

ANNUAL REPORT 2015-16



सत्यमेव जयते

DEPARTMENT OF BIOTECHNOLOGY

**Ministry of Science & Technology
Government of India**

ANNUAL REPORT

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Department of Biotechnology
Ministry of Science & Technology
Government of India



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The Department of Biotechnology (DBT) has celebrated the 30th Foundation Day on 26th February, 2016. From the setting up of a National Biotechnology Board in 1982, to a full-fledged Department in 1986, the DBT had attained several milestones in its 30 years journey. These 30th years have been crucial for the growth of Life Sciences and Biotechnology in the Country and DBT's impact has been both national and global. To mark this event, a series of scientific activities including town-hall lectures, debates and other interactions with our eminent scientists as well as from overseas were organized in association with the autonomous institutes and star colleges. The events also showcased the contributions and impact which Life Sciences and Biotechnology have made on society and, importantly, recognized the contribution of key stakeholders - Individuals, Institutions (including Universities), Industry and Society. Further the occasion was used to explore new opportunities and build new partnerships nationally and globally.

Towards this the DBT also organized a two-day "Global Biotechnology Summit" on 5th & 6th February 2016 at Vigyan Bhawan, New Delhi. The summit brought together around 1500 participants (eminent scientists, entrepreneurs, policymakers and civil society) to discuss opportunities, collaborate and prepare a joint action plan for achieving the target for its biotech sector of \$100 billion by 2020. There were key plenary talks by Prof Ada E Yonath, Nobel Laureate, Weizmann Institute of Science, Israel and Prof Maria Leptin, EMBO- Excellence in Life Sciences,

Heidelberg, Germany. The Summit focused on themes such as Make in India, Start-up India - Nurturing Bio Entrepreneurship, Skill India, Biotech Opportunities and Action for Swachh Bharat and Swasth Bharat, Biotechnology Cooperation, Biotechnology Innovation for Inclusive Development, Biotechnology and Society etc. Steered under the leadership of brilliant minds over the years, biotechnology in India has crossed significant milestones. With the experience of 30 years, DBT's endeavors to further improve the processes and culture so as to expand the reach and depth effectively.

The Department also unveiled the National Biotechnology Development Strategy (NBDS) 2015-20 by Hon'ble Minister for Science & Technology and Earth Sciences Dr. Harsh Vardhan and Hon'ble Minister of State for Science & Technology and Earth Sciences Shri. Y.S Chowdary.

The NBDS 2015-20 is the direct result of formal and informal consultations over the past two years with over 300 stakeholders including scientists, educators, policy makers, leaders of industry and civil society, voluntary and non-government organizations, regulators and international experts. The consultations offered an opportunity to discuss and evaluate technological, societal and policy aspirations, critical success factors as well as barriers that will impede growth and put them in newer and broader perspective and action plan.

The envisaged mission is:

- Provide impetus to utilising the knowledge

and tools to the advantage of Humanity

- Launch a major well directed mission backed with significant investment for generation of new Biotech Products
- Empower scientifically and technologically India's incomparable Human Resource
- Create a strong Infrastructure for R&D and Commercialisation
- Establish India as a world class Biomanufacturing Hub

The Key elements of the Strategy are:

- Building a Skilled Workforce and Leadership
- Revitalizing the knowledge environment at par with the growing bioeconomy
- Enhance Research opportunities in basic, disciplinary and inter-disciplinary sciences
- Encourage use-inspired discovery research
- Focus on biotechnology tools for inclusive development
- Nurturing innovation, translational capacity and entrepreneurship
- Ensuring a transparent, efficient and globally best Regulatory system and communication strategy
- Biotechnology cooperation- Fostering global and national alliances
- Strengthen Institutional Capacity with redesigned governance models
- Create a matrix of measurement of processes as well as outcome

A roundtable discussion was held with key stakeholders to discuss the roadmap for 2020.

The key elements would be implemented in collaboration and partnership with Other

Ministries, Departments, State Governments and international agencies towards achieving:

- Making India ready to meet the challenge of achieving US\$100 billion by 2025
- Launching Four Major Missions - Healthcare, Food and Nutrition, Clean Energy and Education
- Creating a Technology Development and Translation network across the country with global partnership-5 new clusters, 40 Biotech incubators, 150 Technology Transfer Organizations (TTOs), 20 Bioconnect centres
- Strategic and focussed investment in building the Human Capital by creating a Life Sciences and Biotechnology Education Council.

HUMAN RESOURCE DEVELOPMENT PROGRAMMES

The Department is implementing an Integrated Human Resource Development (HRD) Programme in Biotechnology comprising of post graduate teaching programme, short term training courses for upgradation of skills of mid-career scientists and faculty engaged in teaching and R&D, industrial training of students fellowship for doctoral and post-doctoral research training in frontier areas of life sciences. Under HRD scheme, Department is generating critical mass of trained and skilled manpower required for overall development of Biotechnology in the country.

CENTRES OF EXCELLENCE (COEs) IN BIOTECHNOLOGY

The programme provides a flexible model of long-term support for highly innovative research, both basic and translational to create high quality state-of-art facilities for R&D and promote quality publications and intellectual property.



The specific goal is to enhance the innovative ability of the institutions and investigators with well-developed multi-disciplinary research programme in specific areas of biotechnology. In the present year, 224 proposals were received in response to call. These were shortlisted, peer-reviewed and thereafter evaluated by Technical and Apex Committees. Around 30 proposals were recommended for final support. Out of them, Six new “Centres of Excellence (including one Phase II)”, two new “Long-term R&D Project” and five proposals have been funded in “Programme Support (including one Phase II)” during the year. The supported research activities range from basic sciences leading to new understanding of neurofibrils formation, Plasmodium molecular machinery to translational research focusing on development of Pneumococcal vaccine, dental and orthopaedic implants and developing resilient rice.

BIOTECH FACILITIES

The Department has made a considerable progress in establishing and creating the research related

infrastructural facilities in several universities/ Institutions. The major facilities created are next generation DNA sequencing, Proteomics, Platform for agriculture and veterinary science, Animal Resource Facility at Faridabad, Biocluster and Facilities for educational, teaching and training purpose. In addition, extension of the availability of synchrotron beamline facility at Grenoble carried out for the science community. Furthermore, the existing repositories and depositories have been strengthened.

RESEARCH & DEVELOPMENT

The Department supports research programmes in basic and specialized areas of biotechnology. All proposals received in the Department of subject to fair, uniform and transparent screening-cum-selection process comprising of internal screening, peer review by experts and Task Forces/Expert Committees.

An illustrative list showing number of project proposals received and sanctioned during 2015-16 in different areas is given at Table-I

S.No	Area Name	No. of Proposals Received	No. of Projects Sanctioned
1	Agriculture Biotechnology I	11	2
2	Agriculture Biotechnology II	16	9
3	Agriculture Biotechnology III	20	6
4	Animal Biotechnology	32	6
5	Animal Diagnostic and Vaccine	19	4
6	Aquaculture and Marine Biotechnology	86	15
7	Basic Plant Biology, Agriculture and Frontier Area	77	14
8	Basic Research in Modern Biology	97	35
9	BIOCARE	4	11
10	Bioengineering	146	1
11	Bioinformatics R&D Projects	216	22
12	Biopesticides and Crop Management	0	1

S.No	Area Name	No. of Proposals Received	No. of Projects Sanctioned
13	Bioresource Development & utilization - Bioprospecting & Bioresources	32	12
14	Biosystems & Bioprocess Engineering	140	4
15	Biotech Based Programmes for Rural Development	24	3
16	Biotech Based Programmes for SC/ST	30	3
17	Biotech Based Programmes for Women	13	1
18	Biotechnology of Biofertilisers	0	1
19	Centers of Excellence	25 (224-LOIs)	14
20	Energy Biosciences - Biofuels	24	4
21	Environmental Biotechnology	31	7
22	Genome Engineering & Technologies	65	8
23	Infrastructure Facilities	11	3
24	International Collaboration-I	3	0
25	International Collaboration-II	1	1
26	Ipr and Biosafety	1	0
27	Medical Biotechnology - Human Developmental and Disease Biology (HDDB)	45	2
28	Medical Biotechnology - Human Genetics and Genome	22	4
29	Medical Biotechnology - Infectious Diseases	80	8
30	Medical Biotechnology - Non-Infectious Diseases	129	12
31	Medical Biotechnology - Stem Cell Biology	40	5
32	Medical Biotechnology-Vaccine Research and Diagnostics	33	3
33	Nanoscience and Nanotechnology	228	14
34	North Eastern Region (NER BPMC)	543	0
35	Plant Biotechnology	0	8
36	Public Health Food and Nutrition	205	14
37	RNAi Technology	0	8
38	Rapid - General Biotechnology	1	0
39	Technology Development in Silk and its application in biomaterials	19	0
40	Translational Research on Medicinal and Aromatic Plants products	51	1
	Total	2520	266

BIOTECHNOLOGY BASED PROGRAMME FOR SOCIETAL DEVELOPMENT

The Department has been supporting projects aiming to promote use of biotechnological processes and tools for the benefit of the disadvantaged section of the society comprising women, rural population and SC/STs in ecologically compatible manner. The programme aims to create platform for self-employment generation among the target population by diffusion of proven and field-tested technologies through demonstration, training and extension activities. The focused areas are fish production and rearing, poultry farming, pig production, floriculture, hybrid seed production, integrated farming, entrepreneurship development, vermicomposting, spirulina and mentha cultivation, bio-resource utilization, plant disease management, women and child health, hygiene and nutrition. Large number of rural, SC/ST and women population including youth have been benefited through implementation of these projects.

(1) BIOTECH PRODUCT AND PROCESS DEVELOPMENT

BIOSYSTEMS AND BIOPROCESS ENGINEERING

Towards development and improvement of sustainable bioprocesses of commercial interest, Biosystems and Bioprocess Engineering Task Force has been formed to find innovative and efficient solutions addressing the challenges involved in the production processes. In this financial year, a Call for Proposals was issued in areas: (a) Host and Metabolic Engineering (b) Biotransformation and enzyme Engineering (c) Biosystems Engineering. The Department has received 106 proposals in response to the Call and finally 13 proposals have been recommended for financial support.

(2) PUBLIC HEALTH, FOOD AND NUTRITION BIOLOGY

Research and Development endeavours have been continued in food biotechnology and nutrition Biology, Addressal of micro and macro nutrient deficiencies through development of fortified foods with generation of clinical evidence, Health care products/ Nutraceuticals/ Dietary food supplements; Probiotics for holistic health; Addressal of Celiac diseases; Addressal of Vitamin B12 deficiency; Nutriepigenomics; Postharvest processing and value addition; Food safety & allergenicity, shelf life extension of perishable foods etc. In addition, Public health research from a nutrition perspective was also initiated. Proposals were solicited in the areas of "Food Allergy" and "Food to Food Fortification". A multi centric study has been initiated to evaluate the extent of the burden of vitamin B12 deficiency across the country and also to identify the dietary as well as genetic factors associated with low levels of vitamin B12 in various age groups. From a National Public Health policy perspective, this study would address the question whether Vitamin B12 is to be added in conjunction with folate and iron for alleviation of anemia in India.

(3) BIOSAFETY RESEARCH

The program envisages and ensures safety from the use of Genetically Engineered (GE) Organisms and products thereof in research and development by all stake holders as well as to the environment, following rules, 1989 of Environment (Protection) Act, 1986 for the manufacture, use/import/export and storage of hazardous microorganisms/ genetically engineered organisms or cells. Rules, 1989 further highlights the functioning and deliberations of six competent authorities/ committees such as Recombinant DNA Advisory Committee (RDAC), Genetic Engineering Appraisal Committee

(GEAC), Review Committee on Genetic Manipulation (RCGM), Institutional Biosafety Committees (IBSCs), State Biotechnology Co-ordination Committees (SBCCs) and District Level Committees (DLCs).

A three tier mechanism comprising Institutional Biosafety Committees (IBSCs), which operate directly from the premises of the institutions and ensures on-site assessment and monitoring of adherence to the biosafety guidelines with overall oversight of the regulatory process, at the institutional level; the Review Committee on Genetic Manipulation (RCGM) functioning from the Department of Biotechnology; and the Genetic Engineering Appraisal Committee (GEAC) in the Ministry of Environment, Forest and Climate Change, has been established for evaluation, approval and monitoring of safety aspects associated with handling of recombinant DNA (rDNA) products in healthcare and agricultural sectors leading to their commercial/ environmental release. RCGM monitor and review all ongoing research projects involving high risk category and confined field experiments and ensure the compliance of biosafety rules and regulations while conducting rDNA research.

Techno Management and IPR Capacity Building

The main objective of Biotechnology Patent Facilitating Cell (BPFC) is to provide administrative and financial support to biologists and biotechnologists in filing of patent applications in Indian Patent Office (IPO), United States Patent and Trademark Office (USPTO) and other countries and creation of awareness and understanding relating to Intellectual Property Rights (IPR) among students, scientists, faculty of colleges, universities and research institutes. The BPFC supports filing of patent application on inventions pertaining to Life Sciences and

Biotechnology after a rigorous scrutiny. The patent filing is being done through empaneled IPR firms.

BIOTECHNOLOGY INFORMATION SYSTEM NETWORK (BTISNET)

The Biotechnology Information System Network (BTISnet) of the Department established in the year 1986 is now spread across the country with 170 centres. Based on the infrastructure, developments and capabilities the network centres are in various levels and include Centres of Excellence (COEs), Distributed Information Centres (DICs), Distributed Information Sub-Centres (DISCs) and Bioinformatics Infrastructure Facilities (BIFs). The network houses one Supercomputer Facility for Bioinformatics and six Interactive Graphics Facilities. Large numbers of R&D projects in bioinformatics are also being supported through bioinformatics programme. The network supports teaching program in M.Sc., M.Tech. and Ph.D. in Bioinformatics and Computational Biology to generate skilled manpower in Bioinformatics. Further, the BTISnet centres are conducting short term trainings/ workshops for the benefit of research community including experimental biologists. Large numbers of peer-reviewed publications have been emanated during this year. These publications are being compiled into a compendium. These centres also provide services to the scientific community. These activities are being coordinated by the Apex Biotechnology Information Centre (BTIC) which is located at the Bioinformatics division of DBT.

INTERNATIONAL COLLABORATION

Without effective international collaboration we would have limited access to breakthrough scientific knowledge generated by researchers in other countries; the quality of the scientific knowledge generated locally would decline and; our industries would be unable to obtain



innovative technological information and knowledge needed to maintain their competitive edge. The future of our health system depends on having a critical mass of health scientists with the international knowledge and intercultural skills necessary to meet globalization's challenges. With climate change impacting global agriculture, marine and aquatic life and the threat of new emerging pandemic diseases; international collaborations become exigent. The Department has in this year not just expanded International Collaborations but have developed partnerships which address the most challenging issues in marine biology, agriculture, health or human resources.

AUTONOMOUS INSTITUTIONS

The Department has established a number of autonomous institutions for basic, applied and translational research in the field of Life Sciences and Biotechnology.

National Institute of Immunology (NII), New Delhi

The programmes of the NII are focused to study frontier areas of modern biology pertaining to disease processes with special emphasis on the functional aspects of the immune system. During the reporting period the Institute continued expansion of scientific programmes in a multi-investigators driven mode to address challenging questions in biology for improvement of healthcare. The scientific findings have so far been published in 93 reputed journals.

National Centre for Cell Science (NCCS), Pune

In keeping with the vision of NCCS to expand into newer research areas, new initiatives were undertaken through new faculty members, with research investigating the molecular machinery underlying long-lasting memory and exploring

mammalian long non-coding RNAs to develop a mechanistic understanding of how mammalian lncRNAs regulate events associated with oncogenesis.

Towards nurturing young scientific talent, NCCS admitted twenty seven research scholars into its PhD programme, and fifteen research scholars of NCCS registered as Ph.D. students with the University, bringing the total number of research scholars who are registered for a Ph.D. to 133 during this year. NCCS also trained 21 summer trainees and 44 project trainees.

Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad

CDFD provides services in the areas of DNA fingerprinting, diagnostic tests for human genetic disorders and analysis of basmati rice for purity, and is also engaged in basic research activities in different disciplines of modern biology. The Centre has witnessed significant growth in all phases of activities, and several new frontiers of research have been initiated.

National Brain Research Centre (NBRC), Manesar

NBRC conducts research on brain function in health and disease at the molecular and systemic levels including neuroimaging and on disease biology. This year has been extraordinary in the number of research leads that have been shown to be ready for implementation on a large scale. These include dyslexia screening in four Indian languages and a marker for Alzheimer's disease and the possible use of the same as a therapeutic target. An interdisciplinary centre for the state-of-art research in epilepsy and brain mapping has been inaugurated. NBRC has also set a model of the interdisciplinary teaching of the Neurosciences fulfilling its mandate as a deemed university.

Institute of Life Sciences (ILS), Bhubaneswar

Three major areas of research in the institute centered around infectious disease biology, various aspects of gene function as well as regulation and translational research through technology development.

National Institute of Biomedical Genomics (NIBMG), Kalyani

NIBMG is engaged in accelerating genomics for health and disease. NIBMG engages in discovering genomic evidence that underpins disease and health-related traits. NIBMG is the nodal institution for implementing the India to initiative on oral cancer under the aegis of the International Cancer Genome Consortium. The Institute has also undertaken two projects: (a) to discover the biological and environmental correlates of pre-term birth – a multi-institutional project anchored in the DBT-aided institute, THSTI in Faridabad – and (b) a population cohort study, the Kalyani Cohort Study, to study natural histories of diseases and health-related traits. The Institute has a vibrant short-term training program and an outreach program.

Regional Centre for Biotechnology (RCB), Faridabad

The centre moved to the permanent home in the National Capital Region- Biotech Sciences Cluster in Faridabad with minimal disruption in ongoing research programs. At present, the centre has close to hundred scientific personnel engaged in conducting cutting-edge research. The scientists in RCB were involved in publishing a number of research articles and reviews and were the recipients of important distinctions, award and honors. RCB is also engaged in a number of multi-institutional programs that enable scientists at the centre and all over the country to conduct their

experiments. Overall, the academic activities of RCB increased in depth and scale over the year.

Institute for Stem Cell Science and Regenerative Medicine (InStem), Bangalore

In the short period of its existence, inStem has successfully attracted outstanding investigators, who have initiated theme driven programmes. These have been crystallized into six major programmes at Bangalore and the translational, clinical unit at Vellore. inStem scientists have published 36 research papers from the Bangalore campus, building on the advantages of theme driven collaborations from both within the institute and outside. The research demonstrates the breath of enquiry – from atomic resolution work to animal models and the depth of understanding it generates in mechanisms of regeneration to use of stem cells as a model to understand disease pathophysiology. In the coming years, with the completion of the new building and the available expanded space and resources, the institute hopes to grow its science exponentially.

National Agri - Food Biotechnology Centre (NABI), Mohali

NABI anticipates that biotechnology based innovations in agriculture and food sector can provide sustainable and meaningful answers towards quality nutrition. In the coming years, NABI will be able to provide multiple biotechnological and inventive products in agriculture and food sector, which will serve the local interests and also will have wide outreach. Some of these products could include wheat-variety with low phytate concentration, wheat variety with higher micronutrient density in endosperm, wheat varieties with better processing and nutritional qualities, provitamin-A rich Indian banana variety, post-



harvest advancements in shelf life and quality of fruits, development of functional foods and formulations, and dietary recommendations, all of which will collectively enhance the nutritional status of the country.

Center of Innovative and Applied Bioprocessing (CIAB), Mohali

Center of Innovative and Applied Bioprocessing (CIAB) is a national institute representing Secondary Agriculture Initiative (SAI) of the DBT to catalyze research, innovations and knowledge translation for production of secondary agriculture bioproducts (SAB). The institute's current mandate is focused on evolving processing scopes of agri-farm and food-industry spare biomass through chemical, biological and biotechnological (biosynthetic technology/synthetic biology) approaches. Rice and other crop straws fruit and vegetable pomace, processed seed residues etc. are being researched for value-added products. The institute has several research leads including IPR/Patents on liquid whey, solanesol, scented and natural tartaric acid, best flavor rose oxide isomer, lycopene, synthetic biology route production of alternate non-energy sweet sugar etc.

National Institute of Animal Biotechnology (NIAB), Hyderabad

The research at NIAB is focused broadly on Infectious diseases, Reproductive Biology, Animal Genetics and Genomics, Bio-informatics and Nutrition Enrichment with respect to livestock and poultry animals. Scientists have initiated projects on Infectious diseases, Reproductive problems, Antibiotic resistance and Bioinformatics. Major infectious diseases studied are Brucellosis, Theileriosis, Babesiosis, Newcastle disease virus (NDV), Leptospirosis, Toxoplasmosis, Mastitis, Peste des petits ruminants virus (PPR) and Foot and Mouth

Disease (FMD) with focus on developing new tools for diagnosing and preventing the diseases.

Translational Health Science and Technology Institute (THSTI), Faridabad

THSTI is designed to be a dynamic and interactive organization with a mission to integrate the fields of medicine, science, engineering and technology into translational knowledge and make the resulting biomedical innovations accessible to public health. The institution strives to effectively enhance the quality of human life by inculcating a culture of shared excellence through amalgamation of various disciplines.

National Institute of Plant Genome Research (NIPGR), Delhi

The institute has played an important role in the past 16 years in contributing to basic plant science and applied agricultural research in frontier areas of plant genomics. In the current year, apart from core research, NIPGR has also made attempts to translate some of the technologies developed through basic research activities for their application in agriculture. Salient research findings are in important crops namely, chickpea, tomato, rice, foxtail millet and mustard.

Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram

RGCB's main focus is on research programmes around the central theme of disease biology. This framework includes basic and applied programmes in human diseases, animal diseases and plant diseases. Research programme themes include chronic disease biology, tropical disease biology and disease biotechnology. Centered in these three programmes are state-of-the-art discovery research programmes in cancer research, cardiovascular and diabetes biology, pathogen biology, neurobiology and

genetics, chemical and environment biology, reproductive biology and plant disease biology and biotechnology. The Department has taken an initiative to create a specialized ecosystem called Bio-Innovation Center (BIC) at the institute. This will be a unique knowledge center and hub for mid and high level innovation founded on deep and advanced level technical platforms, multidisciplinary cores that will seed growth and innovation. RGC B has started a major initiative on "Ayurveda Inspired Discovery".

Institute of Bioresources and Sustainable Development (IBSD), Imphal

The main mandate of this institute is conservation and sustainable utilization of bioresources for the socio-economic development of the North Eastern region. Research and Development activities are pursued under core areas such as medicinal and aromatic plants, horticulture, algae, microbes, insects, fisheries, wildlife and other aquatic bioresources with emphasis on bioresources database development, bioresources education, Human Resources Development.

Biotech Science Clusters

Bangalore Life Sciences Cluster for multiscale basic and applied research in Biological Sciences (B-Life) has been established in January, 2015. The cluster partnering institutes are: Institute for Stem Cell Science and Regenerative Medicine (inStem) Bangalore; National Centre for Biological Sciences (NCBS), Bangalore; Centre for Cellular and Molecular Platforms (C-CAMP), Bangalore; and Institute of Bioinformatics and Applied Biotechnology (IBAB), Bangalore. DBT has also established NCR Biotech Science Cluster involving five autonomous institutes of DBT (NII, NIPGR, NBRC, THSTI and RCB) registered as legal entity under the Societies Registration Act 1860. The mandate of the cluster are to support discovery of basic mechanisms in biology and

development of novel technologies; to facilitate public-private partnerships for the development of biotechnology business incubators and parks; to network with the potential constituent institutions to create a synergistic ecosystem for accelerating discoveries and facilitating translational research and to provide, in terms of infrastructure, state-of-the-art technology platform center, animal facilities and bio safety containment laboratories.

PUBLIC SECTOR UNDERTAKINGS

Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL)

BIBCOL is a Central Public Sector Unit (PSU), under the administrative control of the DBT. The company has its oral polio vaccine (OPV) plant in Uttar Pradesh. BIBCOL's principal mission is to save the lives of millions of children from avoidable disability, through polio vaccination. Since its inception, it has contributed significantly to the eradication of Polio in the country through the National Immunization Program. BIBCOL is continually growing and secured its position among the top 20 Biotech companies in India, as revealed by recent market surveys only due to its cGMP certified infrastructure, highly skilled manpower and constant support from DBT.

Indian vaccines corporation ltd (IVCOL)

Indian Vaccines Corporation Limited was incorporated in March 1989 as a Joint Venture Company promoted by Govt. of India (Dept. of Biotechnology-DBT,) Pasteur Merieux Serum & Vaccines (PMSV) France and Indian Petrochemicals Corpn. Ltd. (IPCL- a PSU) with a paid up capital of Rs. 18.78 crores, with the objective of manufacturing vaccines based on Verocell Technology to be supplied by PMSV France. The company came into existence after a joint ventures was signed on 1st February 1989. The

company has no trading or commercial activity at present and is maintaining establishment to look after site and complying with the statutory obligations under the company's act 2013.

Biotechnology Industry Research Assistance Council (BIRAC)

BIRAC, is a not-for-profit PSU under the aegis of DBT. BIRAC being a unique organization in the biotechnology ecosystem, works as an interface agency of the DBT, Ministry of Science & Technology, and has the mandate of fostering and nurturing the Biotech Enterprises specially start-ups and SME's for enhancing their innovation research capacities and promoting affordable product development. BIRAC supports Industry-Academia interaction, serve as a single window for the emerging biotech industry, helps establish connectivity with professional and institutional networks, and provides financial support for quality innovation targeted at affordable solutions and product development.

BIRAC is working towards providing enabling support and empowering the entire innovation ecosystem and today more than 310 companies – large, small, medium and start-ups; and more than 170 entrepreneurs are a part of BIRAC's Innovators network. Biotechnology Industry Research Assistance Council (BIRAC) has its registered office in the National Capital Territory of Delhi with an authorized capital of Rs. 1 crores divided into 10,000 equity shares of Rs. 1,000 each.

INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY (ICGEB)

The centre has made a significant progress in molecular biology and biotechnology research. During the year, one Indian Patent application entitled "a novel selectable marker system for

transgenic plants" has been granted and three new Indian patent applications and one PCT have been filed. The Center has also conducted two training programs: (a) Discovery of new Drugs against Malaria and (b) MicroRNAs in Plant Development stress, respectively. The research at the Centre can be broadly categorized in nine areas viz. Malaria, Virology, Immunology, Recombinant Gene Products, Structural and Computational Biology, Plant Molecular Biology, Insect Resistance, Plant Transformation and Synthetic Biology and Biofuels.

PROMOTION OF BIOTECHNOLOGY IN NORTH EASTERN REGION (NER) OF INDIA

The North East Region (NER), of India is a treasure house of exceptional natural beauty, floral and faunal biodiversity and abundant mineral, water and forest resources. It has been identified as one of the biodiversity hotspots of the world. Rich bioresources spread across NER's diverse ecosystems and nurtured by indigenous communities, provide ample opportunities for furthering economic development of the region. However, NER has remained arguably the most backward region of the country, prompting the Government of India to make unprecedented commitment to allocate 10% of its total budget for the development of NER. Accordingly, the Department of Biotechnology (DBT) has earmarked 10% of its total annual budget towards biotechnology-backed development activities in the North Eastern Region of India. Towards this commitment, DBT established the North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) in 2009-10, functioning through Biotech Consortium India Limited (BCIL), for implementation and monitoring of biotechnology programmes in the NER. The NER-BPMC is working in close cooperation with various Government Ministries/ Departments/

Agencies at the Central and State level along with universities and R&D institutions for development and implementation of various programmes.

Of the several programs launched by NER-BPMC since 2009-10, the R&D Twinning Programme has made a huge impact by catalysing vibrant collaborations between institutions from NER and those from the rest of India, evolving NER-specific projects and their implementation across all eight states of the region. More than 300 Twinning projects have been implemented, addressing issues in Healthcare (Medical biotechnology), Agriculture (Agri-biotechnology), Livestock & Fisheries (Animal and Aquaculture Biotechnology), and in the areas of Environment, Medicinal and Aromatic Plants (MAP) with specific relevance to developmental needs of the region; nearly 200 research papers have been published in peer-reviewed journals and more than 400 young scientists of NER have been trained in advanced biotechnology.

ADMINISTRATION AND FINANCE

Administration is responsible for providing a good and ambient working atmosphere for the

in-house scientists, officers and staff. Logistic supports were given for organizing various Task Force & Expert Committee meetings successfully. Modern office equipments like laptops, computers, multimedia projectors, photocopiers, etc.were made available within the Department to maximize the work output. Being a scientific department, a large number of meetings, interactions and quick referral with technical experts, specialists, academicians and scholars from far reaching places and across the world are held. An additional office space of about 11,000 sq.ft. in Block 3, CGO Complex has been acquired, renovated and being occupied .The DBT geared up its employees to launch “Swachh Bharat Mission” from 25th September, 2015 to 31st October,2015 and 18th December ,2015 to 27th December,2015. Hindi Fortnight was organised in the Department during 1st to 15th September, 2015. The Department of Biotechnology was allocated an amount of Rs.1625.14 crore (Rs. 1606.80 crore under Plan and 18.34 crore under Non-Plan) for the year 2015-16. This was revised to Rs.1624.35 crore (Rs. 1606.80 crore under Plan and Rs.17.55 crore under Non-Plan.)

HUMAN RESOURCE DEVELOPMENT PROGRAMME

The Department is implementing an Integrated Human Resource Development Programme in Biotechnology comprising of post graduate teaching programme, short term training courses for upgradation of skills of mid-career scientists and faculty engaged in teaching and R&D, industrial training of students fellowship for doctoral and post-doctoral research training in frontier areas of life sciences. Under HRD scheme, Department is generating critical mass of trained and skilled manpower required for overall development of Biotechnology in the country.

(A) TEACHING PROGRAMMES:

(1) Postgraduate teaching programmes (M.Sc./M.Tech./M.VSc.)

Postgraduate teaching programmes were initiated in close collaboration with University Grants Commission, Department of Ocean Development (DOD) during 1985-86 in six universities, and have been expanded to over 71 universities offering general biotechnology courses and specialized courses such as medical, agricultural, marine, veterinary, industrial, food and pharmaceutical biotechnology, molecular & human genetics, and neuroscience (Fig 1). These universities have been selected on the basis of in-house core faculty strength, existing infrastructural facilities, R&D grants received on competitive funding basis, proximity to other institutions engaged in biotechnology R&D etc. Department provides liberal grants for equipment essentially required for class room teaching, recurring grants for consumables, studentship, books and journals, travel, visiting faculty, contingency, equipment maintenance and thesis

grant for in-house dissertation to ensure quality teaching and intensive hands on training. Six months in-house dissertation is mandatory for all the students admitted in DBT supported teaching programme.

Students for DBT supported PG teaching programmes are selected through a Common Entrance Test (CET) conducted by Jawaharlal Nehru University or IIT-Joint admission test or In a few universities with different academic calendar or geographical location in North-East or J&K, students are admitted through all India written test conducted by the respective universities. All selected candidates are offered studentships. Students passing out of DBT supported teaching programmes have consistently performed well at national level competitive exams conducted by CSIR, UGC, DBT, and ICMR for doctoral fellowships. During the year 2015-16, six new PG proposals were processed for peer review and considered by DBT-HRD Task Force. One time support was provided to M.Sc. Biotechnology teaching programme at Manipur University, Imphal and proposal for starting M.Tech. Pharmaceutical Biotechnology at Institute of Chemical Technology, Mumbai is under consideration for support.

Independent evaluation of HRD Scheme and ranking of DBT supported PG teaching programmes:

Department assigned independent evaluation of DBT supported teaching programmes and based on the performance ranking accorded to 71 teaching programmes, support to three PG teaching programmes viz., M.Sc. Biotechnology

at T. M. Bhagalpur University, Bhagalpur, University of Burdwan, Burdwan and M.Sc. Agriculture Biotechnology at Narendra Deva University of Agriculture and Technology, Faizabad has been discontinued.



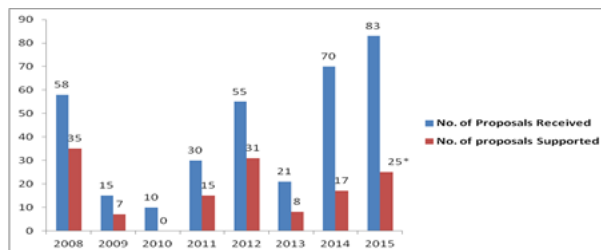
- M.Sc. GENERAL BIOTECHNOLOGY
- M.V.Sc. ANIMAL BIOTECHNOLOGY
- M.Sc. MARINE BIOTECHNOLOGY
- M.Sc. NEUROSCIENCE
- M.Tech. FOOD BIOTECHNOLOGY
- M.Sc. ENVIRONMENTAL BIOTECHNOLOGY
- M.Tech. PHARMACEUTICAL BIOTECHNOLOGY
- M.Sc. AGRICULTURAL BIOTECHNOLOGY
- MASTER IN MEDICAL BIOTECHNOLOGY
- MASTER IN MOLECULAR AND HUMAN GENETICS
- M.Sc. INDUSTRIAL BIOTECHNOLOGY
- M.Tech. BIOCHEMISTRY ENGG. & BIOTECHNOLOGY
- M.Sc. BIORESOURCES AND BIOTECHNOLOGY

Map showing location of Universities/institutes offering DBT supported M.Sc./M.Tech./M.V.Sc. programmes in Biotechnology

(2) Star College Scheme:

Star College Scheme is a unique scheme initiated by the Department with an aim to nurture excellence in science education at Under Graduate level. The main objective was to strengthen the under-graduate science departments by providing academic and physical infrastructure to the colleges, imparting hands-on training to UG students, promoting faculty improvement programme, networking with neighbouring

colleges and institutions, providing better library facilities, motivating students towards research and even encouraging out-reach activities for students in the neighbouring school & colleges. The college is selected for the “Strengthening Component” where the college is awarded one-time non-recurring grant of Rs 5.00 lakhs and Rs 2.00 lakhs for three years under recurring head per department. The college is evaluated for its progress annually and after completion of three years, they are eligible to be reviewed for either upgradation to the “Star Status” or continuation under the existing “Strengthening” component for another two years or discontinuation from the Scheme. There are currently 85 ongoing Colleges and support to 10 colleges has been discontinued on successful completion of one tenure after review in the year 2014-15 (Fig.2). Participating departments in 16 colleges have been accorded Star Status. The Star College programme has led to revival of interest in science stream as evidenced by increase in the cut off percentage at the time of admission to UG courses, decline of dropout rates, better result at UG level and enhanced enrolment of students for higher studies in sciences at PG level. Efforts are being made to expand out-reach of the programme.



***Recommended proposals under consideration**

Star College Scheme: Proposal Received and Supported from 2008-2015

A Foldscope workshop-cum-public lecture was conducted by the Department in collaboration with Prakash Labs, Stanford University at Delhi, Guwahati and Kaziranga. This was a first of its

kind in bringing the foldscope to the masses and Star college scheme was chosen to be the first starting place to explore a pilot programme to bring Foldscope to the scientific community of teachers, ecologists and explorers based in India. Foldscope, conceived by Prakash Lab is an innovative line for mass manufacturing of optical microscopes that can be printed-and-folded from a single flat sheet of paper, similar to Origami. This shall be enabling tool in field and areas where access to sophisticated instruments is limited.



Foldscope workshop in India organized by DBT Sri Venkateswara College, New Delhi

(B) FELLOWSHIP PROGRAMME:

(1) DBT-Junior Research Fellowship

The DBT-JRF programme is being supported by Department of Biotechnology since 2004 with an objective to provide opportunities for pursuing Ph.D in biotechnology. The DBT-JRF Program has provision to select JRFs according to merit in Biotechnology Entrance Test (BET) under two Categories namely Category I and Category II.

Category I:

The programme has provision to select 275 JRF's each year under this Category on the basis of all India online entrance examination conducted at 50 centres in 12 cities. At present, there are total 680 JRFs and SRFs registered for their

PhDs in around 139 institutes / universities. The fellowships are provided as per DBT/ DST norms to Research fellows selected through BET (Biotechnology Entrance Test).

Category II:

Under this category, 100 students are selected and these students are eligible to join any DBT sponsored project. They can avail fellowship equivalent to NET/GATE qualification from the projects as per DBT/ DST guidelines. The JRFs are selected in the projects through the selection procedures adopted by respective institute/ university.

(2) DBT-Research Associateship

Department initiated DBT Research Associateship programme in 2001 for providing post-doctoral exposure in frontier areas of research in Biotechnology in premier institutes engaged in major biotechnological research activities in India. The programme is being implemented by IISc, Bangalore. Candidates with Ph.D. Degree in Science, engineering, MD or MS (Medical) in any area of medicine with research interest in Biotechnology and life Sciences with good academic record are eligible for the Research Associateship. Candidates are selected on the basis of their CV and performance in interview before selection committee. Selection is held twice a year. The selected candidates are eligible for Associateship at par with DST guidelines.

During the year (2015-16), total 692 applications were received and 217 applicants appeared for the interview. Fellowships have been offered to 76 Research Associates.



PROGRAMMES FOR NORTH EASTERN STATES:

In an effort to bring North Eastern Region at par with the mainstream national biotechnology programmes, Department has built special provision in the existing HRD schemes namely DBT-RA programme, BITP programme and Entrepreneurship development programme for the students/ candidates from the North Eastern Region of country.

(1) DBT-RA for North East

The Department initiated DBT-RA programme in 2010 for students with domicile of North-East or those who have studied for past 3 years in university/ institute in North Eastern states. The Programme is being coordinated by Indian Institute of Science, Bengaluru. During the year, total 65 applications were received, 31 applicants appeared for interview and 15 candidates have been selected. The Programme has been well received by the students as evident from increase in no. of applicants in last 3 years.

(2) BITP for North East

Biotech Industrial Training Programme for North Eastern region offers industrial training to fresh B.Tech. / M.Sc. / M.Tech. / M.VSc. students in biotechnology in industry for a period of 6 months. This programme is being coordinated by Biotech consortium India Limited, New Delhi (BCIL). There is a provision for placement of 100 candidates in industries for 6 month industrial training under BITP-NER. During the year, total 126 applications were received, 88 candidates appeared for interview and 80 candidates have been selected for training. Programme has gained popularity among the Biotechnology students from NE region as shown in the figure below.

(3) Entrepreneurship Development Programme in North Eastern Region

Department is providing support for organizing entrepreneurship development programme in Biotechnology for training and setting up of new viable biotech venture by prospective entrepreneurs in North Eastern Region of country. An entrepreneurship development programme (Phase II) for advanced training and setting up of small biotech industry in North Eastern Region was sanctioned to Biotech Consortium India Ltd, New Delhi. The objective of programme was to provide assistance to budding entrepreneurs by technical support at different stages from concept to commissioning for setting up of biotech ventures in North Eastern Region. BCIL, New Delhi conducted intensive entrepreneurship development programme in five areas namely micropropagation, biofertilizers and biopesticides production, herbal plant extraction, orchid culture and secondary agriculture. Four biotech companies have been setup as an offshoot of this hand -holding and mentoring workshop.

DBT AWARDS

RGYI- Rapid Grant for Young Investigators

Rapid Grant for Young Investigators fosters creative research in various fields of biotechnology (Medical, Agriculture, Animal Biotech, Environment and Industry etc.) to enhance early career development of young investigators below 40 years of age. The programme aims to provide first grant to establish the lab and initiate research in the frontier areas of biotechnology. Over the years, there has been overwhelming response to this scheme as more than 3000 proposals have been received and about 600 projects recommended (based on their merit) and

implemented so far. Thus RGYI has provided start-up grants to young investigators across the country working in different settings such as central government funded institutions, State Government funded University departments, scientists at DSIR approved private institutions etc. The major outputs from RGYI projects were in terms of good scientific publications, patents and trained manpower.

FELLOWSHIPS FOR SCIENTISTS

Ramalingaswami Re-entry Fellowship

The Ramalingaswami Re-entry Fellowship was conceived in the year 2006-07 with the idea of encouraging scientists (Indian Nationals) working outside the country, and who would like to return to the home country to pursue their research interests in life sciences, biotechnology and other related areas. Each fellow receives a

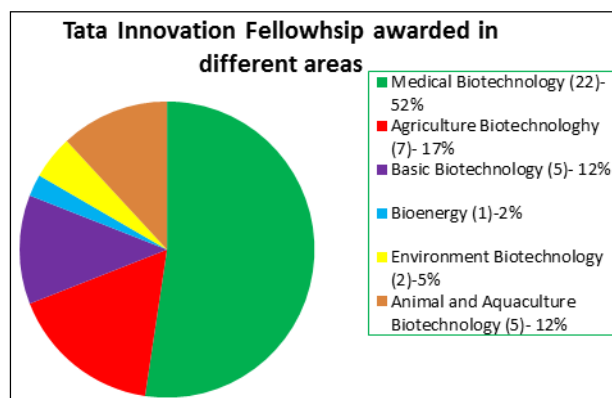
fellowship amount of Rs. 85,000/pm; HRA @ Rs 7,500 pm and research/contingency grant of Rs. 10 lakhs for first year; Rs.7.5 lakhs for 2nd year and Rs. 5 lakhs 3rd year onwards. Fellows retain an option for drawing either the fellowship or salary if they are appointed at a suitable permanent scientific position. Applicants who have returned in less than a year are also eligible. Awardees are eligible to apply for research grants to any of the funding agencies towards accomplishment of research proposal. The tenure of fellowship is initially for five years. It is further extendable for another term on fresh appraisal of performance of the fellow. Based on the current data available, it is quite apparent that people want to relocate themselves to Indian Institutes/National R&D laboratories as these institutes are now providing excellent research facilities to do high quality research.

Status of the candidates applied & selected as on Jan, 2016

Year	Applications Received	Eligible	Selected	Joined	Did not Accept	Accepted but did not join	Absorbed as Faculty	Expected to join
2007-08	83	63	10	7	1	2	6	-
2008-09	42	41	15	14	-	1	14	-
2009-10	131	121	27	23	1	3	18	-
2010-11	133	123	45	31	10	4	27	-
2011-12	170	160	50	35	10	5	26	-
2012-13	137	126	50	40	-	10	20	1
2013-14	220	210	50	45	-	-	20	5
2014-15	205	177	50	07				
Total	1121	1021	297	202	22	25	131	6

Tata Innovation Fellowship

The department initiated the scheme in 2006 to reward the scientists engaged in innovation and in the pursuit of path breaking solutions to major challenges, interdisciplinary work and an emphasis on translational research in life sciences, agriculture, biomedical science and related areas of biotechnology. The awardees are provided a fellowship of Rs. 25,000/- per month in addition to regular salary and contingency grant of Rs. 6 lakhs per annum. The duration of the fellowship is initially for three years which can be extended further by two years on a fresh appraisal. A maximum five fellowships can be provided in a year. During the current year, five scientists have been awarded Tata Innovation Fellowship in the areas of Medical Biotechnology, Agricultural Biotechnology and Environmental Biotechnology. Altogether, 42 scientists have been awarded the fellowship since its inception

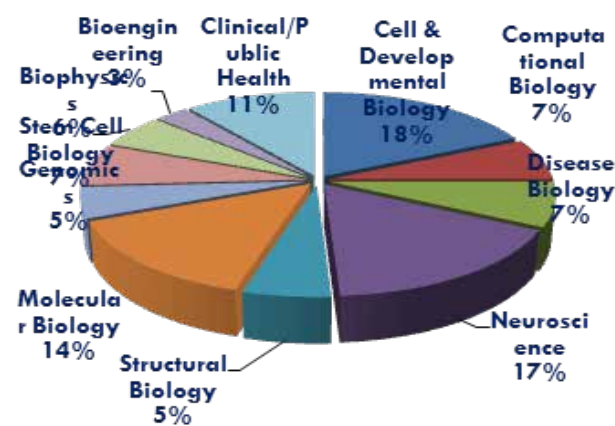


Wellcome Trust/DBT India Alliance (India Alliance) :-

The Wellcome Trust/DBT India Alliance (India Alliance) was set up in 2008-09 as a 10-year £160 Million equally co-funded programme between the Wellcome Trust, UK and the Department of Biotechnology, Government of India. The broad aim of India Alliance is to build excellence in the Indian biomedical scientific community by identifying and supporting the best researchers to

become future leaders. India Alliance Fellowships are broadly divided into 3 categories - Basic Biomedical Sciences, Clinical & Public Health Research (CPH) and Margdarshi Fellowships. The Basic and CPH Fellowships are given at Early, Intermediate and Senior career stages; the Margdarshi is a very senior Fellowship scheme, the mandate of which is to support established leaders to seed centers of excellence in India. The Research Training Fellowships for Clinicians is a unique scheme under the CPH category, which aims to provide training opportunities for clinicians who wish to pursue a career in patient-oriented research. By November 2015, India Alliance has made 202 awards at 65 different institutions across India.

Clinical and Public health research area has been recently included in the programme and constituted 11% of the research areas funded by India Alliance.



Broad areas funded by India Alliance

Fellowship awards in 2015-16 included (i) 23 Fellowships were awarded under the Basic Sciences category in 2015 consisting of 6 Early, 15 Intermediate and 2 Senior Fellowships. (ii) 14 Fellowships were awarded under the CPH category in 2015, consisting of 5 Research Training Fellowships and (iii) Two Margdarshi Fellowships were awarded in 2015 to Prof

Satyajit Mayor (NCBS, Bangalore) and Prof. Akhilesh Pandey (Johns Hopkins University and NIMHANS, Bangalore).

OPPORTUNITIES FOR WOMEN SCIENTISTS

Biotechnology Career Advancement and Re-orientation Programme (Bio-CARe) for Women Scientists

In an attempt to enhance the participation of Women Scientists in Biotechnology Research, the Department of Biotechnology launched a Biotechnology Career Advancement and Re-orientation Programme (Bio-CARe) for women Scientists. The programme is mainly for Career Development of employed/ unemployed women Scientists upto 55 years of age for whom it is the first extramural research grant. There is a Research Grant Opportunity (RGO), under which a 3-5 year research grant is provided. The purpose is to build capacities for women Scientists employed fulltime in Universities and small research laboratories or unemployed women Scientists' after a career break so as to help them undertake independent R&D projects. The calls have been announced so far and 214 (113 Employed and 101 Unemployed) women Scientists have been supported under the Bio-CARe scheme. Out of 214 Women Scientists 89 are from Research Institutes and 125 are from Universities. 40 papers have been published and one patent filed. 10 women scientists have got permanent jobs after getting the Bio-CARe project. Few achievements are as below:

Some highlights of completed/ongoing projects supported under BioCare scheme are as follows:

Bio-Care Fellow at Haldia Institute of Technology, West Bengal targeting colchicine site on tubulin of tubulin microtubule system using group of estrogen molecules with structural variations confirmed that **β -Estradiol-6-one 6-(O-carboxy**

methyloxime) [Oxime] has almost equivalent potential compared to 2 methoxy estradiol (2ME). 2ME can serve as a lead compound for the generation of future antimitotic drug of potential interest.

A new wound dressing formulation having multiple abilities like fluid absorption, antibacterial properties and biocompatibility which can easily be removed from the wound site without causing any trauma to the patient has been developed at Sree Chitra Thirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

Seaweeds collected from southern coast India were initially screened for in vitro antidiabetic assays (α -amylase, α -glucosidase, DPP-IV) at Vellore Institute of Technology, Vellore, Tamil Nadu. Among 25 seaweeds, four seaweeds showed highest inhibition towards α -amylase, α -glucosidase and DPP-IV. Some were screened for in vivo antidiabetic activity in rat model.

Aggregation of amyloid β peptide ($A\beta$) is an important event in the progression of Alzheimer's disease, therefore, inhibition of $A\beta$ aggregation is widely studied and is one of the promising approaches for the development of treatments for Alzheimer's disease.

At Directorate of Rice Research, Hyderabad, a total two hundred and forty two lines of converted restorers having both Rf4 and Rf3 and having grain quality traits of recurrent parent's viz., Swarna, Samba Mahsuri and Improved Samba Mahsuri were developed by marker-assisted backcross breeding (MABB). A new restorer "RP 5933-1-19-R-2" having both Rf4 & Rf3 genes and possessing all the importance traits of popular variety Swarna has been nominated for the multi location testing of AICRIP (All India Co-ordinated Rice Improvement Project) during Kharif 2015.

BIOTECH FACILITIES, TECHNOLOGY PLATFORMS & RESEARCH RESOURCES

CENTRES OF EXCELLENCE (COEs) IN BIOTECHNOLOGY

The programme provides a flexible model of long-term support for highly innovative research, both basic and translational to create high quality state-of-art facilities for R&D and promote quality publications and intellectual property. The specific goal is to enhance the innovative ability of the institutions and investigators with well-developed multi-disciplinary research programme in specific areas of biotechnology.

In the present year, 224 concept proposals were received in response to call. They were shortlisted, peer-reviewed and thereafter evaluated by Technical and Apex committees. Around 30 proposals were recommended for final support. Out of them, six new “Centres of Excellence (including one Phase II)”, two new “Long-term R&D Projects” and five proposals have been funded in “Programme Support mode (including one Phase II)” during the year. The supported research activity ranges from basic sciences leading to new understanding of bacterial toxin-antitoxin system, neurofibrils formation, Plasmodium molecular machinery to translational research focusing on development of Pneumococcal vaccine, dental & orthopaedic implants and developing resilient rice. Apart from this, about 50 projects are at present being supported. The salient achievements under the programme:

Coordinated Research on Tuberculosis

Vaccine against tuberculosis is being explored jointly at the research centres at ICGEB, New Delhi and UDSC, New Delhi. The results from animal

models show that genes for antigens presented by macrophages where immunized as DNA vaccine confer protection against subsequent challenge with the pathogen. Nature of immune response and degree of protection offered is being studied in detail.

A tool that could either specifically diagnose all forms of TB and /or could guide to estimate the therapeutic response in TB patients under treatment is urgently needed. With this background the investigators continued Phase II research of this established, CoE was towards investigating the usefulness of various lead molecules that were the outcome of Phase-I. Human resistin, mycobacterial hupB and various members of fadE group (fadE20, 26 and 28) and a combination thereof were identified as potential markers for determining TB treatment endpoint. Apart from large-scale validation of *M. tuberculosis* novel signature sequence probes for high specificity and high sensitivity diagnosis of TB is underway.

Research on Hepatitis C Virus

Purified active components of herbal extracts *Boerhavia diffusa* and Plum showed efficient inhibition of HCV entry to liver cells in the study carried out at IISc., Bangalore. Further they have successfully optimized the nano-particles for selected delivery of HCV DNA into the animal liver.

Genome Science and Predictive Medicine

UDSC, New Delhi in collaboration with six other institutions constructed molecular networks in Ulcerative Colitis and eight cell type specific

networks in Rheumatoid Arthritis through Genome-wide association studies (GWAS). Identification of potential lead molecules in these two disorders are being attempted in Phase II study for translating the findings.

Computational and System Biology Research

Computational biology labs at NCBS, Bangalore have developed sensitive methods to connect protein families through designed sequences for accurate detection of distantly related sequences. Firm platform to specifically design point mutations or small molecules at the site of different protein-protein interactions has been accomplished. These are accompanied with function-test experiments on well-characterized systems for better understanding of protein interactions.

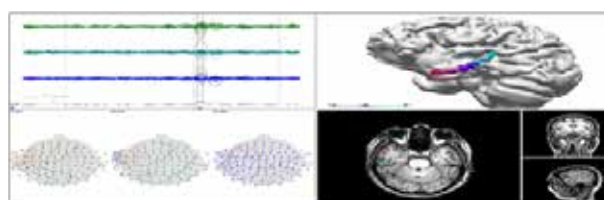
Epigenetics Research

The transparency of Zebrafish embryos allows detailed analysis of phenotype and its fecundity enabled adaptation of Zebrafish for high throughput screening of vast libraries of molecules, on a scale not possible with other vertebrates. Using this, the researches at IISER, Pune developed *in vivo* chemical screen in Zebrafish to identify novel anti-cancer compounds. A series of microtubule destabilizing compounds are presently being screened using Zebrafish embryos, in collaboration with IICT, Hyderabad. The study has so far identified few pyrazole-oxindole and Imidazopyridine-oxindole analogues that bind to colchicine binding pocket of tubulin, as potent anti-mitotic compounds in Zebrafish embryos. These analogues could be potential chemotherapeutic leads for cancer.

Epilepsy Research

COE for Epilepsy is one of its kind centre in India which brings together a premier medical science institute (AIIMS) and a dedicated neuroscience research centre (NBRC) to study drug-resistant

epilepsy (DRE). The main aim of the centre is to understand epileptogenic network and identify potential biomarkers for accurate localization of epileptogenic zone using a systems biology approach. For a comprehensive study the AIIMS is using magnetic resonance imaging (MRI), electroencephalography (EEG), video EEG, as well as functional imaging techniques like positron emission tomography (PET) and single photon emission tomography (SPECT) to locate the epileptogenic area. The NBRC is using non-invasive protocol of magnetoencephalography (MEG) for the source localization. Correlation of the imaging and electrophysiological parameters with the molecular/cellular properties of neurons is the hallmark of this multi-disciplinary centre.



Magnetoencephalography analysis

Translational Research in Eye Diseases

New strides have been achieved in regenerative medicine at LVPEI, Hyderabad. Genome editing technologies has been undertaken for correcting gene mutations in patient derived induced pluripotent stem cells (iPSC) lines and studies are underway in establishing it for gene therapy.

Genome Mapping and Molecular Breeding in Mustard

UDSC, New Delhi and University of Delhi, Delhi has undertaken extensive research in mustard on genome mapping and molecular breeding for improving oil content and protecting the plant against major diseases. In the completed Phase I study, the group carried out genome mapping and fine mapping using SNP markers the genetic loci of seed glucosinolates, erucic acid, seed coat colour and white rust resistance. Further studies

are underway in Phase II support towards improving oil content and achieving disease resistance varieties.

Microbial Biology

In the Centre of Excellence on Microbial Biology significant new understanding of bacterial cell wall synthesis and replication has been achieved at CDFD, Hyderabad. During bacterial cell wall synthesis, a new 'space-maker' regulation mechanism has been identified that involves proteolytic cleavage of the peptidoglycan hydrolase MepS by the combined action of two proteins NlpI and Prc. Export of the basic amino acids lysine and arginine has been shown to occur in *E. coli* through distinct transporters, with a novel exporter YbjE (LysO) mediating lysine export. A model invoking distributed aberrant replication origins from RNA-DNA hybrids (R-loops) has been proposed. The bacterial nucleotide signaling factor ppGpp and the Lon protease have been identified to redundantly contribute for maintenance of the levels of the essential cell division protein FtsZ in *E. coli*.

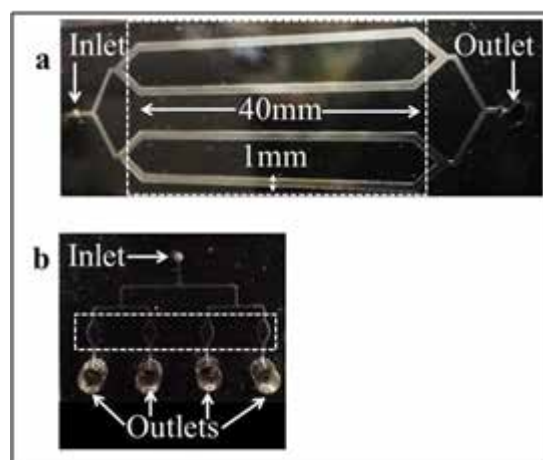
PROGRAMME SUPPORT

Programme Support is given to an identified institution / department (either as single institutional or multi-institutional programme) with multiple investigators in various disciplines to create and strengthen research capabilities at university or institutional level for categorical research by a number of investigators from different disciplines for a joint research effort; or investigators from the same discipline that focus on a common research problem. This mode of support contributes towards enhancing the core competence of the institution/department in biotechnology research. The salient achievements of the ongoing activities are:

- The investigators at University of Calcutta have defined a condition for hyper-activated

spontaneous nodulation in absence of rhizobia in *Arachis*. These inventions that confer a spontaneous nodulation phenotype has utility for the transfer and establishment of nitrogen fixing capability in non-nodulating plants, and thereby reducing the nitrogen fertilizer dependence of non-nodulating crop plants.

- The disease mechanisms, biomarkers, and therapeutic strategies of Retinoblastoma in a multi-faceted manner has been investigated at Vision Research Foundation, Chennai. Several oncogenic and tumor suppressing miRNAs and their relevant target genes known to play an important role in Retinoblastoma (RB) were identified using *in silico* methods and validated by *in vitro* experiments. A microfluidic chip for detecting miR18a (already proven to be specific RB biomarker) and a circulating tumor cell based chip using EPCAM and NCL aptamers were developed. IGF2BP-1 has been identified as a novel target for RB and targeted therapy is being developed against it.



Schematic of the microfluidic devices designed for cell capture studies

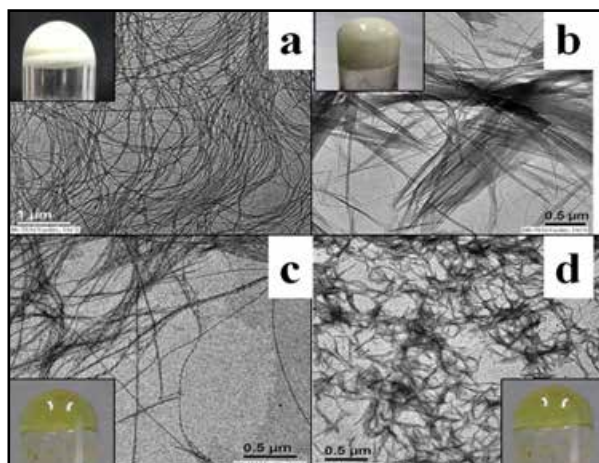
- Prognostic marker for glioblastoma based on Global DNA methylation has been identified at IISc, Bangalore. This is perceived to enable

stratification of patients into low- and high-risk groups. The team is now validating the prognostic signature and novel markers in large clinical samples in a Phase II study.

- Research at JNU, New Delhi for visceral leishmaniasis has led to development of genetically engineered ascorbic acid-deficient live mutants as vaccine candidate.
- ICGEB, New Delhi has achieved major strides in understanding blood stage growth of malaria parasites. A combination of three blood stage parasite proteins has been taken up for product development as a novel blood stage malaria vaccine candidate. PfCDPK1 (as a key effector involved in regulation of microneme release), Heme Detoxification Protein (HDP) and ClpQY protease machinery have been identified as novel drug targets. Signaling mechanisms have been defined that trigger the egress of mature merozoites from mature schizonts and the timely release of parasite ligands from apical organelles enabling receptor engagement during invasion of host erythrocytes.
- Quantitative expression analysis of all genes in each elucidated biosynthetic pathway in three medicinal plant species revealed that multiple genes correlate with the contents of major chemical constituents, suggesting that critical steps in biosynthetic pathways need to be identified so as to plan any genetic intervention strategy towards enhancing the contents of target metabolites. A Phase II research programme on possible genetic intervention has been initiated.
- Understanding the functional significance of non-mitotic role of Aurora Kinases through the phosphorylation of NPM1 (molecular protein), PC4 (non-histone chromatin associated protein) and other novel substrates

was studied at JNCASR, Bangalore. NPM1 is a highly dynamic nucleolar protein that plays an important role in diverse cellular processes. NPM1-mediated induction of p300 autoacetylation was studied in detail. Specific inhibition of Aurora A kinase by a hypertensive drug Felodipine is being explored. Further, non-toxic naphthoquinone derivatives as potent inhibitors for lysine acetyltransferase are being studied.

- Supramolecular synthon and crystal engineering strategies were exploited at NIBMG, West Bengal to convert various NSAIDs to supramolecular gelators for biomedical applications (via topical route) in self-delivery mode where no drug delivery carrier is needed. The easiest reaction such as organic salt formation has been demonstrated to be effective in getting easy access to biocompatible hydrogelators for the first time in literature and with they have isolated and characterized a series of ternary Zn(II)-NSAID complexes of 1,10-phenanthroline-5,6-dione, which display “two-in-one activity” by exhibiting anti-proliferative and anti-inflammatory activities.



Electron micrographs of Hydrogels

- A Programme Support is being implemented at JNTBGRI, Palode towards generation

of knowledge base on bioresources of Western Ghats, sustainable utilization and commercialization of bioresources including bioprospecting for new and novel application and conservation and maintenance of bioresources. So far plant-animal ecology at tropical landscapes is being studied including plant-pollinators interaction.

LONG-TERM R&D PROJECTS

Long-term R&D support to an individual outstanding investigator of high scientific caliber with publications and / or patents record at the highest level is provided in recognition of investigators for their recent performance and planned future work. The salient achievements of long-term R&D projects supported so far under this category are summarized below:

- Curcumin from turmeric was shown to prevent experimental cerebral malaria in mice. A combination of arteether and curcumin prevents and cures experimental cerebral malaria completely providing 100% protection against mortality. Malaria parasite (*P.berghi*) knock out strain for parasite δ -aminolevulinic synthase, the first enzyme of the heme-biosynthetic pathway, was shown to be a potential sporozoite vaccine candidate to prevent liver infection.
- Microbes face various kinds of stresses in a rapidly fluctuating environment. Bacteria sense and respond to the stress via various small signaling nucleotides like guanosine tetra and pentaphosphate ((p)ppGpp) and cyclic diguanosine monophosphate (c-di-GMP). The investigators at IISc, Bangalore have worked on several aspects of the metabolism of these second messengers in Mycobacteria, the pathways regulated by them and developed inhibitors against them. They have synthesized several synthetic glycolipids and (p)ppGpp analogs which

inhibit Mycobacterial biofilm formation. In addition, they have demonstrated molecules like Vitamin C to be natural inhibitors of (p)ppGpp synthesis at high concentrations. The PI has been awarded the one of the highest civilian award for the year for his pioneering work on bacteriology.

- Chromatin remodeling on a global scale is a unique feature of mammalian spermatogenesis during which diploid male germ cells give rise to haploid and highly compacted sperm chromatin. The entire gamut of posttranslational modifications of the three testis and spermatid specific proteins, TP1 TP2 and H1LS1 have been mapped to understand the molecular events that are associated with the histone to protamine transition. Further, the team has discovered one long non coding RNA, mrhlRNA and have shown it to interact with chromatin.
- Significant progress towards understanding the molecular basis of neurodegenerative diseases has been made at NCBS, Bangalore. Multiple pathways have been shown to be operational for amyloid fibril formation by several proteins, including tau and the prion protein, and they have been shown to lead to fibrils of vastly different internal structures and morphologies. In case of the prion protein associated with several prion diseases, the role of oligomers in fibril formation was elucidated, and mechanisms by which oligomers and fibrils could be toxic were delineated. The investigator is further pursuing the leads achieved in a new study.
- Studies at Amity University, Gurgaon, Haryana studied the efflux of incoming antifungal drugs from the cell by drug-resistant pathogenic fungi using membrane-embedded transporters belonging to ABC superfamily including Cdr1 proteins.

Mechanism of acquisition of drug resistance in clinical azole resistant isolates was performed using RNA seq and proteomics. Genes involved in translation, metabolism, transport, respiration and MDR regulation are induced.

BIOTECH FACILITIES

The programme is to promote, upgrade and establish new biotech facilities/infrastructure viz. animal house; gene banks; repositories for microbes, plants, model organisms and infectious organisms; centres for genetic engineering etc. for the up-gradation of research activities of scientific community at regional, National and International level. Furthermore, to promote growth of life science and biotechnology in the university system and linking research to education at every opportunity through creation/reengineering/ remodeling/up-gradation of life science departments in central/state universities. The outcome of the research activities supported for strengthening the research infrastructure in Universities and Institutions is as follows -

1. A DBT-BM14 program coordination unit (DBT-BM14-PCU) at Regional Centre for Biotechnology, Faridabad for providing access to Indian scientific community to synchrotron X-ray beam line (BM14) in Grenoble, France. The project has been extended for two years and an agreement signed between European Molecular Biology Laboratory (EMBL), Germany and Regional Centre for Biotechnology (RCB), Faridabad. A total of 64 peer reviewed publications came out of this support.
2. A project on 'Maintenance of Repository for Filarial Parasites & Reagents (MVR Reddy, Sevagram, MH)' is supported for re-innovation of Repository for Filarial parasites & reagents. A rapid diagnostic kit for filarial IgG4 antibody using filarial recombinant

WbL2 antigen has been developed in collaboration with Ubio Biotechnology Pvt. Ltd., Kerala. Filarial drug studies using green tea extract and piperidine compounds showed that the multiple stages of folate metabolic pathway can be targeted for anti-filarial activity by selectively inhibiting DHFR and thymidylate-synthase enzymes.

3. DBT supported "State-of-the-Art Next-Generation Sequencing Facility" at Centre for Cellular and Molecular Platforms (C-CAMP), Bengaluru, with an objective to provide genomics service to scientists, to train researchers and also work on national genomic projects. Using this set up, 469 samples has been sequenced, including 145 genomes (Bacteria-78, Fungi - 3, Animals-42, Plants - 22) and transcriptomes (Bacteria-82, Fungi-18, Insects-18, Animals- 138, Plants - 44)) from various institutes across India.
4. DBT launched a scheme i.e. DBT-Boost to University Interdisciplinary Departments of Life Sciences for Education and Research (DBT-BUILDER) for advanced education and research for up gradation/reengineering/ remodeling/ creation of Life Science departments in central and state universities. The objective is to promote Interdisciplinary research and technology development at university level. In Shivaji University, Kolhapur; Maharashtra; 11 species and 4 varieties of genus *Mucuna*, a medicinally important plant for treatment of Parkinson's disease (PD) are characterized. Two new *Mucuna* species namely *M. sanjappae* and *M. monosperma* having good amount of L-DOPA (7.3 and 5.2% respectively) and proved to be effective against Parkinson disease are identified. In Calcutta University, Kolkata; bioactive compounds from rare actinomycetes isolated from Sundarbans that are active against a broad range of pathogens



and a potential biomarker (hsa-mir-155) for the early detection of prostate adenocarcinoma is identified. In M.D. University, Rohtak, Haryana, a novel immuno-PCR method was developed, which has advantages of both ELISA and PCR, for an early diagnosis of TB patients. In M.S. University of Baroda, Vadodara, Gujarat; Dr. Vikram Sarabhai Institute of Cell and Molecular Biology is established. In Osmania University, Hyderabad, Telangana; in addition to development of Transgenic varieties of rice tolerant to both drought and salt stresses, Hairy root cultures of *Psoralea corylifolia* (*Cullen corylifolium*) for the production of bioactive isoflavonoids with better yields is developed. In University of Agricultural Sciences, Bengaluru; two important edible mushrooms were isolated and spawn were produced for their cultivation and technology to produce aflatoxin resistant groundnut lines has been developed. During last year, M.S.c fellowships (336), JRF (145), SRF (28), RA (61), PDF (7) awarded the total number of publications under this programme is 62, patent filed are 16 and technology transferred are 7.

5. A International Depository and Microbial Culture Collection Type (MTCC)' at IMTECH, Chandigarh is supported. MTCC has an objective of *ex-situ* conservation of microbial resources of India, to provide authentic microbial cultures to industries as well as academic and research institutes, to act as a depository of patent cultures, to take up research activities on microbial diversity, taxonomy, phylogeny and related areas in microbiology and to train researchers on microbial diversity, taxonomy, phylogeny and related areas. During last year, microflora from sea coast of Bhavnagar, Visakhapatnam, Puga Valley and Tsomoriri salt lake were

characterized. Characterization of two potential novel species using polyphasic approach is being processed. MTCC has supplied about 7,000 microbial cultures to customers from various organization including schools, colleges, universities, Govt. Funded Research organization and several pharma and biotech industries. More than 450 microbial cultures were identified during this period and 140 cultures were deposited for general deposit in MTCC collection. One hundred and twenty cultures were received for deposit under Budapest Treaty during this period and about 1/3 of them are from the industries. Four genomes were sequenced and the data deposited in NCBI. Eight international publications are published, 14 Ph.D. students were trained and 12 Project Assistants are working in the project.

6. A NMR facility (700Mhz) is established at Bose Institute, Kolkata. Dr. Harsh Vardhan, Hon'ble Ministry of Science & Technology and Earth Sciences visited the facility on 3rd May, 2015 (Figure-A). As a result of support, a total of 18 Ph.D. students are trained and Scientists from 14 departments/ Institutes from Eastern India are benefitted. In addition, an X-ray facility established at National Centre for Biological Sciences and two publications came out of this support.



NMR facility established at Bose Institute, Kolkata

DBT-IISC PARTNERSHIP PROGRAMME

Indian Institute of Science (IISc.) Bengaluru has immensely contributed in lifting the face of Indian academic Life-science sector; therefore, DBT supported a 'DBT-Partnership Programme for advanced research in Biological Sciences and Bioengineering' at Division of Biological Sciences, IISc. with major objectives to supplement the already available resources for making the IISc research intensive with added interdisciplinary nature among top institutions of the world through extensive national and international collaborations; to increase the number of publications both in quantity and quality; increase in the number of patents and technology developments/transfers; and increasing the number of undergraduate, Ph.D., students and Post-Doc's in coming years.

Under the Partnership Programme, the major research work is under progress on infectious diseases such as Tuberculosis, Malaria, Pneumonia, Giardiasis, Amboeiasis, Trypanosomiasis, Hepatitis 'C', Diarrhea, Virulence determinants of Japanese encephalitis virus, Enterovirus association with acute and persistent diarrhea, Curcumin-artemisinin combination therapy for the treatment of cerebral malaria, inhibitors for *Theileria annulata* infections in cattle's, Studies on the novel innate immunoregulatory protein, Human Immunodeficiency Virus (HIV) and Chronic diseases such as cancer, thromboerythrosis etc for development of drugs against the selected targets as well as ecological studies of fungal farming by termites, Understanding the pathology of cardiac fibrosis during diabetes, pathogenic mechanisms leading to Alzheimer's disease, role of signaling pathways in the initiation and progression of tumors and oral submucous fibrosis, protein folding, homologous recombination, whole genome sequencing of fungal stains especially *Candida*

species, anticancer from endophytic fungi, vaccine against Abrin intoxication, effect of pesticide especially on endiosulfan on sexual organs, molecular mechanisms of aging-related muscle degeneration, regulation of carbon metabolism, fig microcosmos, bioenergy generation through algal biotechnology, functional genomics of flowering regulators, sensory ecology of pollination networks in a seasonal cloud forest, species delimitation of Himalayan langur, mechanisms of cell wall biosynthesis in pathogenic gram-positive bacteria, determine the various malaria parasite species (*Plasmodium sp.*) infecting non-human primates.

In addition efforts has been made in ecology and environmental biotechnology areas especially in determining species boundaries in the Western Ghats, role of the elephant as a disperser of fruits, rational elicitation of cold sensitive phenotypes, behavior and physiology of peninsula rock agamas, understanding how the brain performs visual perception and object recognition.

Furthermore, the imaging sector has been under tremendous research in the areas such as *in vivo* imaging of mice brain, setting up of the single molecule based super resolution platform, development of novel co-localization algorithms for super-resolution image analysis, understanding the nature of information processing during the planning of sequential movements and coordinated eye hand movements, underlying mechanisms and spatial distribution of Brain rhythms Neural mechanisms of visuospatial selective attention, protocol to obtain thioamidated peptides on solid support, pluripotent stem cell (PSC) differentiation biolog. In total 328 publications were emanated, 70 publications are in internationally peer reviewed journals as a result of direct support through this programme.

AGRICULTURE BIOTECHNOLOGY

1. Crop- wise R&D projects

Rice

A study on cross talk between phosphorus and iron in the maintenance of nutrient homeostasis in rice is being carried out at NRCPB, New Delhi. An efficient hydroponic system for dissecting phosphate deficiency-mediated temporal effects on root traits in rice has been developed.

In the project on comparative genome and transcriptome analysis of *Magnaporthe* (Blast Fungus) isolates from rice and non- rice hosts, investigators have carried out analysis of genome architecture and sequence variation of two of *Magnaporthe oryzae* field isolates, B157 and MG01, of the blast fungus from India. Information from India isolate will contribute to global efforts to understand genetic diversity of *M. oryzae* population and to track the emergence of virulent pathotypes.

In the project on enhancement of starch accumulation and grain filling by dual specificity protein phosphatase AtDSP4 in *Arabidopsis* and OsPP42 in rice, investigators have successfully transformed the *Arabidopsis* and rice and are in the process of generating the transgenic plants, may help to design the better strategies to develop the improved technology for enhancing and increasing the starch quality and quantity in the specific organs such as seeds or other parts of the plants.

In the project on characterization of *Xanthomonas*

oryzae pv. *oryzae* strains from North – West and eastern regions, It has been found that rice pathogen *Xanthomonas oryzae* pv. *oryzae* employs inducible hrp-dependent XopF type III effector protein for its growth, pathogenicity and for suppression of PTI response to induce blight disease.

In the project on exploitation of resistance gene derived markers (GDMs) for the development of blast and bacterial blight resistant version of rice variety, Co-dominant Pi-9 gene-derived markers developed. that will be of utility to rice breeders for the incorporation of broad spectrum blast resistance gene Pi-9 into commercially important rice varieties through marker-assisted selection.

Wheat

Metabolic engineering of phytic acid pathway for improving iron bioavailability in wheat is being attempted at NABI, Mohali that may pave a path for genome editing tools in wheat to develop genetic-germplasm resources.

Phenotyping of mapping populations at hot spots and tagging of major QTLs associated with spot blotch resistance in wheat has been carried out at DWR, Karnal, Three new QTLs namely QSb.iwbr-7B, QSb.iwbr-7D in population Sonalika/BH 1146 and QSb.iwbr-7D in population Kanchan/Chirya 1 have been identified which may be utilized for MAS to improve spot blotch resistance.

Genome-wide molecular characterization of the transcriptome for thermal stress and photosynthetic efficiency in wheat spikes and functional characterization of selected thermal stress associated genes is being carried out at

UDSC, New Delhi. Research outcomes will be helpful in developing wheat varieties suitable for climatic changes and for marginal and stressed environmental conditions.

In the project on improvement of biscuit making quality of Indian wheats utilizing molecular approach, trials have done for identification of superior cultivars. Baking tests of these advanced lines showed higher biscuit spread factor and thus suitable for biscuit making quality. After evaluation for yield and disease resistance, the superior lines will be identified.

Oilseeds

In the project on metabolic engineering of oil biosynthetic pathway in safflower (*Carthamus tinctorius*) for fortification with Omega 3 FA, a reproducible protocol of regeneration *Agrobacterium* mediated transformation of hypocotyls into healthy plants is optimized in safflower under *in vitro* conditions. The modified protocols can be utilized for raising more transgenic plants in long term research. Further, omega-3 fatty acid production achieved in this project in safflower provides a proof of concept for production of transgenic safflower with alpha linolenic acid in seed oil.

Erucic acid profiling and Introgression of low erucic acid trait in cultivars of *Brassica juncea* L., and Single Nucleotide Polymorphisms (SNPs) for *Brassica juncea* are attempted at SKUAST, Jammu. Delhi University is working on introduction of very-long-chain polyunsaturated fatty acids biosynthesis pathway in Indian mustard, diversification of canola quality traits to some important Indian cultivars of *Brassica juncea* through marker-assisted backcross breeding, and also on development of low sinapine mustard (*Brassica juncea*) lines through antisense and RNAi technology

Soybean

Mapping of Mungbean yellow Mosaic Virus resistance loci in soybean is being done at NIPGR, New Delhi and GBPUA&T, Pantnagar. Study has generated SNPs from a RIL population, which will facilitate the dissection of complex traits as well as identification and exploitation of SNPs associated with favourable variants.

In the network project on marker assisted selection for development of kunitz trypsin inhibitor (KTI) free soybean varieties, five Indian soybean varieties were freed from KTI through Marker Assisted Backcross Breeding, SSR markers across the genome. This led to the identification of 9 KTI-free lines in the background of 'JS97-52', 6 KTI-free lines in the background of 'NRC7', 3 KTI-free lines each in the background of 'MACS450' & 'JS93-05' and 2 KTI-free lines in the background of 'DS97-12'. Introgression in varieties 'JS97-52' & 'NRC7' was carried out at ICAR-Directorate of Soybean Research, Indore; in 'JS93-05' & 'MACS450' at Agarkar Research Institute, Pune; and in 'DS97-12' at IARI, New Delhi. Seeds of introgressed lines have been multiplied for multilocation trial.

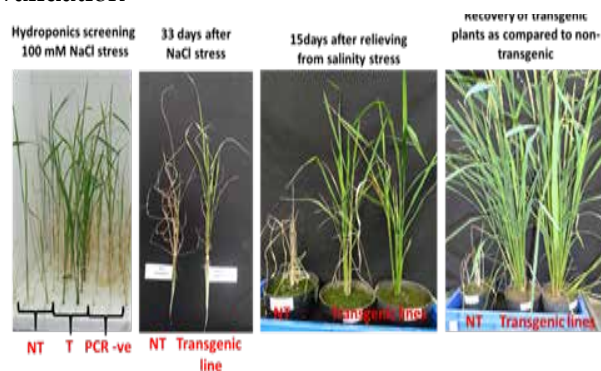
Lentil

Genetics and molecular tagging of drought tolerance gene(s) in lentil is being attempted at IARI, New Delhi. Molecular diversity of 278 lentil genotypes (wild and cultivated) and its cluster analysis will be done for selecting contrasting genotypes for future breeding programmes for improving drought tolerance in lentil. This will help in developing linkage map & tagging drought resistance genes.

Millets

Isolation and validation of salt tolerant genes in Ragi (*Eleusine coracana* L.) was done at TNAU, Coimbatore. Laboratory screening protocols have been standardized to understand genetic

variation for salinity tolerance in rice and ragi germplasm. Salinity responsive transcriptome profiling through RNA-Seq analysis revealed that Trichy1 had specific up-regulation of genes involved in transport, sugar metabolism, lipid metabolism and transcription. Putative candidate gene namely NAC transcription factor (EcNAC67) has been cloned from ragi (Trichy 1) and confirmed by sequencing. Transgenic rice (ASD16) plants over-expressing EcNAC67 were generated and confirmed through PCR and Southern analysis. EcNAC67 over-expressed rice transgenic lines exhibited enhanced level of tolerance against drought and salinity. Few other candidate genes like, Ethylene Response factor, Glycosyl transferase have also been isolated from finger millet which needs further experimental validation



Evaluation of rice (ASD16) transgenic lines engineered with EcNAC67 against salinity (100 mM NaCl) stress; NT = Non-transgenic ASD16; T = Transgenic ASD16 line; PCR -ve = T2 transgenic ASD16 lines negative for the transgene

Sugarcane

Genetic engineering of sugarcane for water deficit stress tolerance is being carried out at SBI, Coimbatore and ICGEB, New Delhi. It has been noted that DREB2, HSP70 and PDH45 genes play an important role in improving the cell membrane thermostability, higher level of abiotic stress related genes expression, higher relative water content and gas exchange parameters, chlorophyll content and photosynthetic efficiency,

which might contribute for the increased drought stress tolerance. Further to confirm the drought tolerance of these transgenic events under field conditions, application was submitted to RCGM for approval of confined field trial for selection of drought tolerant sugarcane transgenic events.

Cotton

Saturated genetic linkage map for *Gossypium hirsutum* L. using SSR and SNP markers is being developed at CICR, Nagpur and NBRI, Lucknow. Indian genotype based cotton SNP-chip has been developed.

Study on identification and mapping of QTLs linked to Jassid (*Amraca devastans*) tolerance in cotton (*Gossypium spp.*) being carried out in TNAU, Coimbatore. Two RIL populations of the cross combinations KC 2 (*G.hirsutum*) X Suvin (*G. barbadense*) and KC 2 (*G.hirsutum*) x MCU 5 (*G.hirsutum*) were developed and are in F6 generation.

2.0 Crop Molecular Breeding

2.1 Rice:

In the network project on development of biotic stress resistant rice through marker assisted breeding, at IIRR, Hyderabad, 3-gene and 5-gene pyramid lines (i.e. backcross derived lines) possessing resistance against bacterial blight + blast, bacterial blight + blast + gall midge, bacterial blight + blast + BPH have been developed in each background and some of these have been nominated for All India trials under gall midge screening nursery, planthopper screening nursery and disease screening nursery

Pup1 QTL containing lines have been developed in the genetic background of ISM, MTU1010 and IR-64. Pup1 introgressed line of ISM also have a high level of bacterial blight resistance conferred by the Xa21, xa13 and xa5. The promising Pup1 introgressed lines were identified in all the three genetic backgrounds. These lines will also serve

as donors for improvement of other elite rice varieties for low P tolerance and bacterial blight resistance.

Development of salinity stress resistance in rice varieties have been attempted with the objective of introgressing the 'Saltol' QTL selectively into three popular rice varieties PB1121 (IARI), Improved White Ponni (Coimbatore) and ADT 43 (Trichy) to confer seedling stage salinity tolerance in the respective salt sensitive rice varieties. Advance lines of PB 1121 'Saltol', IWP 'Saltol' and ADT 43 'Saltol' have been developed using Marker Assisted Back Cross Breeding technique and they are being evaluated both in National and State Level yield trials. The outcome of the project clearly indicated the effectiveness of 'Saltol' in conferring the seedling stage salt tolerance in rice and also the advantage of MABC in developing salt tolerant rice varieties

2.2 Wheat:

In the network project on mobilizing QTL / Genes for quality traits into high yielding wheat varieties through marker assisted selection, systematic and successful transfer and pyramiding genes/ QTL for high grain protein content (GPC), pre-harvest sprouting tolerance (PHST), grain weight (GW), gluten strength (GS), yellow pigment content (YPC), lipoxygenase (Lpx) and leaf rust resistance into 13 popular Indian wheat varieties was achieved using marker-assisted selection (MAS). Currently, several of these MAS-derived lines are being evaluated in All India Wheat Improvement Project.

In the network Project on molecular marker assisted development of biotic stress resistant wheat varieties, improved line of HD2932 with rust resistance genes Lr19/Sr25 +Sr26 is under second and final year of testing under SPL-MABB-IR-LS-CZ/PZ trial of All India Coordinated Wheat and Barley Improvement Project.

2.3 Chickpea:

In the network project on deployment of molecular markers in chickpea breeding for developing superior cultivars with enhanced disease resistance, work has been undertaken for enhancing resistance to Fusarium wilt (FW) and Ascochyta blight (AB) two major constraints to chickpea (*Cicer arietinum L.*) production. The back cross progenies with enhanced resistance to FW and AB have been identified which may be tested in different locations through AICRP trials. Further, the lines developed by pyramiding both FW and AB resistance can further be advanced and tested for resistance to both diseases in disease hot spot regions to identify the superior lines with enhanced resistance to both the diseases.

2.4 Groundnut

In the project on integrated marker assisted selection to develop groundnut varieties for resistance to foliar fungal diseases -Rust and Late Leaf Spot, two generations viz., BC3F1 (rabi 2014-15) and BC3F2 (kharif 2015) were raised during the year. Promising plants with QTLs were identified and forwarded to next generation. The resultant progenies have improved resistance than the parental genotypes. All these progenies are also possessing similar level of oil content as that of parental genotypes.



Performance of BC3F2 population of cross (VRI 2 × GPBD 4): Foreground confirmed progeny shows resistance to both LLS and Rust compare to its recurrent parent VRI 2.



Rust resistant genotypes of groundnut varieties by marker assisted transfer of QTL are being developed at UAS, Dharwad. Investigators have developed a large number of backcross breeding lines in JL 24 and TMV 2 for improving late leaf spot and rust resistance using a Spanish variety (GPBD 4) and interspecific derivatives (ICGV 86699 and ICGV 99005) as donors. They have also developed several mapping populations (RILs, ILs/AB-QTL and epi-RILs), mutant resources and heterogeneous inbred family (HIF)-derived near isogenic lines (NILs) for mapping late leaf spot and rust resistance.

3. Network projects

3.1 Physical Mapping and Sample Sequencing of Wheat Chromosome 2A

Sequencing of wheat genome was taken up as an international effort with 16 participating countries. India participated for sequencing of one of the 21 chromosomes, designated as 2A. Whole genome shotgun sequencing of both the arms i.e. 2AS and 2AL using Roche 454 and Illumina platforms to a depth of ~100 coverage with Illumina and 5-7X coverage with Roche 454 has been completed. The resulting assembly represented about 65% of the whole chromosome i.e. ~600Mb of the total 900Mb of the chromosome, thus confirming the belief of IWGSC that whole genome shotgun sequencing may not give complete sequence. This is because of highly repetitive nature of the wheat genome. This approach, however, has given wheat scientific community immediate access to 50,000 of SSR markers and large number of genes identified. Investigators have also completed high information content fingerprinting (HICF - a high throughput technique for fingerprinting of individual BACs) of almost all the 133,000 BACs and generated the Minimum Tilling Path (MTP). A high density map, based on 120 genes, generated for chromosome 2A.

3.2 Root Development and Nutrition

The project has target to identify genes related to root development and manipulate those genes and the genetic variation present within the root system to develop robust root system for better utilization of water and nutrient by the plant. Mitogen-activated protein kinase (MAPK) transduces signals for cellular reorganization, and Purple acid phosphatase (PAP) solubilizes organic phosphates in the soil for its uptake in plants. Two genes, MAPK6 and PAP, when highly expressed in transgenic rice produced robust root system were identified from rice by gene expression screening. Three genes have showed better root development when expressed in *Arabidopsis*.

3.3 Analysis of diversity in yield components (seed size and weight) at transcriptome and epigenome levels for association/genetic mapping of loci in rice and chickpea

The whole genome sequence, methylome sequence and transcriptome sequence of two contrasting low and high seed/grain weight rice (LGR and Sonasal) and two chickpea genotypes were decoded to understand the global seed/grain weight diversity in these genotypes at genome, transcriptome and epigenome level. The information regarding genomic sequence polymorphisms, epigenetic marks and differentially expressed genes/transcripts scanned from different low and high grain weight rice and chickpea genotypes are being integrated for molecular dissection of complex grain weight trait in rice and chickpea. An integrated genomic approach identified functionally relevant molecular tags (novel genes/QTLs, alleles and haplotypes) regulating grain weight for genomics-assisted crop improvement of rice and chickpea.

3.4 Identification and Functional Analysis of Genes Related to Yield and Biotic Stresses in Rice

At IIRR, Hyderabad, OsGsk11 from *O. rufipogon* was shown to be a candidate gene for yield increase and out of nine differentially expressed genes underlying yld2.1, remorin-like gene showed association to yield. In studies related to bacterial blight resistance serine-threonine kinase gene found to be associated with BB resistant gene Xa33 and characterization of *Xanthomonas oryzae pv. Oryzae* isolates. At PAU, Ludhiana, Xa38 BB resistance gene candidate gene is being validated and a novel BB resistance gene from *O. glaberrima* is being characterized. At CCMB, Hyderabad, transcriptional profiling of rice gene expression suggested that the jasmonic acid (JA) defense response pathway is involved in elaboration of cell wall damage induced innate immunity. At NRCPB, New Delhi, genome wide co-expression of genes in the transgenic rice line containing Pi54 gene related genes, sub-cellular localization on Pi54 protein in the cell membrane. At IIRR, Hyderabad, two and three gene pyramids gene introgressed lines with Pi-1, Pi-2 and Pi54 (Pi-Kh) in the background of BPT5204 and Swarna were evaluated. In studies related to brown planthopper resistance, two major QTLs viz., for WBPH damage score (PV 84%) on chromosome 6 and for days to wilt trait on chromosome 1 (PV 61%) were identified. At CRRI, a major effect QTL on chromosome 4 (PV 73.4%), and two minor QTL on chromosomes 3 and 12 were identified. At TNAU, using QTL and *in silico* analysis, three candidate genes found to be associated with BPH resistance. In studies related to tungro virus resistance, a candidate gene LOC_Os07g29820 encoding NBS-LRR protein was functionally characterized for disease resistance from a major QTL qRTV-7. Sixty seven research publications came out from this network project in total project duration. Towards product development

six improved rice lines obtained from this project have been nominated for advanced varietal trials.

3.5 Functional Characterization of Genetic and Epigenetic Regulatory Networks Involved in the Reproductive Development in Rice

The major developmental pathways targeted in this project are, (a) photoreception and transduction of light signal for vegetative to floral transition, (b) architecture and development of floral structures, (c) pollen development, and (d) seed development. It has been found that over expression of OsCRY2, those codes for a rice cryptochrome photoreceptor can reduce flowering time and reduction in plant height. Since both these traits are agronomically important traits their molecular delineation is underway. Similarly, an E-class MADS-box transcription factor, OsMADS1, has been found to function during its establishment of floral, floret-organ patterning and contributes to meristem termination by affecting auxin and cytokinin homeostasis. Identification of direct targets of OsMADS1 by using ChIP-seq is underway and is expected to reveal regulators of panicle branching, and those controlling floral organ formations. In the area of male gametophyte (pollen) development, two F-box genes and a bHLH transcription factor have been found to play important roles. The leads obtained from these fundamental aspects of plant reproductive biology would provide primers for translational work aimed augmenting not only yield but also quality of rice and cereal crops in general.

4. Crop Biofortification

4.1 Biofortification of Wheat for Micronutrients through Conventional and Molecular Approaches

The project aimed at finding major QTLs for grain iron, zinc, protein and yellow pigment and



transferring them in adapted backgrounds. In a biparental population of 286 RILs, chromosomes 2A, 5A, 7A and 7B were found to be harboring the QTLs for grain iron concentration and chromosomes 2A, 4A, 5A, 7A and 7B were associated with gain zinc concentration. In a backcross population derived from a cross between an introgression line developed from *T boeoticum* and a durum parent, QTL for grain Zn is mapped on chromosome 5A in the marker interval *barc180-wmc150*. Various species of *Aegilops* have been used to transfer the chromosome segments from their addition/substitution lines with high micronutrient content to high yielding and rust resistant derivatives of cv PBW343. Induced homoeologous pairing technique was also used for interstitial transfers and further reduction of linkage drag. Hybridization of wheat cultivars with irradiated pollen of donor alien species was also targeted for selecting lines with high harvest index, yield and micronutrient content. Six lines (in F4 generation) were selected with minimum linkage drag and high Fe (upto 71.45 mg/kg) and Zn (upto 59.27 mg/kg) content on the basis of genomic *in situ* hybridization, molecular marker and Fe and Zn analysis.

4.2 Development of Micronutrient Enriched Maize through Molecular Breeding

Efforts have been directed to enrich maize with provitamin A, Fe and Zn. A rare genetic variant of *crtRB1* gene, capable of increasing β -carotene enormously, was successfully introgressed into seven elite parental inbreds, viz., VQL1, VQL2, V335, V345, HKI1105, HKI323 and HKI161; using marker-assisted backcross breeding. These inbreds are parents of four high yielding commercial maize hybrids in India, viz., Vivek QPM-9, Vivek Hybrid-27, HM-4 and HM-8. The improved inbreds contained kernel β -carotene ranging from 8.6 to 17.5 $\mu\text{g/g}$. The reconstituted

hybrids developed from improved parental inbreds showed enhanced kernel β -carotene as high as 21.7 $\mu\text{g/g}$, compared to 2.6 $\mu\text{g/g}$ in the original hybrid. These improved hybrids possess similar ear- and plant- characteristics coupled with high grain yield potential with respect to the original hybrids. The β -carotene rich version of Vivek QPM-9 and Vivek Hybrid-27 are currently under multi-location testing. This is the first ever example of development of provitamin A-rich maize in the country.

4.3.1 Bio fortification of Sorghum

The project reported identification of new QTLs for grain Fe and Zn in sorghum. High heritability was observed for all traits in sorghum RIL populations, which is a prerequisite for effective QTL mapping and marker assisted selection. Investigators have identified large number (167 QTLs) of small main-effect QTLs controlling Fe and Zn concentration can be used to develop superior genotypes with grain high Fe and Zn concentration through Genomic selection / Marker-assisted recurrent selection (MARS). QTLs/candidate genes along with the marker/genetic resources identified through this study can be used for gene expression study for Fe and Zn concentration in the contrasting sorghum genotypes, identification of transcripts/genes showing presence of SNPs/indels and candidate genes for Fe and Zn concentration. Overall, genomic and phenotypic resources developed through this project will help in developing sorghum lines with high Fe and Zn concentration in a cost-effective and efficient manner.

5. Programme Support to the State Agricultural Universities (SAUs)

Programme support has been given to TNAU, Coimbatore for R&D in agriculture Biotechnology. The support has shown significant outcomes in terms of research and human

resource development. Research programmes on engineering resistance against banana bunchy top virus through RNAi approach, Molecular marker assisted selection and identifying resistance gene analogs (RGAs) associated with resistance to MYMV in mungbean (*Vigna radiata* Wilzck) and rice bean (*V. umbellata*) interspecific crosses, development of drought tolerant rice (*Oryza sativa* L.) cultivars by identification and deployment of candidate genes and fine mapping of QTLs linked to drought resistance traits, development of cotton for drought resistance and fibre quality, functional genomics of drought tolerance related traits in rice and development of low phytate maize hybrids using marker assisted breeding have been undertaken. Significant leads have been obtained. In last three years twenty seven research publications have been resulted from this programme support. Recently, Hon'ble Union Minister for S&T and ES visited TNAU and reviewed the programme.



Visit of Hon'ble Union Minister for Science & Technology and Earth Sciences, Dr Harsh Vardhan to TNAU, Coimbatore

6. Next Generation Challenge Programme on Chickpea Genomics

In the first phase of this programme investigators have generated useful information on genome sequence, transcriptome characterization, gene expression analyses, genome diversity, marker

development, molecular mapping, and gene function. The work led to development of several genomic resources/tools, which provides a framework for future research work. Based on the leads available and outcome of first phase of the project, phase two has recently been initiated with the broad objectives of exploring transcriptome dynamics of chickpea development for candidate gene discovery and defining regulatory elements/modules, functional genomics of stress tolerance in chickpea, and functional genomics of chickpea seed development and nutrition. The outcomes are expected to serve as key components for future research on chickpea functional genomics and molecular breeding for genetic enhancement of important agronomic traits. All the data generated in this research programme are being made publicly available which provides genomic resources for the chickpea research community of the country.

7. DBT-IRRI network programme on QTL to Variety - Marker Assisted Breeding of Rice with Major QTLs for Drought, Flooding and Salt Tolerance

In this multi-institutional network project, the main focus of this project is to improve rice productivity in the fragile ecosystems of eastern, north eastern and southern part of the country, which bear the brunt of one or the other abiotic stresses frequently. Seven consistent QTLs for grain yield under drought are being transferred into submergence tolerant versions of three high yielding mega rice varieties, Swarna-Sub1, Samba Mahsuri-Sub1 and IR64-Sub1. To address the problem of complete submergence due to flash floods in the major river basins, the Sub1 gene is being transferred into ten highly popular locally adapted rice varieties namely, ADT 39, ADT 46, Bahadur, HUR 105, MTU 1075, Pooja, Pratikshya, Rajendra Mahsuri, Ranjit, and Sarjoo 52. Further, to address the problem of soil salinity, Saltol, a



major QTL for salt tolerance is being transferred into seven popular locally adapted rice varieties, namely, ADT 45, CR 1009, Gayatri, MTU 1010, PR 114, Pusa 44 and Sarjoo 52. Genotypic background selection is being done after BC2F2 stage using an in-house designed 50K SNP chip on a set of twenty lines for each combination, identified with phenotypic similarity in the field to the recipient parent. Near-isogenic lines with more than 90% similarity to the recipient parent are now in advanced generation field trials. These climate smart varieties are expected to improve rice productivity in the adverse ecologies and contribute to the farmer's livelihood.



Field performance of backcross derived lines of Swarna-Sub1/DTY1.1 under drought condition.

8. Marker Assisted Introgression of Different Traits to Develop New Generation Rice Varieties

The network project aims to improve twelve popular rice varieties for major biotic (Blast, BLB, BPH, Gall midge) and abiotic (Drought, Submergence, Cold, Salt) stresses by introgressing known genes/QTLs through marker-assisted breeding for their better adaptation to climate change conditions. Different set of gene specific/linked SSR markers were screened for each trait among donor and recipient parents and located in

genic region or closely linked with target genes/QTLs. The project expects the development of climate-adapted varieties that combine tolerance of various abiotic and biotic stresses that are likely to reduce rice yield in different parts of India because of the ongoing climate-change scenario. Further, efforts are also being made on capacity building of young scientists from different institutes involved in the project on marker-assisted breeding and in QTL pyramiding.

9. Centre for Advanced Research and Innovation on Plant Stress and Developmental Biology

The projects focus on the characterization of genes associated with abiotic stress response in rice. Genes have been expressed in rice using stress inducible promoters (NBS-Str and RD29). These transgenic lines have been carried forward to T1/T2 generation and phenotypic analysis is in progress. To alter plant height and flowering time, investigators are exploiting the potential of light signalling components. The cryptochrome 2 (CRY2) when over-expressed in *Brassica juncea* caused early flowering by modulating the expression of flowering pathway genes. It also acted redundantly with CRY1 in controlling plant height at lower energies of blue light. Likewise, OsbZIP48, a bZIP transcription factor, caused a drastic reduction in height when over-expressed in rice, indicating its role in regulating plant height.

10. Biotechnological Approaches of Improving Agricultural Productivity of Coastal Region.

A second round of CO₂ treatments in the FACE rings were carried out for 4 months with two different transgenic rice lines, IR20 introgressed with AmSOD1 genes and Pusa Basmati introgressed with AmAPX and AmMDAR genes (double construct) and non-transgenic cultivars

(control) were grown in 500 ppm of CO₂ and / or 100 mM NaCl integrated treatment. Rice seeds were germinated in the lab and seedlings were transferred to the FACE and ambient rings grown hydroponically in pots with vermiculite. The rice seedlings were exposed to CO₂ with the target above 500 ppm and continued till maturing stage. Results indicate that AmAPX gene expression was upregulated in CO₂ and 100mM NaCl integrated treatment. Elevated CO₂ alone resulted in the upregulation of AmAPX transcripts compared to ambient condition. AmMDAR gene did not show any differential gene expression under either treatment. Additional treatments for extended period is being done to understand the physiological response of rice plant to elevated CO₂ under saline conditions, which mimics the impact of climate change in Indian conditions.

BASIC PLANT BIOLOGY AGRICULTURE AND FRONTIER AREAS

The main focus of the program is to address fundamental plant biology issues and take up path-breaking research in frontier areas of plant biology with potential applications in agriculture. During the current year various projects have been supported with special emphasis on understanding the basic plant developmental mechanisms such as flowering, root development fruit ripening and nutrition. Projects concerning characterization of germplasm, mapping of genes linked to disease resistance and their application in crop improvement using combination of plant breeding technologies and genetic engineering tools received special impetus. The program covers large array of horticultural and plantation crops and also forest trees. Network programs on Metabolomics, Saffron, Apple, Eucalyptus and Solanaceae Phase II program continued to receive support. The completed and ongoing projects culminated in adding new scientific knowledge

in the concerned area of research leading to publications in scientific journals and developing new technologies that can minimize the gap between laboratories to farm. The progress made under various projects supported during the current year is summarized as under:

Basic Research

Several projects have been supported under basic research during the year. Study was supported at Dept. of Botany, University of Kashmir to generate cold tolerant tomato transgenic plants. The cold resistant gene Crp1 from *Brassica oleracea* and LeMPK3 (MAP kinase 3) from *Solanum lycopersicum* were cloned under stress inducible promoter rd29A and putative transgenic tomato lines were generated. Further, molecular analysis of these lines is under way. At TERI, New Delhi, research was undertaken to decipher the role of FT in flowering in *Brassica juncea*. Also, the knockdown plants generated using artificial micro RNAs (B. ju FT-amiR1 and B. ju FT-amiR2), displayed prolonged vegetative phase.

Project was supported at University of Delhi South Campus (UDSC), New Delhi to generate marker free transgenic tomato plants with delayed fruit ripening. Studies are underway to carryout marker free transgenic tomato plants with delayed ripening at T1 and T2 generations.

At University of Agricultural Sciences, Bangalore QTLs researchers have developed Recombinant Inbred Lines (RILS) with high shelf life of more than 40 days under room temperature (24 °C).

Host Pathogen Interaction

At Sharda University, Greater Noida, a diagnostic kit for the onsite detection and identification of Banana Bunchy Top Virus (BBTV) was developed. In another study conducted at Madurai Kamraj University, onsite diagnostic kit is being developed against various isolates of



Cardamom mosaic virus. Study was supported at Sher-e-Kashmir University of Agricultural Sciences & Technology -Jammu to identify and characterize viruses of solanaceous crops in different agro-climatic zones of Jammu region. In Jammu district, the incidence of the tomato leaf curl disease ranged from 29.6 to 45.6 per cent while in Kathua and Udhampur the incidence of the disease ranged from 31.2 to 39.2 and 33.6 to 42.4 per cent, respectively. The overall incidence of potato leaf roll disease ranged from 20.0 to 37.6 per cent in Jammu district while in Kathua and Udhampur districts, the incidence of the disease was 33.6 to 44.8 and 25.6 to 33.6 per cent respectively.

Metabolomics network

At SLS, JNU omics based approaches were adapted to understand the salinity stress response using contrasting rice genotypes IR64 (Susceptible) and Pokkali (Tolerant) variety. Mutant lines with contrasting traits were also generated. The results demonstrated a strong relationship between these metabolic pathways under salinity stress.

For biofortification of tomato with carotenoids and folate, research was supported at University of Hyderabad. Tomato cultivars (natural accessions) enriched with folate / carotenoids were identified. PKM-1 a tomato cultivar predominantly grown in Tamil Nadu has highest folate level (50 µg per 100 gm weight) of tomato fruit. Efforts are on to introgress these traits in to commercially grown cultivars (Arka Vikas and Pusa Early Dwarf).

At University of Delhi, emphasis was given on generation of RNA-seq data to establish global modulation in the expression of both protein coding genes as well as miRNA genes. The analysis indicated that several genes related to folate metabolism were predicted to be targeted by miRNA.

At Jammu University, carotenoid profile analysis of tomato accessions collected from different areas of the State or received from University of Hyderabad was performed. Sequencing and characterization of carotenoid genes in the accession having maximum amount of carotenoids has been done.

In order to deliver a web based secure data repository and comprehensive metabolomics tool for plant biology research was supported at School of Computational and Integrative Sciences, JNU, New Delhi and IIIT, Hyderabad, Hyderabad. Comprehensive software modules have been developed for analysis of data generated through metabolomics.

User friendly GUI of CCPM v. 3.4



SOL Phase-II Network

Various projects have been supported this year under SOL Phase 2 program to understand the basic development mechanisms, enhance nutrition, and engineer disease resistance in tomato plants.

In a study supported at University of Rajasthan to understand root development in tomato, three ESTs (EX149581.1, EX149586.1 and EX149669.1) coding for putative SIHSP90.2 (*S. lycopersicum* Heat Shock protein 90.2), SIAT (*S. lycopersicum* Amino Acid Transporter) and SINAP (*S. lycopersicum* Nucleosome Assembly Protein), showed root and/or stage specific expression in 8d and 40day old plants. The selected genes (AAT, NAP, HSP, EF1α) from Real-time PCR analysis have been PCR amplified and cloning into plant expression vectors is underway to

further characterize these proteins.

In order to engineer ToLCV resistance in tomato, at University of Delhi South Campus, Delhi, polycistronic construct (bi-cistronic construct) targeting the RNAi suppressor genes and pre-coat protein gene namely, AC4, AC2, AV2, was synthesized. Synthetic Rep mutant construct (393 bp) has been cloned and the sequence is being ascertained for mutation.

At Indian Institute of Horticultural Research (IIHR), Bangalore, research is supported to develop ToLCV resistant tomato cultivars by pyramiding of ToLCV resistance genes Ty2, Ty3, Ty5 and Ty6 using molecular markers. Also, efforts are underway to identify new source of resistance in breeding lines and to develop mapping populations for resistance to ToLCV.

In a project supported at NIPGR, *Solanum lycopersicum* 26S-proteasomal subunit RPT4 (SIRPT4), Armadillo-repeat protein gene (SIARM) Ubiquitin conjugating enzyme-2 (SIUCE2), differentially expressed after Tomato leaf curl New Delhi virus (ToLCNDV) infection in tolerant cultivar H-88-78-1 have been functionally characterized by virus induced gene silencing (VIGS). Moreover, 16 novel interacting partners of SIRPT4 protein have been identified; these interactions may play an important role in plant defence against ToLCNDV.

Research is also supported to improve fruit quality of tomato under ripening network program. At University of Hyderabad, introgression of Nps mutant, which is defective in phototropin and has a phenotype of delayed ripening and high lycopene into Arka Vikas cultivar, is being carried out. The groups at Lucknow University and University of Delhi are trying to achieve improvement of fruit quality via manipulation of genes for Ethylene Responsive Factors (ERFs).

Forestry, Horticulture and Plantation Crops

Three multi-location trials of the mapping population developed from *Eucalyptus tereticornis* X *E. grandis* has been established at Channagiri and Hosakoppa, Shimoga district, Karnataka and Nellore district, Andhra Pradesh. The populations developed will be used for multi-environment phenotyping for wood property traits.

Research has been supported for various horticultural crops like chilli, grapevine and cucurbits etc. At Punjab Agricultural University, Ludhiana two markers linked to the nuclear sterility gene ms10 in chilli pepper (*Capsicum annum L.*) have been identified and validated. Efforts are on to develop new male sterile lines (DL161, SD463 and SL461) using these markers.

To gain insights into the mechanism of salt stress in grapevine, an integrated transcriptome and proteome approach was adapted at National Research Centre (NRC) on Grapes, Pune. Differentially expressed genes were identified in salt stressed grapevine (leaf sample). Gene enrichment revealed predominance of transcription factors. Metabolome analysis was performed for treated and control samples and 15 most differentially expressed metabolites have been selected for further annotation and validation.

Studies are also supported to understand cytogenetic diversity in some genera of Cucurbitaceae and characterization of sex linked genes in *Coccinia*. Fluorescence banding in native populations of *Coccinia grandis* showed cytological distinction in chromosomal CMA signals between the genders.

Saffron network programme

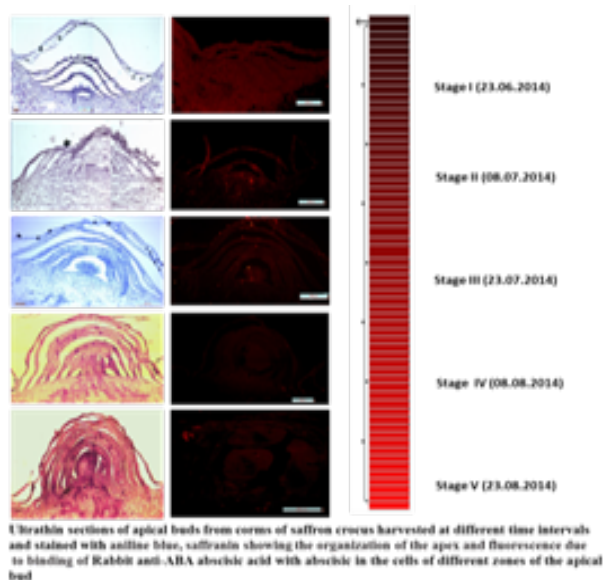
Support is being continued for an ongoing network programme on Saffron involving North Eastern Hill University, Shillong; University of Jammu, Jammu; Kashmir University, Srinagar; National institute of Plant Genome Research,



New Delhi; Jawaharlal Nehru University, New Delhi and IHBT, Palampur. In a study supported at University of Kashmir/ IHBT Palampur tissue culture protocol for saffron cormlet with desired size was developed and corm size up to 5.1gm was achieved. Both, normal growth regulators and standards were constantly used for cormlet weight improvement. Besides, 4 isolates from Kashmir University and 4 culture filtrates from IHBT, Palampur showed significant impact on the weight gain of cormlets.

In a study supported to identify and characterize PGPRs influencing growth of saffron, a total of 4146 bacteria were isolated and 4 bacilli i.e. *B. aryabhatai*, *B. amyloliquefaciens*, *B. megaterium*, and *B. thuringiensis* showed best PGP and biocontrol activities. These were further used to develop consortia in different combinations.

At IHBT, a total of 2073 rhizobacteria were isolated and resolved into 113 morphotypes. The efficient PGPR isolates were further tested for antifungal activity against fungal pathogens. Efforts are on to undertake field trials using PGPR based inoculum.



In order to understand the regulation of synthesis and accumulation of apocarotenoids in saffron (*Crocus sativus* L), the stages of bud development

were characterized. It was observed that the bud development correlated with changes in ABA levels in the apical buds and corms. The expression profile of selected apocarotenoid pathway genes in different floral organs and genes at different developmental stages has been developed.

In addition, transcript profiles of corms and buds, at pre-dormancy stage and during dormancy have been worked out at NIPGR, New Delhi. Experiments are in progress to generate comprehensive expression profiles of saffron transcripts in different tissues and further analyze important metabolic pathways.

Apple Network programme

In an ongoing network programme on apple involving 5 institutions KU & JU from J & K, YSPUH & F from HP, GBPIHED from Uttarakhand and CSIR-CCMB, Hyderabad, DNA typing of 250 identified apple genotypes using 78 SSR markers has been achieved. Preliminary allelic diversity analysis suggests a region specific variability in the apple germplasm is available in India. Further, >180 SSR markers showing parental polymorphism useful for linkage analysis have been identified and mapping progenies have been evaluated. Large land resources (30/20 canals) have been granted at Baderwah, Zakura, and Kinnaur, the off-campus Research stations of Jammu, Kashmir and YSPUH Universities, respectively, and Chubatia Garden, Almora for establishment of "Apple mapping orchards". In addition, seed-derived mapping population as well as grafted or cloned progenies has been established in the orchard at Zakura campus. The scionwood of the same is being prepared for transfer to the above referred locations for establishing clonal mapping populations. In order to take leads obtained under this program to a logical conclusion, Phase II apple network program has already been initiated.

TRANSLATIONAL RESEARCH ON MEDICINAL AND AROMATIC PLANTS

Programme has been remodeled in the last year focusing on taking forward the research leads to their logical conclusion through multi-disciplinary approach. An Expert Group Translational Research for Products and Processes from Medicinal and Aromatic Plants constituted has been successfully promoting research efforts in the area. The Group has identified the following priority areas to be taken up for support: (a) Taking forward the research leads available for developing viable products and processes, (b) Developing products from medicinal and aromatic plants for animal healthcare, and (c) Technology development in aromatic crops and aroma engineering.

A Brainstorming Session on Herbal Products for Animal Healthcare was organized by DBT on 11th May, 2015 in which eminent scientists along with representatives from eight industries participated. Various priority areas were identified for support.

A Brainstorming Session on Technology Development in Aromatic Crops and Aroma Engineering was organized by DBT on July 3-4, 2015 at Fragrance and Flavour Development Centre (FFDC), Kannauj, UP in which eminent scientists along with representatives from Essential Oils Association of India (EOAI) and representatives from 10 industries participated. Priority areas for support were identified. Significant achievements are summarized below:

Ex-situ Conservation, Characterization and Agrotechnology:

Quantitative surveys were completed for populations of *Symplocos racemosa*, *Pterocarpus marsupium* and *Saraca asoca* in Eastern Ghats of

India at Siksha-O-Anusandhan (SOA) University, Bhubaneswar. Molecular characterization of different populations of target taxa with SSRs, AFLP and other sequence-based primers are being done for formulation of appropriate conservation strategies.

Based on essential oil yield (0.8 to 0.9%), rhizome yield and cyperene contents (24 to 26%), two elite accessions of *Cyperus scariosus* (Nagarmotha) and *C. rotundus* (Motha) have been selected out of 80 accessions collected from various parts of the country at Fragrance and Flavour Development Centre (FFDC), Kannauj. Post-harvest technology including distillation of these plants has also been standardized.



A Field view of Mature crop of Nagarmotha



A view of Nagarmotha germplasm at the time of collection from Betwa

Etymological analysis of Ayurvedic synonyms of Meda-Mahameda and Shatavari have been carried out at FRLHT, Bangalore to compare

the morphological characters of the candidates described in ancient Ayurvedic texts with their taxonomical features. Both *Polygonatum cirrhifolium* and *Polygonatum verticillatum* match the Ayurvedic descriptions such as Nakhachchedya, shalyaparnika, manichidra /purushadantika.

Ecology based chemotyping has been done in *Zingiber zerumbet*, *Hedychium coronarium* and *Curcuma caesia* through collection of germplasms from different ecoregion of Odisha and West Bengal jointly at SOA University, Bhubaneswar and RKMV Centenary College, Kolkata. This has revealed significant variation in yield and quality of drug through analysis of essential oil and extracts using GC-MS and HPTLC analysis. Chemical fingerprint has been developed for essential oil of 3 species using GC-MS. Genotyping work is in progress.

Mint farmers of Northern India have been suffering severe economic losses from Begomovirus infection in the cash crops, menthol mint. For this, a dipstick-based diagnostic kit for

early detection of Begomovirus infection in mint (*Mentha arvensis*) has been developed at CSIR-CIMAP, Lucknow from the viral coat protein.

An end-to-end demonstration project on field demonstration of cultivation and processing of selected aromatic crops has been implemented in Dhar block (Kandi Area) of district Pathankot, Punjab by Punjab State Council for Science & Technology in collaboration with Kelkar's Scientific Research Centre, Mumbai and linkage institutions – Regional Research Station of Punjab Agriculture University, Ludhiana and Unati Cooperative Society, Talwara, Punjab. A total of 48.5 acres farmers' fields in villages Jungath, Patti, Bhabbar, Roug, Dhar Kalan, Bhangoori, Phaguli, Simbhal and Durnag Khad have been brought under cultivation of aromatic grasses – lemon grass, citronella and palmarosa, in a phased manner. The essential oils extracted from these aromatic crops are being marketed through linkage organizations at the rate ranging from Rs. 750/- to Rs. 900/- per liter.



Cultivation of Aromatic Crops at Farmers'



Fields in village Phaguli, Dhar Block, Punjab



Steam Distillation Units at farmers' fields



About 170 germplasm of three medicinal plants – *Rauwolfia serpentine*, *Glycyrrhiza glabra* and *Andrographis paniculata* were collected from 13 different locations of the country including the states of Haryana, Chandigarh, Uttarakhand, Himachal Pradesh and Uttar Pradesh. The plants are in the green house of the CPB, Hisar and will soon transferred to the nursery in the CPB campus.

Kewda flower and leaf samples have been collected from ten identified kewda patches. Extraction of essential oil has been completed. Chemical and molecular profiling is in progress.

Novel Bioactive Agents and Herbal Formulation:

Tribulus terrestris and *Achyranthes aspera* were studied in detailed experiments for their potential effects in kidney stone mediated renal injury at JUIT, Solan. They were found to inhibit calcium phosphate (CaP) nucleation and the demineralization of the preformed mineral phase effectively. Aqueous extracts of *T. terrestris* reduced renal injury, the sites for CaOx deposition. Further, butanol fraction of *T. terrestris* was found to be better than *A. aspera*. Purified protein from *Tribulus terrestris* also exhibited cytoprotective effects on renal cell lines.

Ethanol extracts of mycelial culture of the mushroom strains, *Pleurotus ostreatus* showed anti-apoptotic effect in human colon carcinoma cells.

Syzygium cumini, *Costus speciosus*, *Momordica charantia*, *Gymnema sylvestre* and *Azadirachta indica* were studied to identify a potent molecule with anti-diabetic and anti-adipogenic activity at Anna University, Chennai. Oleanolic acid 3-glucoside (OAG) from *S. cumini* has been identified using bioactive guided fractionation and structural characterisation. OAG was found to be a bifunctional molecule showing antidiabetic

and antiadipogenic effects through inhibition of PTP1B and partial agonism to PPAR γ . A pure molecule with anti-diabetic potential from *C. speciosus* was identified using bioactive guided fractionation and the structure of the bioactive molecule is being elucidated.

Bioactivity guided fractionation of *Tinospora cordifolia* fractions led to the isolation of biologically active compound, TCD5-F3-B (TC-B) jointly at Manipal College of Pharmaceutical Sciences (MCPS), Manipal and Indian Institute of Science, Bangalore. TC-B showed dose-dependent depletion of side population and inhibition of the multi-drug resistance (MDR) transporters (ABC-B1 and ABC-G2) in human epithelial cancer cells.

Butanol fraction of *Anogeissus acuminata*, ethyl acetate fraction of *Punica granatum* and *n-hexane* fraction of *Soymida febrifuga* exhibited potent antibacterial activity against *Staphylococcus aureus* at SOA University, Bhubaneswar. The *n-hexane* fraction of *S. febrifugais* being further pursued for isolation of bioactive compounds.

Cardioprotective effect of curcumin on doxorubicin induced cardiotoxicity has been demonstrated at Jaypee Institute of Information Technology (JUIT), Noida. Curcumin was found to reverse cellular hypertrophy through inhibition of MMPs.

A modified valproic acid induced model of Autistic Spectrum Disorder (ASD) and experimentally induced epilepsy in rats, a new animal model of autism has been established at PGIMER, Chandigarh. Effects of Risperidone and *Withania somnifera* extract is being studied on neuro development biochemical pathways.

Anti-obesity properties of piperine were studied in experimental rats at SV University, Tirupati. The observations strongly suggest that piperine, a major phytoconstituent of black pepper



serves as an effective therapeutic agent for the management of obesity and hypertension.

Prophylactic potential of *Terminalia arjuna* bark extract against osteoblastogenesis, osteoclastogenesis and adipogenesis in in-vitro model is being studied at Mahatma Gandhi Medical College and Research Institute, Puducherry. The aqueous extract facilitated osteoblastogenesis as evidenced by the presence of calcium nodules, osteocalcin, collagen, matrix mineralization and increase in alkaline phosphatase activity and calcium secretion compared to other extracts showing pro-osteogenic potential.

Oral bioavailability of tenofovir, an HIV drug, was enhanced by over 80% when co-administered along with 3', 5-dihydroxyflavone-7-O- β -D-Galacturonide-4'-O- β -D-glucopyranoside (FG-3) or piperine at Dr. Babasaheb Ambedkar Marathwada University, Aurangabad. FG-3 enhanced the oral bioavailability of tenofovir by inhibiting the p-glycoprotein function and for piperine it is via inhibition of CYP 450 mediated metabolism.

Methanolic extract of *Puraria tuberosa tuber* significantly prevented the rise in serum urea and creatinine level along with high albumin in urine demonstrating promising role in the prevention of diabetes nephropathy at BHU, Varanasi.

Bioactivity guided solvent extraction of leaf extracts of *Phyllanthus acidus*, *P. emblica* and *Leucas aspera* has led to select the fraction enriched with anti-plasmodial activity against chloroquine sensitive and resistant strains of *Plasmodium falciparum* at ICGEB, New Delhi.

Genomics and Biosynthetic Pathways:

Mentha piperata is economically important aromatic and medicinal crop. The terpene synthases in relation to metabolite channeling in

Mentha piperita was studied. 11 full length novel genes were obtained through RACE. Among these genes, the genes for viridifloral biosynthesis was studied in detail through expression in suitable host as this terpene provides smoothness and sweetness to the flavor of essential oil. Expression analysis of viridiflorol synthase gene showed correlates with viridiflorol content of *Mentha* oil. Overexpression of viridiflorol synthase gene in *M. piperita* is under progress.

ENVIRONMENTAL BIOTECHNOLOGY

Bioremediation/ Biodegradation

Assessment of arsenic pollution and bioremediation of arsenic contamination from agricultural soils has been carried out at NBRI, Lucknow. Soil fungal strains having significant arsenic tolerance were tested for their plant growth promoting abilities and they were not exhibiting any pathogenic symptoms to test crops. It has been concluded that these fungal strains can be effectively used for the arsenic bioremediation in arsenic-contaminated agricultural soils.

Study on the mechanism of microbial degradation of xenobiotic nitro-aromatic pollutants carried out at NEERI, Nagpur. A bacterial culture capable of biodegrading nitroaromatics was isolated from a contaminated site. It was identified as *Cupriavidus* strain by 16S rRNA gene sequencing.

A proof-of-concept has been developed at IIIT, Noida, demonstrating the ability of selected PGPM strains to remediate organophosphate pesticides commonly used in agriculture.

In the project on developing efficient microbial inocula for degradation of textile dyes and their amines at GNDU, Amritsar, biotransformation of C.I. Acid Blue 113 and other dyes by *Shewanella* species and biodegradation of 4-aminobenzenesulfonate by indigenous isolate *Shinella yambaruensis* have been demonstrated.

The work has been validated in lab scale bioreactors and the process for their on-site testing is in process.

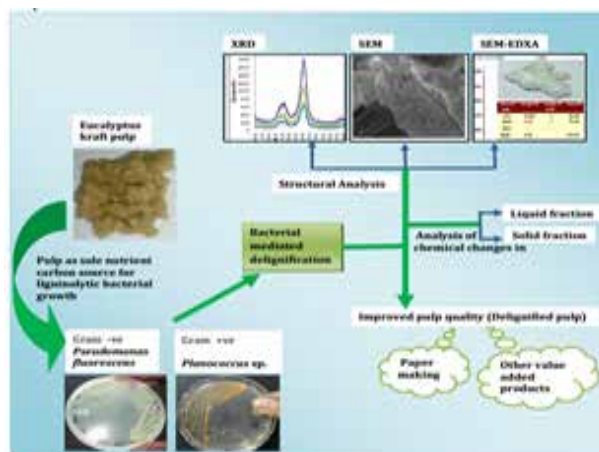
In the biomineralization studies of manganese from wastes and natural resources at SOAU, Bhubaneswar, isolation of indigenous bacterial and fungal strains from mining quarry have been attempted. Molecular identification of selected potential Mn bioleaching microorganisms done using molecular tools. The fungal strains were identified as *Aspergillus terreus*, *Aspergillus oryzae*, *Penicillium* species, *Penicillium* species, *Penicillium dalea*, *Penicillium* species. The bacterial strains were identified as *Bacillus anthracis*, *Acinetobacter* sp, *Lysinibacillus* sp.

In the study related to biodegradation of high molecular weight polycyclic aromatic hydrocarbon by fungal culture at NVP College of Pure and Applied Sciences, Vidyanagar, Gujarat, optimization for laccase production in solid state fermentation using fungal isolate *Agaricomycetes* sp AGAT and its role in degradation of pyrene have been delineated.

Genomic and biochemical characterization of bacterial isolates degrading atrazine and its application in herbicide bioremediation are being carried out at NEERI, Nagpur. Sequence analysis of identified isolate *Pseudomonas* sp. EGD-AKN5 revealed the complete atrazine degradation pathway. Besides degradation of the herbicide, the isolate may also be able to degrade phenol, demonstrating a multi-substrate degradation property making it a good candidate for bioremediation of environmental niches.

Development of a green technology for improvement of paper quality and to minimize the generation of genotoxic effluents has been carried out at NIT, Durgapur. A proof of concept has been developed to provide the paper pulp mills an economic feasible strategy involving direct application of *Planococcus* sp. and *Pseudomonas*

fluorescence whole cells in pre-bleaching of pulp.



Pictorial representation illustrating the improvement in the quality of raw eucalyptus kraft pulp by bacterial mediated delignification

Metabolites characterization and detection of functional genome of melanoidin degrading enzyme involved during the decolourisation of post methanated distillery effluent have been carried out at IITR, Lucknow. The potential bacterial consortium has been developed and noted to produce extracellular Ligninolytic enzyme i.e. Manganese Peroxidase (MnP) and laccase capable for degradation of molasses Melanoidin, resulted in decolourisation of post methanated distillery effluent (PMDE) in presence of glucose (1.0%) and peptone (0.5%) as carbon and nitrogen source at high BOD and COD level. The developed microbial consortium and process can be further optimised as technology after reduction of Total Dissolved Solid (TDS) of high TDS containing PMDE for detoxification and re-use of treated wastewater for economic growth (aquaculture, green belt development, industrial use of treated water and in agricultural practices) and sustainable development.

Phytoremediation/ Bio restoration

In the project on construction of wetland for phytoremediation treatment process for the degradation of dyes from textile industrial



effluent, phytoremediation of textile effluents and dyes has been demonstrated by *Alternanthera philoxeroides*, *Ipomoea hederifolia* rooted soil bed and *Ipomoea aquatica* rhizofiltration coupled phytoreactors for efficient treatment of textile wastewater.

Endophytic microbe mediated growth promotion mechanisms in an arsenic accumulator terrestrial plant and a heavy metal accumulator aquatic macrophyte *Typha angustifolia* has been studied at Culcutta University, Kolkata. A consortium of endophytic microbes isolated from *Typha angustifolia* collected from a Uranium mining site was found to significantly promote growth in *Typha*. The microbes were tolerant to both Fe and Mn and appeared to impart increased tolerance to *Typha* towards these metals. In a study with rice it was noted that *Typha* endophytes also promoted growth in rice.

Bioremediation of degraded mangrove forest along the embankment of the river Ramganga and related molecular study for the loss of mangrove ecosystem homeostasis is being done at WBSU, Kolkata. Investigators have been able to restore considerable area of the degraded site which was earlier completely barren, with established grassy patches of *Porteresia coarctata*, *Myriostachya withiana*, *Paspalum vaginatum* and *Sporobolus virginicus*. Mangrove seedlings are regularly multiplied in the nursery depending on the availability of propagules in different seasons. The team has started transplanting the already well grown seedlings to the site of restoration Technologies to multiply *Heritiera fomes* (endangered), *Xylocarpus* spp., *Phoenix paludosa* (near threatened), *Lumnitzera racemosa* and *Nypa fruticans* (both very rare locally) in large scale have been developed to be utilized for mangrove restoration.

A specific portion of the degraded Ramganga site is being restored by our developed technology



Development and optimization of a plant growth-promoting rhizobacteria assisted technology is being attempted for phytostabilization of mine tailings in the Sukinda chromite mining area. Forty four plant growth promoting bacterial strains were selected after screening of chromium resistant (Cr [VI]) isolates from the rhizosphere of native plants of different mining sites in Sukinda, Jajpur district of Odisha. The results of this study may provide data on the spatiotemporal patterns in the bacterial communities and will identify bacterial groups that are specifically present or absent in overburden soils compared to control samples.

Environmental Metagenomics

In the network project on understanding genome organization and gene expression in response to different Hexachlorocyclohexane (HCH) isomers in HCH degrading bacteria and the HCH dumpsite, *in-situ* characterization of the microbial community present at the hexachlorocyclohexane(HCH) dumpsite was performed using metagenomic approach to analyze the community structure and function. The application of 16S rRNA amplicon and shotgun metagenomic sequencing methods

revealed an enrichment of unknown archeal, bacterial and fungal taxa under high saline condition prevalent at the dumpsite. In addition to this a clear abundance of *lin* genes, transposons, plasmids, prophages, ABC transporters and genes associated with chemotaxis/motility and membrane transport were abundant. The work was further extended by reconstruction of the common ancestor of *Sphingobium japonicum* UT26 and *Sphingobium indicum* B90A; isolated from two discrete geographical locations, Japan and India, respectively and are capable of degrading HCH using metagenomic data from an HCH dumpsite.

A study on physio-chemical and microbial community structure of soil is being carried out to understand ecological perspective of Rann of Kachchh. Investigators have developed a protocol for indirect cell lysis for metagenomic DNA extraction from saline soil, yielding 4.6 µg DNA per gram of soil, capable for down stream molecular processing without additional purification steps. The whole metagenome sequencing revealed the anticipated pre-dominance of archaeal species at Kuchchh desert, with abundance of *Halorubrum* sp. and *Salinibacter* sp. of bacterial community. The functional annotations suggested that microbial community were adapted for various stress at desert ecology amongst the unique gene features. The cultivable dependent analysis revealed the dominance of *Bacillus* in all three seasons.

In the study on characterization of lipase producing clones and microbial diversity of hot springs of Odisha through metagenomic approach, screening of metagenomic library constructed from Taptapani hot spring (Odisha) yielded a positive lipase clone. Sequence analysis showed an ORF of 416 amino acid residues. Sequence analysis at protein level revealed the conserved Ala-His-Ser-Gln-Gly motif consistent with the consensus motif Ala-X-Ser-X-Gly. This ORF also contained a Zn²⁺ binding consensus sequence which confirms that the present lipase is matching with

the members of family. Ala-Ser-Leu-Arg-Ala (Ala-X-X-X-Ala) motif of pUC-lip479 could be responsible for its thermal stability. AXXXA motif lead to dimerization of protein causing better stability by strong Vander Waals interaction in thermostable lipase at elevated temperature.

In the project on exploration of microbial diversity and function in acid mine drainage and mine tailings at IITK, Kharagpur, one hundred thirty four bacterial strains were isolated from different sites. Metabolic characterization indicated abundance of acidophilic, autotrophic nature with higher resistance to Zn followed by Cu and anaerobic growth. Transmission electron microscopy indicated intracellular Cu sequestration ability of selected bacteria. The study revealed the characteristics of indigenous microbial community in AMD of Malanjkhanda Cu mine and their potential role in situ bioremediation.

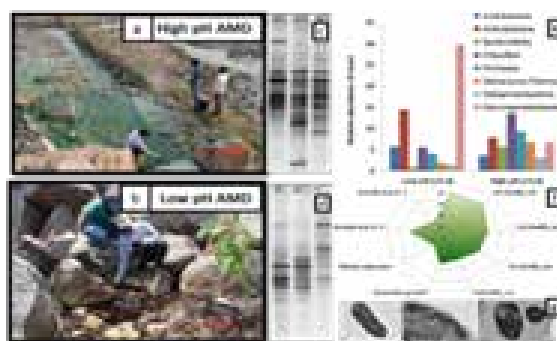
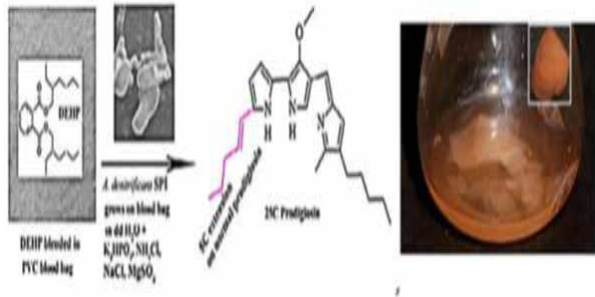


Fig. AMD sites at Malanjkhanda Cu mine, high pH (>5.0) (a); low pH (<5.0) (b); 16S rRNA gene DOGE profiles (c) high pH, d low pH); NGS based community composition (a); metabolic profiles of isolated bacteria (b); transmission electron micrographs of cells grown with copper, showing intracellular metal deposition (c)

Products from Waste

In a pilot scale study for the bioconversion of hazardous DEHP plasticizer in plastics into a drug by *Achromobacter denitrificans*, it was shown to produce a 25C prodigiosin analog in a simple basal salt medium supplemented with free (ex situ) di(2-ethylhexyl)phthalate (DEHP) or DEHP blended (in situ) blood bag (which contained 35% w/w phthalate as the plasticizer) as the sole source of carbon. The production conditions were optimized statistically. In silico analysis using

Glide, this 25C prodigiosin indicates its analgesic and anti-inflammatory potentials



DEHP blended in blood bag, *A. denitrificans* growing attached on blood bag, structure of 25C prodigiosin analog, and *A. denitrificans* growing in BSM-blood bag medium produces prodigiosin (the orange-red colour).

Design of pilot scale process for extraction of protease from the fish processing waste and its application in dehairing is being carried out at CLRI, Chennai. In this project stability of long term storage, immobilization and shelf life of an enzyme derived from the fish waste is being studied in order to transfer the proposed technology for commercialization in leather industry.

In the project on utilization of cassava bagasse as a substrate for the production of microbial exopolysaccharides (xanthan and curdlan), new bacterial strains capable of producing exopolysaccharides namely curdlan and xanthan isolated from roots of infected plants have been identified. Microbial exopolysaccharides namely xanthan gum and curdlan were produced from agricultural wastes like, cassava bagasse and jackfruit seed using environmental isolates and strains obtained from the culture banks independently. In order to recover maximum fermentable sugars, agrowastes were subjected thermal, acid and enzyme pre-treatments. The process conditions are being optimized for each pretreatment.

Biodiversity Conservation and Characterization

Animal Biodiversity

Patterns of distribution and diversification in select snake genera in the Western Ghats and North-East India has been studied at IISc, Bangalore. Study revealed that there are different patterns of distribution and diversification associated within each genus, discovery of new lineages and cryptic diversity of taxa. Currently, with six species of *Ahaetulla*, this study recovered two new lineages (species) within the group. The *Ahaetulla* ancestors appear to have dispersed to the Western Ghats from North-East India and dispersed back to the other parts of India dry lands thereafter. Investigators discovered five new lineages within *Trimeresurus* genus and it appears that North-Eastern India may not have played a role in colonization of *Trimeresurus* into Peninsular India.



Members of the snake considered for study

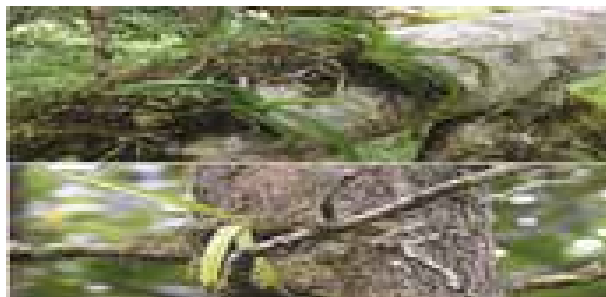
Initial results of the study on population genetic structure of gaur (*Bos gaurus gaurus*) from Melghat Tiger Reserve (MTR) of Amravati District (Maharashtra), predicts moderate (around 0.52) genetic diversity in the current gaur population inhabiting fragmented pockets in the reserve and suggest possible measure to connect this pockets through some corridor to reinforce gene flow so as to enhance the genetic diversity in the existing gaur population.

Initial results of the study on determining the taxonomic and conservation status of the Forest Owlet (*Heteroglaux blewitti*), using mitochondrial and nuclear markers does not indicate hybridization between Spotted Owlet and Forest Owlet from the samples collected. This is the first time that molecular data has been generated on the Forest Owlet which is endemic to Central India and is listed as Critically Endangered under the IUCN Red List.

Plant Biodiversity

In the Pan India network project on preventing extinction and improving conservation status of threatened plants through application of biotechnological tools a total of 858 new populations belonging to 90 species have been inventoried since the beginning of the project. Ecological niche models for all the species were improved during the period and predictive modelling and field validation for 79 species have been completed. Inter-population variation in active principles has been studied in two species viz., *Angelica glauca* and *Podophyllum hexandrum*, based on which elite populations were identified. Standardization of macro-propagation methods was completed for 16 species. Micro-propagation protocols were developed for six species. With this, macro-propagation methods for 55 species and micro-propagation methods for 26 species have been standardized during the project period. Study on reproductive biology was completed for three species during the period under report. Reintroduction in the field was achieved for 38 species, and a total of 13,297 seedlings were reintroduced in the field during April to November, 2015. So far, 26,837 seedlings have been successfully reintroduced in the field. Out of 94 species, 50 species were reported to have medicinal value. Of these, the propagation techniques for 24 species have been standardized, and seedlings are now available for transplanting.

Conservation of *Vanda thwaitesii*, *V.wightii* and *Eulophia cullenii*-three endangered orchids of Western Ghats through micropropagation and restoration with tribal participation have been carried out. The studies revealed habitat destruction as the main reason for depletion of all three species. Asymbiotic culture of seeds from natural populations was performed and produced 1306 seedlings of *V. wightii*, 1494 seedlings of *V. thwaitesii* and 725 seedlings of *E. cullenii*. Reinforcement of *V. wightii* (350), *V. thwaitesii* (308) and *E. cullenii* (325) seedlings was undertaken at sites approved by Kerala State Forest and JNTBGRI campus through the participation of EDC/VSS members from the particular region. Reinforced seedlings of *E. cullenii* exhibited 85% establishment in the native localities. The preliminary data showed 65-75% survival/establishment of *V. wightii* and *V. thwaitesii* seedlings in the native localities.



Reinforced *V. thwaitesii* (top) and *V. wightii* (Bottom) seedlings at Wayanadu and Idukki showing establishment

Climate Change/ Carbon Sequestration

In the project on exploring the efficiency of carbon sequestration potential of tree species under elevated CO₂ level at University of Hyderabad, it has been concluded that Gmelina and Mulberry are suitable candidate tree species for short rotation coppice forestry in future climate change scenarios to mitigate increased atmospheric CO₂ as well as for the production of renewable bio-energy.

Outcome of the project on evaluation of impact of elevated carbon dioxide on crop productivity and carbon sequestration reveals that in changing high CO₂ climatic conditions, Brassica juncea (mustard) plants will have increased plant productivity and higher seed yield. There was no down regulation of photosynthesis and Ribulose-bisphosphate carboxylase/oxygenase (Rubisco) in high CO₂ environment with optimum input of fertilizers including green manure to the soil.



Free Air Carbon dioxide enrichment (FACE) facility built in JNU. Mustard (Brassica) plants are grown inside FACE Rings maintained at elevated CO₂ (550 ppm)

Environmental Impact Assessment

Impacts of habitat fragmentation on host parasite interaction in endemic and endangered animals of Western Ghats has been studied at LaCONES, CCMB, Hyderabad, to examine the host parasite interaction in endangered and endemic animals inhabiting the fragmented rainforests of Anamalai Hills, Western Ghats. Analysis revealed that animals inhabiting small and disturbed forest fragments with human settlements nearby had higher gastrointestinal parasite species richness and greater percentage prevalence of parasitic infection as compared to animals of large and undisturbed forest fragments with no proximity to human settlements.

Characterization of anuran species as indicators of environmental quality in human dominated

landscapes is being carried out at CCMB, Hyderabad. Results obtained so far of this first amphibian radio telemetry study from India add a new dimension to understanding impacts of linear barriers on wildlife. The findings of this study would contribute to developing mitigation measures for the impact of fast expanding linear infrastructure in the country and restore ecosystem function.

Cytopathological and biochemical fish biomarkers of pollution are being studied for water quality assessment at Patna University, Patna. Fish biomarkers of pollution may act as biological early warning system of adverse effect in line with the “precautionary principle” which may be adopted in national monitoring programme of aquatic pollution

In the project on molecular investigation of epigenetic modifications in exposure to environmental pollution using *Neurospora crassa* as a model system at IITG, Guwahati, investigators have identified key role of three calcium signaling genes that play as molecular mediators that turn the environmental signal into phenotypic output in *N. crassa*. Further work will identify epigenetic changes of these genes in response to environmental stimuli

NATIONAL BIORESOURCE DEVELOPMENT BOARD

The National Bioresource Development Board (NBDB) was set up in 1999 with a mission to evolve a broad policy framework for R&D for sustainable utilization of bioresources and an effective plan of action for economic prosperity of the nation through accelerated R&D using modern tools of biosciences. NBDB focuses on the application of biotechnological and related scientific approaches for R&D and development of new products and processes sustainably utilizing the rich biodiversity of our country.

During the 12th Plan period, the thrust under National Bioresource Development Board on value added products from Biomass and Bioresource. With the rich Biomass and Bioresource reserve, the main emphasis is to move towards a Biobased economy to achieve this programmes are supported for both basic and translational research. These on in three major categories:-

- (A) Energy Biosciences
- (B) Bioresource Development and Utilization
- (C) Plant Tissue Culture (National Certification System for Tissue Culture Raised Plants (NCS-TCP)

The salient achievements of the programmes in 2015-16 are as follows:

ENERGY BIOSCIENCE (BIOFUEL) PROGRAMME

Energy Bioscience is one of the key areas of Department of Biotechnology. This program is being supported through various schemes and major emphasis is on development of 2nd generation biofuels. DBT has established a large network of more than 100 scientists in the country, who are working to realize the goals set in National Biofuel Policy. Efforts continued to support the R&D toward development of cost effective next generation biofuels like algal-biodiesel, cellulosic ethanol, bio butanol and bio hydrogen.

Department has established four Bioenergy Centers in country, specifically to strengthen the research base in the country in biofuel area and to promote translation of process and technologies from research to scale up and commercialization. These centers have the state of art facility and research teams are working in interdisciplinary areas related to Bioenergy. Various technologies

including cellulosic ethanol have been developed. Lignocellulosic technology developed by one of the Centers is being demonstrated at a pilot scale. Performance of these centers is reviewed by an Oversight Committee of DBT comprising senior members both national and from overseas.

Under International Cooperation in Clean Energy, Indo-US Joint Research and Development Center is being supported with a large consortium of 15 partners from academia and industry from both countries. Energy Bioscience Overseas Fellowship program has helped to bring 10 young scientists to back to home country. Very recently a Bioenergy Awards for Cutting Edge Research (B-ACER) launched for training of young scientist and Ph.D. students in leading institutes in USA. The purpose of this award is to nurture future innovators and thought leaders in Biofuel and Bioenergy.

Leads obtained from various programs are detailed below:

A. Bioenergy Centers

Following four DBT-Bioenergy Centers exists with specific goals and targets set by Department aligned to National Biofuel Policy :

- i) DBT-ICT Centre for Energy Biosciences, Matunga, Mumbai
- ii) DBT-IOC Centre for Advanced Bioenergy, Faridabad
- iii) DBT-ICGEB Centre for Advanced Bioenergy, New Delhi
- iv) DBT-Pan-IIT Centre for Bioenergy (participating 5 IITs)

Each one of these Centers is unique with respect to their capabilities and strengths in interdisciplinary research, process development and commercialization etc. Progress of these Centers is reviewed by an Oversight Committee

comprising 3 members from Overseas. Each Center is overall managed by an independent Scientific Advisory Committee and Governing Council. The Centers have developed more than 10 product and process technologies with protected IP and also these are working in close coordination with other Bioenergy Centers to complement joint research activities.

i) DBT-ICT Centre for Energy Biosciences, Institute of Chemical Technology, Mumbai

This is the first Bioenergy Center of Department and currently support extended for Phase II to take forward the leads from Phase I activities. Following are the highlights of achievements :

- Based on DBT-ICT Cellulosic ethanol technology first national facility developed at IGL Kashipur. Fully continuous intensified biomass-to-ethanol demonstration plant (of capacity 10 T biomass /day) will be commissioned by June, 2016. This 2G-Ethanol Technology has several novel features and is patent protected worldwide. The technology is devised to overcome all the drawbacks of the contemporary technologies and can produce ethanol from any agricultural residue feedstock. The technology is relatively low on both CAPEX and OPEX. Imminently scalable, the globally competitive DBT-ICT Technology is ideally suited to Indian conditions as it is feedstock agnostic and can operate well at any scale upwards from 100 ton/day biomass.
- 1000L Flat panel photo-bioreactors designed for autotrophy as well as mixotrophy growth of algae. Commissioning of the photo-bioreactors is underway.
- The Centre has developed a novel 'Hybrid Technology' for the treatment of municipal solid waste (MSW) and municipal liquid waste (MLW) and in convert in to value

added products in cost effective way. The novel 'Hybrid Technology' will be demonstrated at pilot scale in 2016.

- High throughput assay methods developed for any feedstock and in-process biomass composition analysis.
- Feed agnostic hydrolysis of pretreated biomass (96-99% cellulose) has been achieved.
- A series of template plasmids have been constructed for *Escherichia coli* genome engineering. This platform enables control of different promoters with the ability to modify/replace promoters of native genes for controlled expression of the gene product.
- Simulation software based on modified model with scientific parameters is developed to determine and predict the conditions for selective adsorptive separations of mono sugars and their dimers. Methods developed for scalable membrane separation of monomers from dimers and trimers with >90% purity and consistent yield.
- Methods optimized for isolating intact chloroplast and isolation of thylakoid membranes in progress for antenna size determination in microalgae.



DBT-ICT Centre 2G Ethanol Technology & pilot plant at (10 Tons biomass/day) IGL Kashipur



Algal laboratory at DBT-ICT CEB, Mumbai

ii). DBT-IOC, Centre for Advanced Bioenergy Research, Faridabad

DBT IOC Centre has completed three years and the major thrust of the centre has been to develop viable 2nd generation biofuel technologies in new areas of second and third generation biofuels, such as ligno-cellulosic ethanol and algal fuels. The Centre got equipped with state of art facilities in Liquid Chromatography - Mass Spectrometry (LC-MS) for the complete analysis of pretreated biomass degradation products & proteomics, 3000 litre Algae tubular photo-bioreactor pilot plant for scalable algal cultivation, Membrane filtration, Refinery Gas Analyzer etc.

- Pretreatment process optimization done 250 kg/day pilot scale for rice straw at lower cost (Capex) and low acid concentration, to produce high sugars at minimum inhibitors.
- Bench scale process optimization done for high productivity of enzyme production in mutant strains (productivity of 80-100 FPU/litre/hr). Enzyme production initiated in 10 litre fermenters which shall be scaled up in 150 litre Fermenter facility.
- Developed NIR model for one feedstock for fast biomass composition analysis to understand structure and process for pretreatment completed for 10 different biomasses.

- Development of high performance mutant algae strains which are producing high lipid content and have high temperature tolerance.
- Setting up of 3000 Liter Algae tubular photo-bioreactor for cultivation of high performance mutant algae strains.
- For the first time in India, Life Cycle Analysis (LCA) of cellulosic ethanol from rice straw initiated by this Center. Also, LCA and Net Energy ratio (NER) for fuel ethanol from sugarcane molasses and its impact on Indian biofuel program studied and published. NER of fuel ethanol from sugarcane molasses in India under different scenario established.
- Center has filed one patent and published 7 papers in last one year.



3000 litre Tubular Algae Photo Bioreactor facility at DBT-IOC Center Faridabad

iii) DBT-ICGEB Centre for Advanced Bioenergy Research, ICGEB

This is the third Bioenergy Center of DBT and research focus is on use of molecular tools to engineer microbes, Cellulytic enzymes, algae for enhanced biofuel production. Recently the center has developed capabilities in Systems biology. The major achievements in this year are as below.



(A) Enzyme and microbial engineering

- A hypercellulytic fungus, *Penicillium funiculosum* has been identified for higher hydrolytic efficiency at par with best commercially available cellulase cocktails. Genome of this hypercellulytic fungus sequenced, annotated and molecular tools developed for increased enzyme secretion ability.
- An ethanologenic engineered strain *E. coli* SSY10 further engineered to utilize cellobiose present in the hydrolyzate by cloning, expressing and secreting beta-glucosidase.
- Identified *Saccharomyces cerevisiae* natural isolate capable of fermenting ethanol with the yield of 0.39 g/g and productivity of 1.6 g/l/h at 40°C.

(B) Algal biofuels

- High lipid producing seven new green algae isolated and their genetic identification is established.
- A green microalga *Chlamydomonas* successfully engineered to enhance neutral lipid with diglyceride acyltransferase-II gene of rapeseed.
- A marine alga *Parachlorella Kessleri-I* was engineered for increase in biomass and lipid content via Carbon Concentrating Mechanism (CCM). Magnet based harvesting of the algal species is developed. Mixotrophic growth of algal species was optimized using wastewater for generate biomass and reduce the cost of cultivation.

(C) Systems Biology

- The latest genome scale metabolic model of *E. coli* was analyzed to identify targets for ethanol production from glucose and xylose

(primary sugars released from the hydrolysis of lignocellulosic biomass) using FBA-based methods.

- The ethanol yield from these knock-out strains was predicted utilizing advanced FBA-based methods and previously published ¹³C-MFA data, and compared to previously reported ethanologenic strain from our group.
- Genome scale model of a gut cellulolytic symbiont *Paenibacillus polymyxa* ICGEB2008 has been constructed and validated experimentally.
- In a year this Centers has published 25 papers and filed 3 patents as a research outcome.

iv). DBT-PanIITCenter for Bioenergy

This is the largest virtual Bioenergy Center recently established by DBT comprising 22 sub-projects under seven group. The group wise achievements are briefed below. Cyanobacterial Biofuels

¹³C flux analysis of cyanobacteria was initiated and results were obtained for dynamic flux analysis of *Synechococcus* sp. PCC 7002. A fully annotated and validated genome scale metabolic model was developed for *Synechococcus* sp PCC 7002. Approximately 50% of the proteome was covered by means of LCMS analysis and 1160 proteins were detected from the protein extracts genetic engineering of algae

Few algal strains were screened for starch content, and analysis revealed that the *Chlorella* sp. accumulated more starch (~22%) compared to *Scenedesmus* sp. (10%) after 30 days of growth.

Algal Bioenergy: Process Engineering

Harvesting of *Chlorella* MJ11/11 and *Synechocystis* PCC 6803 performed using flocculation with efficiency of 98% and 85%, respectively, with

ferric chloride (400 mg L⁻¹), and 98-98, 5% with chitosan (25 mg L⁻¹).

Algal pretreatment for H₂ production performed by HCl, heat, autoclaving, sonication, and H₂O₂; H₂ producing bacterial strains (*Klebsiella pneumoniae* IITBT-08, *Citrobacter freundii*) identified in lab, with H₂ production of 1330 mL/L.

Design and fabrication of dual chamber and sediment MCC completed). Clay/Pd based catalysts turned effective for model compound (squalene) for algae oil conversion. These catalysts were found to be promising for algal oil saturation/hydrogenation.

V) Rational strategies for enzyme and strain improvement

Sequence & structure comparison of Ct43Araf (*Clostridium thermocellum*) with HiAXHd3 (*Humicola insolens*) showing conserved sub-site residues F165, G183 and N184 were mutated to Alanine. The above mutations are directed towards enhanced activity of Ct43Araf. Out of the strains procured, it was found that *C. acetobutylicum* MTCC 11274 and *C. sporogenes* NCIM 2918 produced 11.8 g/L and 11.7 g/L of butanol respectively, when grown on optimized media. Solvent tolerance experiments showed butanol toxicity at 10-15 g/L. Kinetics studies based on differential acid phase and solvent phase are being carried out.

VI) Bioreactor Design

An initial, non-adaptive, version of the proposed Predictive Control (AMPC) toolbox for control of a fed-batch simultaneous saccharification and fermentation system has been developed and experimentally verified. VII) Techno-economic and life cycle analysis of biomass and algae-derived fuels initiated Work initiated on testing and debugging of the model.

2. Virtual Enzyme Center

This is a network project involving 6 partner institutes with complementary expertise of microbe engineering to product commercialization. The 6 work packages are divided among JNU, South Campus Delhi University, DBT-IOC Centre Faridabad, IIT Madras, Anna University, IIT Bombay. The purpose of establishing this network of 6 partner institutes is to develop robust and cost effective indigenous enzyme for cellulosic ethanol production.

Achievements of various Work Packages in first year are as below

- Isolation of fungal strains showing enhanced cellulase activity in SSF (WP1)
- Improved saccharification efficiency in packed bed reactors in comparison to slurry reactors (WP2)
- Improved host platform designed for recombinant protein production (WP3)
- Transformation protocol for *P.citrinum* and isolation of cellulase genes (WP4)
- Development of *E.coli* with furfural tolerance and pyruvate production (WP5)
- Optimization of pre-treatment, Standardization of enzyme assays and activity comparison between strains (WP6)
- Cellulase enzyme developed with good activity (FPase U/g, 17 CMCase U/g and 70 β -glucosidase U/g)

3. International Collaborations

Indo-US Joint Clean Energy Research and Development Centre (JCERDC)

(JCERDC) is being coordinated by Department and Biofuel consortium is supported by



Department. The consortium is co-led by the Indian Institute of Chemical Technology-Hyderabad and the University of Florida-Gainesville. An independent Project Monitoring Committee reviews progress of this collaborative project twice in a year. A joint presentation was made during Indo-US Energy Dialogue held on September 2, 2015 in Washington DC which was Co-chaired by Minister of Power, from GOI and Secretary, DoE US.

The U.S.-India Consortium for development of Sustainable Advanced Lignocellulosic Biofuel Systems emphasizes on sustainable feedstock cultivation and supply, biochemical conversion technologies for production of second generation biofuels with minimal environmental impact, and analysis of overall sustainability and supply chain of feedstock.

High biomass sorghum, pearl millet and bamboo have been identified as feedstock from India side. Out of 36 genotypes of high biomass sorghum genotypes tested for various agronomic traits (plant height, fresh yield, stover yield, etc.) 10 genotypes showed superior stalk yields during post rainy season. Also a good draught tolerant line identified based on multi location trial. Vegetative propagation of 20 bamboo germplasm is in progress. Abellon, one of the Industry partners has collected 20 different bamboo germplasm from various parts of India after consulting with National Bamboo Mission (NBM). Six out of 20 germplasm lines have been established at Modasa for further studies, while others are in the process of being established.

For conversion of sorghum biomass, 21 cellulolytic fungi have been isolated at TNAU. Standardization of alcohol fermentation to establish base levels on glucose substrate using in-house *Saccharomyces cerevisiae* has been initiated at IIT-D. Similarly, standardization of pre-treatment

variables of the biomass samples, isolation of microbial strains from various biosphere zones, and screening of biomass degrading-enzymes (xylanase and cellulase) have been initiated at IICT.

Socio economic study is being conducted with the farmers from Gujarat and Madhya Pradesh for cultivation of above three feedstock by Consortia partners - ICRISAT, DSR and RVSKVV, CESS. Baseline survey fieldwork has been completed in Madhya Pradesh by CESS. Preliminary survey findings showed mono-cropping being predominant in the study areas.

4. Capacity Building

“Energy Biosciences Overseas Fellowship” is a re-entry scheme for scientists of Indian origin who are working outside the country in the field of Energy Biosciences. Over the past few years since 2009, ten awardees with diverse expertise have returned to India and are working with the DBT Bioenergy Centers-IISER, IITs and other institutes. Two of these awardees/fellows have been absorbed in host institutes viz; IIT Guwahati and IIT Delhi. Thus, the program has been successful and proven to be the right platform for scientists who wish to return to India and contribute to nation. Energy Bioscience Chair awarded to a senior scientist is currently working at DBT-IOC Center and leading a team of researchers in the area of biomass characterization.

Recently, Bioenergy Awards for Cutting Edge Research ‘B-ACER’ launched for Ph.D. students and young scientists from India to interact with American peers and help build long term R&D linkages. The purpose of this award is to nurture future innovators and thought leaders in Biofuel and Bioenergy. More than 50 applications received from young scientist and students working in Bioenergy related area.

5. Various ongoing R&D Projects and leads so far

Feedstock Development for cellulosic ethanol

Availability and sustainability of feedstock is the major limitation for production of 2nd Generation biofuel. Hence efforts are continued by Department to develop alternate and suitable feedstock for cellulosic ethanol production ensuring the requirement of fodder and land use for agriculture crops. Indian Institute of Millets Research (IIMR, formerly DSR) and ICRISAT at Hyderabad have developed 28 high biomass varieties of sorghum (without affecting grain production) and 20 brown midrib derivatives.

- Two multi-location trials with 28 high biomass entries and 20 brown midrib derivatives were conducted across the rainfed environments of Maharashtra (Solapur), Karnataka (Gulbarga) and Tamil Nadu (Coimbatore) during Kharif 2015
- The entries SPV 2070 and SSV 20 recorded significantly high yields of fresh biomass (54 - 57 t/ha) and dry biomass yields (25-26 t/ha). Similarly under the Brown midrib trial, the brown midrib (bmr) entry IS 11861 exhibited a high fresh and dry biomass 50 t/ha and 23 t/ha
- Under bmr 6 introgression, about 53 F4 and 60 F3 generations were advanced and 15 BC3F1:2, 4BC3F2:3 and 12BC2F2:3 were produced
- A total of 43 BC2F1s with bmr 12 allele in sweet sorghum and high biomass backgrounds were generated.

Recently a network project started among private sugar industries and 4 institutions viz; Indian Institute of Millets Research (IIMR), National Federation of Cooperative Sugar Factories

(NFCFSF), Jawaharlal Nehru Technological University (JNTU) and ICRISAT involving 29 scientists and managers. The purpose of study is to commercialize sweet sorghum for biofuel production. To identify the most adapted genotype for a given location a multilocation trial with five sweet sorghum varieties conducted during the early raining season of 2015 in the sugar mill areas of three states Gujarat, Maharashtra and Tamil Nadu. In addition with the interest of sugar mills the trials were also taken up at sugar mills in Telangana, Puducherry, Karnataka. The data collection and harvesting is in progress at various locations.

Pretreatment is one of the important step in cellulosic ethanol, which helps to separate the lignin from cellulose and hemicellulose and making the material amenable for hydrolysis. There are several thermochemical pretreatments are available however the major issue is that many inhibitors/toxic compounds are formed which affect the enzymatic hydrolysis in a significant way. Therefore, Department has supported work on development of enzymatic delignification at various institutes.

At Venkateshwara University, after isolation and screening many ligninolytic fungi obtained from industrial area. Further characterization was done by sequencing of 18S rRNA of laccase potent strains (*Flaodius flavus* (KT714246), *Flaodius species* (KT714247) and *Xylaria* sp. (in process and cultivation conditions were optimized in submerged fermentation to increase the yield of laccase production by potent fungal strains.

Laccase mediated delignification

The process established at IIT Kharagpur for bioethanol production from lignocellulosic biomass is entirely through biological route using in house developed enzymes. The advantage of enzymatic pretreatment or delignification



is that no formation of harmful inhibitors in process which otherwise are formed during thermochemical treatments and hence better hydrolytic and fermentation efficiency could be obtained. So far, delignification process has been standardized at 40 °C resulting 75-80% lignin removal in 5-6 hrs. Pilot trials conducted for 50 kg biomass (dry weight) for bioethanol production. Koji room facility for large scale enzyme production has been established from this project within IIT-Kharagpur premises. The yellow laccase mediated delignification process for lignocellulosic biomass has been patented by IIT K.

An integrated approach for the development of microwave systems for pretreatment of lignocellulosic biomass is being studied at Central University of Rajasthan. Ferric chloride pretreatment and ammonium salts showed great potential to be used as microwave sensitizer chemicals for pretreatment of rice straw and sugarcane baggase respectively. Process for production of xylanases and cellulases enzyme cocktail from *Aspergillus niger* ADH-11 using microwave treated wheat straw as a substrate has been developed.

Ethanol from food waste

At Punjab University four strategies have been successfully used to convert putrescible food waste residues into ethanol at various level of fermentation. The four strategies include i) separate hydrolysis and fermentation (SHF), ii) separate partial hydrolysis and fermentation (SPHF), iii) simultaneous hydrolysis and fermentation (SSF), and iv) consolidated bioprocessing (CBP). The highest ethanol yield was obtained by the process of SSF (33.78 mg/g wet weight) followed by SPHF (32.99 mg/g wet weight), SHF (31.90 mg/g wet weight) and CBP (29.80 mg/g wet weight). More experimentation

and optimization is being done to further improve the ethanol yields in 100 L fermenter by using different consortia of appropriate hexose and pentose fermenting yeast strains.

Ethanol from textile mill waste

The cotton waste from the textile mills were collected, pooled together and the highest total sugar was observed of exactly 58%. The amount of glucose released after pretreatment was found to be 127 mg/g in the treated pooled cotton waste. The proper combination of pretreatment and enzymes for a given biomass enables high yields of sugars from both hemicelluloses and cellulose components. Enzymatic hydrolysis of pretreated cotton waste was performed through fungus (*Trichoderma reesei*) at optimum condition through response surface methodology. The sugar release was higher in treated cotton waste (Chemical followed by enzymatic hydrolysis) and the amount of 62% of free sugar was converted from complex form. The fermentation of the treated cotton wastes was performed using immobilized cells of *Zymomonas mobilis*. The estimation of the ethanol production was unerringly 0.48 % in 1 ml of treated cotton sample.

Biodiesel -Microalgae as a feedstock

Microalgae and Cyanobacteria Repository

One thousand seven hundred and eight (1708) microalgal strains including cyanobacteria are being maintained & preserved in the National Repository for Cyanobacteria & Microgreen algae (Freshwater) at IBSD, Imphal using conventional and modern techniques. Potent and fast growing cyanobacterial strain were investigated for the production of pigments, total soluble proteins, total carbohydrates, extracellular ammonia excretion etc. Sample bar coding of the strains using 16S rRNA & ITS markers has been taken up and submitted the nucleotide sequences to NCBI

GenBank database. Accession number have been allotted for 176 strains.



Another National repository, established at Bharathidasan University, Tiruchirappalli exclusively for Microalgae and Cyanobacteria includes marine and freshwater. Presently the repository houses marine mesophiles, hypersaline forms, thermophiles and psychrophiles. NFMC has established new germplasm and culture room for psychrophilic organisms in addition to mesophilic organisms at $4 \pm 2^\circ\text{C}$ and $15 \pm 2^\circ\text{C}$. This houses isolates of Arctic and Antarctic strains collected through Arctic and Antarctic expeditions.

This year 23 cultures supplied for research purpose to 15 institutes of 9 states from NRMC. Three institutes have deposited their strains at NRMC.

The details regarding available culture at Repository with their microscopic images and GPS data are available on Website www.nfmc.res.in

Photobioreactor design for algae production

A photobioreactor design based on the distribution of excess sunlight was developed at TERI New Delhi with 2-4 times higher areal productivity. A

simultaneous growth-harvest methodology also been developed which involves settling of select strains and collection of the settled cells in the growth system itself. This methodology has been repeatedly tested in the various growth systems employing an interval of about 45 minutes. This method has now become the norm by which algae are harvested from outdoor growth systems (350 L to 1800 L). A 10,000 L photobioreactor-harvest system is now in the process of construction.

A CFD model predicting the effect of delta wings hydrodynamics and pond geometry on velocity distribution profile and mixing for 1000L capacity open outdoor raceway pond was developed at IISc Bangalore. A simulated CFD model was developed to predict water velocity and gas hold-up profile, interfacial area concentration of air bubble and volumetric mass transfer coefficient in an internal draft-tube air-lift photo-bioreactor.

The growth of *Spirulina platensis* in open outdoor raceway was modelled using genetic expression programming (GEP). The growth, biomass productivity and biochemical response profile of *Scenedesmus obtusus* was studied in open ponds (under natural light and temperature conditions) and indoor enclosed photo-bioreactor (PBR) system. The studies on effect of hydrodynamic parameters, light intensity and photoperiod on growth and biochemical characteristics of microalgain the closed PBR are in progress.

In another study at PES Institute of Technology a process of production and extra-cellular secretion of lipid has been developed and process is being patented.

Algae production in industrial waste water

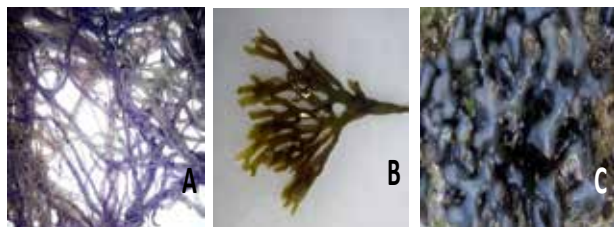
Rubber waste water collected by TERI Guwahati and was analysed for nutrients levels, BOD and COD were found to be 12300 and 3920



respectively. Various algal consortia were tested in this water and the consortium 3a (*Chlorella*, *Chlamydomonas*, *Chlorococcum*, *Volvox*) found best w.r.t. biomass and chlorophyll a & b production. Around 0.7g/l dry biomass was achieved in 100% rubber waste water in a photobioreactor. A photo illumination model developed for fine tuning Photosynthetically Active Radiation (400-700nm). This model could regulate intensity and duration of required light of various wavelengths

Macroalgae/Seaweeds

Three species of *Gracilaria* collected from Tamil Nadu coasts. The enzymatic saccharification of macroalgal pulp is being developed at Delhi University.



Biohydrogen

Currently, there is a huge demand for hydrogen and one of the usage is as alternate fuel. Several strategies for the production of hydrogen by fermentation in lab-scale have been found in literature. However no strategies for industrial-scale productions have been found. In one of the DBT supported project at Phototrophic bacteria from waste waters of South India has been isolated and characterized. Optimization of cultural conditions has been done to improve the production of hydrogen of the most promising phototrophic bacterial strains

Genetic engineering of *Rhodobacter sphaeroides* by knocking out the hydrogen reuptake hydrogenase gene is underway.

Hydrogen production through biotechnological route using various carbon sources (food and

non-food) is being studied at TERI New Delhi and Motilal Nehru Institute of Technology.

Various bio-wastes for biohydrogen production have been identified and tested fermentation using *Bacillus firmus* NMBL-03. The process has been optimized using starch as a substrate. However, starch being food /feed source efforts are continued to use cellulosic biomass as a feedstock. With hydrogen production as 2428 mL/L which yielded 2.168 moles H₂/mole of glucose.

A microbial based bioprocess developed for hydrogen production by *Enterobacter cloacae* strain DT-1 from baggase and wheat straw at TERI, New Delhi. Encouraging yields of H₂ obtained with acid treated biomass hydrolysate at 30 L fermentation.

Experimental set up at TERI New Delhi, for hydrogen production by *Enterobacter cloacae* DT-1 from acid treated wheat straw pre-hydrolysate and pretreated wheat straw enzymatic hydrolysate (both obtained from DBT-Bioenergy Centers)

Jatropha seed oil improvement by genetic engineering

Key genes contributing to high seed oil content in a genetically superior genotype (IC561235) have been identified through comparative expression analysis in a low seed oil content genotype across two geographical locations. This has been done for the first time in *Jatropha curcas* so as to rule out the influence of genotype and environment on expression status of FA/TAG pathway genes. Key 8 genes of 4 *Jatropha* genotypes with high seed oil content (42%) and higher female to male flower ratio (1:10) have been identified and used to develop gene markers using Eco-TILLING and sequencing.

In a breeding study at IFP Ranchi, eight parents of

Jatropha curcas were selected on the basis of yield and growth performance. Half diallel crossing was done among these parents. Diallel crossing without reciprocal was made using eight parents. So, a total of 28 different crosses were made during April – June, 2015. The highest seed setting was observed in cross 6 × 8 (79.61 %), whereas the lowest seed setting was observed in cross 1 × 6 (45.81 %). The maximum (92.23 %) and minimum (55.78%) seed germination was obtained in cross 4 × 6 and 3 × 8, respectively. Total 36 populations (8 parents + 28 F1 progenies) have been planted for evaluation in RBD fashion with 5 replications and growth data are being recorded periodically.

Based on inputs from various Ministries and Government Agencies, a consolidated report generated on 'Jatropha quality planting material and performance assessment through multi location trials'. DBT Inter-ministerial workshop on 'Quality Feedstock for Biodiesel' was organized by the Department of Biotechnology on 23rd July 2015 at TERI, New Delhi. The objective of this workshop was to consolidate information, bring out status of Jatropha in the country and plan a road map for future efforts towards production of feedstock for biodiesel. The meeting was represented by various Ministries and Departments and key recommendations were brought out after discussions and deliberations.

(A) Bioresource Development and Utilization

Efforts are being continued to support the research for bioprospecting, inventorization and characterization, value addition and sustainable utilization of bioresources along with relevant training, capacity building and awareness generation under the Task Force on "Value added Biomass and Product from Natural Resources".

The salient achievements of the major programmes during 2015-16 are as follows:

1. Mission programme on microbial prospecting:

Drugs from Microbes - a public private partnership

Under the DBT Microbial Mission programme involving nine institutions and Piramal Healthcare Limited (PHL) in a public private partnership model, nearly 200 thousand microbes were collected from various niche areas and screened for activities anti-cancer, anti-diabetes, anti-Inflammation and Anti-infectives. Nearly 16000 Hits have been identified. In the next phase, 1000 potent extracts were taken for 'Chemical characterization'.

One New Chemical Entity with anticancer and anti-inflammatory activity and 12 probable new uses of compounds were identified. One US patent has been filed and few are under process. A catalogue of 133 compounds has been prepared mentioning the bioactivity and all other details of the microbes and also classifications. Efforts are being made to explore the strategies for moving some of the active molecules obtained in the Microbial Mission program from discovery to Pre- Investigational New Drug (IND) studies.

2. Establishment of Microbial Repository

Department has established a Country's largest Microbial Culture Collection Centre (MCC) at NCCS, Pune which has IDA recognition. MCC has made significant progress towards achieving a premier culture collection status. With more than 180,000 microorganisms (archaea, bacteria, fungi including yeasts) in its collection at present, MCC is the single largest culture collection in the world, and has put India in the top three countries with the largest collections after USA and Japan. In continuation with its efforts to document the microbial diversity of the country, MCC scientists have described 13 novel taxa that have been published in international journals.

MCC also provides a variety of culture deposition (including deposits under Budapest Treaty),

supply and identification services. The details of services offered by MCC are as follows:

Cultures deposited in MCC under public access (Bacteria)	1210
Cultures deposited in MCC under public access (Fungal)	189
Total general deposit Cultures supplied by MCC	185
16S rRNA gene sequencing as an identification service	70
ITS /18S rRNA gene sequencing as an identification service	20
Phylogenetic analysis	21
Lyophilization provided as a service	168
FAME analysis	7
DNA-DNA hybridization	75
% GC content for general deposit cultures	34
Polar lipid profiling for general deposit cultures	12
Deposits under Budapest Treaty	75
Cultures as safe deposits	2

The status of Microbial Repository at NCCS, Pune as an IDA makes it mandatory for it to have a continuous existence. Efforts are underway towards upgradation of existing Microbial Collection Culture (MCC) to a National Centre for Microbial Resources. The IDA recognized National Repository will be expanded to cater to the country's requirement of collection and conservation of the rich microbial diversity. This would be crucial and critical to achieve India's Road Map on bio-economy.

- A Microbial Repository has also been established at IBSD, Imphal with an aim to act as the nodal centre for the supply of authentic microbial cultures collected in this region and help in the training of the researchers in the NER in conservation and characterizations of microbes. More than 20,000 cultures of bacteria, actinomycetes,

fungi and yeasts had been preserved and maintained in the repository. Efforts are being underway for expansion of Microbial Repository at IBSD, Imphal in collaboration with all North Eastern states to have a collection of microbes from all unique ecological niche areas of North East.

3. Biodiversity Characterization and Digitized Inventorization:

- Indian Bioresource Information Network has been launched towards developing a single window gateway to access distributed bioresource database. Its major goal was to network and promote an open ended, co-evolutionary growth among all the digital databases related to biological resources of the country and to add value to the databases by integration. This is the largest interactive database including information on data on 39,000 species of plants, animals, marine organisms and microbes including the spatial database. All the distributed data providers are now retrievable through a single window (www.ibin.gov.in). Efforts are underway for expansion of Indian Bioresource Information Network, which is today the largest single window portal providing complete information on the biodiversity of Hot spots in India and integration of IBIN data on Bhuvan Geo-portal.
- A first ever systematic attempt has been made for quantitative assessment of plant resources of Andaman and Nicobar islands. This assessment has been done in a grid based manner and compiled the data in the form of database. Over 70,000 images and 7,514 herbarium have been collected for over 2200 species of A& NB islands. Nine new species were identified & five species were

re-discovered from the project teams.

4. Prospecting of Genes and Molecules for Product Development

Projects have been supported for prospecting of novel genes, molecules, enzymes etc. from plants, microbes, fungi, lichens for production of potential products of industrial importance.

- A network project involving eight institutions has been supported to bioprospect for novel bioactive molecules from forest resources of the country. Three important species have been chosen, namely *Dysoxylum binectariferum*, *Saraca asoca* and *Lagerstromia speciosa*. Important leads have been obtained with regard to identifying new bioactivities, new biomolecules and new sources of important metabolites such as rohitukine and corosolic acid from *Dysoxylum binectariferum*, and *Lagerstroemia speciosa*. Based on the rohitukine scaffold, 55 NCE's have been generated and screening for anti-CDK activities accomplished.
- Plant species of the Western Ghats with high concentrations of Shikimic acid have been identified. One of the species belonging to the Araucariaceae family yielded the highest levels of shikimic acid (5.02%).
- New plant sources of camptothecin have been identified. Among the species, seeds of two species, *Miquelia dentata* and *Pyrenacantha volubilis* were found to have the highest ever reported content of camptothecin (1 to 1.4 %). Efforts are in progress for developing agro-forestry technology for the mass multiplication and developing a sustainable model of camptothecin production.
- Guggulsterone E and Guggulsterone Z were isolated from hexane extract of *Commiphora mukul*. Total six analogues of Z-guggulesterone were synthesized in very good yields. Boswellic acid, 3-Hydroxy-tirucallic acid, β -boswellic acid, acetyl- β -boswellic acid, keto- β -boswellic acid and acetyl-keto β -boswellic acid were isolated from *Boswellia serrata*. More than 20 compounds from the essential oils of *B. serrata* were also isolated. Ten analogues of boswellic and 11-keto-boswellic acid were synthesized. Five samples showed anti-inflammatory activity with > 50% inhibition of Carrageenan induced paw oedema in rats. 3, oxotirucallic acid isolated from *B. serrata* exhibited 87 % anti-inflammatory activity.
- Under the Lichen Bioprospecting Programme, one novel lichen molecule MSSRF/TE/04 isolated from *Trypethelium eluteriae* found to be active against seven clinically isolated *Mycobacterium tuberculosis* strains, non-tuberculosis mycobacterial strains as well as 20 strains of Methicillin-resistant *Staphylococcus aureus* (MRSA) and 7 gram positive human pathogenic bacteria at a concentration 12.5 μ g/ml.
- A high-throughput procedure for screening for carbapenemase inhibitors has been developed and validated using known inhibitors.
- A TLC Biotransformation Autography screening technique was validated using natural products and synthetic compounds. The technique was successful in identifying the formation of biotransformed products, as well as, simultaneously identifying the antifungal activity of the parent compounds (eg. Zaluzanin D).
- In a project aimed at studies on isolation, identification, characterization of an anti-inflammatory compound and formulation of herbal gel from a mangrove plant species

Rhizophora mucronata, the leaves extract of *Rhizophora mucronata* showed potential anti-inflammatory activity.

- The Department has launched a Network programme on prospecting of 'Fungi' for industrial important biomolecules. It is aimed to establish a network programme for prospecting of Fungal resources (known and new Fungi) for novel compounds. Under this network programme a total of 10 projects have been supported.

5. Resource Based Network Programmes

Several programmes have been launched to screen, characterize and improve important resources.

- Department has established a Hippophae Germplasm Resource Centre at Lahaul (HP) and at present 183 accessions of Hippophae from Himachal and one accession each from Russia and China are being maintained at the centre. A network project has been supported to consolidate Hippophae accessions from different regions of the country.
- A network project was supported for characterization, conservation, and value addition of Agarwood (*Aquilaria malaccensis*) using biotechnological approaches. Chemical markers for identification of infection in natural and artificially inoculated population have been identified. Specific microbes that have capacity to induce production of agarwood and developed artificial infection methods have been identified. By using these organisms agarwood production in *Aquilaria tree* within 3 months of infection can be induced. Diversity of endophytes in *Aquilaria malaccensis* in North Eastern part of India has been studied and artificial infection

method for oleoresin production has been developed.

- Under the Zingibers Network Programme, projects have been funded for production of superior quality planting material through macro and microrhizome formation, development of molecular markers in curcuma and prospecting of selected zingers for flavour compounds. In order to accomplish the ex situ conservation of gingers, the 'Ginger Park' at JNTBGRI was created. 7000 SSR markers of *Curcuma* have been identified and validated 20 novel polymorphic genomic microsatellite markers for use in *Curcuma* spp. and related members of Zingiberaceae. Methods were developed for assuring pathogen free nature of microrhizomes using DNA diagnostic markers for *Ralstonia solanacearum*, the pathogen causing bacterial wilt in ginger.
- A Phase-II Honeybee network programme has been launched so that the rich diversity of entire India is known and documented which will bridge this lacuna and map the complete diversity of honey bees and stingless bees from entire Indian subcontinent with authentic documentation and publication.

(B) Plant Tissue Culture: National Certification System for Tissue Culture Raised Plants (NCS- TCP)

Realizing the potential of plant tissue culture to revolutionize the growth of agriculture in India, Department of Biotechnology established National Certification System for Tissue Culture Raised Plants in 2006 under Seeds Act 1966 with the objective of mentoring the tissue culture companies for production and distribution of disease free and quality tissue culture plants. NCS-TCP ensure certification of Tissue Culture

Plant by Accredited Test Laboratories (ATLs) and Recognition of Tissue Culture Production Facilities which meet NCS-TCP guidelines, includes assisting tissue culture production units in strengthening their capacities for production of quality planting material, developing standard testing protocols and updating them from time to time, developing Standard Operating Procedures (SOPs) for Accredited Test Laboratories and Tissue Culture Production Facilities.

For implementing the NCS-TCP in country, DBT has established a well-defined operational structure. NCS-TCP Management Cell was established at Biotech Consortium India Limited (BCIL) whereas new Referral Centre for Genetic Fidelity Testing was established at NRC Plant Biotechnology, New Delhi. Advanced Centre for Plant Virology, IARI, New Delhi continued as Referral Centre for Virus Indexing. Two new Test Laboratories namely ICAR-Indian Institute of Sugarcane Research (IISR), Lucknow and Vasantdada Sugar Institute (VSI), Pune were also accredited leading to establishment of total five Accredited Test Laboratories (ATLs). Number of recognized companies has increased to 100 from 88 in 2014 from last year which includes all the leading companies. This year 29.47 million tissue culture plants have been certified by ATLs and 31,470 labels were issued. So far total 76.88 million tissue culture raised plants have been certified and 82,544 certification labels have been issued.

NCS-TCP is building capacity of tissue culture companies by increasing their visibility at national and international level. This system is also proving cost effective and accessible quality control mechanism to companies. Farmers are getting virus free and true to type tissue culture raised plants from the NCS-TCP recognized companies. Number of incidence of virus infection has been significantly reduced and no major virus outbreak has been reported during last few years since implementation of certification p r o g r a m m e .



Map illustrating the distribution of tissue culture production facilities and ATLs across India

ANIMAL BIOTECHNOLOGY

Animal Production

Livestock production is becoming increasingly important to economic growth of the country and therefore application of biotechnological tools to enhance the productivity of livestock sector is continued through R&D interventions supported by the department. Some of the achievements of the programme are as follows:

Animal reproduction and allied areas:

The structural and functional characterization of follicle stimulating hormone (FSH) of marmoset (*Callithrix jacchus*), an animal model, was studied at National Institute for Research in Reproductive Health, Mumbai. The recombinant mFSH was produced using yeast, *Pichia pastoris*, expression system and the purified protein preparation demonstrated immunoactivity, receptor binding ability and signalling competence. For antibody development, synthetic peptide corresponding to L2 loop region of mFSH β -subunit was synthesized and polyclonal antibody was raised against the peptide. The antibody was able to bind to mFSH in the recombinant preparation and also in biological samples like marmoset plasma and pituitary sections. It was demonstrated that the L2 loop region displayed distinct properties between mFSH β and hFSH β using the peptide



and anti-peptide antibody. *In silico* modeling and docking study showed differences in the structure and interactions between marmoset (m) FSH-mFSH receptor (R) complex and human (h) FSH-hFSHR complex. The recombinant mFSH and antibody would be useful for developing mFSH immunoassay and for further structural characterization of the protein.

The role of neutrophils in maintenance of pregnancy and their possible use in diagnosis of early pregnancy in buffalo is being attempted at National Dairy Research Institute (NDRI), Karnal. A two way communication during implantation between the conceptus and mother's immune system was observed and neutrophils showed changes in their expression pattern which was measured by isolating these cells during days 12 to 20 post insemination. There was a downstreaming of adhesion molecules of neutrophils along with pro-inflammatory cytokines in pregnant cows and up-regulation of interferon stimulated genes like ISG15, OAS1, MX, IFI16 which clearly indicates their possible roles in successful implantation. The study conducted so far suggests that neutrophilic genes and plasma cytokines may determine the outcome of pregnancy.

At National Institute of Animal Nutrition and Physiology (NIANP), Bangalore transcript of buffalo pregnancy associated glycoproteins (PAGs) were identified, amplified, cloned, sequenced and compared with the existing database to confirm the predominant transcript in buffalo placentome. The PAGs were produced and antibody against the recombinant protein was raised and the immuno-reactive epitopes were determined by testing the reactivity of antibody with the overlap biotinylated peptides. The recombinant partial PAG coding regions of PAG7 sequence was expressed. Three buffalo PAG specific antisera were generated, out of

which two were based on 20aa peptide epitopes and one was partial recombinant PAG protein. The immuno-reactivity of all the three antisera were tested and two antisera were identified as possible candidate for developing immuno capture ELISA. In another study, identification of newer protein and miRNA biomarkers from serum and urine of early pregnant buffaloes were carried out in an attempt to diagnose early pregnancy in buffalo. The urinary proteins SLAMF9, MARK1 and PDK1 were identified as possible marker having biological significance during pregnancy

At Indian Institute of Science (IISc.), Bangalore, cDNAs encoding the bovine and bubaline FSH subunits were cloned into a mammalian expression vector and used to transfect CHO cells to produce recombinant bovine gonadotropins. In both cases the cells expressed the hormones that were active *in vivo*. The *Pichia* cells were engineered to produce the recombinant hormones with human-like glycan moiety. The hormones produced using this *Pichia* host exhibit the glycan moiety with five mannose residues or three mannose residues with 2 N-acetyl glucosamine. Recombinant bubaline FSH was purified and *in vivo* biological activity was confirmed.

Expression and localization of autocrine and paracrine factors and their receptors regulating corpus luteum function during the estrous cycle of buffaloes (*Bubalus bubalis*) is being studied at IVRI, Izatnagar. The insulin like growth factor (IGF) genes were expressed in both granulosa cells (GC) and theca interna (TI) cells. The relative expression of IGF-I and IGF receptor I (IGFR-I) genes increased with follicle size and was greatest in the pre-ovulatory follicle. Expression of IGF-II and IGFR-II genes was minimal in GC but was readily detected in TI cells. In TI cells, the gene expression was greater in medium and large as compared to small and pre-ovulatory follicles.

The expression of all binding protein genes was detected in both GC and TI cells. The result indicated evidence of an autocrine/paracrine role of IGFs in follicular development and a stimulatory role of IGF1 in steroid production in GC of preovulatory follicles in the bubaline species.

The effects of metabolic stresses on follicular and oocyte development were studied in buffalo at NIANP, Bangalore. The maturation, cleavage and morulae/blastocyst production rates were found to be significantly lowered in media containing ammonia, urea, high combo NEFA and OHB. The increased ammonia caused maximum impairment to preantral follicle growth compared to other stressors. Apoptosis, lipid peroxidation and oxidative DNA damage in preantral follicles and COCs increased with increased dose in the order ammonia>NEFA> β -OHB>urea. The study will help in elucidation of the basic mechanisms involved in fertility in relation with metabolic stresses.

At IVRI, Izatnagar, effect of omega-3 poly unsaturated fatty acid in the ovarian and uterian function of goat is being studied. It was noted that the supplementation of omega-3 enriched diet resulted increase in the diameter of corpus luteum (CL) of goats on day 5 post-estrus. The preliminary result indicates a positive influence of ω 3 enriched diet on the ovarian function in the goat.

At Banaras Hindu University, Varanasi, cellular and molecular changes of ovum in rat model was studied during postovulatory aging to understand molecular regulation of mammalian oocyte maturation and aging. Postovulatory aging *in vitro* as well as *in vivo* leads to several morphological, cellular and molecular changes in eggs. Aging eggs were unable to handle increased cytosolic free Ca^{2+} level that leads to the generation of ROS. SNAP prevented postovulatory aging-

mediated abortive SEA in rat eggs cultured *in vitro* in a concentration-dependent manner and prevented postovulatory aging-mediated changes in specific phosphorylations of Cdk1 resulting in stabilized MPF and M-II arrest in eggs cultured *in vitro*. Decrease in cyclin B1 level was observed during postovulatory eggs aging together with changes in specific phosphorylation status of Cdk1 leading to destabilized form of MPF, which is the main cause associated with abortive SEA. MPF destabilization during abortive SEA might be associated with reduced Nlrp2 expression during postovulatory egg aging.

Transgenic and cloning:

Buffalo mammary gland specific expression vector containing human insulin and buffalo SCD gene was constructed and introduced into buffalo fetal fibroblast cells to prepare competent transgenic donor cells at NDRI, Karnal. The transgene integration was confirmed in transgenic buffalo fibroblast cells and cloned buffalo embryos were produced using hand guided cloning technique. The transgene expression in the embryos was also confirmed. The study confirmed the possibility of production of transgenic buffaloes and using its mammary gland as bioreactor for the production of human proteins in its milk.

Buffalo beta casein promoter gene was isolated from buffalo genome, characterized and sequenced at NII, New Delhi. This was confirmed using human breast cancer cell lines and primary cultures of buffalo mammary epithelial cells, by expressing tagged gene (GFP) in these cells. The transgenic mice line was developed using this construct and confirmed that the GFP is expressed only in the mammary gland of the transgenic mice. Human gamma interferon was also cloned under this promoter and transgenic mice expressing human protein in the breast gland

of mice were generated. The study confirmed that the mammary gland can be targeted for the production of desired human protein in the milk of animal.

A transgenic mice line expressing the echidna EchAMP gene in its mammary gland was developed to understand the role of EchAMP protein in the background of experimentally induced mastitis at Centre for Cellular and Molecular Biology, Hyderabad. Bioactivity (anti-bacterial and anti-inflammatory properties) of EchAMP protein was demonstrated with the help of EchAMP transgenic mice. Whey protein isolated from milk of transgenic EchAMP mice showed antibacterial activities against *Staphylococcus aureus* and *Bacillus subtilis* whereas EchAMP expressing milk showed bacteriostatic action against *Pseudomonas aeruginosa*. The study have significant and long-term impact in the area of antimicrobials.

At NDRI, Karnal, efforts are continued to enhance the efficiency of hand-made cloning technique for the production of cloned buffalo embryos using somatic cell nuclear transfer (SCNT). Trophectoderm (TE) cell lines were produced from IVF, SCNT and parthenogenetically derived blastocysts. A feeder-free in vitro culture system was developed which enabled long-term culture of TE cells derived from both IVF and SCNT buffalo embryos. Buffalo embryos were produced from various cells by hand-made cloning and their developmental competence, quality, epigenetic status and gene expression pattern was studied. The developmental competence and quality were lower, and the epigenetic status and expression level of many important genes was different in TE cell-derived blastocysts than those produced from fetal or adult fibroblasts or their counterparts produced by IVF. The developmental competence of cloned embryos produced from tail skin and urine derived cells

was similar to that of embryos produced from ear skin cells (controls) in terms of the blastocyst rate. The blastocysts produced from tail skin and urine cells were superior to those produced from ear skin cells, as indicated by lower apoptotic index.

The pluripotent stem cell (PSC) lines of EGFP-expressing transgenic 'green' mice were developed at IISc., Bangalore. Comparative efficiencies of differentiation of PSC lines towards cardiac and neural lineages were assessed with the accompanied gene expression profiles. It was noted that both PSCs showed superior differentiation efficiencies vis-a-vis the wild-type D3-cell line. Global gene expression profiles of GS-2 and N9 iPS cell lines were performed and compared with wild-type D3 ES-cell line. During the course of study, a defined and efficient ES-cell derived in vitro neurogenesis model was established, providing opportunities in terms of enhancing in vitro neurogenesis using ES-cells and developing disease models, screening of molecules and in studying molecular regulation of neurogenesis.

Host pathogen interaction

At IVRI, Izatnagar, elucidation of gene network, host pathogen interaction and molecular pathway involved in susceptibility/ resistant of Peste des petits ruminants virus (PPRV) has been taken up. The temporal dynamics of immune response in PBMCs infected with Sungri/96 vaccine was surveyed by transcriptome analysis. Infected goat PBMCs at 48 h and 120 h post infection revealed 2540 and 2000 differentially expressed genes (DEGs), respectively, on comparison with controls. Functional analysis of DEGs reflected enrichment of TLR signaling pathways, innate immune response, inflammatory response, positive regulation of signal transduction, cytokine production and MAPK cascade. The upregulation of innate immune genes during

early phase (between 2-5 days) and interactome analysis indicated induction of broad-spectrum anti-viral state. The cytoskeleton proteins responsible for maintaining cell shape and integrity were dysregulated in PPRV infected PBMCs, which corroborates with transient leucopenia induced by the virus. The study indicated that the involvement of both innate and adaptive immune systems with the enrichment of complement cascade observed at 120 h p.i., suggestive of a link between innate and adaptive response.

Animal byproduct:

Utilization of animal cartilage of caprine origin for surgical implantation in microtia and rhinoplasty of human patient was taken up at WBUAFS, Kolkata. The goat choncal cartilage was chemically processed and its biocompatibility in xeno-transplanted rabbit model was carried out successfully. Treated cartilage was implanted in human volunteers at R. G. Kar Medical College, Kolkata and samples were retrieved for histological and histochemical examinations including one rhinoplasty operation. Quantitative estimation of glycosaminoglycan, elastin, fibronectin, TGF β , TGF β 1, TGF β 2 showed higher concentration than the untreated samples respectively. Histochemically, well organized collagen fibres which interwoven the architectural matrix between cells and other supported structures were observed. Samples extracted from human volunteer had normal arrangement of the cartilaginous cells without any inflammatory or exudative reactions. The rhinoplasty operation utilizing the treated acellular animal cartilage showed satisfactory recovery resulting improved facial look.

Nutrition

A process for extraction of xylan and production of xylooligosaccharides from agricultural waste

was standardized with an aim to produce quality animal feed at NIANP, Bangalore. The tartaric acid was effective in production of xylooligosaccharides from the xylan of agricultural waste and highest concentration of xylooligosaccharides production was recorded from the xylan of Bajra stalks. The xylanase was effective in production of xylooligosaccharides with different degree of polymerization including xylobiose, xylotriose, xylotetrose and xylopantose. Most of the applied variables exhibited significant effect on the xylooligosaccharides production. The efficacy trial of xylan on microflora dynamics of sheep and also on the growth of animals is being carried out.

Nutritional strategies to enhance the conjugated linoleic acid (CLA) in the milk and meat of ruminants were taken up at NDRI, Karnal. The diversity of CLA producing indigenous *Butyrivibrio spp.* was carried out and their utilization as a probiotic for animal and enzymes involved in biohydrogenation of fatty acids were studied. *Butyrivibrio fibrisolvens* 4a strain and In-1 strain, isolated from ruminants, found to alter the bio-hydrogenation of fatty acids in ruminants and manipulate ruminal microbiota to increase the vaccenic acid and PUFA in rumen fluid which ultimately enhances CLA, especially cis-9, trans-11 CLA in meat and milk. The study confirmed that the CLA content in meat and milk is enhanced by administration of indigenous *Butyrivibrio fibrisolvens sp.* as a feed additive to increase CLA content in ruminant's meat and milk.

Animal Production:

An attempt to enhance milk production through mammary stem cells in goats using xenthosine treatment is being made at Guru Angad Dev Veterinary and Animal Sciences University,



Ludhiana. Expression of steroid receptor hormones on prepubertal, lactating, non-lactating and mastitic goats was carried out. The prepubertal goats reported to have highest (45.6% of mammary epithelial cells, MEC) expression of ESR1 while mastitic goats have lowest (5% of total MEC) expression. The study suggests that mastitis not only damage MEC, milk secreting cells, but also reduce cell proliferation signals. Further study on understanding of abnormal lactation (like short lactation), cessation of lactation etc. is underway.

Animal Vaccines and Diagnostics

Introduction:

The Department is supporting R & D programmes for development of affordable new generation vaccines and diagnostics against various animal diseases of economic importance. The emphasis is given to the 'commercialization of the leads, products and processes developed in the R & D programmes. A thrust in this direction is given through multi-faceted approaches such as collaborative translational research, consolidation of existing projects with potential leads and generation of network programmes around major animal diseases of national importance.

Major Initiatives:

During the year, several new projects have been supported on epidemiological studies of mastitis, development of therapeutics for brucellosis, development of diagnostics for theileriosis, and development of vaccines against Hemorrhagic septicaemia, Infectious Bursal disease, Porcine circovirus, Hepatitis Hydropericardium Syndrome virus, etc.

A Brain Storming meeting was organized in which it was decided to generate a canine health programme with aim to create Centre of Excellence (COE), knowledge repository,

services, national and international linkages, consortium, etc.

Based on the excellent progress made in the DBT Network Program on Brucellosis, the program was extended for another two years to perform third party validation of diagnostic kits and phase two studies of the animal vaccine developed under the program.

Salient achievements:

Network Programs

DBT Network Program on Brucellosis

The Network Program on Brucellosis has successfully completed the first phase. A repository was established for storing and cataloguing different Brucella species. A novel penside diagnostic, lateral flow assay kit, indirect ELISA kit against Brucella species and a hand held ELISA reader have been developed.



Translational Research Platform for Veterinary Biologicals (TRPVB)

TRPVB is partnership programme between the Department of Biotechnology and Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai with the aim to translate veterinary vaccines, diagnostics and other Biologicals for field application. During the year several technologies were transferred/

commercialized viz. Quick Heal topical wound healing cream, Bovine TB alert Kit, ABT Choice Kit and EndoMetB, Wild TB alert kit, and Bovine platelet lysate.

Vaccine and Diagnostics Research and Development:

Recombinant vaccine against *Mycobacterium avium* for goats, vaccine for canine mammary tumor, Nano-Newcastle disease virus vaccine, recombinant antigen based diagnostics and chimeric plant virus-like particle based vaccine for infectious bursal disease virus (IBDV) were developed. Studies to develop dip-strips to detect acaricide resistant ticks, biosensors for detection of peste des petits ruminants (PPR), and economic diagnostics for surra have been done. LAMP based assay was developed for the detection of animal by-products in feedstuffs and indirect ELISA was developed for the diagnosis of *Mycobacterium bovis*.

AQUACULTURE & MARINE BIOTECHNOLOGY

Fish Genomics and Transcriptomics:

Transcriptome profiling of immune responsive genes in Golden mahseer (*Tor putitora*) was carried out at DCFR, Bhimtal. The Golden Mahseer (*Tor putitora*) is one of the most important coldwater fish species. The study was formulated to create a reference transcriptome database of *Tor putitora* and to identify cascade of immune responsive genes against *Aeromonas hydrophila* (a common pathogenic agent existing in most of the aquatic environment). Full transcriptome including organ specific genes have been constructed of the species. 629 transcripts involved in various pathways of Immune system were also identified along with 14 immune related transcripts were identified for qRT-PCR validation.

A network programme on whole genome

sequencing and development of allied genomic resources in two commercially important fish - *Labeo rohita* and *Clarias batrachus* has been implemented at NBFGR Lucknow, CIFA Bhubaneswar, IASRI, New Delhi and AAU, Gujarat. Whole genome multi platform sequencing (Illumina, Roche 454 and Ion Torrent) have been done for *L. rohita* and *C. batrachus*, followed by quality checking of data and trimming of the low quality reads. SSR mining was done from the assembled contigs in both the fish, followed by the development of webserver. A tool has been developed, which automates the process of segregating SSRs, as per their location in the genome. The work for the construction of genetic linkage map has been initiated in *C. batrachus*.

Antimicrobial and Immunostimulants:

Antimicrobial and immunostimulatory activities of actinomycetes for aquatic animal health management were implemented at C. Abdul Hakeem College, Melvisharam, Tamilnadu. The antibacterial activity of actinomycetes against bacterial pathogens of fish, shrimp and prawn (*Vibrio harveyi*, *V. anguillarum*, *Aeromonas hydrophila*, *A. caviae* and *Edwardsiella tarda*) is being tested.

Studies on immunostimulatory activity of brown seaweeds in shrimp *penaeus monodon* was carried out at Centre for Marine Science and Technology, M.S. University, Tamilnadu. Polysaccharide fucoidan was extracted from five different brown seaweeds (*Sargassum wightii*, *S. duplicatum*, *S. polycystum*, *S. tenerimum* and *Turbinaria ornata*). The primary screening of these fucoidans on antimicrobial activity against WSSV and *Vibrio* pathogens displayed best performance by *S. wightii* fucoidan. The study concluded that the *S. wightii* fucoidan had enhanced the innate immunity and decreased the pathogenic infection in shrimp *P. monodon*.

Health and Vaccine:

Development of WSSV free brooders for seed production was implemented by C. Abdul Hakeem College, Melvisharam, Tamilnadu by using indigenous shrimp, *Penaeus indicus* as a model. The dsRNA specific to VP28 gene of white spot syndrome virus (WSSV) of shrimp was synthesized in *Escherichia coli* in large scale. Fermentation process for large scale production of dsRNA-VP28 has been standardized and dsRNA has been produced in large scale. The efficacy of dsRNA to protect the shrimp from WSSV infection was tested and the effective dosage of dsRNA has been determined.

Development of nanodelivery system of DNA based RNAi vaccine against WSSV in tiger shrimp, *Penaeus monodon* was implemented by CIFE, Mumbai. Two different methods used for delivery of DNA vaccine encapsulated with nanoparticles. In first experiment, immersion or bath treatment was used for delivery of DNA vaccine. Three nanoparticles, viz. chitosan, polylactic-co-glycolic acid (PLGA) and sodium alginate were synthesized and characterized. Relative percentage of survival was found highest in chitosan (87.3%) followed by PLGA (84.6%) SA (80%) PGA (79.23%) CP (77.45%) and BP (63.25%) treatments, respectively.

Bioactive Molecules and Biomaterials:

A project on antipathogenic potential of marine cyanobacteria in preventing quorum sensing dependent bacterial infections among aquaculture organisms was implemented by Alagappa University, Tamilnadu. The aim of this study was to find out potential antipathogenic compounds from marine cyanobacteria as an alternative strategy to combat the infections caused by antibiotic resistant bacterial pathogens specifically Vibriosis in aquaculture. It was observed that the treatment of Hexadecanoic

Acid (HDA) drastically reduced the intestinal colonization of bacterial pathogens in aquatic animal model *A. franciscana*.

Studies on purification, characterization, functional analysis and structural elucidation of pattern recognition molecule - β -1, 3-glucan-binding protein and antimicrobial peptides from crustaceans were carried out at Alagappa University, Tamilnadu. β -glucan binding protein (β -GBP) was purified from green tiger shrimp *Penaeus semisulcatus*, mangrove crab *Episesarma tetragonum* and blue swimmer crab *Portunus pelagicus*. Antibacterial and antibiofilm activity of purified β -GBP reaction product was determined.

Highthroughput selection and production of Polyhydroxy Alkanoates (PHA) from the metagenome of marine sponge(s) was implemented by Pondicherry University. Metagenomic library of a marine sponge was screened for the PHB synthase using mixed fosmid preparations (each from 384 clones). The study showed that PHB inhibits the phenotypic expression quorum sensing molecule of pathogenic *Vibrio sp.*

A comprehensive analysis on cyanobacterial Glutathione S-Transferases: new insights and perspectives was implemented by Bharathidasan University, Tiruchirappalli. Glutathione S-transferases (GSTs) a detoxification enzyme acts as a second line of defense in all living organisms. The study has explored the cyanobacteria GST's for the first time. The expression of GST in the higher forms in the presence of pesticides was also substantiated by *in vivo studies*.

Marine bacterial carrageenase for production of carrageenan oligosaccharides useful in food and biomedical applications was implemented by CFTRI, Mysore. Potential carrageenolytic isolates showing degradation of carrageenan in carrageenan containing solid medium were evaluated for carrageenase production using

carrageenan containing minimal medium. The purity of the enzyme was increased by 5.15 fold by precipitation at 80% ammonium sulphate saturation.

Radical scavenging activity of Antioxidant Peptides from the mantles of three marine Cephalopods was implemented by SRM University, Tamilnadu. Identification of antioxidant peptides were carried out from three marine cephalopod mantles, like cuttlefish (*Sepia brevimana*), squid (*Loligo duvauceli*) and octopus (*Octopus aegina*) using three different enzymes (trypsin, α -chymotrypsin and pepsin) for 12 hours hydrolysis. The trypsin hydrolysate of Cuttlefish, α -chymotrypsin hydrolysate of Squid and pepsin hydrolysate of Octopus mantles showed maximum radical scavenging activities.

Molecular characterization of biofilm produced by coral associated bacteria isolated from Andaman Sea has been implemented at Institute of Life Sciences, Bhubaneswar. This study shed light on the biofilm forming capability of marine bacteria isolated from Andaman Sea. Initial screening of the isolates indicated the differential biofilm forming capability of the isolates. The studies on the interactions between bacteria within a biofilm showed antagonistic interactions between *Vibrio spp.* and *Pseudoalteromonas spp.* when grown together in a biofilm.

DNA Barcoding of Marine Ascidians: DNA barcoding of marine ascidians was carried out at Islamiah College, Vaniyambadi, Tamilnadu. 69 species inclusive of six new species (*Botryllus sp 1*, *Botryllus sp 2*, *Botrylloides sp 1*, *Botrylloides sp 2*, *Botrylloides sp 3* and *Botrylloides sp 4*), two new record (*Monandrocampa sp* and *Diplosoma simileguwa*) covering 26 genera and 9 families were recorded from 26 stations from Dhanushkodi to Kanyakumari along the Gulf of Mannar. Investigation of the levels of intra- and interspecific genetic variation using

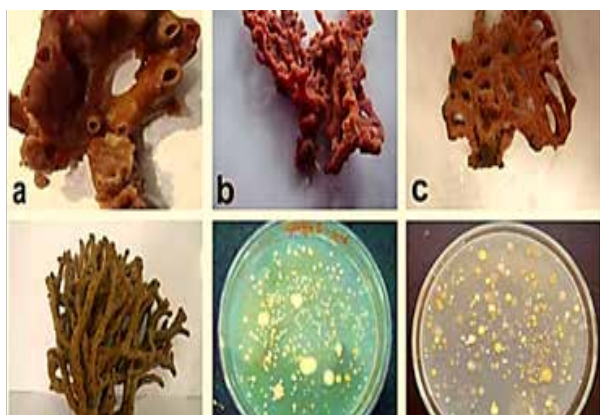
NJ tree and K2P showed a clear gap between these interspecific and the intraspecific ones. It was found that analysis of the COI sequences presented in this work is a powerful tool for identification of ascidian species.

Fish Brain Development: A study of neurotrophic factors in relation to calcium binding proteins during fish brain development was implemented at Department of Zoology, RTM Nagpur University, Nagpur. Localization of the mRNA expressions of CaBPs, calretinin (CR) and calbindin (CB) by performing In-Situ hybridization (ISH) have been done along with mRNA expression. The study concluded that both CR and CB genes may play an important role in the development of eye, brain, spinal cord and other tissues during early development of the fish.

Biomarker: Project on ddd Gene programming Biomarker used to perceive the DMSP (Dimethyl Sulphonio Propionate) phytoplankton species originates in the Cochin Estuarine System was carried out at Cochin University of Science & Technology, Cochin. 106 phytoplankton species were identified in Cochin estuary during the first sampling, the major algal species identified were *Melosira granulate*, *Tabelaria fenestrata*, *Nitzschia spp.*, *Cyclotella striata*, *Actinocyclus spp.*, *Thalassiosira weissflogi*, *Cylindrotheca closterium*, *Pinnularia spp.*, *Surirella spp.*, *Navicula spp* and *Fragellariopsis spp.* The freshwater species included *Arthrodesmus spp.*, *Staurodesmus spp.*, *Staurastrum spp* and *Dictyosphaerium pulchellum* and 103 phytoplankton species were identified during second sampling. The major algal species identified were *Actinocyclus spp.*, *Cosinodiscus radiates*, *Melosira granulate*, *Thalassiosira weissflogi*, *Actinocyclus spp.*, *Cylindrotheca closterium*, *Pinnularia spp.*, *Surirella spp.*, *Naviculaspp.*, *Fragellariopsis spp.*, *Micrasterias foliacea*, *Dictyosphaerium pulchellum*, *Scenedesmus quadricauda*, *Alexandrium spp.*, *Prorocentrum spp.* and *Peridinium spp.* For the study of the bacteria

with DMSP-lyase activity the samples were cultured and the isolates were screened, cultured and characterized using molecular biology techniques and sequenced.

Bio-surfactants: Production of biosurfactants from marine bacteria was implemented in Bharathidasan University. The agro-based substrate tamarind kernel powder enhanced the bio-surfactant production of *Alcaligenes* sp. MB-I9 followed by corn powder. The maximum bio-surfactant production (6.76 g/l) attained by *B. amyloliquefaciens* MB-101 in point prediction method validated experimentally and 6.75 ± 0.05 g/l of biosurfactant yield was obtained. The use of metal (Fe) nanoparticles as supplement was found to increase the bio-surfactant production under solid state fermentation (SSF). Recycling of spent substrate remains after production cycle in SSF as biofertilizer to achieve zero-waste production process. It was demonstrated that bio-surfactants and the fermented substrate promotes germination of *Vigna radiata* seeds and growth of plant seedlings. This approach was the first demonstration of utilizing fermentation waste for bio-fertilizer development based on the existing literature. Marine sponge associated bacteria was demonstrated as potential bio-surfactants.



Marine sponge associated bacteria was demonstrated as potential bio-surfactants

Development of Diagnostics: Genetic Diversity of *Clostridium botulinum* in seafoods and

Development of Lateral Flow Immuno Assay (LFIA) for toxinotyping was implemented at CIFT, Cochin. Survey in major cities in India has been conducted to collect various packed fish products for *C. botulinum* contamination. 94 food samples comprising of ready to eat (23), ready to cook (49) and fresh fish samples (22) from retail outlets and super market of major cities in India including Kochi, Bengaluru, Chennai, Gujarat, Mumbai, Visakhapatnam and Delhi were screened. Mouse bioassay and 16S rRNA sequence analysis of two samples confirmed them as *C. botulinum* type B. Studies are being initiated to develop a Lateral flow immunoassay (LFIA) for *C. botulinum* toxinotyping.

Identification of etiology of Monodon Slow Growth Syndrome (MSGs) of black tiger shrimp in India and development of rapid diagnostic tools was studied at CIBA, Chennai. 320 farmed shrimp samples were collected from 60 shrimp farms located in Andhra Pradesh (AP), Gujarat, Tamilnadu (TN) and West Bengal (WB) and screened for White spot syndrome virus (WSSV), Infectious hypodermal and haematopoietic necrosis virus (IHHNV), Hepatopancreatic parvovirus (HPV), *monodon* baculovirus (MBV) and Laem-Singh Virus (LSNV) by PCR technique. PCR products from five IHHNV positive samples were sequenced and the phylogenetic tree constructed.



Growth Syndrome (MSGs) of black tiger shrimp

Marine Actinobacteria: Diversity (cultivable and culture independent), ex situ conservation and bio-prospecting of marine actinobacteria for antibiotics, anti-HIV and immunomodulatory substances was carried out at three institutes namely Annamalai University, Sathyabama University, Periyar University, Tamilnadu. At Annamalai University samples were collected from various sites of Andaman islands and 19 morphologically distinct strains of marine actinobacteria were isolated. Two psychrophilic actinobacterial strains (Nocardiopsis-3 and Streptomyces-1) were isolated from the Polar Frontal waters of the Southern Ocean (Antarctica) and 52 strains isolated from the coastal and marine habitats of the Andaman and Nicobar islands. Assaying of antioxidant activity is under progress.

BASIC RESEARCH IN MODERN BIOLOGY

The Department of Biotechnology has developed a very strong bench for basic research in modern biology. Basic research efforts are directed at conceiving and developing fundamental new ideas, approaches, and methods for addressing some of the most intriguing and challenging aspects of the living organisms. DBT through its initiative to strengthen basic research in the country has supported a number of research programmes to increase the understanding of basic principles and to provide scientific information and theories that lays down the foundation for the applied science that follows. Noteworthy achievements of some of some of the projects supported by the division are presented below:

Studies conducted to decipher the BMP signaling network in developing bone at IIT Kanpur have revealed 58 BMP dependent bone-specific transcripts by performing large-scale

transcriptomic studies in combination with in-house meta-analysis of data derived from publicly available Big-Data repositories. Subsequent in-vivo experiments in mice, chicken and in-vitro experiments with their patented cell lines have helped in elucidating function of two such genes in bone development and limb pattern formation.

Study initiated at NIPGR, New Delhi on Functional characterization of sugar- and auxin-regulated DUF581 domain containing genes encoding expressed proteins of unknown functions in model plant system has led to the identification of a novel class of plant-specific zinc finger proteins. At the physiological level, these genes were found to be essential in mediating adaptive responses during light and energy-limited growth conditions and stress.

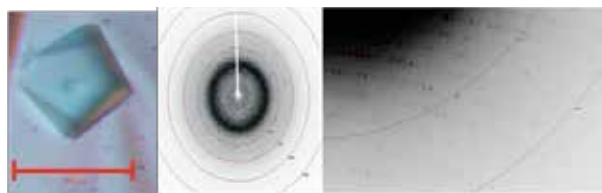
Work undertaken to study chromatin remodeling for activation of systemic acquired resistance in Arabidopsis at NIPGR, New Delhi has revealed an epigenetic regulator that modulates both flowering and SAR. In fact process of flowering and SAR development is highly interconnected.

Scientists working on exploring stationary phase genome dynamics in *E. coli* using next-generation sequencing at NCBS, Bangalore have shown that bacteria display increased sequence diversity over time, and that this may be a result of evolutionary selection.

Scientists working to Elucidate protein level interactions to define arrangement of subunits in the plant Mediator complex at NIPGR, New Delhi have analysed the Intrinsic Disordered Regions (IDRs) of Mediator proteins. They have found that the overall disorder of the whole complex increased from simpler to complex organisms. The study has provided the basis of the well noticed flexible behaviour of Mediator complex in terms of its association and dissociation with other protein(s) and complexes.

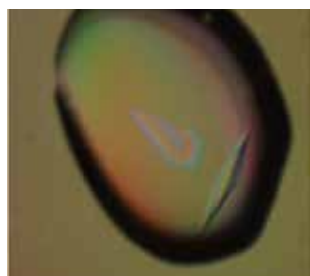
Work carried out at IACS, Kolkata to understand Differential Recognition of G-Quadruplex DNA Binding Small Molecules Using Dynamic Combinatorial Chemistry have reported two simple bis-triazolylcarbazole derivatives that can inhibit c-MYC transcription, possibly by stabilizing the c-MYC G-quadruplex.

Structural studies carried out at ICGEB, New Delhi on delineation of EcpD chaperone in formation of Yad fimbriae in uropathogenic *Escherichia coli* have cloned, over-expressed and purified EcpD chaperone. After getting initial hits in different conditions and several manual optimizations, the group has successfully obtained a diffraction quality crystal. The structure reveals a unique fold and a conserved pocket that can be targeted for inhibitor discovery for urinary tract infection.

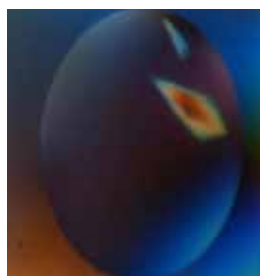


(A) Crystal of EcpD (B) X-ray diffraction pattern of EcpD crystal

Structural investigations of surface nano scale assembly in a gut bacterium being carried out at RCB, Faridabad have crystallized pilus proteins (SpaA and SpaD) that forms hair-like surface organelle called 'pili' on probiotic *L. rhamnosus* GG. High resolution X-ray diffraction data have been collected for determining three-dimensional atomic structure and understanding the pilus formation/adhesion.



Crystals of Spa A



Crystals of SpaD

Scientists working on elucidating the regulatory role for RunX proteins in CD40 gene expression and its impact on murine dendritic cell activation at IMTech, Chandigarh has established a novel role for Runx transcription factors in dual regulation of Cd40 expression in dendritic cells.

Scientists working on *Drosophila* embryo as a model system to study the onset of polarised distribution of proteins at IISER, Pune have found asymmetric distribution of proteins in the X-Y and X-Z axis of the syncytial plasma membrane. Further, the stage at which hexagonal architecture of the plasma membrane develops in embryogenesis was also elucidated.

Researchers at RGCB, Thiruvananthapuram working on cancer stem cells isolated from colorectal cancer patient's tumor and surrounding cells have found many critical drug resistant proteins expressed on such cells which could be detrimental for a patient's healthy post-operative life. On the basis of cancer stem cell presence in tumor and its surrounding tissue a minimum resection margin was defined which could be enough to remove these cells and help in proper prognosis of a CRC patient.

Studies conducted on unraveling the link between cellular stress response, carcinogenesis and anti-cancer drug screening using *Drosophila* model at BHU, Varanasi have revealed the role of the stress-inducible Hsp70 in metastasis and the cell-fate specific induction of tumours. Further, depletion of Hsp83 or Hsp27 in *Igl4*^{-/-}-somatic clones affected clone growth and metastasis, indicating the essentiality of these proteins for tumour development.

Scientists working on understanding the effects of perturbation of pRb-Fzr1-Skp2 axis on mammalian cell cycle regulation at JNU have shown that a single mutation in Fzr1 can deregulate two important cancer related proteins, the oncogene Skp2 and the tumor suppressor p27.

Ongoing research at ACTREC, Mumbai aimed at understanding the regulation of centrosome duplication by 14-3-3 proteins have reported that both 14-3-3 ϵ and 14-3-3 γ are required to prevent centrosome over-duplication. Further, deletion mutants of γ -tubulin (GC1) and GCP-2 (GC1 and GC2) that do not localize to the centrosome have also been revealed.

Studies aimed to discover a panel of candidate markers for LB and HE subtypes using complementary gel based 2-D DIGE and gel free iTRAQ approaches at NCCS, Pune has revealed the potential markers which can discriminate LB and HE subtypes.

In vitro study of input-output robustness of MprAB signalling pathway in *Mycobacterium tuberculosis* at Bose Institute, Kolkata resulted in a mCherry reporter assay that permits monitoring the interaction of tRNA polymerase with its promoter *in vivo*. This novel recombinant reporter assay is expected to render a new and efficient avenue to monitor the interactions among *M. tuberculosis* RNAP, transcription factors and their cognate promoters *in vivo* without the hazard of handling the pathogenic, slow growing bacteria.

SILK BIOTECHNOLOGY

The Programme was reoriented in the last year towards focus on addressing newer and emerging technologies in silk and its applications under the stewardship of the Expert Group on Research on Technology Development in Silk and its Applications in BioMaterials. Based on the earlier brainstorming meeting, an interactive meeting was conducted at UAS, Bangalore in July 2015 for mulberry crop improvement program. The network partners have developed a multi-component draft proposal focusing on mulberry genome sequencing and resequencing of 40 accessions, evaluation of leaf quality, silkworm metabolome studies etc. A working committee

has been constituted for finalizing the network program involving various partners.

Significant achievements on various research programs being implemented under the scheme are summarized as follows:

Development of Improved Races of Silkworm for Enhanced Productivity:

3D BAC pools of silkworm genomic library was generated at CDFD, Hyderabad to identify W chromosome derived BAC clones. More than 100 BAC clones that are W derived have been identified and characterized. The female specific gene Bmz1 shows negative regulation over the male specific gene Bmimp and also has an effect on the Bmdsx splicing. The genome of Lepidopteran insect *B. huttoni*, a close outgroup of the domesticated silkworm *B. mori* was sequenced to test the generality of the faster-Z pattern. They show that silkworms experience faster-Z evolution, but unlike in birds, the faster-Z effect appears to be attributable to more efficient positive selection in females.

Phylogenetic analysis has shown that Andhra local and Bhandara ecoraces were found to be genetically close in a study performed at Kakatiya University, Warangal. EST (Expressed sequence tags) primers were designed and screened for polymorphism among samples from each of the 7 ecotypes. Phylogenetic analysis was carried out. The sequencing results have shown that the gene belonged to lipoprotein superfamily. Within the gene, the ecorace Sukinda has shown much variability.

A sex-limited breed for cocoon colour (SLO1) available in the bivoltine silkworm germplasm of Andhra Pradesh State Sericulture Research and Development Institute, Hindupur (APSSRDI) was selected as donor parent for introducing the sex-limited character into 10 productive bivoltine

breeds. At present, the sex-limited breeding lines have completed two generations successfully and entered into F3 generation.

Development of Disease Control Measures:

Extensive research was carried out at Seribiotech Research Laboratory, Bangalore on the infection of *B. mori* larvae by the microsporidian (uzifly maggot). The studies demonstrated enhanced expression of host response proteins indicating early appearance of humoral immunity markers in haemolymph against the microsporidian infection. Further, humoral lectin and hemocytin (discoïdin domain) showed significant reduction in expression in early days of infection revealing suppression of the recognition proteins by microsporidian infection. Apolipophorin showed *enhanced* presence in microsporidian - infected *B. mori* larva which is a recognition protein with multiple functions in inducing immunity in insects.

Improvement of Host Plants:

Work has been continued under a Consortium Project on Mulberry Genomics (CPMG) involving four institutions- Central Sericultural Research & Training Institute(CSR&TI), Mysore, Central Sericultural Germplasm Research Centre(CSGRC), Hosur, University of Agriculture Sciences (UAS), Bengaluru and University of Delhi South Campus (UDSC), New Delhi. A total of 751 mulberry specific SSR markers have been developed. Out of these, 511 SSRs have been standardized as locus specific out of the 511 locus specific markers 450 markers were found to be polymorphic between Dudia white and UP105, the parents of a mapping population segregating for root traits. As the population developed from heterozygous parents, a pseudo-test cross strategy was adopted to develop a linkage map. Hence, 262 markers segregating in 1:1 ratio were

further used to develop a linkage map. Of these markers, 134 markers were linked in 14 linkage groups with a total linkage distance of 4263.5 cM. The mapping population was also extensively phenotyped for root traits, WUE (based on $\Delta 13C$) and other drought adaptive traits. The outcome of the project has offered promising potential for genetic improvement of mulberry with superior growth under water-limited conditions.



Multiplication of wild type and transgenic plants of mulberry A: cuttings of transgenic mulberry and wild type plants having 2-3 buds; B: Cuttings were treated with Indole butyric acid, for early establishment of roots; C and D: Establishment of mulberry cuttings in polybags in containment facility

A comparative transcriptome has been achieved and several ESTs were characterized with in mulberry respect to their expression profile under abiotic stresses like simulated drought, salinity and cold stress. Due to absence of diverse genomic information available within the species of mulberry, two additional species, i.e. *M. laevigata* and *M. serrata*, were shortlisted for cDNA library preparation and genomic resource generation. The cDNA library prepared has been sequenced. Additionally, their transferability to other closely related species has also been explored. Towards functional validation of novel genes from mulberry, a vacuolar Na-hydrogen

transporter (NHX1) and a halotolerance protein (HAL3) have been cloned and successfully used for mulberry transformation. Significant genomic resources have been developed for mulberry improvement.

The mulberry transgenic plants expressing HVA1, Osmotin and bch1 was developed by UDSC, New Delhi and established at UAS Bangalore under green-house condition. These plants are being multiplied and examined for their stress response and growth in comparison with true wild-type and a leading variety (V1). Transgenic material developed is also being characterized. Initial *in vitro* experiments indicated improvement in cellular tolerance in transgenic plants when compared to wild-type mulberry.

An extensive survey was undertaken in the mulberry root rot infested sericultural areas of South India for assessment of genetic variability and diversity among the pathogens causing the disease. A total of 95 fungal isolates associated with root rot disease belonging to *Fusarium spp.*, *Macrophomina phaseolina* and *Botrydipodium theobromae* were collected and characterized by cultural, morphological and molecular markers. 156 germplasm were subjected to screening using a virulent strain of *M. phaseolina* and the resistance response was evaluated in pot grown plants. A total of 20 germplasm were found to be resistant (< 25% root rot). Further, 50 were classified as moderately resistant with (26 - 50% root rot) and 39 were found to be susceptible (51-75% root rot). The rest, 47 mulberry germplasm were found to have > 75% root rot and were considered highly susceptible. The minimum root rot infection of 9.85% was observed in the *M. cathayana* (Hybrid). The genetic divergence among the contrasting lines (resistant and susceptible) was estimated based on 50 microsatellite marker data.

Silk Proteins as Potential Biomaterials:

Large scale rearing of *Antheraea mylitta* was undertaken. Cocoonase was collected from 3000 tasar silkworm cocoons at CTR&TI, Ranchi. Further, sericin has been recognized as natural substrate of cocoonase and it is established that cocoonase directly acts on the sericin without affecting the fibroin protein. Molecular matching of *Antheraea spp.* cocoonase was also performed in order to identify the possible analogues available in nature.



Pupal-adult emergence of *Antheraea mylitta*.



Proteolytic enzyme cocoonase was collected during emergence

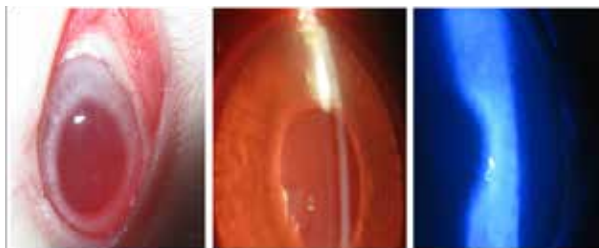
Four significant eco-friendly technologies have been developed towards sericin based value added finishes - extraction of high quality sericin



using IR assisted aqueous method; production of sericin peptides using organic acids, development of multifunctional finish on polyester for medicinal and sports application; and sericin based finish for shrink proofing of wool. Further, industry partner interested in putting up the plant for recovery of sericin on commercial scale has been identified.

The waste of silk industry was utilized to prepare nanometer size proteins. The waste water of silk industries was used to prepare clean sericin powder at R.V. College of Engineering, Bangalore. The fibroin fibers were obtained from split cocoons by degumming process. The wound dressing membrane of fibroin prepared with different composites healed wounds much faster. The hydrogels of nano sericin have very good water absorption and retention capacity. Thus, they were used in preparation of hydrogels for the growth of saplings. The hydrogels of nano sericin are being exposed for use in sanitary napkins, baby diaper and in tissue culture.

The investigators at West Bengal University of Animal and Fisheries Science, Kolkata and IIT, Kharagpur evaluated *Antheraea mylitta* silk films as scaffold for corneal cells *in vitro*, and tested the biocompatibility of these silk films in rabbit cornea. Study showed films from *A. mylitta* have biophysical characteristics for use in cornea. It is transparent and has refractive index comparable to natural cornea. Further, the investigators found that the *A. mylitta* silk films support corneal cell attachment and proliferation. Extensive biocompatibility studies conducted in rabbit eye showed these films are safe for use in cornea.

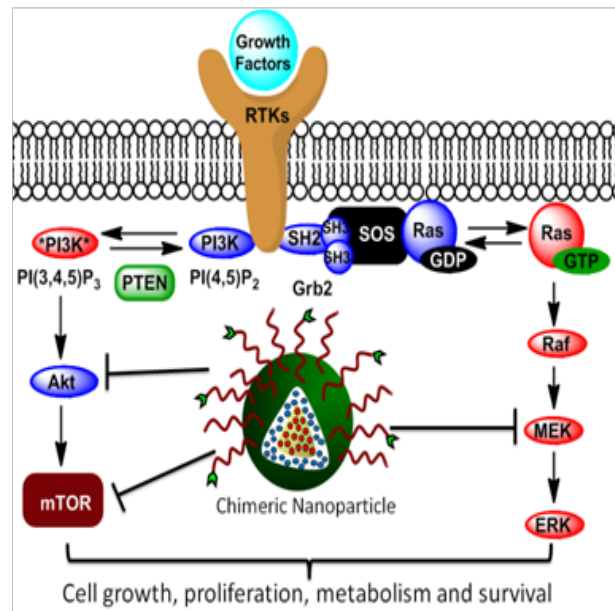


Implantation of Am films within the cornea

NANOBIOTECHNOLOGY

The recent focus of the nanobiotechnology program has been focused in the areas of nanomedicine, nanosensors, Imaging technologies and developing smart nanomaterial for various biomedical applications. Highlights on some of the work accomplished in the year have been presented in the following section:

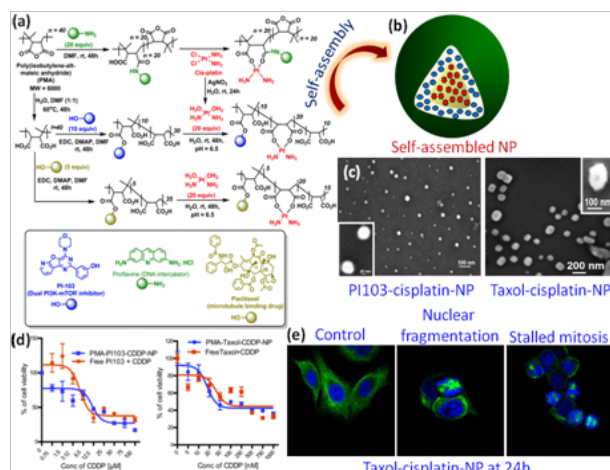
Work is being carried out at IISER, Pune to develop chimeric nanoparticle based platform, which can enable spatiotemporal targeting of aberrant MAPK, PI3K, and mTOR signaling network within a tumor to avoid off-target toxicity and drug resistance.



Chimeric Nanoparticle to target MAPK-PI3K-mTOR signalling hub.

The polymeric self-assembled nanoparticle contains PI103 (PI3K inhibitor) and cisplatin (DNA damaging clinically approved drug), using poly-maleic anhydride (PMA) as the starting polymer, which has multiple sites for attaching several drug molecules. First, chemically conjugated proflavine (DNA intercalating drug) or PI103 or paclitaxel (tubulin binding clinically

approved drug) with PMA were synthesized and finally conjugated with cisplatin (a). Interestingly, cisplatin induced the self-assembly of the polymer into spherical nanoparticles (b) which were characterized by field-emission scanning electron microscopy (FESEM, (c)). PMA-PI103-Cisplatin-NP and PMA-Paclitaxel-Cisplatin-NPs showed improved cytotoxicity in MCF7 breast cancer cells compared to free drug combinations (d). Furthermore, PMA-Paclitaxel-Cisplatin-NPs showed interesting fragmentation of cellular nucleus and stalled cell division in the mitosis stage, characterized by confocal laser scanning microscopy (CLSM, (e)). Work being continued to further engineer the chimeric nanoparticle, which can preferentially home into tumor, by $\alpha\beta 3$ integrin mediated active targeting for better efficacy and to reduce off-target toxicity. These self-assembled polymeric NPs may provide a platform for developing novel combination therapy for cancer patients.



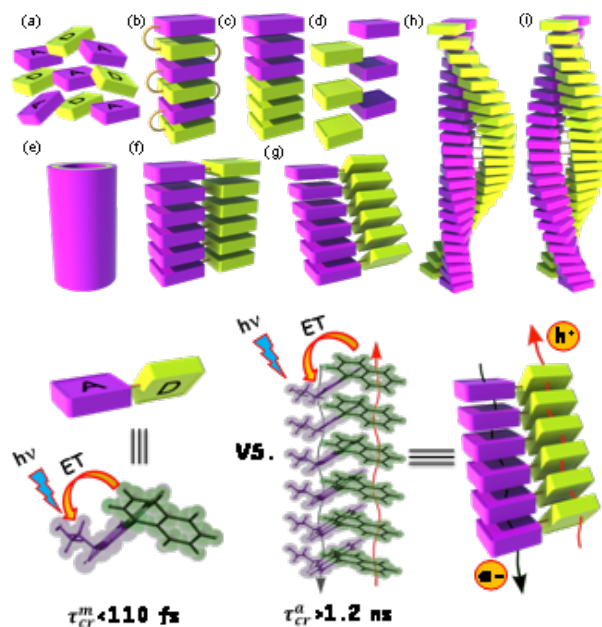
Engineering and biological evaluation of self-assembled PMA.

Work has been carried out at BHU, Varanasi to develop a Graphene Oxide (GO) enabled biosensor to detect Platelet-derived-microparticles (PMPs) in blood samples. The sensor was developed by modifying glassy Carbon electrode with GO coating which provided carboxyl groups

(CO=) for covalent linking of PAC-1 antibody (specific against active conformation of surface glycoprotein IIb-IIIa complex, present on PMPs).

Early translational research being carried out at ICT, Mumbai to develop a Nano particulate system of anti-tubercular drugs for targeting lungs through oral delivery based on demonstrated proof of concept that there was higher lung uptake of nanoparticles of Gantrez, a hydrophilic polymer. Detailed studies were carried out to optimize the Gantrez based nano-formulation. In vivo studies at 40mg/Kg (extrapolated human dose) of the Gantrez NP showed a relative bioavailability of ~125% and higher lung uptake at 8 hr. Gantrez NP revealed prolonged retention in the GIT, which could be useful for sustained release. Studies on uptake of the NP by the Peyer's patches showed a lot of accumulation of Gantrez NP at the villi border with limited uptake due to high muco-adhesion and revealed significant uptake by the Peyer's Patches. During this uptake was monitored in the plasma, lung and other organ. A significant accumulation of the drug was observed in the lungs. ADME studies on various parameters such as absorption, distribution, metabolism, excretion etc are in progress to evaluate the efficacy of the drug in animal model.

Research being carried out at IISER, Trivendrum to minimize charge recombination by separating the donor and acceptor portions of the molecule on different spatial planes at nanoscale. A naphthalimide-naphthalene dyad has been synthesized where the donor and acceptor units are twisted into different planes. The twisted monomers also assemble into a stacked tower. When illuminated by ultraviolet light, the charge separated state of the stack can last more than 1.2 ns, 10,000 times longer than in the monomeric dyad.



Representative strategies adopted to spatially organize electron donors and acceptors for emergent properties.

To further enhance the lifetime of the charge separated states, the developed donor acceptor scaffold was covalently attached to DNA. The survival time of charge separated states, upon photoexcitation of naphthalimide connected to DNA, exhibited a significant increase ca. 600 ns upto 3 base-pair separation. Such assembly could be a novel nanoscaffold for light harvesting, molecular electronics, or new light-induced electronic applications.

Research work is being carried out at IISER Trivendrum to develop drug delivery carriers using DNA based amphiphilicity-driven self-assembly approach. Synthesis was carried out to show self-assembly of DNA-oligo(phenyleneethynylene) (DNA-OPE) based hybrid amphiphiles into vesicular nanostructures. The surface of the vesicular nanostructure was decorated with Au-NPs. This was achieved by the surface modification of the Au-NPs with a DNA sequence, which is complementary to the DNA on the surface of the vesicle. It was envisioned that the replacement of alkyl chains tethered

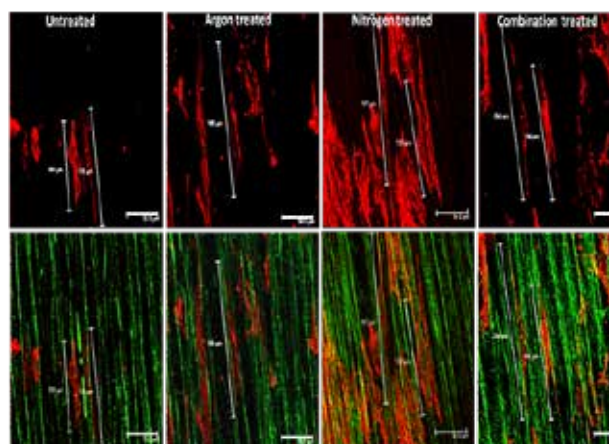
OPE segment of the amphiphile with a strongly π -stacking hydrophobic core such as alkyl chains tethered hexa-peri-benzocoronene (HBC) could lead the self-assembly of the amphiphile into DNA decorated nanosheets due to the strong π -stacking of HBC core in one dimension and the van der Waals interaction of the alkyl chains in other dimension. With this rationale, a series of DNA π -HBC hybrid amphiphiles were designed. Microscopic analyses showed that DNA-HBC amphiphiles self-assemble into high-aspect-ratio nanosheets with remarkable thermal stability. The present research findings suggest that nanostructures of this kind would be an ideal candidate for the targeted cancer therapy.

Studies were carried out at IISc, Bangalore to develop a Nano carrier using coat-protein of sesbania mosaic virus (SeMV) that self-assembles to form VLPs with T=3 icosahedral that can effectively bind to antibodies. For antibody binding, B domain of Staphylococcus aureus protein A (SpA), that is known to bind to Fc portion of various IgGs were chosen. CP was modified to create a VLP expressing B domain at the HI loop (SeMV loop B-SLB). It was shown that SLB self-assemble into VLPs (37 nm) and showed 43 times better antibody binding affinity as compared to SpA. The results highlight the potential of SLB as a universal nanocarrier for intracellular delivery of antibodies.

Research work is being carried out at CIFE, Mumbai to develop optical fiber-based whole cell prokaryotic biosensor device for sensing heavy metal pollutants. Three prokaryotic biosensors, pLDR9-Hg, pLDR9-Pb and pLDR9-Zn responsive to mercury, lead and zinc, respectively developed are being integrated into an optical-fibre device for field application. The heavy metal detection range of pLDR9-Hg, pLDR9-Pb and pLDR9-Zn biosensors was 0.002 - 0.02 ppm of Hg²⁺, 10 - 50 ppm of Pb²⁺ and 3 - 800 ppm of Zn²⁺, respectively as per the the lowest heavy metal concentration used. Detailed studies are being

conducted to establish sensitivity in terms of lowest and highest detectable ion concentration. The specificity of Pb, Hg and Zn biosensors was tested by co-induction with other heavy metals like Cu²⁺, Ni²⁺, Co²⁺ and Cr^{2O7}²⁻ including their specific metal ion using the standardized induction conditions. All the three biosensors showed maximum response to the respective heavy metal, while negligible response was observed with other heavy metals. Specificity of biosensors in response to heavy metal mixtures is being determined to establish interference if any.

In continuation of the ongoing research efforts at AIMS, Kochi, various marine based polymeric scaffolds were fabricated and combination of argon and nitrogen plasma treatment was carried out to improve its bio-responsiveness. The developed chitin/PHBV and chitin/PCL/nCS scaffolds showed enhanced hydrophilicity, protein adsorption, cell attachment and proliferation. The addition of polar functional groups on the fibers by plasma treatment modified its property from hydrophobic to hydrophilic nature thereby increasing the applicability of this material. Protein adsorption was also enhanced. The developed membrane would prove beneficial for tendon tissue engineering after plasma treatment.



Extent of hMSCs attachment on untreated and plasma treated fibers after 48 hours was imaged using confocal microscopy

The work was carried out on fabrication of Neurospecific nanogels for targeted drug delivery, molecular imaging and analysis in APO-E-GFP Zebrafish model at Satyabhama University, Chennai. Delivery of drug to the zebrafish brain was achieved by overcoming the blood brain barrier by synthesizing the poly N-isopropyl acrylamide nanogels (PNIPAM) with 20 nm size for sustained drug release. PNIPAM nanogel was prepared and functionalized with polysorbate 80 for sustained donepezil delivery. The entrapment of donepezil in the nanogel was quantified as 87.5% by HPLC and its sustained drug release pattern was achieved at 37 °C using Janus green dye release assay. Studies are in progress to generate relevant data to enhance the translational value of the work.

Non-invasive radiofrequency (RF) electric fields as an energy source for thermal activation of nanoparticles and thereby delivering drugs within cancer cells could be a valuable addition to nano-mediated RF based cancer therapies. Utilizing the high penetration of RF waves would be useful for the controlled release of encapsulated drug molecules from smart thermo- and pH-responsive nanoparticles. With this rationale, novel biodegradable thermo-responsive nano-vehicles (curcumin encapsulated chitosan-graft-poly (N-vinyl caprolactam with gold nanoparticles (Au-CRC-TRC-NPs) were synthesized at AIMS, Kochi. The prepared nanoparticles were shown to have cyto- and hemo- compatibility. Breast cancer cells could selectively internalize 170± 20 nm sized Au-CRC-TRC-NPs. After optimum RF exposure at 40 watts for 5 minutes, Au-CRC-TRC-NPs absorbed and dissipated energy as heat in the range of 42°C, which is the lower critical solution temperature (LCST) of chitosan-graft-poly(N-vinyl caprolactam), causing controlled curcumin release and inducing apoptosis to 4T1 breast cancer cells. Further, the tumor localization studies on orthotopic breast cancer models



revealed that Au-CRC-TRC-NPs could selectively accumulate at primary and secondary tumors as confirmed by in vivo live imaging followed by ex vivo tissue imaging and HPLC studies. These preclinical results throw light on their feasibility as a better tumor targetable nanomedicine for RF-assisted breast treatment modalities.

Studies were carried out at AIIMS, New Delhi to entrap hepatitis B surface antigen (HbSAg) in 14kd polycaprolactone (PCL) nanoparticles (NPs) (61.2±20 nm) and use them as an oral delivery vehicle comparing the efficacy with parenteral routes of immunization in mice. It was demonstrated that there were robust and significant production of anti-HBsAg antibody till 2 months following onetime oral administration which was superior than other routes of immunization including that of conventional alum based HBsAg vaccine in mouse and guinea pig models. The nanoparticles and the antigen were found in the macrophages in small intestinal villi, peripheral lymph nodes and other reticuloendothelial organs 2 months after immunization through the oral route in the animals. This system has capability of antigen cross presentation with expansion of cytotoxic T cells and memory T cells documented by flowcytometric studies. This study with HbSAg suggests the efficacy of this nanocarrier system for efficient antigen presentation through oral route with a prolonged antibody response which can minimize the requirement of booster dose. Thus this novel nanoadjuvant can help to develop oral vaccination platform for several infections especially for intracellular organisms.

GENOME ENGINEERING TECHNOLOGIES AND THEIR APPLICATIONS

Recognizing the emergence of powerful technologies, tools and processes to study and

manipulate the genome, DBT has recently started a program on “Genome Engineering Technology and Their Application” with a vision to foster innovation and promote development of Genome-wide analysis and engineering technologies to make them accessible and affordable for wider use in Life Sciences. Initially, the program has been mandated to help establish accessible facilities on emerging technologies such as (i) Genome Manipulation, Editing and Interference by CRISPER, TALENS and RNAi (ii) CLIPS, ChIPs for genetic variations and chromatin remodeling and, (iii) Single Cell Genomics. These technologies are only examples and the program may both support and make efforts to lead in new areas as well as, adapt and improve current ones, and also develop human resources. This is envisaged that the support under this program will help create, for example, a larger user base and enable it to address important basic questions, applications in the study of emerging diseases, to manipulate/engineer genomes, develop transgenic systems and develop genome based diagnostics.

So far, through two rounds of call for proposals, out of 250 submission only 8 proposals were recommended for financial support in the areas of optimization of CRISPR/Cas system of genome editing in plant e.g. Brassica juncea, creating animal models for disease e.g. retinal dystrophy using genome editing methods, generation of genome-edited mice using CRISPR/Cas-9 based knock-out/knock-in technology, high throughput design, synthesis and validation of TALENs for targeted genome engineering, genome engineering using CRISPR to enable discovery in lipid signaling etc. Rest of proposals did not match the mandate of the task force as the proposal lack the basic components towards- (A) development of methods, tools, processes and platforms for genome-wide studies and, (B) Application of genome wide

technology platform, s including genome-editing method. Or did not involve the (i) large scale manipulation/editing of genomes of established model organisms as well as pathogens, or (ii) address novel biological questions using OMICS based technologies or other emerging methods, or (iii) study large-scale expression, genotyping, methylation, multi-dimensional data analyses, single cell measurements and data analytics. Such observations clearly indicated that there has been a lack critical mass in terms of expertise to catch up with the growth of this area to harness the benefit of the technology for basic or applied use in larger context.

Genomic tools and technologies are growing fast and have shown transformative potential in understanding the genomic phenomena, genome measurement and manipulation to address issues in health and agriculture sectors. An urgent need has been realized to promote overall growth of this area in India to adopt, innovate and leverage such technologies for wider applications in biotech sector. With this backdrop, the program is being expanded to undertake a range of activities for overall growth and promotion of the various aspects of genome engineering and their applications such as (i) Advancing research and fostering innovations through grant support and creation of core facilities for making state-of-the-art genomic technologies accessible, Pre-, post-, and genomic pipelines and platforms, and innovation on existing technologies for easy adoption, new applications of existing genomic technologies (ii) Human resource development through support of National and overseas fellowship, Special courses/short term schools, support of workshops, training, and symposia etc, (iii) Creating specialized centers in the thematic areas such as Personalized Medicine, Synthetic Biology etc. (iv) fostering international collaboration to make researchers accessible to international facilities and blending expertise and

knowledge in the focused areas through visit and exchange programs and holding joint symposia / workshops

BIOENGINEERING

Bioengineering is a highly interdisciplinary field of research wherein principles and methodologies of engineering and other quantitative sciences are applied to unravel the complexities of biological systems to provide novel cost-effective solutions for healthcare and medicine. In this financial year Department has issued a Call for Proposal wherein more than hundred proposals have been received and further short-listed for financial support. Proposals are also received in areas of 'Robotics in Medicine' following the brainstorming workshop conducted in last year. In addition, conscious efforts are being undertaken for promoting the scientific advancements in its various identified areas and other emerging areas. Some of the significant achievements made during this period are:

Spatio-functional characterization of skin using multimodal OCT and multispectral imaging Scientists at IIT Kharagpur are studying non-invasive investigation of skin wounds using multimodal imaging and computational modelling. They are trying to employ in vivo high-resolution optical imaging technologies along with state-of-the-art computational processes for correlating imaging properties with tissue in health and pathology; thus facilitating development of in vivo histology techniques and processes for skin characterization. Scientists have assembled hardware units for in vivo imaging and optimized methods for simultaneous in vivo multimodal OCT (Optical Coherence Tomography) and multispectral optical imaging, image registration, image archival and retrieval. The histo-and molecular pathology of cutaneous wound have been studied and OCT images

corroborated with histological images.

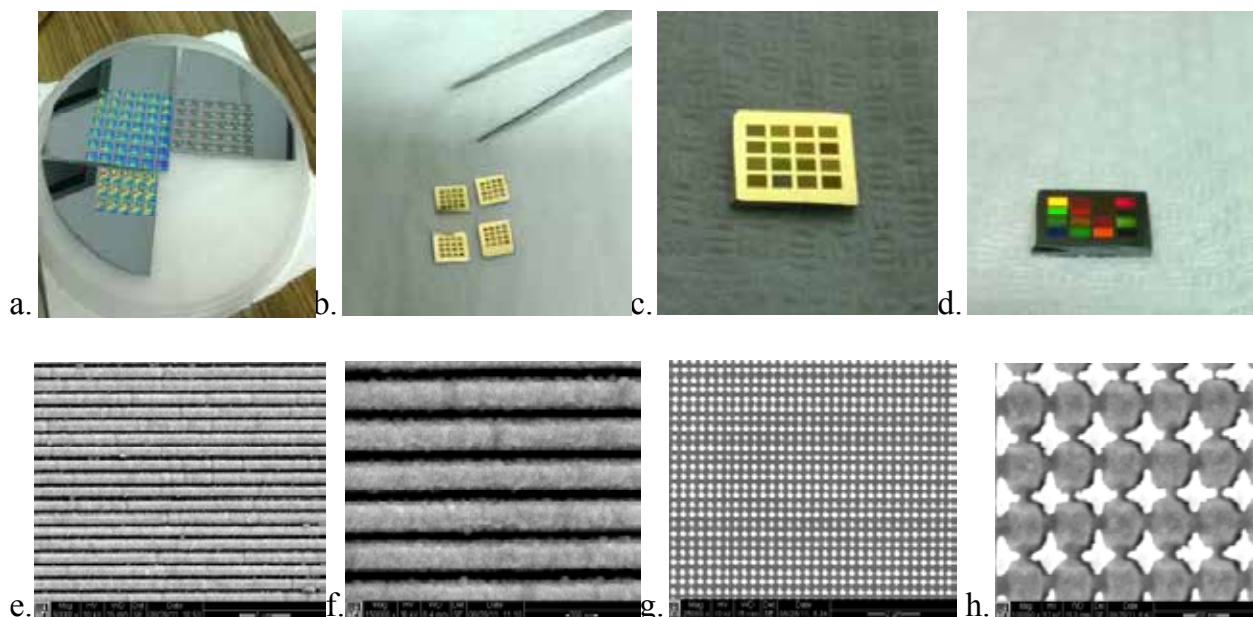
Imaging signaling dynamics with fluorescent biosensors

Scientists at NCBS are in process to develop and use a new class of fluorescence-based biosensors that can be used to visualize cellular events in real time. Under this project they are developing biosensor variants that work on the principle of fluorescence resonance energy transfer (FRET) and understand the dynamic regulation of critical cellular enzymes – the Src family kinases. Src kinases are among the first known oncogenes and influence almost all aspects of cell fate and behavior, and are relevant in diseases like cancer, inflammation, heart diseases as well as infection. Specifically sensors for Fyn kinase, a key SFK member important in cell physiology have been developed so far. Further these sensors are being

validated and improved for the dynamic range through targeted protein engineering, leading to detailed imaging of SFK dynamics.

SERS based sensing and imaging for early breast cancer diagnosis

Scientists at IIT Delhi are developing nanostructure biochips (NSB) to detect RNA biomarkers for use in early breast cancer detection. SERS substrates consisting of one dimensional nanoline and two dimensional nanopillar arrays have been fabricated on 6-inch wafers-scale using Deep UV Lithography. Raman measurements on gold and silver nanoparticles in solution have been carried out to show that SERS can be employed for multiplexed detection of multiple SERS-active dyes.



(a) Image showing parts of a 6-inch silicon wafer on which nanostructured regions were fabricated using deep UV lithography, (b) Gold-coated chips that are cleaved from a 6-inch wafer. (c) Image of a chip showing a 4 by 4 array of regions containing different geometries of gold-coated silicon nanostructures. (d) Nano-structured regions showing different colors as regions having different geometries have different scattering and absorption cross-sections. SEM images of the nanostructured silicon chips: (e) and (f) 1D array of gold-coated silicon nanolines, (g) A 2D Silicon nanodiamond array, (h) A 2D Silicon nanodiamond array coated with gold employed as a SERS substrate.

Micro-Diffractive Interference Contrast Cell Imaging

Scientists at IISc are trying to explore quantitative phase imaging of cells and the sensing of mechanical properties of a cell using a diffractive technique. The idea is based on the fact that due to the internal, as well as external mechanical motion of the cell, there is redistribution of refractive index within the probe beam volume. The scientists are modifying the existing lab system to have a smaller probe beam covering only a single cell, procure cells of different types, such as RBCs, bacteria and yeast cells and acquire the diffraction pattern using a fast camera. They are also trying to develop algorithms to estimate the lateral movement of the cell and cell stiffness parameters from the dynamically modulated 2D diffraction pattern.

Non-invasive long-term in vivo vascular imaging

Scientists from CMC Vellore, are trying to delineate real-time events of angiogenesis or vasculogenesis in vivo and the interaction of different cell types in their biologically relevant microenvironment in vascular constructs via non-invasive in vivo vascular imaging using multiphoton laser scanning microscopy. For this, placental vascular cells are being labeled with fluorophores, in a Collagen 1- fibronectin scaffold that would provide the microenvironment that is conducive for their growth and formation of tubes. To prevent immune rejection in the murine host, the tissue engineered constructs are implanted in a cranial window model in the Severe Combined Immunodeficiency Deficiency (SCID) mice, which would allow long term evaluation of vascular cells.

High Resolution Holographic Microscope for 3D Imaging of Live Biological Cells

Scientists at IIT Delhi are establishing high resolution holographic microscope technology prototype for label free and fluorescence based 3D imaging of live cells. They have demonstrated methodology for accurate high resolution quantitative phase imaging of biological cell samples. The basic results involve fundamental new developments in Physics where breaking of the standard resolution limit in single shot holography is demonstrated. Additionally, in an experiment performed at low photon levels, for the first time ever, they have demonstrated sub-shot noise phase measurement with classical interferometry. New methodologies for phase measurement using direct far-field diffraction data and spiral phase diversity have also been established. These methodologies have significant future potential for cell imaging.

Non-invasive imaging modality for blood pulsation monitoring

In another study undergoing at IIT Delhi a non-contact noninvasive method for blood pulsation monitoring is being developed using the polarization properties of light. The study is investigating the effect of blood pulsation variation on the polarization properties of linearly polarized light and presents a new monitoring technique. Experiments have been performed to measure the partial polarization state using degree of linear polarization (DoLP) with varying combinations of polarizers in the incident optical path and transmission path. The experiments show an exponential relationship between DoLP of transmitted and reflected part of linearly polarized incident light and the heart blood pulsation rate.

Novel 3D Nanocomposite Scaffolds for Tissue Engineering/drug delivery

Scientists at IISc, Bangalore have successfully developed smart biodegradable polymers from different low cost renewable sources for use in tissue engineering and drug delivery. A number of novel systems based on polyanhydrides and polyesters have been synthesized and the physico-chemical characterization is being done. The cytocompatibility of the polymers in vitro has been established. Currently work is being carried out to modify them to introduce drugs in to the backbone of the polymers to impart bioactivity to these polymers.

Biodegradable Hybrid Polymer-Peptide System for Efficient Intraocular Drug Delivery Scientists at Anna University of Technology are trying to develop biodegradable hybrid polymer-peptide system, consisting of temperature responsive and pH responsive peptide suitable for encapsulation and delivery of therapeutic drugs to the eyes for treatment of glaucoma. The newly synthesised conjugated system formed a gel at eye physiological conditions. The drug delivery system has been developed and characterised successfully with synthesised conjugated system.

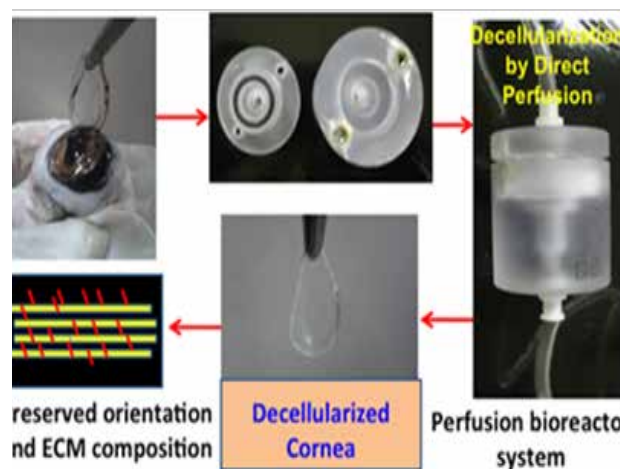
Cellular Programming using Bioactive Scaffolds for Immunotherapy

Scientists at IIT Bombay trying to focus on Adoptive T cell therapy by developing a material based system of biofunctional three-dimensional matrices that can be implanted in vivo to recruit and transduce T cells with CAR (chimeric antigen receptors) thereby regulating their trafficking and activation in situ. They are trying to transduce T cells via the scaffold system. They successfully made functional GFP lentiviruses and infected HEK 293 FT cells encapsulated in a collagen scaffold and on tissue culture plate. They also have optimized transduction of HEK cells in a 3D

collagen scaffold.

Characterization of Decellularized Cornea for Tissue Engineering

In eye banks, many donated corneas cannot be transplanted and get discarded. Scientists at IIT Delhi are trying to use the discarded human corneas or easily available goat corneas to generate functional corneal constructs. The extracellular matrix (ECM) of corneal tissue or its derivative is being used as an inductive template for constructive remodeling of the tissue. They have devised an efficient and relatively simple protocol for corneal decellularization followed by recellularization of goat keratinocytes on corneal matrix. The study demonstrated that the process of corneal decellularization causes conformational changes in the corneal collagen molecules due to the effect of detergent treatment and shear stress.



Schematic diagram showing the process and perfusion bioreactor used for corneal decellularization

Customized skin graft

Scientists from IIT, Kharagpur successfully isolated Collagen type I from Mrigal scale, a widely-available fresh water fish. Collagen I is a promising material with various applications in biomedical field. The collagen has been isolated,

characterized and purity assessed by various methods. The biological response of collagen sponge in wound healing on rat animal model has been studied. The faster wound healing capacity and closeness of thermal stability of extracted mrigal scale collagen offers a good choice for its usability in biomedical, pharmaceutical and tissue engineering application. Therefore, the scale of mrigal fish could be an alternative source of collagen which is otherwise discarded as fish processing waste.

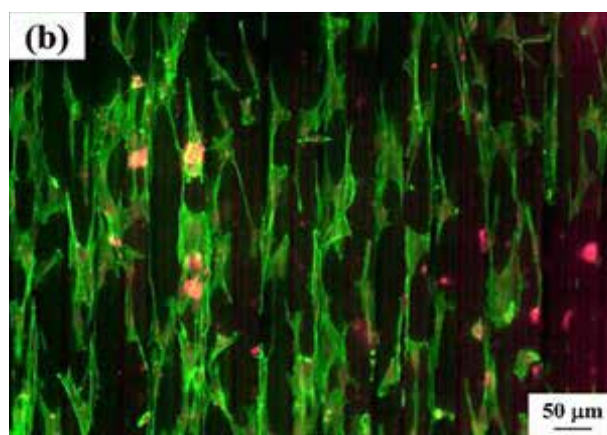
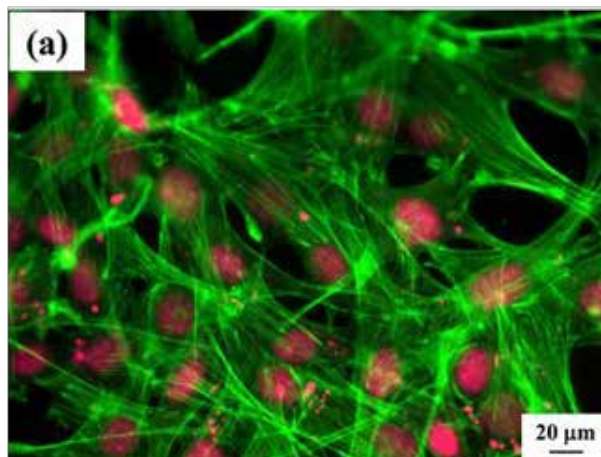
Underpinning mechanism of cell migration in microchannels with physico-chemical gradients

Scientists from IIT Bombay are aiming to investigate the adhesion, migratory behaviour, growth and differentiation of mesenchymal stem cells in presence of physical (substrate stiffness) and chemical (chemokine) cues. To start with, PDMS (Polydimethylsiloxane) substrates of varying stiffness have been prepared to study the effect of stiffness on cell behaviour. In addition to this, a microfluidic device is designed and simulated using COMSOL and then fabricated to experimentally visualize the gradient formation. Fibroblasts are used to study the effect of stiffness and gelatin (extracellular matrix protein) concentration on cell area, circularity and motility. The experiments reveal that adhesivity dominates the responses; however, the motility of cells is found to decrease with decreasing stiffness and increasing gelatin concentration.

Porous Bio-active Ti-based Composite for Bio-implant Application

Scientists at IIT, Kharagpur are aiming at development of bio-mimetic titanium based porous component by powder metallurgy route for orthopaedic application with detailed evaluation of its mechanical, electrochemical and bio-activity. Porous titanium has been developed using cenosphere and NaCl as filler

materials. It is observed that there is a significant decrease in coefficient of friction and corrosion rate as compared to pure Titanium in the porous composites. Initial trial on in-vitro tests also indicated that porous titanium at certain combination exhibits comparable biological response to the control.



Fluorescent micrographs of (a) as received and (b) laser surface textured Ti6Al4V showing the attachment of MC3T3-E1 mouse fibroblast cell on the surface.

BIODESIGN PROGRAMME

The Department has implemented the Biodesign Programme to foster and promote development of indigenous affordable medical technologies and building capacity for innovative research, prototyping, validation and testing of medical

technologies. Under the programme, biodesign centres have been established at AIIMS, New Delhi; IIT, Madras; THSTI, Faridabad; IISc Bangalore and a multi-institutional alliance, i.e. National Biodesign Alliance (NBA).

School of International Biodesign Programme (SIB)

This programme was implemented as Stanford-India Biodesign (SIB) programme as a joint programme between a medical school (AIIMS) and an engineering institution (IIT-Delhi) in collaboration with international partner, Stanford University, USA. However, during the last couple of years the collaboration has been expanded with Australia and Japan as well. Accordingly the programme has been now renamed as 'School of International Biodesign Programme' with a focus on invention and early-stage development of affordable implants and devices for Indian population. This is facilitated through a fellowship programme (i fellowships) and organizing events such as Medtech summits and workshops. The overall goal of the program is to 'Identify in India, Invent in India and Implement globally'. During the year six fellows joined the iFellowship Program from India and two Fellows from Queensland University, Australia. Additionally, three Fellows successfully completed Phase I of their Fellowship in Stanford University, USA and Phase II in India.

This year has led to conceptualization of 5 inventions from Fellows and iFellows under expert mentorship of faculties from AIIMS and IIT-Delhi. Two inventions viz. 'Endo-Nasal Air Purification System (ENAPS)' and 'Filter-Less Air Purification' were developed by 2015 batch of Fellows. Four inventions i.e. 'Asthma Monitoring Device', 'Hemorrhoid Treatment Device', 'Baby Weighing Device' and 'Hydration Assessment Device' have been conceptualized by iFellows-2015 batch; 5 provisional patent

applications were filed; 2 Industrial Design applications were filed i.e. 'Sphinx- Ostomy Management Appliance' and 'Hansure- Portable Device for Hand Sanitization'; 3 trademarks have been filed .e., Spinaflex- Posture Support Device, pleuraGoh- Aspiration Device and FlexiOH- A Breathable & Customized Cast for Immobilization of Fractured Limb. A technology of 'A Breathable and Customized Cast for Immobilization of Fractured Limb' was licensed to a Start-Up Company- M/s. J C Orthoheal Pvt. Ltd., Gujarat. During the year a workshop on 'Indo-AusBioDesign & Frugal Innovation Seminar & Networking' and the 9th Medtech Summit was organized with participation of representatives from academia, industry, government, medicine, engineering, design, venture capitalists & entrepreneurs. The Fellows of the programme have received awards and fundings from various prestigious national & international agencies.

The 'Accufeed', 'Hi-Care Limo', 'Fecal Incontinence Management Device', 'Neobreathe', 'FlexiOH', 'IO device' technologies developed under SIB were showcased in Vigyan Rail - Science Exhibition on wheels, which was a unique concept in bringing India's scientific heritage and recent achievements to the doorsteps of the people.

Centre for Biodesign and in-vitroDiagnostics (CBD), Translational Health Science and Technology Institute, Faridabad

The Center for Biodesign at THSTI has a focus on *in-vitro diagnostics*. The aim is to transform the field by creating a novel medical technology enterprise in India for affordable health care through a "biodesign process", which essentially utilizes inputs from clinical-care settings to innovate or improve existing designs. The Centre is also promoting an effective translational route for basic findings into routine applications through a multidisciplinary

approach, combining new biomarkers, novel technological concepts and clinical insights. This Centre has established collaboration with various Departments of AIIMS, Delhi.

The major achievements during the year are: a) Development of diagnostic tests for MTb, acute febrile syndrome b) Development of platform technologies for improved stability and yield of recombinant protein. A total of four patents have been filed in India and various products that are in final stage of development are: i) A rapid diagnostic test for typhoid ii) A rapid filtration device for improved smear microscopy for TB iii) An aptamer based tool for TB diagnostics.

Biodesign-Bioengineering initiative, IISc Bangalore:

The Biodesign-Bioengineering programme at IISc Bangalore was implemented in collaboration with St. John's Medical College and Narayana Hridalyala Bangalore, with an aim to facilitate collaboration among the faculty in the Indian Institute of Science and clinicians in Bengaluru hospitals. Various projects have been undertaken at this Centre covering biodesign, basic and translational research—experimental as well as computational work. Under the Biodesign part, various medical devices/aids are being developed. Some of them are: a device that helps transferring a patient from one bed to another with the bed-sheet staying out in its place during the transfer; transferring a patient from a stretcher into an ambulance and vice versa irrespective of the heights of the stretcher and ambulance; designing and building an exercise-cum-gaming chair for patients suffering from cerebral palsy and to develop an Intensive Care Unit (ICU) simulator. Under the bioengineering part, the focus is on three diseases, namely, cardiovascular diseases related to thoracic aorta, estrogen-receptor negative breast cancer, and hemoglobin disorders. The first two focus on mechano-

biology studies to understand the disease in terms of diagnostics and eventual therapeutics. The third is an analytical study comprising experimental and computational studies. Some of the major achievements are 1) Design, prototyping, and initial testing of a bed-to-bed Patient transfer device is complete 2) Design and prototyping of stretcher-to-ambulance and vice versa completed. 3) A therapeutic exerciser-gaming chair for cerebral palsy patients has been designed, prototyped, and tested 4) The design and prototype of the ICU simulator is completed and being tested in the St. John's Medical Hospital 5) Experimentation on a custom-built equi-biaxial stretcher instrument in progress. 6) Designed multi-bioreactor perfusion culture system and cost effective miniature peristaltic pump with separate reservoirs for the medium, and electronics for setting the perfusion rate. 7) An in situ cell-stretching device is designed, microfabricated, and tested. 8) Successfully established the Xenograft model system in immunocompromised mice using the IVC system procured for this purpose 9) Blood samples from normal (HbA) and variant (HbE) individuals were collected and hemolysates were prepared and characterized in order to find the secondary structural changes in the variant molecule 10) Two invention disclosures have been filed.

Healthcare Technology and Innovation Centre (HTIC), IIT-M

Healthcare Technology Innovation Centre (HTIC) has been established to bring together technologists, engineers, doctors and healthcare professionals, industry and government to develop healthcare technologies for the country. Several technologies in areas of ophthalmology, cardiovascular, ultrasound, neonatal, oncology, intensive care, are under development in collaboration with leading organisations. HTIC has successfully developed various technologies namely, Mobile Eye Surgical Unit (MESU); Eye



PAC™; ARTSENS™; an improved design for a Neonatal Transport Unit; a highly efficient, practical and useful technology for performing accurate contouring of surgical plates used in reconstruction surgery; technology to evaluate feasibility and appropriateness of LBC in cervical cancer screening in resource-constrained settings of India; and a wearable health status monitor for Chronic Obstructive Pulmonary Disorder (COPD). HTIC has established collaborations with: a) J Mitra to develop affordable diagnostic instrumentation; b) HealthSensei to develop wearable monitor for Chronic Obstructive Pulmonary Disorder (COPD) applications; and c) GE Healthcare in the area of practical, affordable incubator for resource constrained settings.

Based on the multi-centric cross-sectional study to evaluate feasibility and appropriateness of LBC in cervical cancer screening in resource-constrained settings of India the following three key reports were delivered: (1) report on analysis of clinical performance of screening tests, (2) Health Technology Assessment (HTA) report on cost-effectiveness of LBC technology, and (3) report on end-to-end feasibility of implementation of LBC technology in resource constrained settings. A brief video summary of HTIC is available in the following link: <http://htic.iitm.ac.in/?q=ftp%20page%205>

National Biodesign Alliance (NBA)

The National Biodesign Alliance (NBA) was initiated by the Department as a multi-institutional partnership program in Biodesign and in-vitro diagnostics, anchored through a coordination secretariat at THSTI, Faridabad. The National partners for the alliance are Translational Health Science & Technology Institute, Regional Centre for Biotechnology, International Centre for Genetic Engineering and Biotechnology, All India Institute of Medical Sciences, Indian Institute of

Technology Delhi, IIT Chennai and Ramachandra Hospital, Christian Medical College Vellore and University of Turku, Finland as international partner. Various new initiatives have been undertaken by the Alliance focused on platforms technologies, diagnostics for infectious diseases, diagnostics for non-communicable diseases, etc. The Alliance is also focusing on training module for a process of need identification and filtration through clinical immersion for diagnostics

HUMAN GENETICS AND GENOME ANALYSIS

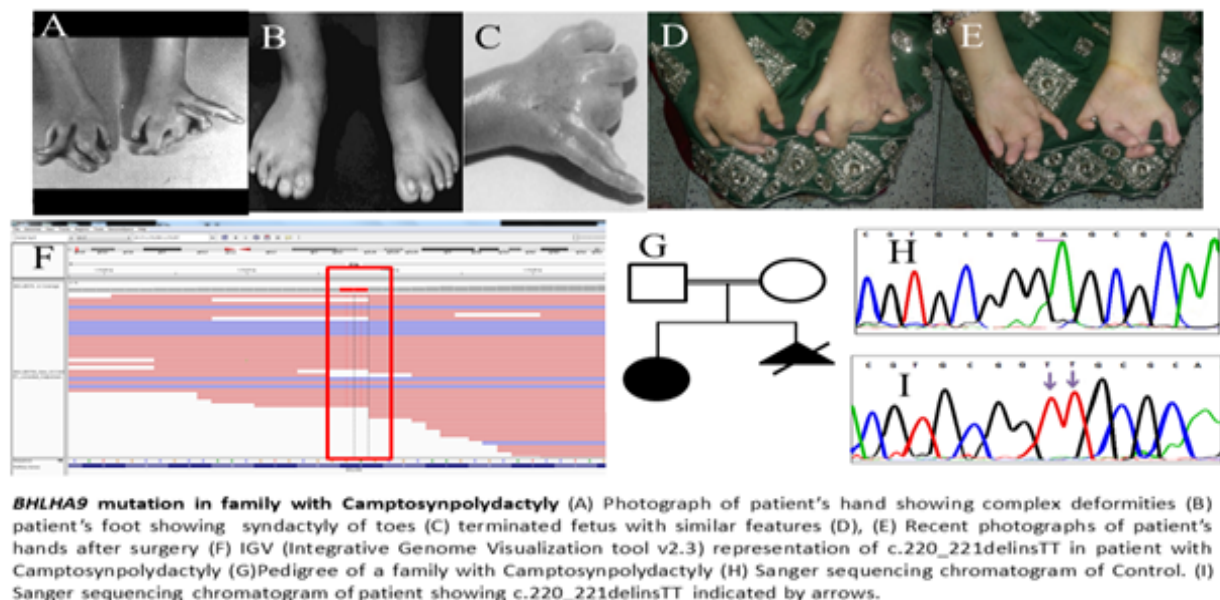
Introduction: The present emphasis of this program is to support studies in the areas of human genetics, clinical genomics, and translational proteomics and to promote education and training in emerging areas of human genetics. The program also supports activities to provide services to affected families for diagnosis and counseling to reduce genetic disorder burden. Highlights have been mentioned below of the salient research activities and achievements in the present year.

Single gene disorders are individually rare but collectively they form an important group of human diseases. Research in single gene diseases helps both in understanding pathophysiology of these diseases as well as that of common multifactorial diseases. Till date causative genes for about 4000 diseases are known, which means more than 20000 disease causative genes are still not known. Traditional methods of gene identification like linkage analysis have many disadvantages. With this background, research was carried out at CDFD, Hyderabad using contemporary techniques of array comparative genomic hybridization and exome sequencing to identify causative genes in rare Mendelian diseases identified in Indian families. BHLHA9 and HERC1 were found out as causative genes

with phenotype of Complex Campto syn polydactyly and Syndromic Intellectual Disability and identified for these diseases respectively. Availability of consanguineous families with

genetic diseases in Indian population is very helpful for identification of novel autosomal recessive genes.

Identification of BHLHA9 as causative gene for Complex Camptosynpolydactyly



Sickle cell anaemia (SCA) is a hereditary (genetic) red blood cell disorder and is prevalent in malarial endemic regions in the world. Burden of SCA is high among tribal populations in India. Studies were carried out to screen 14,325 individuals from Koya and Konda Reddy tribes in West Godavari District, Andhra Pradesh to identify sickle cell trait (SCT) and SCA. By performing biochemical tests (solubility test and NESTROFT), 1406 (9.82%) individuals were identified to be SCT (carriers) and 11 (0.08%) individuals to be Beta-thalassemia (BTT) positive. The distribution of the ABO blood group was studied and O group was found to be predominant followed by B group. Molecular screening was performed on 1042 biochemically positive individuals, which showed that mutant allele was present in 63.44% of the 1042 individuals demonstrating that advance molecular testing has to be implemented

for definitive identification of SCT and SCA. Nine individuals were found to be SCA by molecular testing. This is the first time that in India a novel synonymous SNP c.9T>C (NM_000518.4) was identified addition to the pathogenic sickle cell mutant allele in this population. The novel SNP is 11 base pairs upstream to the sickle cell variant. The novel variant is seen in all individuals with sickle cell trait. Additionally this variant is also seen in individuals without sickle cell trait. Synonymous polymorphic variants can affect mRNA splicing, stability, and structure as well as protein folding.

Work was carried out at PGI Chandigarh to study the structure function relationship of four novel defective beta myosin heavy chain (MYH7 mutations) previously identified in North Indian Cardiomyopathy patients (Tyr266Cys, Gly377Ser, Met515Thr and Arg721Lys) employing three



different approaches such as confocal microscopy studies to check the effect of these mutations on sarcomeric structural arrangements, electron microscopy studies to observe ultra structure changes and integrity of cardiomyocytes and functional genomics studies to study the effect of these mutations on the expression of other genes which are involved either in signaling pathways leading to hypertrophy or in sarcomeric organization and contraction. Cytoplasmic aggregates were observed with all the mutant constructs in transfected neonatal rat cardiomyocytes NRCM. In contrast, the wild type construct assembled into filamentous networks. Cardiomyocytes containing mutant eGFP-MHC constructs showed that eGFP-MHC did not incorporate into cardiomyocytes sarcomeres, while WT eGFP-MHC incorporated normally. Electron microscopic analysis revealed ultra structural changes in different compartments of the transfected NRCMs cells. Mutant transfected NRCMs showed increased number and mitochondrial size, nuclear envelope abnormalities and accumulation of myelin figures in different organelles as compared to no abnormality in nuclear membrane, mitochondria size and shape and absence of myelin formation in cells transfected with wild type construct. Expression of Rho A, involved in myocyte hypertrophy was significantly decreased in three mutant constructs (p. Gly377Ser, p. Met515Thr & p.Arg721Lys) as compared to wild type at both mRNA as well as protein level. Thus the present findings provide molecular basis of these MYH7 gene mutations in the pathogenesis of HCM/DCM via formation of defective MYH7 protein. Our findings suggest that these mutations result in defective MYH7 proteins which may form protein aggregates and inhibit the incorporation of defective protein into thick filaments. Mutated protein aggregates may also impair the sarcomeric contractility and increase cellular stress, which

finally leads to cellular hypertrophy.

Studies were also carried out at PGI Chandigarh to customize re-sequencing array based indigenous comprehensive cardio-chip for genetic analysis of HCM/DCM for India population. Efforts were made to employ chip based target enrichment of exonic regions of a large number of known and unknown genes associated with cardiac diseases followed by NGS re-sequencing of enriched genomic regions to identify disease causing variants in a North Indian cohort of HCM/DCM patients. This method allowed a higher variant detection rate (100% in current cohort) along with detection of genetic variants in several new genes for the first time in Indian cohort. Present studies indicated that Targeted exome sequencing allows reliable variant detection in a large number of disease associated genes in shorter turn around time. Gene panel sequencing is more sensitive and specific than Sanger sequencing as compared to Sanger sequencing and re-sequencing arrays. Using this cardio myopathy micro array panel a large number of gene sets might be screened directly in the laboratory at lower cost, which is beneficial for patients. The identification of mutation in patients can help in their clinical management and also aid in identifying asymptomatic carriers for targeted clinical monitoring to minimize adverse outcomes.

At IIT Madras studies and systematic analysis of the regulation of renalase gene, a novel regulator of cardiovascular/metabolic/renal diseases, revealed that microRNAs belonging to miR-29 and miR-146 families play key roles in determining the expression of renalase in pathophysiological conditions including hypertension. It was also discovered that a common functional genetic variation in human renalase (rs10749571) that creates a miR-146a binding site alters blood pressure/glucose/triglyceride levels in various human populations.

Work was carried out at ICGEB, New Delhi on cloning, expression and characterization of proteins of MSP-1 associated complex on the surface of *Plasmodium falciparum* merozoites. Using proteomic analysis, PfMSP-3, PfMSP-6, PfMSP-7, PfMSP-9, PfRhopH3, PfRhopH1, PfRAP-1, PfRAP-2, and two RAP domain-containing proteins were found to constitute this complex. The various proteins or their domains have been cloned, expressed and purified. The recombinant proteins were used to raise antibodies in mice and rabbit and their specificity was confirmed by Western blot analysis. The localization of the various proteins in merozoites was evaluated by immunofluorescence assay. Further the vaccine potential of these proteins that form a part of MSP-1 complex is being evaluated by an *in vitro* invasion inhibition assay in Plasmodium culture and in mice model using P. berghei challenge studies. Ability of Rap, RhopH3 and MSP antibodies was also evaluated to provide protection against malaria by opsonic phagocytosis assay. The antibodies were affinity purified from patient sera and used to opsonize Plasmodium merozoites and their phagocytosis by THP-1 cells evaluated by FACS analysis. Human antibodies affinity-purified against recombinant MSP3 promoted phagocytic activity in this assay. Such findings have important implications in the development of a multi-protein malaria vaccine.

Studies were carried out at SGPGI, Lucknow on molecular profiling of KIR and their clinical relevance to the end stage renal disease (ESRD). The findings suggest that an element of genetic risk exists determining the pathogenesis of end stage renal disease (ESRD) involves deregulation of NK cells, their activity being inclined towards more activating state. This is the first report showing the association of the killer immunoglobulin like receptor (KIR) gene cluster with ESRD. The results demonstrated considerable inter-individual variability in the

degree of systemic inflammatory activation as the cytokine expression and production is under epistatic and oligogenic control. The high degree of polymorphism and the inter-individual variation in both the number and types of KIR genes can account for varied NK cell responses among individuals. This variation can also account for the varied inflammatory activation and a particular KIR genotype can influence the pathogenesis of the ESRD. The KIR genotyping data obtained for the northern Indian ESRD patients has been submitted to the International KIR database (www.allelefreqencies.net). The genetic association of the KIR gene cluster among ESRD associated basic diseases like CGN, HTN, CIN, PKD, and type-I and II DM were also studied which revealed risk association with activating KIR genes. Further it was observed that the KIR gene and HLA ligand incompatibility due to the presence/absence of KIR in the recipient and the corresponding HLA ligand in the allograft may impact graft survival in solid organ transplantation. The findings conclude that the presence of inhibitory KIR gene leads to better survival; whereas activating motifs show no significant role in renal allograft survival. The particularly susceptible as well as protective combinations obtained are further studied for the allelic variants of KIR genes through direct sequence-based typing. This revealed long term renal allograft survival for subjects positive for KIR3DL1/HLA-Bw4 combination in comparison to KIR3DS1/HLA-Bw4 combination. Identification of risk factors that influence the incidence and severity of acute rejection remains the priority of transplant biologists and this study can contribute an additional tool of donor-recipient matching prior to going for transplantation. Software named MASSKIR Analyzer has been developed for ease in KIR genotyping data analysis (<http://sourceforge.net/projects/masskiranalyzer>)



Studies were undertaken at Bhartiya Vidyapeeth University, Pune to examine the changes in maternal plasma levels of angiogenic (VEGF and PlGF) and anti-angiogenic (sFlt-1) factors, erythrocyte antioxidant enzyme (SOD, GPx and eNOS) across gestation and their association with blood pressure, cord levels at delivery and birth weight in women with normotensive and PE. It was demonstrated that higher levels of lipid peroxidation may contribute to the pathophysiology of preeclampsia (PE) and further may affect fetal growth and development. Maternal angiogenic imbalance with lower angiogenic factors (VEGF and PlGF) and higher anti-angiogenic factors (sFlt-1 and sFlt-1/PlGF ratio) exist in women with PE from early gestation. Altered placental VEGF mRNA expression and CpG methylation patterns was also observed in women with PE. Thus, measurement of angiogenic factors in early pregnancy may be a useful to predict women who may be prone for development of preeclampsia.

Collaborative studies were carried out on screening of intra-genic variants of disease causing, drug metabolizing, drug response and modifier candidate genes in various cardiomyopathies involving Delhi University; All India Institute of Medical Sciences; CSIR-Institute of Genomics and Integrative Biology. Families suffering from Hypertrophic Cardiomyopathy were selected for this study. A total of 85 individuals from 22 families were included in this study. Next generation sequencing was successfully undertaken for all the samples. Bioinformatics analysis has been completed of Whole Exome Sequencing of 12 individuals (5 affected + 7 unaffected) from two families and actionable variations were identified. In one family, a rare variant in a candidate gene TNNT2 was found to be segregating with the disease, which is associated with sudden death in other populations; being reported first time in Indian

population. In the second family, a putative novel deleterious variant was identified in a gene previously not associated with the disease and this variation segregated in all the three affected family members. The putative novel gene was subjected to functional validation in a zebra fish model system. Morpholino mediated knock down of the novel gene in zebra fish resulted in cardiac abnormalities. Further studies are ongoing to characterize this putative novel gene and its role in causing HCM.

Chronic Otitis Media (COME) is a most common childhood disease characterized by middle ear infection, which leads to hearing impairment. It is considered as multi factorial disorder arising from complex interactions between environmental (bacterial infection) and genetic risk factors. Prevalence of Chronic Otitis Media is higher in India however; the true cause and pathogenesis are not well understood. Studies were carried out at ILS, Bhubaneswar Identification of Genetic Susceptibility to Chronic or Recurrent Otitis Media with Effusion. It was reported that about 27% of the COME cases have more than one affected family member indicating genetic basis for the condition. Total blood count analysis of COME subjects in the present study showed an abnormally high eosinophil count (ranging from 7-24%) in 42.59% of cases. This study reported the genetic association of ISL1 (rs2303751 & rs121913540), FBXO11 (rs12712997), TLR4 (rs4986791) and TGFB1 (rs1800470 & rs1800471) gene polymorphisms with otitis media in Indian population for the first time. The risk alleles for rs2303751, rs12712997 and rs4986791 polymorphisms were found to be associated with elevated level of eosinophil in otitis media cases. In addition, it was shown that the over expression of TLR4 in the blood monocyte of the COME patients carrying the risk allele for the causative SNP rs4986791 when compared to the controls. This study firmly investigated the genetic and

molecular contributions of ISL1, TLR4, FGF3, TGFB1 and FBXO11 gene polymorphisms in the pathogenesis of COME development in Indian population.

Education and training in emerging areas of human genetics: Considering the paramount need for preventing the birth of affected children and reduce the socio-economic burden of genetic disorders through genetic screening, prenatal & antenatal diagnosis and counseling, the Department partnered with National Board of Examinations, New Delhi to establish strong linkages in the field of capacity building and education in biotechnology and Medical Genetics. DNB Medical Genetics is a National level initiative in this direction offering a postdoctoral medical education programme at Center of Medical Genetics, Sir Ganga Ram Hospital, New Delhi; National Institute of Biomedical Genomics, Kalyani, West Bengal, and Nizam's Institute of Medical Sciences, Hyderabad. The program is being implemented through NBE with responsibilities to prescribe minimum standards and requirements for faculty infrastructure, library, laboratories, equipment and such resources etc. as are required for introducing and governance of this academic programme. The programme was initiated in 2015 and 6 DNB candidates are currently undergoing their training at above mentioned institutions.

NON-COMMUNICABLE DISEASE (NCDs)

India at present is undergoing an epidemiological transition, thanks to the rising socio economic status. Prevalence of communicable diseases is on the decline and that of non-communicable diseases is rising sharply. Non-Communicable Diseases (NCDs) have started contributing to substantial disease burden and 60% of all deaths in India are now due to NCDs.

Hence, DBT through multiple Task Forces and Expert Groups is focusing on R & D and Capacity Building in:

- Cancer Biology
- Neuro-Disease Biology
- Metabolic Disorders/Diseases
- Renal Biology/Nephrology
- Auto-Immune Diseases
- Reproductive Biology

Cancer Biology:

During the year, major focus was put to redefine strategies in the area of Cancer Disease Biology. The Task Force specially constituted for this purpose aims on:

- 1) Policy, Planning and Strategic thinking for Cancer Disease Biology Research and Translational Medicine on short-term, medium term & long term basis
- 2) Guidance on setting-up Center of Excellence/ Theme Based Research Units
- 3) Suggesting novel HRD schemes in critical areas
- 4) Developing partnerships & collaboration both national & International

In addition to the R & D projects, DBT has strengthened resources around established "Leaders in Cancer Biology" in the form of Unit of Excellence (UOE); six UOEs have been supported during the current financial year. The Department is trying to connect "Excellence in Small Places" in the form of Virtual National Cancer Institute (VNCI). Theme-based research centers on major cancers afflicting Indians i.e. oral, cervical, lung, breast, gall-bladder, gastric etc. have been planned and final round of consultations are in progress for VNCI on Breast Cancer and Virtual National Oral Cancer Institute (VNOCI).

Recognizing the importance of collaborative

& complimentary research so as to consolidate resources and pool talent, DBT has signed an MoU with the upcoming National Cancer Institute, AIIMS at Jhajjar Campus in area of cancer research to:

- Co-design and Co-develop research labs/facilities at NCI located at AIIMS-Jhajjar campus
- Manpower Training
- Jointly support and forge partnership with industry for the development and evaluation of products for public health through Public Private Partnership

Following the visit of Hon'ble PM to US in September 2014, followed by the visit of President Obama, a US- Indo Joint Statement identified Cancer Research as an area of co-operation and collaboration. A Bilateral-Tripartite MoU for cooperation in cancer research, prevention and control with NCI-NIH, USA and ICMR-MoH&FW and DBT has been signed during June 2015. The MOU proposes to establish general framework of collaboration by promoting and conducting high-quality research in cancer prevention, bio-marker discovery, treatment and control.

A National Clinical Oncology Research Fellowship (NCORF) for clinicians desirous of pursuing research as a career is planned to cater to translational medicine.

Neuro-Disease Biology:

The Department envisages to initiate a Dementia Science Programme that aims to address the concerns of reliable and valid estimation of prevalence and incidence through a robust study design and use of internationally acceptable instruments validated in Indian context across sites. The study aims to set-up Population and Hospital-based cohorts with Bio-banks to find out the incidence/prevalence rates of dementia

in different parts of the country; identify risk factors and distinguish between normal ageing and mild cognitive impairment/early dementia. The proposed study shall use DSM-5 criteria and will also be an opportunity to obtain DNA and other biomarkers for detailed workup as well as for creating large bio-database which can be employed for future research. The study will facilitate identification of possible risk factors, their contribution to neurocognitive disorders burden and preparation of a framework of interventions, to lay foundations for a national program for this emerging health problem with extensive societal, financial, health system and family level implications.

Metabolic Disorder/Diseases:

India with its unique BMI is topping prevalence & incidence of metabolic diseases. Among the NCDs, diabetes is one of the most common and most easily measurable NCD. India is currently facing an uncertain future in relation to the potential burden that diabetes may impose upon the country. The practical management of diabetes is difficult due to poor accessibility, lack of effective services and costly treatment compliance, especially for sub-urban and rural areas. In alignment with the Health Policy, 2015, DBT has initiated studies on: Gene environment interactions; Inflammation, innate immunity and adaptive immune response; Toxicity of energy (glucose and lipids) fuels; Micro- and macro-vascular complications of diabetes; Host-microbiome interactions. Joint Cohort Development addressing basic and clinical questions and monitoring structures with long-term funding options are being explored with the clinicians at the tertiary care hospitals.

Renal Biology:

Chronic kidney disease (CKD) has become a growing public health problem worldwide

with a serious socioeconomic impact. CKD increases patient morbidity and mortality with disproportionate increase in the risk of cardiovascular disease (CVD). The progression of CKD and CVD in the setting of CKD is highly variable and the factors determining progression and complications are largely unknown. Hence, a long-term population based Indian Chronic Kidney Disease (ICKD) study is aimed to establish a large cohort of Indian patients with moderate kidney failure (40-60% reduction in kidney function) by enrolling 5000 patients in 8 centers nationwide, who will be prospectively followed for a minimum of five years and to develop prediction algorithms using a) Traditional and non-traditional clinical parameters; and b) Biologically relevant biomarkers.

ICKD study will be comparable to similar large scale studies underway globally so as to allow comparative analysis that would provide new scientific insights into the disparities in the risk factors, the progression and the predictors of CKD, as well as the large burden of DVD and associated mortality. Other identified for R & D areas include:

- I. Development of accurate and reproducible equation for estimation of glomerular filtration rate in Indian populations.
- II. Identification of novel biomarkers for early detection and progression of acute kidney injury and chronic kidney disease
- III. The role of genetic factors and/or gene-environment interaction in development and/or progression of diabetic and non-diabetic kidney diseases
- IV. Development of cohorts to study the natural history of diabetic and non-diabetic kidney diseases in Indian populations.
- V. Develop technology of membrane filters for

dialysis in India.

Pediatric Renal Biology Program:

The proposed study seeks to develop a multi-centric collaboration for research on nephrotic syndrome, the most common cause of chronic renal disease in children. The research will allow to characterize the burden of monogenic nephrotic syndrome in India including discovery of new genetic variants that cause the condition or act as disease modifiers. Information on genetic mutations will help to develop an appropriate and rational genetic screening algorithm that is cost effective and also provide molecular drug target for therapeutic interventions. In addition, a bioinformatics platform will be used to establish links between working groups on nephrotic syndrome within the country to enable integration of disease cohorts followed prospectively at individual centers into an anonymized national disease registry for pediatric nephrotic syndrome.

Auto-immune Disease:

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with prevalence varying from 5-10 per 10,000 population globally but with no data from India. Since it mainly affects women in the reproductive age group, it poses significant social and economic burden to the society. In India, about 20% of SLE starts in childhood, posing a huge challenge. Till date most of the work on SLE has been done on describing the clinical phenotype. Owing to its increasing significance, DBT organized a Brain Storming Session on SLE. An outcome of this meeting has been identification of clinicians and basic researchers to develop Multi-centric Network Program on SLE. The group would develop and establish a clinical cohort of SLE from different geographical regions in India to study differences in clinical phenotype, relationship between phenotype and autoantibody response, biochemical predictors of

long term outcome, major causes of mortality and establishment of a bio-repository.

DBT proposes to initiate a multi-centric network program on Osteoporosis and Bone Biology to address both clinical and basic questions with long-term funding and monitoring structures.

Reproductive Health: Under Reproductive Health programme, it is planned to invite/generate projects on: Basic issues associated with infertility: Endometriosis; Implantation failure; Paternal Factors contributing to infertility; Poly Cystic Ovary Syndrome that has become a major health issues in young population; Reproductive Tract Infections: HIV; HSV-2; HPV and Vaginal Ecology

Infectious Diseases

Tuberculosis:

DBT has been funding research on Tuberculosis for the past two decades with focus on: Diagnostics, Vaccine Development, Immunomodulation, Basic Biology; and early & late stage drug-development. There are about 60 on-going R & D projects covering above aspects.

In order to convert scientific leads into products, DBT has signed an MoU with ICMR/ DHR on “Validation of indigenously developed technologies for diagnosis of pulmonary tuberculosis and multi-drug resistant tuberculosis” with an aim to replace imported kits with locally developed technologies. Four major institutions and two Indian companies are involved in a tightly governed exercise. It is planned to offer them to the Revised National Tuberculosis Control Programme, if found cost-effective and scientifically matching.

India TB forum: In a joint initiative between DBT, ICMR, Central TB Division/MOH&FW, DBT is planning to set-up an India TB Research Forum with a purpose to undertake activities

pertaining to diagnostics/treatment/prevention of TB/MDR-TB on a long term basis. Placed under an “Expert Committee”, the forum would be collective Indian Voice on Tuberculosis in all National & Global meetings/fora. It would review the achievements under TB research and identify strengths and gaps; convene joint meetings/ consultations to formulate India-specific guidelines for the programme; formulate guidelines for multi-disciplinary research contributing to TB elimination and pool the resources and promote funding in Innovative Research.

Medical Biotechnology for the North Eastern Region

Since 2009 DBT Nodal Centre for Medical Colleges and Biomedical Research Institutes of North East India, set-up in Tezpur University, Assam has been mandated to facilitate the implementation of two projects:1) “Development/Upgradation of Infrastructure in Medical Colleges in North Eastern States of India”, and 2) “Research Grants to Support MD/MS Thesis to Medical Students in North Eastern Region”. During the FY 2015-16, there has been remarkable increase in the volume of applications for MD/MS thesis grant & participating medical institutions in NER. Over 200 research grants have been awarded thus far and the processing of grant applications for Phase IX are in progress for 2015-2016. There has been notable increase in travel grants for participation in national seminars and workshops by awardees of MD/MS thesis grant with concurrent increase in presentations and publications.

DBT Healthcare Molecular Diagnostic Laboratory, Dept. of Microbiology Regional Institute of Medical Sciences, Imphal has been recognized as one of the viral load testing platforms under NACP. This Lab has successfully participated in the RCPA Quality Assurance

Programs (Molecular HIV Program 2015; on HIV -1 RNA viral load testing), conducted/assessed by RCPA Quality Assurance Programs Pvt. Ltd (Serology Team), NSW, Australia.

DBT Healthcare Molecular Biology/Virology Laboratory, Dept. of Microbiology, Assam Medical College & Hospital, Assam is under consideration for becoming an APEX laboratory for surveillance of AES cases. It is also a part of the departmental NABL Accreditation.

VACCINE RESEARCH & DEVELOPMENT

Vaccines remain the most effective public health tool that provide safe, cost effective and efficient means of preventing morbidity and mortality and constitute critical component of a national health security. DBT has made concerted efforts in vaccine research and development since its inception in 1986-87 through: Task Force on Medical Biotechnology, National technology Mission on Immunization and National Jai-Vigyan Mission on S&T for the generation of new and improved vaccines. Currently, vaccine research and development efforts are being implemented through Vaccine Grand Challenge Programme (VGCP) and Indo-US Vaccine Action Programme (VAP) with major objective to accelerate development of candidate vaccines for which earlier leads are available and to take them through pre-clinical, clinical development and commercialization.

I. Vaccine Grand Challenge Programme

VGCP encourages novel and innovative vaccine related discoveries, accelerated development of candidate vaccines for which earlier leads are available, research of basic & applied nature to improvise current understanding of vaccine science and to strengthen the scientific basis for future vaccine design. Support has been provided

to R&D projects through VGCP focusing on:

Development of candidate vaccines such as: Recombinant combination blood stage vaccines for *P. falciparum* malaria (JAIVAC-2 & JAIVAC-3), rBCG85C -a candidate TB vaccine, Dengue Virus-like particle (VLP) vaccine candidates, BAC-EBV vector-based vaccine approach for Hepatitis C, Inhalable DNA Vaccines for Tuberculosis, novel candidate vaccines against *Salmonella enterica* serovar *Typhi* and *Paratyphi*.

Development of vaccine related technologies such as: Novel Adjuvants for Mucosal Priming, adenovirus based novel viral vector for vaccine delivery, Vitamin D supplementation to improve immune responses to vaccines, *Mycobacterium indicus pranii* (MIP) as a booster to BCG, Chemoenzymatic assembly of defined protein dendrimers for vaccine use.

II. INDO-US Vaccine Action Programme (VAP)

The VAP is a bilateral Indo-US program, which supports a broad spectrum of activities relating to new and improved vaccines. The program was designed to encompass laboratory-based research, evaluation of candidate vaccine development, testing for clinical development, vaccine quality control, delivery of vaccines etc. All work is carried out within areas designated as VAP priorities by the VAP Joint Working Group (JWG) which is comprised of eminent scientists and policymakers from both countries.

This programme popularly known as VAP aims to reduce the burden of vaccine-preventable diseases of public health significance in India, US and other parts of the world, and promotes vaccines as one of the most cost-effective health technologies. VAP-supported research projects have directly addressed critical health problems relevant to both countries.

III. Progress of Major Vaccine Development Projects

- **Rotavirus Vaccine**

ROTAVIRUS VACCINE-(ROTAVAC®) is the first indigenous rotavirus vaccine, developed from an Indian strain- by an Indian company, and tested by Indian investigators in an effort led by the Indian government and supported by several national and global partners. The vaccine has been developed by a unique social innovation of public-private sectors along with institutional collaboration.

Department supported the development of first rotaviral diarrhoea vaccine 116E in India at All India Institute of Medical Sciences (AIIMS), New Delhi in collaboration with Centers for Disease Control and Prevention (CDC), USA. With continued financial support from DBT, National Institute of Health (NIH) & Programme for Appropriate Technology in Health (PATH), the vaccine completed Phase III clinical trials at three sites: Society for Applied Studies (SAS), Delhi (ii) Christian Medical College (CMC), Vellore and (iii) KEM Hospital, Pune. Data from the trial, showed ROTAVAC® to have an excellent safety and efficacy profile. The clinical study demonstrated for the first time that the India-developed rotavirus vaccine is efficacious in preventing severe rotavirus diarrhoea in low-resource settings in India.

The vaccine is manufactured in India by M/s Bharat Biotech International Limited, Hyderabad under cGMP conditions. Bharat Biotech announced a price of US\$ 1.00/dose (or approximately INR 54/dose) for and will soon file for registration of the vaccine in India. It is licensed by the Drugs Controller General of India (DCGI) and is a more affordable alternative to the rotavirus vaccines already on the market. The vaccine has been commercialized and based on

the recommendations of NTAGI; ROTAVAC® has been introduced in the EPI programme of Himachal Pradesh and is being considered for introduction in Andhra Pradesh, Orissa, and Maharashtra.

- **Blood-Stage Malaria Vaccines**

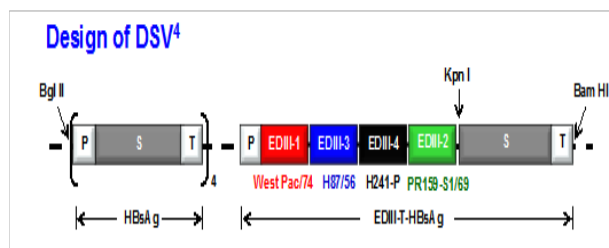
The development of blood-stage malaria vaccines in the past has focussed primarily on two essential antigens, MSP-142 and AMA-1, which both play a crucial role in red cell invasion but are under immense immune pressure. As a result, these antigens exhibit a high degree of polymorphism such that their respective antibodies exhibit neutralizing activity only against homologous *P. falciparum* strains and not against the heterologous strains, thus impeding their potential as vaccine targets. Hence, the primary goal in the development of efficacious blood-stage malaria vaccines has been the identification of essential target antigens that conserved and can elicit strain-transcending neutralizing antibodies. In this regard, the group at ICGEB and JNU has identified essential novel antigens (PfRH5, CyRPA) and produced them in recombinant form that elicits potent strain-transcending invasion inhibitory antibodies. These target antigens hold great promise as efficacious blood-stage vaccine candidates.

- **Dengue Vaccine**

Department has been supporting the group at ICGEB, for the development of safe, efficacious and inexpensive tetravalent dengue vaccine.

The ICGEB has developed a tetravalent Dengue Subunit VLP (DSV4) based vaccine candidate, expressed using the methylotrophic yeast *Pichia pastoris*. This candidate is based on EDIII. Unlike domains EDI and EDII, which elicit largely flavivirus cross-reactive and weakly-neutralizing or non-neutralizing antibodies, EDIII elicits potent serotype-specific virus-neutralizing

antibodies. The ICGEB's 'four-in-one', tetravalent vaccine candidate incorporates the EDIIIs of all four DENVs spliced together through flexible linkers in a single translational reading frame. Further, it is genetically fused with Hepatitis-B surface antigen (HBsAg) and co-expressed with four expression cassettes of HBsAg in order to display EDIIIs on the surface of HBsAg virus-like-particles (VLPs).



Key points of validation attained:

1. DSV4 assembles into VLPs and displays critical DENV neutralizing epitopes of all 4 serotypes.
2. It is immunogenic in mice and macaques.
3. It elicits serotype-specific neutralizing antibodies against all four DENVs in mice. These antibodies exhibit breadth of neutralization against various genotypes of each serotype. Additionally, these antibodies are protective in dengue sensitive AG129 mice.

IV. Major Initiatives Implemented under Indo-US VAP

• Regional Prospective Observational Research for Tuberculosis - Report India Initiative

RePORT India is a bi-lateral multi-organizational collaborative effort designed to advance regional basic and clinical tuberculosis (TB) science in India. The goal of this program is to establish long term longitudinal cohorts of TB patients

in India to strengthen TB research capacity and infrastructure, and foster research collaboration within India and with other countries.

The RePORT Consortium is comprised of research organizations in India with their U.S.-based partners. The primary funding for Consortium research activities comes from the Indian DBT, Ministry of Science and Technology, U.S. National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), U.S. National Institutes of Health (NIH), and Office of AIDS Research (OAR).

The RePORT India Consortium consists of five distinct TB cohorts mainly in Southern India working in collaboration to address a wide array of scientific objectives and to institute a unified common prospective observational research protocol (Common Protocol) that is supported by a central biorepository, a central data management center. It aims at the utilization of harmonized data elements and specimen collection standard operating procedures (SOPs).

RePORT India Leadership Meetings: The leadership to the RePORT Consortium is provided by the governing committee comprising of principal investigators (PIs) from CRUs and their US partner organization, representatives from the funding organizations. The face-to-face meetings and interactions were held with various stakeholders during the meeting that help in (i) Approval of the policies and overall procedures of the Consortium (ii) Review and prioritization of study concepts (iii) Monitoring the performance of the CRUs (iv) Cross-study coordination of timelines, standardization of procedures, means for resource sharing, and other broad operational issues for effective implementation of the research agenda across all study sites.

The Third RePORT India Leadership Group (LG) Meeting in Pune, India: This RePORT India



LG Meeting took place on March 03-05, 2015 at Pune, India. The Byramjee Jeejeebhoy Medical College (BJMC) hosted the event and the meeting was well-attended by representatives from the DBT, NIH, U.S. Embassy, and investigators, scientists, and other participants from India, the U.S., Europe, South Africa, Indonesia, and Brazil. Representatives from other RePORT Consortia in Brazil, South Africa, RePORT India Consortium and Indonesia presented overviews of their work. The meeting covered a wide breadth of scientific, programmatic and operational topics. Days two and three were co-sponsored as part of the Fogarty Workshop.

The Fourth RePORT India Leadership Group Meeting in Boston, USA: This was held in conjunction with the first RePORT International Joint Leadership Group Meeting at the Marriott Newton, and at Boston University Medical Center in Massachusetts, USA on September 23-25, 2015. This meeting brought together renowned TB researchers from the Boston Area and other locations, NIH, DBT and ICMR leadership and program representatives, RePORT investigators and Boston area scientists

- **Human Immune Phenotyping and Infectious Disease Initiative**

The goal of this funding program is to promote U.S.-India collaborative research on human immunophenotyping in the context of infectious disease and vaccine development, and in collaboration with investigators of the HIPC (Human Immunology Project Consortium). Both NIAID (through HIPC) and DBT have allocated funds to support joint activities pursued under this program.

28TH JOINT WORKING GROUP MEETING OF INDO-US VACCINE ACTION PROGRAMME HELD ON JANUARY 27-29, 2016 AT NEW DELHI



The 28th meeting of the Joint Working Group (JWG) of Indo–US Vaccine Action Programme (VAP) was held on January 27-28, 2016 at New Delhi. The JWG was attended by the Indian and US members and the investigators of various vaccine programmes both from India and US. The opening session of the meeting was also attended by Mr. Richard R. Verma, US Ambassador in India. The JWG discussed the progress of various initiatives being implemented under Indo-US VAP and also discussed the development of affordable vaccines for Dengue, RSV, Malaria etc.

INFECTIOUS DISEASE BIOLOGY (IDB) TASK

The mandate of the program is to establish an integrated R&D approach for the development of preventive, therapeutic and diagnostic tools for infectious diseases. Research & Development activities in the important infectious diseases caused by various pathogenic agents including bacteria, viruses, parasites, fungi etc. viz., HIV/AIDS, Hepatitis, Influenza, Chikungunya,

Dengue, Malaria, Leishmaniasis etc have been funded. The 2nd & 3rd meeting of the reconstituted IDB Task Force considered 54 new proposals, reviewed progress of 83 ongoing projects and outcome of 20 completed projects. 20 important R&D proposals on HIV/AIDS, Influenza, Hepatitis, Sepsis & Leishmaniasis etc. were recommended for funding.

Salient achievements from projects funded in 2015-2016:

- Even though the HCV targeting drug Sofosbuvir has entered the market, a large number of patients with HCV infection progress to cancer requiring liver transplant. The recent work using both in vitro culture work and also using patient samples at ILBS reveals a subtle role of epithelial to mesenchymal transition (EMT) in the progression of neoplasia. Elevated level of inflammation molecule viz., PAI1 was noted in patient with HCV genotype 3. Using cell culture assay, HCV-NS2 gene resulted in relocalization E-cadherin from membrane to nucleus with a subtle change in EMT phenotype. Intriguingly, the work revealed that NS2 gene when over-expressed resulted in growth arrest of HCC cell line, Huh7 cells.
- In an effort to understand the molecular mechanism of host cell interaction by Hepatitis A Virus, the interaction of capsid protein VP1 with the HAV receptor HAVCr-1/TIM-1 has led to the discovery that HAV VP1 can form capsomeres (capsid morphological intermediates) upon bacterial expression under specific conditions. Biophysical and immunological studies are being carried out on these oligomers. If these are found to be immunogenic and antigenic, they might serve as effective material for vaccination and diagnostic efforts.
- The effects of interaction of Hepatitis C Virus protein NS5A with host translation machinery on HCV pathogenesis has revealed that HCV NS5A sequesters eukaryotic cap binding protein eIF4E to 40S ribosome and forms a complex ENR. Further studies required identification of mRNAs that are differentially translated in HCV infected cells by state of the art technology “Ribosome Profiling” and the protocol has been standardized for this.
- Isolation and characterization of recombinant strain of Hepatitis C Virus, genotype 1a/3a from Kolkata is the first report of this recombinant strain from East and North East India. It has several new subtypes (3e, 3g, 3i, 6n and 6u).
- Over the years many compounds of medicinal value have been isolated from Indian Medicinal Plants. Recently a search found potent anti HCV activity to be present in the semi-purified sub-fraction of methanolic extract prepared from *V. wallichii* root.
- In a study for identifying the role of mTOR on HCV life cycle, studies are suggesting that mTORC1 is assisting the cells to contain the virus flourish as its inhibition caused increased viral replication. Studies also suggest that mTORC1 also regulates autophagy during HCV infection through an unknown mechanism.
- A natural source of potent antiviral activity against all four dengue virus serotypes has been identified that could provide a safe, affordable and efficacious solution to the dengue menace. A tetravalent Virus-like Particle based recombinant dengue vaccine candidate has been expressed in yeast and



an international patent has been filed.

- In a study to understand the molecular basis of pyrethroid resistance in *Aedes aegypti*, a novel kdr (knockdown resistance) mutation in the voltage gated sodium channel has been identified which confer resistance against synthetic pyrethroids. Also a, PCR-based method has been developed for identification of novel kdr mutation.
- In another study on NS3/NS2b dengue proteases, investigator has discovered crucial interactions between NS3/NS2b and flnA, between NS2b and newly discovered protein SAR1, and between flnA and ICAM1. The new Interactions of dengue proteases NS3/NS2b discovered may have huge impact in discovering the drug targets of other candidates of Flaviviridae, once proven to affect the dengue pathogenesis in vivo.
- By implementing proteomic approach to understand the etiology of Neuro-pathogenesis induced by Chandipura Virus infection, it was seen that Chandipura Virus Perturbs Cholesterol Homeostasis Leading to Neuronal Apoptosis. With help from Graph theoretic network analysis the research group has further revealed protein pathways underlying cell death following neurotropic viral infection.
- In a study to understand the biology of Chikungunya Virus infection in permissive cell lines and mosquito vectors, its observed that Heat Shock Cognate 70 protein interacts with CHIKV in C6/36 cells. Experiments to confirm the role of HSC 70 as a putative receptor for CHIKV in C6/36 cells are in progress.
- A study on visceral leishmaniasis, probing the role of Arabinosylated Lipo

arabinomannan (Ara-LAM), has shown a strong immunomodulatory role for the TLR2-ligand isolated from avirulent *Mycobacterium smegmatis*. Ara-LAM increases IFN- γ by JAK-STAT pathway and also reciprocally modulates IRF4 and IRF 8 expression. This reinstates anti-leishmanial TH1 response, thereby initiating CD4+ and CD8+ proliferation. This reduced the parasite load in spleen and liver infected by *L. donovani*. Thus a new principle for immunomodulation by IFN- γ has been established. In another study targeting histone acetyl transferase HAT3 in kalaazar causing parasite *Leishmania donovani*, HAT3 mediated PCNA acetylation was found to act as a flag for PCNA ubiquitination, a modification required for DNA repair.

- In a study, for understanding the nature of liver-stage specific CD8+T cells generated following infectious sporozoite challenge that ensue long-lived protection against Plasmodia infection, an insectarium have been established to rear the mosquitoes. The parasite has been grown in mosquito which successfully infected mice. Protection model has also been established using radiation attenuated sporozoite (RAS) which were used in all our studies. CD8+ T central (TCM) and effector (TEM) memory cells as CD44hiCD62Llo and CD44hiCD62Lhi cells were characterized, respectively. Both of these memory cells accumulated in liver upon challenge. Furthermore, the qualitative change in expression of CXCR3, and to some extent CXCR6 on both TCM and TEM cells that reside in liver was also observed. The exclusive expression of CXCL16 in challenge group strongly supports the hypothesis for maintenance of memory T cells for a long time. However, the survival potential of memory T cells for

extended period remains to be determined. Currently groups of mice are being immunized to study the survival potential of memory CD8 T cells in kinetic manner.

- In a comparative study of Gene characterization of Influenza A pandemic (H1N1) 2009 viruses from virus isolates of 2009 pandemic and 2012 re-emerging viruses in western Rajasthan it was found that samples collected from Barmer district showed more than double mutations as compared to viruses from Jodhpur district.
- Studies on antifungal susceptibility testing and genotyping of Cryptococcal isolates from Delhi and other parts of India, have shown increase in resistance to various antifungals (Amphotericin B: 8/61 =13.11%, Fluconazole: 4/61 =6.55%), which in turn will affect the present treatment options and prophylaxis. A novel strain (ST194), previously reported only in China, has been found in India. Studies have also revealed that SUMOylation is an essential process in *C. glabrata* and that adaptation to stress involves changes in global SUMOylation. Importantly, loss of deSUMOylating enzyme *ulp2* leads to impaired growth, sensitivity to multiple stress conditions, reduced adherence to epithelial cells and poor colonization of specific tissues in mice. New potential drug candidates for use as antifungal agents are being screened and some leads have been found. Indigenous diagnostic kits for detection of antibodies to *Aspergillus fumigatus*, AfuPEPLISA, in patients of bronchial asthma and pulmonary TB are being devised and trials are ongoing at various hospitals.
- In a study on sepsis, it was observed that Wnt5a facilitates both uptake and killing of pathogenic bacteria belonging

to the *Streptococcus*, *Hemophilus* and *Pseudomonas* species, which are known to promote sepsis.

Maternal and Child Health Programme

A taskforce on Human Developmental and Disease Biology (HDDDB) has been functional to give due emphasis on research activities related to pregnancy complication, factors of adverse pregnancy outcome, neonatal development and associated diseases. The projects focused on preeclampsia, IUGR, recurrent miscarriages, effect of maternal nutritional status on pregnancy outcome, development of neonatal immune system and neonatal sepsis. The overall goal is to support both basic research and application centric discovery under the programme.

Human Placental Research

An international meeting on “Provocative Ideas on Human Placental Research” was organized on 1st& 2nd December 2015 by Translational Health Science and Technology Institute (THSTI) along with Regional Centre for Biotechnology (RCB), Faridabad and NIBMG, Kalyani, to develop a roadmap for placental biology research in our country. Eminent global experts were invited to evolve provocative questions and identify scientific priorities for advancing our understanding of placental research.

Salient achievements in ongoing program

- Some interesting outcomes have been noted in the ongoing projects. PBXIP1 gene was for the first time reported to be associated with preeclampsia. Additionally while understanding its role in trophoblast differentiation, significantly low expression of HPIP was noted in human preeclampsia (PE), indicating HPIP as a potential biomarker.



- Studies on maternal nutrition status showed that supply of dietary Docosahexaenoic acid (DHA) was important for fetal growth and development, placental angiogenesis and vascular remodeling during early pregnancy. This stresses on the requirement of further studies to test effect of other nutritional components on pregnancy and development.
- Study evaluating the role of Sirtuins showed that increased expression of SIRT2 is a novel marker of cellular senescence. The first evidence for an important role of miR-99a in human MK development was found, and was identified as a molecular regulator of the differences between neonatal and adult MKs.
- Using Deuterium dilution technique for the first time in India, fat and fat-free mass was calculated for a large cohort of neonates. Results showed birth weight was positively correlated with fat as well as fat-free mass. However fat mass % correlated with the gain in weight from birth and was comparable to their Western counterparts.
- In one of the first studies which documents reference values for Indian infants' PFT indices, normative data has been prepared. Changes in the IPFT values were observed due to acute respiratory infection by viral agents, thereby indicating increase in airway resistance. Children with multiple episodes of ARI, RSV infections and LRTI had more abnormalities in PFT indices.
- Based on mouse model studies of endometriosis, it was found that endometrium survived and proliferated at ectopic locations, but its responsiveness to steroids is altered. This is due to the fact that endometrotic tissue doesn't properly express estrogen and progesterone receptors. This alters estrogen sensitivity thereby inducing progesterone resistance. Based on these findings, it was hypothesized that hormone based therapy for endometriosis may not be successful thus need for newer therapeutic targets are evident.
- Identifying biomarkers and understanding pathogenesis of Retinopathy of Prematurity (ROP) is an important area of research. A gene expression analysis of ROP patients showed 142 differentially expressed genes. Inflammation mediated by chemokine and cytokine, endothelin signaling, toll receptor signaling, CCKR signaling and gonadotrophin releasing hormone receptors pathways were the major pathways involved. Proteome analysis of vitreous humor of ROP patients and controls showed differential expression especially in pathways involved in coagulation cascade, complement activation pathway, angiogenesis and plasminogen activation. These mark an important step towards identifying biomarkers and disease etiology.

Pre-term Birth Programme (PTB)

The Department of Biotechnology has supported the Inter-institutional Preterm Birth programme at an overall cost of approx Rs. 49 crores, at Translational Health Science and Technology Institute (THSTI), Regional Centre for Biotechnology (RCB), Clinical Development Services Agency (CDSA), National Institute of Biomedical Genomics (NIBMG), Gurgaon General Hospital (GGH) & Safdarjung Hospital. A small Molecular Research Unit, (MRU) has been made functional at GGH which processes bio specimens from about 8-10 enrolments per day. Isolation, processing and storage of the samples with unique id have been harmonized across the

centers. The two major activities of the project has been to document clinical & epidemiological determinants of preterm birth, and to conduct proteomics, genomics & microbiome assays for the bio specimens collected. For each of the enrolled participant serial ultrasound, images for placental changes & cervical length has been recorded. The other risk factors that are being documented are social and demographic information, current and past pregnancy events, medical and surgical history treatment history, and maternal anthropometry. 369 women have been assessed out of which 269 were confirmed and enrolled for the study.

DBT-ICMR Joint Working Group finalizing roadmap for Gene Therapy

Gene Therapy has picked up pace as a promising avenue for biomedical science. After skeptic reviews Gene Therapy products have been approved for use in some countries. Hundreds of clinical trials are ongoing across the globe. Researchers in India also have the expertise to delve into the foray. To promote research, infrastructure and clinical trials in the country DBT and ICMR have joined hands towards development of regulatory framework, guidelines and proforma for clinical trials and the drafts are being finalized. Clinical trials and development of vectors are the prioritized sectors.

India-South Africa collaborative research programme on HIV/AIDS and Tuberculosis

TB is the most common opportunistic infection affecting individuals who are HIV positive and is also the most common cause of death in patients with AIDS. Timely diagnosis is prevented due to rapid spread of infection marred by a compromised immune system. Increase in the incidence is alarming, particularly for developing nations, where HIV infection and TB are endemic and resources are limited. To develop clinical

capacity in this area India and South Africa have jointly agreed upon to build a sustainable environment for translational research which promotes discovery of new technologies and products for prevention and management of HIV/AIDS and TB. This program will facilitate collaborative efforts between academia and industry in both India and South Africa.

Inter Ministerial Programme: DBT-ICMR Collaborative Effort on HIV/AIDS & Microbicides:

Mandate of the program & major initiatives:

The mandate of the program is to understand pathogenesis of HIV/ AIDS, design novel vaccine immunogens, adjuvant formulations, microbicides concepts, curtailing HIV replication. This program has been initiated with the collaboration between DBT and ICMR through an MoU during 2007 to promote research in the HIV/AIDS and Microbicides area involving investigators from academia and research laboratories to design HIV antigens/antibodies/ drugs/microbicides. The MoU was further extended for another period of 5 years w.e.f September, 2012. The collaborative activities have been expanded further to Maternal & Child Health.

The 2nd phase of the programme has been implemented and it aims to accelerate research that will generate knowledge and develop state-of-the-art technologies to provide the basis for the development of HIV vaccines and novel therapies against HIV including microbicides. Two subgroups are currently operational viz., Clinical Research Consortium and Natural Product Consortium on HIV/AIDS and Microbicides.

Expert Committee meeting was held to review the progress of 14 ongoing R&D projects. Under Clinical Research Consortium, a proposal for studying intricate relationships between HIV

pathogenesis and immune defense in Long Term Non-Progressors (LTNPs) elite controllers (EC), HIV-Exposed Sero-negative (HESN) and High Risk Sero-negative cohorts was recommended by the Expert Committee & is under active consideration for funding by the Department.

Salient Achievements:

In a study on structure based rational design & synthesis of inhibitors for various enzymes of HIV, few novel leads for HIV-RT inhibition have been identified which can be explored further for lead optimization.

In a study on rapid epitome mapping of neutralizing antibodies & other entry inhibitors of HIV-1, the PI is developing methodology for rapid mapping of epitopes targeted by monoclonal & polyclonal neutralizing antibodies. Further studies to confirm these findings are in progress.

- In a study to identify the factors associated with susceptibility/resistance to heterosexual HIV transmission among sero-discordant couples using proteomics, Human Cervico Vaginal Lavage (CVL) showed significant anti-HIV activity against four HIV-1 isolates with distinct tropism. Further, the samples are being collected from study participants and would be analyzed by iTRAQ proteomics to identify factors present in the secretions of human genital mucosal compartment contributing to susceptibility/resistance against the sexual transmission of HIV.
- In another study relating to Microbicides for prevention of HIV transmission and other sexually transmitted infections: in vitro efficacy and pre-clinical safety evaluation, two new plants with anti-HIV-1 activity have been reported. Formulation-1 comprising of the ethanolic extracts of 3

plants showed potent anti-HIV-1 activity, formulation-1 also has anti-HSV-2 activity, formulation-1 up to 100 µg/ml did not show any significant decrease in the viability of lactobacilli and any adverse effect on the epithelial monolayer, gel formulation-2 comprising of ethanolic extracts from 5 plants were formulated and shown to have anti-HIV-1 activity.

- In another study for Identification of Anti-HIV Leads From Plant Sources and Determination of Mechanism of Action, four acetone/methanol extracts of *Terminalia paniculata* (TP) and *Polygonum glabrum* (PG) and their fractions (total 59) were tested for anti-HIV1 activity using TZM-bl and PBMC assays. The leads were further studied for determining the mechanism of action using cell based (HIV-1 entry and fusion inhibition) and enzymatic assays (protease, reverse transcriptase and integrase inhibition). Three extracts (NCL-51, NCL-52 and NCL-53) showed inhibition of HIV-1 entry and two extracts (NCL-51 and NCL-52) were found as potent protease inhibitors.
- In an effort to isolate and identify anti-HCV natural compounds from selected Indian Medicinal Plant, potent anti HCV activity was confirmed to be present in the semi-purified sub-fraction of methanolic extract prepared from *Valeriana wallichii* root.

BIOSPACE: Policy Center for Biomedical Research (PCBR), THSTI

About the Center:

The Policy Center for Biomedical Research is mandated to carry out systematic assessment of technologies to deal with innovation system issues, carry out gap analysis to help the

Government and other relevant stakeholders to prioritize R&D in the biotechnology sector applied to health. It studies the health system and implementation issues for existing opportunities for intervention and assess the impact of the technologies, to be able to advice on demand generation. It also suggests improvements and incremental innovations needed in a technology that will facilitate its diffusion at appropriate level in the health system. In addition, concepts and designs for newer technologies that are socially relevant and commercially viable are also addressed.

The achievements in the three flagship program are as follows:

Flagship program on Point of Care (PoC) Diagnostics for communicable diseases in India: A comprehensive analysis of health technologies for point of care tuberculosis (TB) diagnostics was carried out in regard to their performance and subsequent challenges. Two of the near mature products based on imaging technology from two commercial companies were identified. These include developing a new technology and validating an indigenous version of prototype of the existing product, through appropriate industry-academia partnership which is being facilitated and monitored by PCBR, interlinked with strategies to accelerate creation of appropriate policy for integration of these diagnostics at various levels of point of care for early diagnosis of TB. Newer platforms for inclusion in this program are being mapped and studied in detail.

Flagship program on cholera vaccine introduction in India: A roadmap for cholera control and prevention in India is being prepared by the PCBR. Currently, as a part of creating an evidence base for disease burden, hot spots and high-risk areas for cholera are being mapped. The Health Department of states that are identified through

this mapping will be partnered with to draw up a national plan. This will also include the use of oral cholera vaccine as an adjunct preventive measure with water and sanitation.

Flagship Program on Leveraging Global Health Technologies to Promote Maternal & Child Health (MCH) in India: A landscape of important parameters affecting attainment of optimum MCH in the country is being prepared. Further, a comparison is being made with neighboring countries like Sri Lanka, Nepal and Bangladesh on their achievements in the same area, so as to identify the deficiencies in our system and recommend policy changes.

STEM CELL RESEARCH AND REGENERATIVE MEDICINE

The Department promotes stem cells and regenerative medicine as one of the thrust areas under its biomedical research. The projects are being supported in the following broad categories: basic research; pre-clinical and clinical research; industry-academia partnership programme, capacity building; and formulation of regulatory framework for stem cell research in India.

During the year, a number of projects have been implemented on various aspects of embryonic, adult and induced pluripotent stem cells. The findings of the studies are promising and intend to develop improved methods and techniques for isolating and culturing stem cells from different origin and ability to create induced pluripotent stem cells to be used in regenerative medicine. A study has been supported wherein protocol for isolating and proliferating multipotent mesenchymal stem cells from the wharton's jelly of umbilical cord of sheep has been developed. In an another study, methods for efficient generation of corneal epithelial cells from dental pulp stem cells to provide an autologous and renewable source of cells for the treatment of blindness



related to corneal disorders was developed. A novel polymer scaffolds - Poly lactic acid-Poly ethylene glycol with optimum degradable nature and stable thermal, mechanical, and porosity properties has been developed and characterized under the study supported at IISc Bangalore. This polymer will be used in a novel designed perfusion bioreactor system for bone regeneration using mesenchymal stem cells. One of the study showed that alcohol activates NOTCH signalling leading to overexpression of ASCL1, a key marker associated with neuronal defects, thereby driving the cells towards differentiation and abnormal neurogenesis. A study to identify and characterize stem cell growth factor from the perivitelline fluid of the fertilized eggs of the Indian horseshoe crab has been supported. In an another study at CMC Vellore, a total of five children with large segmental bone defects have received tissue engineered bone transplant (custom made triphasic hydroxyapatite scaffolds loaded with mesenchymal stem cells) with no serious adverse effects.

As per the Joint Statement issued during visit of the Hon'ble Prime Minister of India to Japan in September, 2014, stem cell research was identified as one of the thrust areas for developing collaborative programmes between both the countries. The focus of the collaboration is on developing treatments for sickle cell anemia, β -thalassemia and brain disorders and creating haplobank relevant to our population in collaboration with CiRA, Kyoto University, Japan. Accordingly the Department formulated and implemented an SFC proposal "Accelerating the application of stem cell technology in human disease" as Indo-Japan collaborative programme with four participating institutions from India, namely: inStem, Bangalore; NCBS, Bangalore; NIMHANS Bangalore; CSCR, CMC Vellore; & CiRA, Kyoto University, Japan as international partner. This proposal aims to develop the

infrastructure and the expertise for India to be a competitive force in the field of regenerative medicine and pluripotent stem cell biology. As part of this programme a comprehensive schedule of activities will be developed to train and equip Indian students, young and senior faculty in the area of stem cells and regenerative medicine. The details of the training component of this programme will be worked out with the Centre for iPS Cell Research and Application (CiRA), Kyoto University, Japan.

Guidelines for Stem Cell Research

A regulatory framework and the guidelines for stem cell research have been formulated jointly by DBT and ICMR and have been revised based on the feedback from all the stakeholders. The government has also constituted a National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT), for effectively reviewing and monitoring the stem cell research in the country. As per the guidelines it is mandatory that any institution/organization involved in stem cell research should be registered with the NAC-SCRT through Institutional Committee for Stem Cell Research (IC-SCR).

CENTRE FOR CELLULAR AND MOLECULAR PLATFORMS (C-CAMP), BANGALORE

C-CAMP was established in 2009 by Department of Biotechnology, Ministry of Science and Technology, Government of India. The objective was to fill a key gap in biotechnology research and entrepreneurship by fulfilling the following goals: i) making available technologies accessible to academia and industry ii) to convert discoveries to innovation and technologies. The mandate of C-CAMP is to stimulate biotechnology research, innovation and entrepreneurship in India by enabling cutting-edge research, making available state-of-the-art technologies, providing training

on these platforms to academia and industry as well as building translation capabilities, and promoting entrepreneurship and innovation. This is the first of its kind in the country to leverage the investment in a research environment to enable creating the link between academia and industry. It was set up as a not-for-profit company under the companies act to allow for maximum flexibility to accomplish the mandate it was given.

Salient achievements

A. High-end Technology:

a) Access to technology for academic and industrial researchers: In pursuit of the goal to stimulate innovation, C-CAMP has till date reached out to and provided high-end platform technology services to 166 organizations across all technology platforms. With access to C-CAMP's high-end platforms and expertise of its platform directors and laboratory personnel, users have benefitted both in terms of high quality data and results as well as the opportunity to gain insight into their scientific question through interactions with C-CAMP experts.

b) High Impact Publications: As a result of this access and interactions with C-CAMP experts, users have been able to publish their work in over 71 publications in high-impact journals such as Cell, Science, Journal of Bacteriology etc. It is to be noted that these are only a few, which have been published and acknowledged. There are few more at the manuscript level and some just about to be published.

c) Technology Training: Availability of trained manpower is often limiting in hi-tech areas. Over the last 6 years, C-CAMP has trained over 800 scientists from academia and industry in these technology platforms who have gone on and successfully used the skills gained from C-CAMP training programs. The impact of C-CAMP's training programs is the number of skilled manpower that it has been able to generate to

allow high-end technologies to be used at their full potential. Technology training is an important function of C-CAMP. This generates valuable human resources for the country's academic and biotech industrial enterprise.

B. Innovation and Entrepreneurship:

a) Entrepreneurship and Innovation Promotion: C-CAMP's involvement as a partner in BIRAC's Biotechnology Ignition Grant (BIG) scheme has further expanded C-CAMP's entrepreneurial support. Currently, a number of small companies have begun incubation and have also shown particular interest in C-CAMP's technology platforms and expertise. C-CAMP has so far supported more than 50 early start-ups and also provided incubation.

b) Early Translation Programme: The Early Translation Accelerator at C-CAMP has been established at C-CAMP with an aim to bridge the gap between discovery and application/s of the technology by bringing in scientists with industry experience to look at an existing early stage discovery and understand the experiments that may be conducted to validate the discovery and establish proof-of-concept to the stage where industry partners can take the technology through further development and possibly onto the market. C-CAMP has 4-5 exciting translation projects underway with academic collaboration.

C) Technology Development: Apart from services, training and entrepreneurial activities, C-CAMP has also been engaged in technology development projects. As an example, C-CAMP, NCBS and IIT-Madras in collaboration have developed a point-of-care, miniaturized flow analyzer with an important application towards HIV immune health monitoring via CD4/CD8 cell count in rural areas where access to flow cytometers for detection is sparse. This technology is also highly affordable and portable and addresses a very important need in rural areas.

Biotechnology Based Programme for Societal Development

Biotechnology Based Programme for Rural Development

Fish Culture:

A project on propagation of culture-based-capture fisheries in selected reservoirs of Konkan and Western Ghat regions of Maharashtra was implemented at College of Fisheries, Ratnagiri for livelihood security of rural fishermen. Training and demonstration programmes were conducted for the tribal fishermen on reservoir fisheries management, production of fish fingerlings in the ponds and cages and ornamental fish production. As an outcome, the average fish production from the reservoirs has been increased from 25 kg/ha to 245 kg/ha with an increased average additional income per family of tribal fishermen Rs. 12000-15000 to 40000-45000 per annum. Due to the implementation of these activities migration has been reduced from 85% to 35% and has increased their income about ten times during the last three years.



Harvesting of fish from reservoir

Another project on backyard fish culture for rural population of Tirunelveli, Tuticorin

and Kanyakumari Districts of Tamilnadu was implemented at Centre for Aquaculture Research and Extension (CARE), St. Xavier's College, Palayamkottai, Tamilnadu. Training programmes were conducted and 553 farmers were trained on various aspects of fish culture. Trainees adopted murrel culture at small scale level and harvested table size murrels (average weight 650 gm) with an average production of 230 kg/farmer and earned an average income of Rs 70,000/per farmer/year.

Quail production:

A project on commercial quail production for rural youth was implemented in Nandurbar district of Maharashtra by Indira Mahila Sewa Society (IMSS), Nandurbar. Demonstration unit of quail was established at IMSS Nandurbar and 9 training and demonstrations programmes were conducted on various aspects of quail rearing including housing, brooding of chick, rearing and feeding of quails, and preparation of feed. Five awareness camps were also organized. The demonstration programme helped the participating tribal youths in the marketing of products and gaining higher profit.



Quail Farming

Integrated Farming:

Project on popularization of Fish Poultry-Vegetable integrated farming for socio-economic upliftment of fish farmers of Kumaun region of Uttarakhand was implemented at KVK, Lohaghat, Champawat, Uttarakhand. Demonstrations on fish poultry and vegetable integrated farming were conducted. Technology was refined and further demonstrated at farmer's fields that produced 61.80 kg fish, 1250 eggs and 61.80 kg poultry meat from 40 chicks in one crop and 175 kg poultry meat from 80 chicks in two crops in a year. 3435 kg vegetables (vegetable pea, cauliflower, cabbage, capsicum, brinjal) were produced from 1000 m² area. 200 fish farmers were given training on integrated fish farming and out of which, 34 farmers have adopted this technology for their livelihood generation.

Awareness Programme for Zoonotic Infections:

A project on capacity building and awareness generation towards combating microbial zoonotic infections in Kamrup and Lakhimpur districts of Assam was implemented at College of Veterinary Science, Assam Agricultural University, Guwahati, Assam. The purpose of this project was creating mass awareness among farmers and vulnerable groups about the various zoonotic diseases in animals, their mode of transmission, prevention and control, scientific management of livestock so as to minimize the incidence of these infections. Several training programmes were organized at various locations of Kamrup and Lakhimpur districts of Assam along with demonstration camps at farmers's field as well as distribution of leaflets on zoonotic diseases.

Entrepreneurship Development:

Entrepreneurship development for the rural population on preparation of dry flower materials and establishing a dry flower small scale cottage industries for improvement of livelihood

was implemented at Tamilnadu Agricultural University, Coimbatore. 18 training programmes on various aspects of preparation of dry flower material were conducted for Self Help Groups, farm women and unemployed rural youth. People from Sivagangai, Dharmapurai, Trichy, Tirupur, Namakkal, Coimbatore, Dindigul and Theni districts were benefited through this training programme. The entrepreneurial training programmes and demonstrations have helped women to form Self Help Groups and to earn additional income. The unemployed rural youth were also benefited through these training programmes for their livelihood generation.

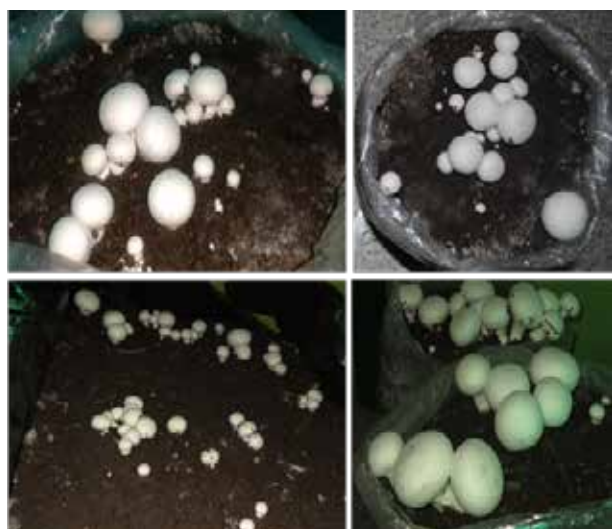
Medicinal Plants:

A project on income generation for rural communities through cultivation and conservation of medicinal plants was implemented at HNB Garhwal University. *Rosmarinus officinalis* L., family Lamiaceae, was introduced for cultivation as it has high medicinal and aromatic value including culinary use. The dry leaves of rosemary have high industrial demand for several pharmaceutical, cosmetic and culinary uses and its essential oil. Training and motivation programmes were conducted in selected 8 villages of Persari Gram Panchayat in a mission mode to produce bulk herbage of Rosemary and organic farming practices. The dry leaves, extraction of essential oil and hydrosol of various herbal products have been developed viz., herbal tea, spice and seasonings, mixing in shampoo, face wash and gel making along with herbal dhoop which broadened the source of income for rural community of the region. Adoption of this practice has helped self-employment opportunities.

Mushroom Cultivation:

Establishment of Rural Bio-resource Complex was implemented at Uttar Banga Krishi Viswa

Vidyalaya and North Bengal University, West Bengal. Two workshops on cultivation and post harvest processing of edible mushroom and exploitation of plant and microbial resources of North Bengal were organized. 1050 people from seven districts of North Bengal were given hands on training for button mushroom cultivation along with value added vermicompost preparation. A book on 'Production and Processing of Edible Mushroom' has been published for the better technical knowledge of the growers. 150 mushroom growers, 35 entrepreneurs and 10 active spawn producers are engaged in edible mushroom production.



Mushroom Production Unit has been set up at the University of North Bengal

Spirulina Cultivation:

A project on small scale backyard cultivation of Spirulina for income generation and as a health supplement was implemented at Shri AMM Murugappa Chettiar Research Centre, Chennai. Awareness cum demonstration camps were organized for spirulina cultivation where 115 farmers participated from NGO's and other individuals from 12 district of Tamilnadu. A spirulina cultivation handbook has been prepared in Tamil language and distributed

to the participants. The fields of NGOs and individual beneficiaries were visited by project staff and 25 beneficiaries were selected based on the land, water availability, sunlight and the environmental conditions for Spirulina tank construction. Spirulina buyback arrangements were made with two different buyers namely Vitasmartzone, Tharangambadi, Nagapattinam Dist and Realgae, Chinnasalem, Villupuram Dist. Both buyers have entered into an agreement with our beneficiaries to purchase the products regularly.

Menthol Cultivation and Disease Management:

A project on propagation and demonstration of nematode disease management in menthol mint for better health was continued at CIMAP, Lucknow. Several awareness programmes were conducted among the farmers in menthol mint growing areas in Barabanki and Lucknow districts of Uttar Pradesh. Farmers were trained on nematode disease management in menthol mint. Kisan Melas were also organized in which large number of farmers participated. adoption of this practice 12 %-15% increased in oil yield and significant reduction in root knot nematode and other disease infestation achieved.



Kisan Mela organized for the farmers by CIMAP

Rehabilitation Programme:

A project on rehabilitation of flash flood affected

area of Uttarakhand through biotechnological interventions was implemented at HESCO, Dehradun. The aim of the project was to provide livelihood options to victims of the flash flood affected areas through biotechnological interventions. Thirty villages in three districts Uttarkashi, Rudraprayag and Chamoli have been selected for implementation of the project. Six Kissan banks (2 in each district) have been set up. Several training programmes have been conducted in various interventions in agri-horticulture crops including value addition of agri-horticulture produce, nursery development, packaging and marketing. Six well equipped Common Facility Centres have been established to provide local resource processes and value addition services. Each centre is shared by 5 villages. 150 bio-digesters have been installed. Animal husbandry practices also introduce to the community as an alternative source of livelihood and goats and poultry suitable to the area have been distributed among the selected group. Six nurseries have been developed in the affected villages for planting material and this has provided a good source of livelihood support to the community. 2707 families from 3 disaster affected district have been benefitted.

Biotechnology Based Programme for SC/ST Population

Fish Seed Production & Rearing:

A project on carp seed production in Fibre-reinforced plastic (FRP) hatchery and development of integrated rearing system for livelihood development of SC/ST communities in Khurda district of Odisha was implemented at ICAR - Central Institute of Freshwater Aquaculture (CIFA), Bhubaneswar. 192 beneficiaries having 9.19 ha pond area have been selected in the project. There FRP carp hatcheries have been operated at Puranapadhan Village, Baliana Block and Kantabada Village, Begunia Block for

carp seed production. The FRP carp hatchery site of Puranapadhan Village has been developed as a model fish seed center, carp breeding operations were conducted and 20.4 million carp spawn (*Labeo rohita*, rohu; *Cirrhinus mrigala*, mrigal; and *Cyprinus carpio*, common carp) were harvested in the monsoon. 233 persons were trained on scientific aquaculture technologies in three orientation programmes conducted in all the three clusters. .



FRP hatchery for Carp seed production at beneficiary's field

Pig Farming:

A project on propagation with up gradation of local pigs of keirak for socio-economic upliftment of schedule castes families of Keirak, Thoubal district was implemented at College of Agriculture CAU, Imphal. 200 farmers were provided training on various aspects of pig farming including importance of piggery, breeding aspects, selection of boar and sow, rearing of pigs, space requirement, construction of shed etc. Adoption of this practice has increased the income.

Vegetable Seed Production:

A project on quality seeds production of some important vegetable crops (tomatoes, brinjal and



okra) was implemented at KVK, Manipur for sustainable economic development. Three subdivisions of Bishnupur district namely, Moirang, Bishnupur and Nambol were selected for the implementation of this project. Two SC villages Leimaram and Sadukoireng in Nambol and one SC village Kwakta in Moirang divisions have included along with four ST villages of Nambol, Onion, Toubul and Sagang in the project. These villages are predominantly vegetable growing areas. 10 self help groups have been constituted from the project villages and they have been given training on vegetable seed production particularly for tomato, brinjal and okra. 20 training programmes have been organised on different aspects of quality vegetable seed production for the farmers.

Vermicomposting:

A project on socio-economic upliftment of the rural and peri urban SC/ST population of Srikakulam district was implemented at Agri Biotech Foundation, Andhra Pradesh. Four training programmes were conducted on rising vegetable seedling using pro tray technology, vermicompost and coir pith compost covering 102 farmers. Resource mobilization was done for construction of vegetable seedling nurseries, vermicompost and coir pith compost unit followed by distribution of nursery implements. Adoption of this technology benefitted 120 farmers.



Training for preparation of seed mixture and vegetable seedlings.

Health & Nutrition:

A project on capacity building including training and demonstration to educate SC/ST and rural community of Kerala for child maternal health by popularizing traditional nutritional/functional food was implemented in Amity Institute for Herbal and Biotech Products Development, Thiruvananthapuram, Kerala. 232 women (between the age group of 18-35 years) and 252 children below the age of 5 years were selected to take up the project activities. Majority of them were under low income group. 20% of the respondents (mothers) and also children from each Gramapanchayat were underweight. Mothers also suffered from chronic diseases like diabetes, thyroid, cholesterol and blood pressure. Medical camps were organized in Vilappil and Aryanad Gramapanchayat of Thiruvananthapuram to provide free medical services to the rural poor, especially mother and children. Awareness programmes were also carried out to improve the health and nutritional status of mother and children.

Biotechnology Based Programme for Women

Health and Hygiene

A project on awareness generation and screening for cervical cancer in women above 30 years age was implemented by Government Medical College, Srinagar, Jammu & Kashmir. 2000 women were screened for cervical cancer through awareness generation cum screening camps pursuant to motivation via printed and electronic media. Though motivating of women for this invasive procedure was very difficult but door to door counselling found very effective. Follow-up, treatment and further intervention were also provided to the identified patients and proper record was maintained as per the hospital protocol. Twenty one comprehensive interacting sessions at various primary health centres were also organized. Around eighty ASHA's workers were made aware of benefits of screening for cervical cancer who were instrumental in motivating the women folk to participate in these camps. Around 8000 women have been provided free consultation for cervical cancer screening by a screening team of gynaecologists, biochemists, pathologists and health care workers through this programme. Women were made aware of benefits of screening for cervical cancer and motivated to come forward for screening for this deadly disease.

Another project on liquid based cytology and its potential for diagnosis of reproductive tract infections & abnormal cervical cytology was implemented at National Institute for Research in Reproductive Health, Mumbai. A survey was conducted in 21 villages covering 3000 household and 705 rural women of low socioeconomic status in the age group of 18 to 60 years attended the camps for diagnosis of reproductive tract infections and abnormal cervical cytology at the institute. 90% of rural women had no knowledge related to reproductive health, infection, pap smears, and

genital hygiene before intervention and after counselling they had improved their knowledge about the same. Eight training programmes have been conducted for 56 beneficiaries including Anganwadi sevika and other health workers.

A Network Project on Breast cancer screening has been supported in four districts of North-East India namely-Manipur, Meghalaya, Mizoram and Tripura through coordinating agency Cancer Foundation of India, Kolkata. 2821 women have been sensitized on breast health in Agartala Govt. Medical College, Tripura. In Civil Hospital, Aizawl, Mizoram, clinical breast examination was done in 1723 women and 54 cases of breast cancer were diagnosed and treated in hospital. 1190 women with benign disease were advised for follow up. In Civil Hospital, Shillong, Meghalaya, 1170 girls were sensitized. In Regional Institute of Medical Sciences, Manipur community awareness programme on breast cancer was also organized and 4342 women were sensitized.



Breast cancer Awareness campaign programme

Livelihood Generation and Skill Development

A project was implemented by The Energy and Resources Institute on livelihood enhancement of agrarian population in Kamrup, Morigaon and Dhubri district of Assam on scientific cultivation of the selected crops, bio-fertilizers and their application, on-farm production of



vermicompost, micro-entrepreneurship etc. 20 low-cost vermicomposting units were constructed in three districts and farmers were provided worms. Turmeric processing units along with a banana fibre extracting units were established for turmeric processing and extraction of banana fibres extraction to strengthen the economic condition of the farmers. The farmers were provided hands-on training for running these two processing units. 75 training programmes were conducted on various scientific method of cultivation of the Turmeric, banana, bio fertilizers and their application, on-farm production of vermicompost in which 2827 farmers attended. Farmers were also helped to establish market linkages for selling of their produce at competitive rates. Adoption of this programme sensitized the farmers about the available technologies and they could utilize these technologies to improve their livelihoods.



Preparation of Vermicompost at the farmer's field

Another network project on Biotechnology Led Socio-economic empowerment of farm women was implemented by IARI, New Delhi, Deendayal Research Institute, Chitrakoot and Participatory Rural Development Foundation, Gorakhpur. Several self help groups (SHGs) of farm women have been formed to implement the project activities. Various nutritional

interventions have been implemented through trainings and introduction of nutrition garden at household level. New crops and varieties of wheat, rice, barseem, mustard, moong, maize, oat, barley, different vegetables, fodder crops etc. were introduced based on soil and water conditions. Rural Biotechnological Innovation and Application Units (RBTIAUs) have been established. These units are working as a single window delivery system for the adopted villages in imparting information on new technologies, improved tools including farm implements. Entrepreneurial potential of the farm women has been scaled up by training them in post harvest management and value addition of the farm produce available in the village. This project has brought perceptible social changes in project area, motivational level of farm women and increased their awareness and knowledge about improved agricultural technologies.

Value addition of meat products

A project on socioeconomic upliftment of rural women through development of value added meat products was implemented by Sher-e-Kashmir University of Agricultural Sciences & Technology, Jammu. The beneficiaries were selected from the families of Jammu who were involved in the rural meat industry or in poultry rearing activities or in meat business. The beneficiaries were provided several trainings for preparation of different meat products, packaging, preservation and market strategy for sale of value added products including creation of awareness about the nutritive value of meat and meat products, benefits of value addition. The participants were also provided training on development of meat pickle, meat biscuits, meat snacks, meat balls, meat nuggets and meat patties.

Natural dyeing technology

A project on empowerment of rural women through

natural dyeing technology was implemented by University of Agricultural Sciences, Dharwad, Karnataka for capacity building of rural families. Intensive skill development training programmes on natural dyeing was conducted in 3 taluks of Dharwad, Belgaum and Uttar Kannada district. Natural dyeing protocol using four different sources viz., arecanut slurry, fountain flower, marigold and teak leaves has been developed and the dyeing technology provided a good opportunity for self-employment in rural areas for women folk. Increasing consciousness among consumers towards health and environment has encouraged the utilization of natural resources for eco-friendly products. 250 rural women from 9 villages of Karnataka state were trained in this project. Possibilities and scope of designing variegated products for enterprise development, cost calculations, marketability avenues were all discussed during the training. Some SHG members have come forward to a produce eco-friendly baby kits for newborns. Establishment of micro-enterprise and market linkage of the natural dyeing technology has also been established.



Natural dyeing technology shown during training programme

Animal Husbandry and Poultry Farming

A project on increasing in the productivity of existing cattle through scientific rearing for upliftment of economic status of women was

implemented by Society for Environment and Development (SED), Digod, Rajasthan. 20 women beneficiaries were given training to increase the productivity of existing cattle through scientific rearing to enhance the income of poor rural women. Various training programme on selection of suitable breed, Housing, Health & hygiene management, Immunization, Feed, Natal care, Storage, transportation and marketing, Animal waste recycling and organic farming were provided to the beneficiaries. A model demonstration unit was established at Gramin Vigyan Kendra of SED in village Digod for cattle rearing.

A project on techno-economic empowerment of rural women through sustainable piglet production units was implemented by College of Veterinary Science and Animal Husbandry in Aizawl, Mizoram. 100 women farmers from 10 villages of Aizawl district of Mizoram were selected for implementation of this project. For technical empowerment of the farmers, hands-on training of five days duration on piggery management for 20 farmers was organized in the Pig farm of the college. Constructions of model ten sow units at college have been done. Ten breeding gilts were purchased from the College Pig farm and these gilts are being used for breeding. Female pigs are being distributed to the selected farmers.

In another project on sustainable livelihood generation for rural women through improved backyard poultry farming was implemented by College of Veterinary Science and Animal Husbandry, Central Agricultural University, Mizoram. 541 parent Vanaraja chicks (80 male birds and 461 female birds) were purchased from Project Directorate of Poultry, Hyderabad. The birds were reared in deep litter system of management in the Instructional Poultry Farm Complex of the College. Ten women from



ten selected villages were imparted training to enhance their skill to serve others as local

service providers in their respective villages and establishment of rural poultry resource centre.



Management of Vanaraja Chicks under the Brooder and Backyard Unit

BIOTECH PRODUCT AND PROCESS DEVELOPMENT

BIOSYSTEMS AND BIOPROCESS ENGINEERING

Towards development and improvement of sustainable bioprocesses of commercial interest, Biosystems and Bioprocess Engineering Task Force has been formed to find innovative and efficient solutions addressing the challenges involved in the production processes. In this financial year a Call for Proposal was issued in areas of (a) Host and Metabolic Engineering (b) Biotransformation and enzyme Engineering (c) Biosystems Engineering. Department received 106 proposals in response to the Call and finally 13 projects have been recommended for financial support. Several technical leads have been obtained from already funded projects and few leads are given below:

Bioprocess development for synthesis of industrially relevant product

Scientists at IIT Bombay are in process of developing an industrial process where microbial oxidoreductases are used to synthesize stereo selective chiral alcohols. This involves high production and expression of alcohol dehydrogenase (ADH), improvement of these candidates for better properties, biotransformation process development and scale up. The group has already selected some candidates, expressed them and estimated their natural capabilities for biotransformation. Random mutagenesis approach is being explored to improve the properties of candidates selected. To screen them for positive phenotype, a medium-high throughput screening assay is being developed simultaneously. Scale-up of biotransformation have been tried with wild type ADH candidate at

high substrate feeding and high conversion rates of ~80% have been observed.

Designing of indigenous adsorbents for purification of therapeutic antibodies

Scientists at ICT-DBT Centre are trying to develop indigenously designed alternative affinity adsorbents for purification of therapeutic antibodies. The feasibility of the technique for purifying polyclonal and monoclonal human IgG using these indigenously designed pseudo bioaffinity adsorbents ['AbSep'] has been evaluated. The characteristics of IgG purified using 'AbSep,' have been found to meet pharmacopoeia specifications in a better way as compared to IgG purified using conventional Protein A adsorbent. Designed pseudo bioaffinity adsorbent can be used for more than 100 cycles without any significant effect on quality of antibodies. Purified antibodies found to be stable without any colloidal and conformational instability. The newly designed adsorbent gives consistent performance for both polyclonal and monoclonal antibodies with the optimized process conditions.

Establishment of Multi-Target Screening Platform useful for Targeted and Combinatorial Drug Development

Scientists at MKU, Madurai are developing multi-parallel assays to facilitate the "rapid hit-to-lead selection process" in combinatorial drug development. The aim is to establish 50 different signaling assays reporting the drug targeting effects of the compounds, and establishing standard operating protocol to perform the multi-target screening cellular assays. Under the study,

researchers have obtained in-vitro signaling pathway activity data for 45 signaling pathway activity in 22 cancer cell lines. By an in-silico and integrative genomics approach, the pathway activity pattern of 1811 gene-sets in 917 cell lines also has been derived. With this in-vitro and in-silico data, they could identify the importance of major signaling pathways to be targeted for cancer therapeutics. Proof-of-concept screening has been performed for two different compound libraries (each with 96 drugs) for two different oncogenic signaling pathways, Wnt& ERK/MAPK. The screenings have identified multiple hits and are being evaluated in additional cell lines.

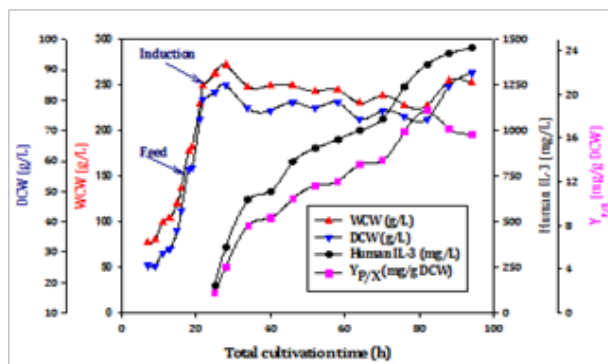
Fabricating microchip for in-situ product monitoring in bioreactor

Scientists at IIT Delhi are developing amperometric detector microchip for in-situ product monitoring in bioreactors. Their first strategy is to fabricate microfluidic devices compatible to capillary electrophoretic amperometric detection (CEAD). So far they have developed (CE-AD) devices based on using micropatterned Indium Tin Oxide (ITO)

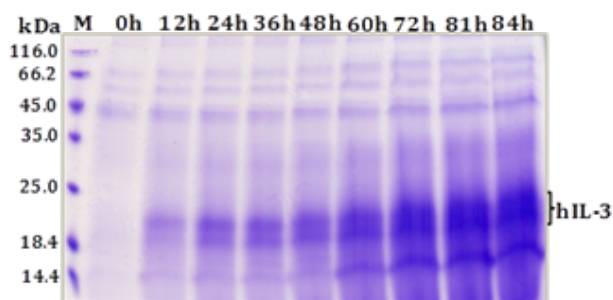
structures and Polydimethylsiloxane(PDMS) based microchannels. A microfluidic device has also been created with gold microelectrodes in order to compare the differences between ITO vs inert electrode such as gold for CE-AD applications. As a trial, dopamine and glucose have been estimated off-the chip on systems designed with LabVIEW control. Microchip fabrication and detection of dummy single analyte instead of multianalytes being tried out so far.

Bioprocess development of recombinant therapeutic in Pichia

Scientist at UDSC, Delhi has developed cost effective production of therapeutically important recombinant hIL-3 in *Pichia pastoris* expression system. They have demonstrated higher level of extracellular and biologically active recombinant hIL-3 protein expression of 2.30 g/L in *Pichia pastoris* culture supernatant after bioprocess optimization. The biological efficacy of the *Pichia* produced hIL-3 is better than the standard control available in the market.



(A). Growth and product profile



(B). SDS-PAGE analysis

Growth profile and SDS-PAGE of hIL-3 expression in optimized fed-batch fermentation

Glucan production from strains of North-East Indian microbial diversity

Scientists at IIT Guwahati are optimizing the production of glucans from hyper-producing LAB strains from North-East Indian microbial diversity. Glucan producing strain, *Weissella cibaria* RBA12 has been isolated from *Citrus maxima* (Pummelo) and Glucan production optimized from this strain. Structure and physico-chemical characterization of glucan also has been carried out. They have also produced and purified glucan sucrose. The strain also has been used to produce Isomalto-oligosaccharides by fermentation.

Optimization of bioconversion process for rare sugar production

Scientists at Charotar University of Science and Technology are aiming at bioconversion of natural sugars to rare sugars and its separation. Under this project they are trying to produce D-allose, D-psicose, D-lyxose and L-ribose from natural products like D-glucose, D-fructose, D-xylose and L-arabinose respectively using enzyme like isomerase and epimerase. Several microorganisms from nearby region have been isolated and subjected to molecular identification and isomerase gene amplification. Bioconversion of L-arabinose to L-ribose and D-xylose to D-lyxose are being done by L-arabinose isomerase and Ribose isomerase respectively. For D-psicose and D-Allose production, single step epimerization have been performed using D-psicose epimerase and D-tagatose epimerase.

Bioprocess optimization for recombinant expression of xylose reductase

Scientists at IIT Madras are targeting towards high yields of enzyme xylose reductase which can be useful for further development of enzyme based xylitol production. For the first time, the

xylose reductase gene from yeast *Debaryomyces nepalensis* was isolated successfully and its gene and protein sequences determined and deposited in National Center for Biotechnology Information (NCBI) database. The gene following its cloning has been heterologously expressed in *Escherichia coli* and purified to homogeneity and high yield of enzyme achieved. Biochemical characterization of enzyme has been performed. In addition they found that the enzyme exhibited remarkable salt tolerance towards NaCl and KCl. The half-life of the enzyme in the presence of 1 M KCl and 1 M NaCl found to be 30 h and 16.5 h respectively. The conformational stability of the enzyme was not affected even at 2 M salt. This property of the enzyme is even more beneficial since it could help develop an economical enzymatic bioprocess for xylitol production from salt contaminated plant biomass hydrolysates at industrial grounds.

Metabolic engineering of biosystem for propionic acid production

Collaborative work at IIT Madras and Anna University Chennai is underway to metabolically engineer the acrylate gene pathways in *Lactococcus lactis* for the production of propionic acid, a widely used food and feed preservative. Acrylate pathway from *Clostridium propionicum* comprising of genes for synthesis of propionic acid from lactate were cloned in lactic acid bacteria to produce propionic acid. The enzymes were expressed successfully and its impact on the host physiology is being studied. The synthesized propionic acid by LAB having GRAS status can be formulated directly with animal feed by separating the cells thus reducing purification cost. Further, kinetic modeling was adopted to understand the impact of the enzymes concentration on the overall flux and metabolite levels in the pathway. The model was developed with the enzyme rate expressions based on the data available in literature. Therefore the model

can be used to calculate flux control coefficients by estimating elasticity coefficients and in the design of synthetic pathway constructed using more efficient enzymes from other organisms.

Green and efficient synthesis of enantio pure alcohols of biological interest

Scientists at IICT, Hyderabad developed a simple, inexpensive and eco-friendly process based on enzyme membrane methodology for the continuous synthesis of chiral alcohols. Chiral alcohols are used as intermediates/building blocks in the synthesis of pharmaceuticals, agrochemicals and flavours. *On* screening for biocatalysts from plant and microbial sources, *D.carota*, has been found to show promising enantio selective bioreduction of prochiral ketones. The enzyme responsible for keto reduction from *D. carota* showed broad substrate specificity and stereoselectivity. From this study it is also observed that the enzyme dehydrogenase is responsible to obtain chiral alcohols. The enzyme immobilization found better on 10% PVDF membrane with higher yields and enantio selectivity. The rate of the reaction catalyzed by the immobilized enzyme found to decrease on every repeated cycle, which may be due to limitation of co-factor (NADPH), which is responsible for enantio selective keto-reduction.

PUBLIC HEALTH, FOOD AND NUTRITION BIOLOGY

Research and Development endeavours were continued in food biotechnology and nutrition biology, addressal of micro & macro nutrient deficiencies through development of fortified foods with generation of clinical evidence, health care products/ nutraceuticals/dietary food supplements; probiotics for holistic health; addressal of celiac diseases; addressal of Vitamin B12 deficiency; nutriepigenomics; postharvest processing and value addition; food safety &

allergenicity, shelf life extension of perishable foods etc. In addition, Public health research from a nutrition perspective was also initiated. Proposals were solicited in the areas of “Food Allergy” and “Food to Food Fortification”. A multi centric study was initiated to evaluate the extent of the burden of vitamin B12 deficiency across the country and also to identify the dietary as well as genetic factors associated with low levels of vitamin B12 in various age groups. From a National Public Health policy perspective, this study would address the question whether Vitamin B12 is to be added in conjunction with folate and iron for alleviation of anemia in India. Research leads in major thematic areas are given below:-

Public Health

Iron Fortified Rice for the addressal of anemia: India is one of the countries which have a high prevalence rate of anemia. The anemia prevalence rates among pregnant women in India are as high as 58%. Chemical fortification is one of the tools to tackle this problem. A programme was initiated in IIT- Kharagpur for the development of iron fortified rice pre-mix which when uniformly mixed with normal rice in a ratio of 1:100 would provide 25% of RDA of iron in 100 grams of rice.

Addressal of severe acute malnutrition in children: In India, the prevalence, and rates of malnutrition in children remain high. Inappropriate feeding and caring practices for the young children, especially during the first two to three years of life is one of the causative factors of malnutrition. Children afflicted with severe acute malnutrition are at an increased risk of death from diarrhea, pneumonia and malaria which could be halted by strengthening our health systems and by increasing the access to simple and affordable interventions.

A multi-centric, randomised controlled trial in

children affected with severe acute malnutrition (SAM) conducted in Delhi, Vellore and Udaipur showed that the recovery rates overall were 43% in augmented home prepared food (AHPF) and 48% through ready to use therapeutic food (RUTF-C). The median weight gain in children who recovered was 1100 g as compared to 600 g in non-recovered children. The maximum treatment duration of 16 weeks was more beneficial than the originally planned duration of 8 weeks. A variation in the prevalence of SAM was noted in the study sites ranging from 0.5% in Vellore, 1.5% in Delhi and 5% in Udaipur. A national consultative meeting was convened to deliberate the results obtained from this study.

NUTRITION BIOLOGY:

Initiation of Integrated M.Sc. & PhD programme in the area of Nutrition Biology: An integrated M.Sc and Ph.D programme was initiated in the area of nutrition biology in Central Food Technological Research Institute, Mysore for capacity building and augmentation of research capacity. This programme has a provision of 10 MSc students per year and 10 PhD students from the third year with a research focus in two areas: (i) Food and Nutrition Based approaches to control obesity and its complication and (ii) Generation of the knowledge as well as experimental evidence based database for natural bioactive molecules.

Potassium counter for estimation of body cell mass in pregnant women and neonates: Low birth weight rates are highly prevalent in Indian babies and are a well-known cause of neonatal mortality. The weight of a new born baby is dependent on various factors such as maternal pre-pregnancy weight, parity, gender and gestational age of the child. Furthermore, the dietary habits of Indian pregnant women do not meet the increased requirement of quality protein during the last trimester of pregnancy

which could impact the weight of the new born. Accurate measurements of body cell mass (protein) accretion during pregnancy along with neonatal body protein content are done using a potassium estimation counter. Total body potassium estimation using whole body counting of naturally occurring radio-active potassium gives an accurate measure of the body cell mass, which is considered as gold standard and is not available in India. Through the Departments' support, St. John's Research Institute, Bangalore has built a potassium counter for measurement of body cell mass. The counters efficiency was measured using anthropomorphic shaped container with a known quantity of potassium chloride, while the measurement of body cell mass in pregnant ladies is ongoing.

Addressal of obesity and metabolic disorder: Obesity is on the rise worldwide and is invariably associated with metabolic complications like diabetes and hypertension. The casual factors include activation of inflammatory pathways and chronic inflammation. Transient receptor ions channels are permeable to calcium and are possible candidates for the alleviation of chronic inflammation. Cinnam aldehyde in high fat fed rats resulted in modulation of anorectic gene patterns in hypothalamus which in turn led to lipolysis in liver and visceral adipose tissue and also anti-inflammatory activity.

In another study, rice bran oil and its minor components which are known for their hypolipidemic and hypoglycemic effect were tested as a therapeutic approach for addressal of diabetes as well as diabetic nephropathy. Oryzanol concentrate, a derivative of rice bran oil ameliorated the metabolic changes in streptozotocin induced diabetic rats. Deposition of total fat, glycoproteins and collagen in glomeruli was significantly decreased in diabetic rats which were indicative of ameliorative effects of oryzanol

against diabetic nephropathy. Administration of oryzanol also reduced the expression of type -iv collagen.

In another study, oral administration of raw carrot juice had significantly reduced high fructose diet induced elevation of free fatty acids, macrophage chemoattractant protein 1 (MCP 1) and c-reactive protein levels which was indicative of alleviation of inflammatory state.

Maternal Micronutrient status, inflammatory markers and risk of pre-eclampsia: Pre-eclampsia is a pregnancy complication which is one of the leading causes of perinatal morbidity and mortality that results in preterm birth as well as low birth weight. Current thinking in this field implicates angiogenic imbalance and excessive inflammation in the development of pre-eclampsia. L-NG-Nitroarginine methyl ester (L-NAME) was administered to pregnant rats in order to develop an *in vivo* model of pre-eclampsia characterized by systolic and diastolic hypertension in pregnant dams, lower pup weight, and significant rise in placental TNF- α levels which were alleviated by the combined supplementation of folate, vitamin B12 and omega-3 fatty acids.

Food Biotechnology

Aptamer based detection system for aflatoxin M1 in milk: Food safety regulations require advanced technology for the detection toxins present in food. Mycotoxins are considered as deleterious contaminants since they cause adverse health effects in animals and humans AFB1 is secreted in milk which is classified as a possible human carcinogen. An aptamer based tool is being developed for detection of Aflatoxin M1 in milk. One particular aptamer, AFAS3-2 was found to possess good affinity towards aflatoxin M1. Efforts are underway for the development of an aptamer based detection system for aflatoxin

M1 in milk.

Quantum dots based detection of Food borne pathogens: Various molecular methods viz, polymerase chain reaction, Enzyme linked immunosorbent assay, reverse passive latex agglutination etc are being routinely employed for the detection of food borne pathogens. On the other hand, detection of food borne pathogens rapidly in real time in field deployable conditions is a real challenge. Nanotechnology based detection approaches can enable rapid detection and monitoring of pathogens and toxin contamination at various steps of food chain. Quantum dot approach is a powerful technique for detection of food borne pathogens. A new method was developed for the synthesis of highly fluorescent Quantum dots. Studies are underway for the development of a highly sensitive and specific aptamer based detection assay.



TEM image of the CdTe-CdS quantum dots showing an average diameter of 2 nm (Scale bar-20nm)

Anti-inflammatory mediators from wild and medicinal mushrooms: Ingestion of mushrooms as food and for medicinal purposes is very popular among the tribes of West Bengal. Decoction of *Ganoderma lucidum* was used for gastralgia, detoxification and chronic tracheitis by the santal tribals from times immemorial.



Numerous examples of this kind are available in the folklore. Carbohydrate complexes extracted from *A.hygrometricus* and *Ganoderma* species, reduced the production of nitric oxide as well as expression levels of pro-inflammatory cytokines and iNOS thus indicating their anti-inflammatory properties. *In vivo* efficacy studies are being carried out in an animal model in Carrageenan induced paw edema model.

Beneficial effects of nutraceuticals and bioactives: Edible products of plant origin possess a plethora of nutraceuticals and bio-active phytochemicals such as flavonoids, anthocyanins, saponins, carotenoids and terpenoids etc. In the recent past, the anti-oxidant and anti-cancer properties of spices and green tea, hypoglycemic effects of fenugreek seeds, anti-cancer effects of isoflavones and phytoestrogens from soy have been vigorously demonstrated. Scientific validation of health claim of traditional foods / medicines and bioactives is an important area of investigation.

Composite processed fruit formulations were evolved based on mango, banana, papaya, bitter orange, pomelo fruit juices, besides supplementation with xanthone extract from mangosteen fruit exocarp. The developed composite fruit processed products, i.e beverages were evaluated for their sensorial acceptability, storage stability at room temperature and for microbiological quality. Bitter orange fruit fractions demonstrated anti-obesity activity *in vitro*. Pomelo fruit fractions displayed anti-diabetic property *in vitro*, while structural elucidation of anti-diabetic component was spelt out as naringin.

Physalis minima and *Carissa spinarum* are known to have strong medicinal and nutraceutical properties. An anthocyanin rich beverage with a good sensory value was prepared from the pulp of *C spinarum*. Callus cultures of *C. spinarum* plants have shown to accumulate pigment during

the first culture itself, indicating that it would be a very efficient system for production of this pigment *in vitro*.

Kodo millet – whole grain/bran supplementation improved the oral glucose tolerance, serum lipid parameters, exerted prebiotic effects on selected gut microbiota and improved short chain fatty acid (SCFA) production, especially acetate, although it did not affect the weight gain. Further Kodo Millet whole grain and Kodo millet bran supplementation alleviated inflammation by preventing the rise in IL-6 and LPS levels in the serum, suggesting reduction of inflammatory state and improved gut barrier function. *In vitro* experiments with finger millet arabinoxylan could significantly inhibited pro-inflammatory responses in mouse macrophage cell line RAW 264.7 challenged with E.coli lipopolysaccharides (LPS). Dissolved nitrite levels were dose dependently decreased after treatment with finger millet arabinoxylan. Expression levels of INOS, NFκβ, IL-6 and TNFα were also down regulated upon treatment with finger millet arabinoxylan at 0.5 and 1 mg/ml doses. Secretion of inflammatory cytokines, TNFα, IL-6 and IL1β in the spent broth were reduced upon finger millet arabinoxylan treatment along with LPS. These results indicated that the finger millet and kodo millet exerts significant anti-inflammatory effects.

Identification of celiac disease epitopes in Indian wheat cultivars: Gluten present in wheat causes celiac disease. A large number of proteins in gluten for example, glutenin and gliadins are immunogenic. Removal of immunogenic proteins could be one of the strategies to combat celiac disease. Some of natural variants of these immunogenic peptides with single amino acid/SNP substitution are non-immunogenic. Identification of such non immunogenic epitope variants needs detailed study before actually targeting them. Anti-gliadin antibody

(polyclonal) based response was analysed in different translocation lines as well as in different wheat cultivars and landraces. The translocation lines were used in the breeding strategy had a lower level of anti-gliadin antibody based response than the wheat cultivars. Varieties like PBW54, HI617 and Kharchia had lower response for the anti-gliadin antibody. In contrast, NP4, NP12 and PBW65 showed higher response. The response was also analysed in diploid wheat e.g. *T. monococcum* (AA), *Ae. speltoides* (BB) and *Ae. tauschii* (DD). A higher number and expression level of alpha gliadins in *T. monococcum*. The screening of different wheat cultivars with monoclonal antibody work is under progress for the presence of specific epitopic sequences (KLQPFQPELPYPQPQ) known as immunogenic sequence. Translocation lines of *Hynaldia villosa* in wheat (6VS.6DL and 6VS.6AL) were used to transfer non-immunogenicity to different types of wheat i.e. hard, soft and color wheat lines. Positive BC3F2 seeds screened from the main season were advanced to BC3F3 in the off season after marker assisted selection. Plants were screened first with 6vs-Bd6 marker for 6VS chromosome and thereafter positive ones with different 6AS and 6DS specific SSR markers.

BIOSAFETY RESEARCH

The Department has re-constituted the Review Committee on Genetic Manipulation (RCGM) w.e.f. 21.08.2015 with 19 experts in their individual capacity and 12 nominees of various Ministries, Departments and State Agricultural Universities.

During the year, the RCGM evaluated about 597 applications in its 6 meetings in the areas of agriculture, healthcare and industrial products. The applications were for import/exchange of recombinant research related materials including seeds, gene constructs, plasmids, and vectors, GMOs / LMOs; for conduct of pre-clinical toxicity

studies and evaluation of pre-clinical study data. Applications for conduct of Event Selection Trials (ESTs)/ Biosafety Research Level 1 (BRL1) trials in confined conditions for seven transgenic crops under development viz. cotton, corn, rice, chickpea, brinjal, sugarcane and potato were also considered from 12 public/private organizations for generation of biosafety data.

Six Central Compliance Committee (CCC) teams with more than 20 experts with expertise in plant breeding, physiology, plant biotechnology, entomology, pathology, etc., along with agriculture experts from the states and members of state agricultural university (SAU) were constituted and visited biosafety research trial sites to interact with the in-charges of the trials and the Directors of Research of the respective SAUs for monitoring the compliance of biosafety rules and regulations while conducting the trials on GM crops as stipulated in "Guidelines for the monitoring of confined field trials of regulated, GE Plants, 2008".

In the pharmaceutical sector, 19 rDNA products were permitted for conducting pre-clinical toxicity studies by 11 private/public institutions & companies. Based on the evaluation of pre-clinical study reports, 12 rDNA products developed by 8 private/public institutions & companies were recommended by RCGM to Drug Controller General of India (DCGI) for appropriate phase of clinical trials.

Apart from the above, RCGM also provided technical recommendations to GEAC to facilitate in decision making on GE organisms/ living modified organisms (LMOs) and products thereof for conducting further research leading to subsequent release into the environment. Since, GEAC had entrusted the responsibility of reviewing applications for commercial release of Bt cotton hybrids expressing approved events to Department of Biotechnology about 250



applications from 36 applicants were considered during 2 meetings of the Standing Committee and based on agronomic performance and other desirable characteristics of the hybrids for profitable and sustainable yield by the cotton farmers, 107 hybrids were recommended to the respective State Agriculture departments for commercial cultivation.

In order to bring awareness about existing laws, rules and guidelines governing biosafety regulation of GMOs among various stakeholders the division organized “Scientific/ Strategic Research on Biosafety & Biosecurity” on February 25, 2015. Envisaging the need to strengthen the biosafety regulations, a training workshop on “Regulating Agricultural Biotechnology: Indian and International perspectives” during September 10-12, 2015 was organized at Hyderabad. The workshop was attended by senior/ middle level officials from state agriculture departments, state agriculture universities, quarantine authority and scientists from various public and private sector organizations.

As a part of reforms and strengthening of biosafety regulation in the country the division has initiated series of consultative processes with various stakeholders. One of the major initiatives is the establishment of Biosafety Support Unit (BSU) in partnership with Regional Centre for Biotechnology (RCB) with trained and skilled scientists with specialization in various scientific disciplines. During the year BSU has acquired new office space and became a fully functional unit. The unit has two risk assessment groups i.e. agriculture and pharma. At present these groups comprise of a team of eleven scientists having different specializations. Major activities undertaken during the year include:

- a) Providing assistance to Review Committee on Genetic Manipulation (RCGM) in scrutiny of applications, preparation of draft agenda

and recommendations of RCGM meetings

- b) Providing logistic and technical support to RCGM and its Sub Committees during meetings.
- c) Prepared draft documents on Biocontainment facilities, requirements for molecular characterization of GM Crops and the approach to risk assessment studies, soil microbial analysis in CFTs of GM crops and a report on evaluation studies for Phase 2 trial for Genetically Modified Mosquito (*Aedes aegypti*)
- d) Initiated development of risk assessment and management (RARM) plan for GE SPT rice, GM mustard, and BGIII RRF cotton hybrids.

Establishment of Indian Biosafety Knowledge Portal (IBKP) reached to a stage of development and would be commenced in next financial year. The portal would ensure compliance adherence at organizational level along with online submission-tracking-review-processing & monitoring of the applications submitted by the organizations to RCGM. The portal would also ensure easy access of information related to trends in biosafety and biosafety regulation of GMOs worldwide.

To facilitate R&D and make the regulatory system efficient and transparent, the Department has brought out “simplified procedures/ guidelines on exchange (inter-state and inter-institutional supply/ receipt within India), import and export of genetically engineered organisms and product(s) thereof for research purpose.”

Since, 2011 the division has initiated an observance of strict compliance of biosafety guidelines for rDNA activities by various universities, institutions, laboratories, and industry through their Institutional Biosafety Committees (IBSCs).

During the period under report, 44 new IBSCs have been constituted, while 67 old IBSCs were renewed.

TECHNO MANAGEMENT AND IPR CAPACITY BUILDING

The main objectives of Biotechnology Patent Facilitating Cell (BPFC) is to provide administrative and financial support to biologists and biotechnologists in filing of patent applications in IPO, USPTO and other countries and creation of awareness and understanding relating to Intellectual Property Rights (IPR)

among students, scientists, faculty of colleges, universities and research institutes. The BPFC supports filing of patent application on inventions pertaining to life sciences and biotechnology after a rigorous scrutiny. The patent filing is done through empaneled IPR firms.

The Department filed 05 Indian patent applications and 04 foreign patent applications through its empaneled IPR firms during the year. Following patents have been granted during 2015-2016:

S. No.	Country & Patent No.	Name of the Inventor(s)/ Applicants	Title
1	US Patent No. 9057058 Dated- 16.06.2015	Dr. ReetaGoel G. B. Pant University of Agriculture and Technology, Pantnagar and Department of Biotechnology	Process for the preparation of talc based formulation for LDPE-degrading bacterial consortia
2	EP No. 2323676 Dated- 15.07.2015	Dr. Manoj Kumar Bhat National Center for Cell Sciences, Pune Department of Biotechnology	Protein based product from fenugreek seeds that regulates dyslipidemia and obesity, and a process for the preparation thereof
3	EP No. 2162742	Dr. R. V. Omkumar	Assay for detection of transient intracellular Ca ²⁺
4	Dated -30.09.2015	Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram	PCR-based detection method for <i>Chlamydia trachomatis</i>
5	US Patent No. 9139883	Department of Biotechnology	Sealbio: a novel non-obturation regenerative technique of endodontic treatment
6	Dated -22.09.2015	Prof. Daman Saluja	Method of producing alkalothermostable xylanase from <i>Bacillus pumilus</i> strain MK001 by solid state fermentation
7	US Patent No. 9,180,072	University of Delhi	Recombinant nitrogen fixing microorganism and uses thereof

IMPORT/EXPORT R & D RECOGNITION AND OTHER ISSUES

Export plays an important and direct role in growth of an economy. The Department fixed and communicated Input Output Norms for Four biotechnological products and communicate comments on export/import of Three restricted items to the concerned authority to facilitate trade.

Research & Development based technological innovation has always been fuel for industrial growth around the world. The Department recommended 18 Research & Development units of biotechnology firms for recognition of their in house R & D to Department of Scientific & Industrial Research.

BIOTECHNOLOGY INFORMATION SYSTEM NETWORK (BTISNET)

The Biotechnology Information System Network (BTISnet) of the Department of Biotechnology established in the year 1986 is now spread across the country with 170 centres. Based on the infrastructure, developments and capabilities the network centres are in various levels and include Centres of Excellence (CoEs), Distributed Information Centres (DICs), Distributed Information Sub-Centres (DISCs) and Bioinformatics Infrastructure Facilities (BIFs). The network houses one Supercomputer Facility for Bioinformatics and six Interactive Graphics Facilities. Large numbers of R&D projects in bioinformatics are also being supported through bioinformatics programme. The network supports

teaching program in M.Sc., M.Tech. and Ph.D. in Bioinformatics and Computational Biology to generate skilled manpower in Bioinformatics. Further, the BTISnet centres are conducting short term trainings/ workshops for the benefit of research community including experimental biologists. Large numbers of peer-reviewed publications have been emerged during this year. These publications are being compiled into a compendium. These centres also provide services to the scientific community. These activities are being coordinated by the Apex Biotechnology Information Centre (BTIC) which is located at the Bioinformatics division of Department of biotechnology (DBT).



Location of BTISnet Centres on India Map

Centres of Excellence (CoE):

Six Centre of Excellence (CoE) in Bioinformatics, Computational and Systems Biology have been established as part of BTISnet. These Centres are well equipped with state of art Bioinformatics infrastructure to support research within the institute as well as neighbouring institutions. The focus of these centres is high quality research, education and services.

Supercomputing facility for bioinformatics & computational biology (scfbio), has been established at IIT-Delhi with a vision to develop personalized medicine using Gene to Drug (Dhanvantari) pathway. Their efforts have resulted in a whole genome analysis methodology and software based on DNA energetics (ChemGenome), an all atom energy based computational protocol for protein tertiary structure prediction (Bhageerath-H), and a binding free energy based methodology for protein/DNA targeted lead molecule design (Sanjeevini). These softwares are web-enabled and made freely accessible from the SCFBio site (www.scfbio-iitd.res.in) to the entire global community of interested scientists and students. With the help of these softwares one can design a lead molecule which could be improved iteratively in combination with experiment to yield personalized medicine. This Gene to Drug pathway is a major step towards finding the right medicine for the right disease for the right person in an automated way with a potential to help the society in a big way. Leadinvent (www.leadinvent.com) incubated at IIT-Delhi from 2006 to 2009 and Novoinformatics (www.novoinformatics.com) under incubation at IIT-Delhi since April 2011 are two start-up companies created by the students and staff of SCFBio based on the Gene to Drug innovations at SCFBio, IIT Delhi. The centre developed software called Distance to native - D2N for to calculate a score

for a given protein structure based on the physico chemical properties of the known structures, to make prediction in unknown cases. The centre has also developed a meta server for protein tertiary structure analysis and validation. The centre has published seven papers in the peer reviewed international journals of high impact

The research focus of the CoE at JNU, New Delhi has been on comparative genomics, structural biology, in-silico drug design, biological evolution, biomolecular simulation, data-mining, analysis of large scale data, systems biology, complex systems and artificial intelligence. A new program on complex systems has been initiated in this year. The facility is ably supported by excellent computational and communication infrastructure, computer clusters, multiprocessors nodes, large memory nodes and GPUs to facilitate specialized research. Four book chapters and 33 publications have emerged from the centre during the year.

The thrust areas of research for the CoE at IISc, Bangalore are genome analysis, development of new algorithms, internet computing, structural analysis of biological macromolecule, structural pharmacology, computational immunology. The centre has developed software packages for structural biology such as CSSP, MIPS, FAIR and SSMBS. The centre supports the Interactive graphics facilities. Twenty four research papers in high impact journals have emerged from the centre.

The CoE in Bose Institute, Kolkata is undertaking research in the area of genome analysis, molecular evolution, genetic engineering, regulatory RNA, stem cell & oncogenomics, structural bioinformatics, ligand-design and network biology. The centre has developed two web servers: PVT (pipeline version of TopHat); PVT Cloud for implementing PVT pipeline in cloud computing systems and has published 21 high



impact papers in the current year. The centre also offers web services in the six selected areas.

The main activity of the centre at MKU, Madurai has been on structural genomics of prophage proteins, structural bioinformatics of membrane proteins, studies on protein aggregation in human diseases. The centre also coordinates the network teaching programme involving MKU, Anna University and Pondicherry University. The centre has published eight research papers

The CoE at Pune University focuses on genomics, proteomics and phylogenetic analysis of infectious viruses such as mumps, rhinovirus, dengue etc. The centre has developed a number of databases and servers viz. RTD – phylogeny server, HRV typer – Human rhinovirus server, BDE – Bio Db extractor, IRESPred server for cellular and viral internal ribosome entry sites prediction, AEROMONAS ML styperto identify the *Aeromonas* sp. and has published about 16 papers and three book chapters during the year.

Distributed Information Centres (DICs):

As part of BTISnet eleven Distributed Information Centres (DICs) in Bioinformatics have been established. The focus of these centres, like CoEs is high quality research, education and services. The DIC at CCMB has developed a database on miRNAs and their targets in breast cancer, sequenced four bacterial genomes including of Psychrophilic bacterium, *Sphingomonas antarcticum*. They have published 21 research papers. CCMB has also developed a tool for identification of histone free regions (HFRS) at HOX loci. The DIC at IARI, New Delhi has divided the research activities in three areas of genomics, proteomics and chemo-informatics.

The IMTECH Chandigarh, DIC has developed 6 web servers and 9 databases including t-RNAmod for prediction of t-RNA modifications, HLP for prediction of half life of peptide in intestine like

environment, ntEGFR – open source web server for predicting inhibitory activities of molecules. The centre has published 22 peer reviewed publications. The most notable achievements by the researchers working at the NII, New Delhi centre is the development of Ten Web Servers including Substrates of PDZ domains, Analysis of miRNA-mRNA base-pairing, Analysis of PKS/NRPS, Motif Discovery, Analysis of enzymes catalyzing novel PTMs, Substrates for MHCs & Kinases. The centre has published 6 research papers. The DIC at Kerala Agriculture University, Thrissur has created new databases DIACAN (Antidiabetic and Anticancer Medicinal Plants Databases) and MangoDB a complete web source for varieties of mango cultivated in Kerala. The DIC at M.S. University, Baroda has divided the research activities in five areas of genetics, molecular biology, immunology, industrial fermentation and biophysics. The centre's two bioinformatics publications got the status of "highly accessed" papers in peer reviewed journals. The researchers working at the University of Calcutta, Kolkata centre has carried out the bacterial clade, Hadobacteria which is famous for the high resistance to gamma & UV radiation as well as their ability to survive in high extreme environment. The centre has also developed novel and simple quantitative measure for automatically evaluating the biological relevance of one or more clusters of genes. The centre has published 18 research papers and two Book-Chapters.

Sub-Distributed Information Centres (DISCs):

Fifty Sub-DICs are functional as part of BTISnet at various Institutions/ Universities. These centres were mainly established with the aim to provide service to the research community. However these centres are now also imparting training in bioinformatics through workshops. Many

centres have now ventured in bioinformatics related R&D activities and have also developed information resources in form of databases.

ACTREC, Mumbai has developed a Histone database and a webserver namely PNAS (Predict Putative Substrates of Proteases). At BHU, Varanasi centre has developed Akriti v1.0 tool for physico-chemical properties calculation for multi FASTA proteins. They have also published nine peer reviewed research papers. The DISC at Bharathidasan University, Tiruchirappalli focuses on Cynobacterial-Bioinformatics. The centre has also developed two important tools namely CKB (Cyanobacterial Knowledge Base) and Syn-R-io, is an interactive R application based on the shiny package for visual exploration of *Synechocystis* 6803 chromosome with simple data extraction. CARL, Port Blair has developed database for corals, horticulture crops, and butterflies in the Andaman and Nicobar island. Central Plantation Crops Research Institute, Kasaragod has developed databases and software packages like (a) COCMAP-Pred: a tool to predict sequences with MAP Kinase domains from coconut transcriptome data. (b) SmiRNA: A ready-made software package for the large-scale of discovery, annotation and prediction of miRNAs in plants. (c) A transcriptome database was created from RNA-Seq of coconut leaves and embryogenic calli on an Illumina Hi Seq 2000 platform. The major thrust areas of the centre at CSTRI, Mysore is Seri-biotechnology and Seri-bioinformatics. A number of databases for silkworm and mulberry have been developed. These include SILKPORT (an annotated protein database for silkworm and Mulberry), SilkTF (for silkworm specific transcription factors), Mulberry genome database, The Silk e-lab (on silkworm genome and proteome) and Soilinfo (providing information on type of soil, its physio-chemical characteristics, nutrient composition etc). IIIM, Jammu has developed theoretical models for the screening

of *Escherichia Coli* (Ec) GlmU protein inhibitors. The centre has also created MedchemDBportal, a compilation of various pathways, crystal structures and target details related to stem cell research. IISR, Calicut has developed Sequence Repository of IISRdatabase, designed to store the sequence information from the projects carried out at IISR and updated Ginger transcriptome database, and *Phytophthora* genome database. The major activities at IIT, Kharagpur include microRNA analysis in *Cajanus cajan*, structural analysis of intrinsically unstructured protein, macromolecular assembly in ribosome, cDNA-microarray analysis of *Entamoeba* genome, protein-RNA interactions, Metagenomics, Immunoinformatics. A Biomaterial database: Biomat_database has been developed by the centre and published in a reputed journal. The National Institute of Oceanography, Goa has developed databases on "Fungi associated with marine sponges of India" and Mangroves of India. The centre has also developed computer aided taxonomic identification system for class: Bivalvia. NIPGR, New Delhi has developed NEXCADE: an online webserver for Perturbation analysis of complex networks, PLecDom : Plant lectin Domain Analysis & ESSOILDB: The essential oil database. NBRI, Lucknow centre has developed databases for Legumes of South East Asia (2030 unique legumes), and plants of India (covering 19000 taxa). The centre has published 27 research papers. TNAU, Coimbatore has established millet and pulses database and ProDisC a stand alone tool to predict the inter atomic distance of proteins. The TBGRI, Thiruvananthapuram has created a database for scanned images of 5000 herbarium specimens of JNTBGRI. Phytochemicals from *Mimosa pudica*, *Phyllanthus amarus*, *Hemidesmus indicus* and *Tamarindus indicus* which were docked with Russell's viper venom proteins and have identified lead molecules having inhibitory effect on the activities of named toxic proteins.

Bioinformatics Infrastructure Facilities (BIFs): For Biology Teaching through Bioinformatics (BTBI)

The aim of these centres is biology and biotechnology teaching through bioinformatics. The scheme is designed to expose teachers, scientists and students to the use of bioinformatics in solving hard core biological problems. The centres uses lecture materials, video clippings, demonstrations, tutorials and online facilities for teaching. Hundred and one educational institutions have so far been supported under this scheme.

The BIF at Alagappa University, Karaikudi has developed two databases: Streptococcus pyogenes enzyme inhibitors using Docking studies (SPEIDS) and Ribosomal database for marine bacteria associated with coral reefs, sponges, marine sediments and sea water. The centre has also published 32 research papers with a good impact factor. The BIF centre at CCS Haryana Agricultural University, Hisar has created a database of pests (plant mites) and found Heterotetramer of AGPase of rice (*Oryza sativa*) having p493A mutant large subunit. The BIF centre at FRI, Dehradun is the National Forest Biodiversity Informatics centre. The centre has developed a web portal of Forest Flora of Manipur: A database of Ligneous Plants of Manipur including plants identification system. The centre has also developed the database of forest pathology herbarium (8600 no. of specimens) and DNA finger prints database of *Cedrus deodara* species. Maharani Lakshmi Ammanni College for Women, Bangalore has created databases for Phytomellitus, BambooDb, and Ectomycorrhiza. Manonmaniam Sundaranar University, Tirunelveli has sequenced and annotated above 10,000 genes of earthworm, *E. eugeniae* which will be helpful to understand the biology of the agronomically important animal earthworm.

The centre at the Presidency College, Chennai has registered for five patents for Novel antiviral combination for treating Asian and East Central South African genotypes of Chikungunya & for treating sensitive, isoniazid resistant strains and Multi Drug Resistant Mycobacterium. The centre at Sher-e-Kashmir University of Agricultural Sciences and Technology of Kashmir, Srinagar has developed a pipeline for annotating protein sequences, Transcriptome profiling of double humped camel and Microarray analysis for differential expression of the genes under cold stress in pashmina goat with qPCR for validation of the microarray data. A centre for Venom informatics has been established at the University of Kerala. The University of North Bengal, Siliguri centre has created a database for North Bengal's bamboo's.

North Eastern Bioinformatics Network (NEBInet):

Under the special drive to strengthen the North Eastern States of the Country a Bioinformatics network 'NEBInet' consisting of 29 Bioinformatics centres was established across 8 states. NEBInet comprises of 2 DICs (at NEHU and AAU), 2 DISCs (at IBSD, and Sikkim State Council of Science and Technology) and 25 BIFs (at various universities, colleges and institutions). In order to monitor the progress of these centres the interactive meeting of NEBInet was organised in Tripura University, Tripura on 18th & 19th November, 2015. The Meeting was attended by the Senior dignitaries including university science fraternity, teachers & students pursuing research in the area of Biotechnology and Bioinformatics.

The DIC centre at NEHU, Shillong has specialization in Animal Husbandry & Dairy Technology, Horticulture and Rural Development. The centre is currently working on Helminth parasite database. Also published

two books entitled Dairy and Food Processing Industry-Recent Trends, in Volume -I & II. The DISC at Sikkim State Council of Science and Technology, Gangtok has completed web database of all *Rhododendron* sp. of Sikkim.

The DIC at AAU, Jorhat has done reconstruction of transcription factor-gene regulatory network in rice and miRNA FeedForward Loops. The research work at Assam University, Silchar has developed one database on anti-diabetic phytochemicals and is named as DiaBank. The centre has also published 16 papers in indexed journals. The BIF CAU, Tripura has developed database on Fisheries Resources of Tripura. The CVSc& AH, Aizawl centre has prepared database on animal disease prevalence in NE region, and the animal genetic resources of NE region. The BIF at College of Veterinary, AAU, Guwahati has developed a database BABRONE for human resource available in the major institute of north east India. Also a globally accessible online server has been developed on "Serotyping of common clinical isolates of Salmonella by Multiplex PCR" in collaboration with the Vaccine Research Institute of San Diego, USA. The BIF at DM college, Imphal has done Morphometrics and Molecular Phylogenetic Analysis of certain fishes found in Manipur river System and Developed a Database on Ethnozoological resources of Bishnupur District in Manipur. The centre at Gauhati University, Guwahati modelled important proteins from different organisms like *Varanus komodoensis*, *Silurana tropicalis*, Silk Worm, Turtles, Fish & HIV-2 pol-polyprotein. The BIF at Gurucharan College, Silchar has carried out research activities about the Role of heavy metal tolerant rhizobacteria in sustainable cultivation of rice and MicroRNA & its application. Manipur University, Imphal centre is actively engaged in development of a comprehensive database for pollen grains found in Manipur state. The Mizoram University, Aizawl centre has distributed their research activities in areas of

Molecular Phylogeny, Human Genome Analysis, Molecular Modeling and Docking. The centre has also published 10 research papers with a good impact factor. The centre at Nagaland University, Kohima has done Nucleotide compositional analysis and statistical clustering of 90 species of *Paphiopedilum* species. The centre has also launched a quarterly e-Newsletter. The BIF at IBSD, Imphal is creating an 'Application Database' for the anti-tuberculosis properties of plants available in Sikkim Himalayan region. At Rajiv Gandhi University, Itanagar research activities mainly focus on creation of area-specific plant databases having medicinal value.

BTISnet website:

The BTISNET programme, envisaged as a National distributed bioinformatics network organization, was launched during 1986-87 and this network is having 170 centres spread all over the country. In order to enhance the information availability a website was designed and hosted at <http://www.btisnet.nic.in> for the dissemination of information. This website contains an overview of the BTISNET programme, its participating institutes, taskforce member details, resources, fellowships etc. This is being updated on a regular basis. The details of each of the individual institute along with their contact details are also given in the website. Number of visitors who have visited this site last year was 123,961 and the average per day is 338.

Coordinator's Meeting of Biotechnology Information System Network (BTISnet):

The 27th BTISnet Annual Coordinators meeting is being organised on 3rd and 4th March, 2016 in Nainital, organised by Kumaun University, Nainital. The focal theme for this meeting is "Bioinformatics at the Forefront of Biotechnology Revolution". The Peer reviewed research papers published in last one year by the Centres have been scrutinised and the incentive



awards for the best publishing centres as well as best publications during the year 2015 will be announced in this meeting. This year a special presentation on PFMS has been arranged for awareness creation and for the benefit of the coordinators so that they can update the UCs timely on the PFMS to help the next year release of grant.

BIOINFORMATICS R&D ACTIVITIES

R&D projects supported under competitive grant scheme:

The first R&D proposal in bioinformatics was received by the department in 1999. Since then the department has supported about 130 projects of which 40 are ongoing. The projects have been supported in various areas such as NGS data analysis; Structural Bioinformatics of proteins and nucleic acid; Computational analysis of metabolic pathways; Large scale network analysis; Computational Image analysis; Large scale data-mining, analysis, integration, curation and storage. Some notable achievements of the ongoing projects are as follows:

Establishment of national database on Tuberculosis:

This database is being developed in a multi-centric mode with NJIL&OMID, Agra; NTL, Bangalore; IOB, Bangalore; JNU, New Delhi; IISC, Bangalore and TRC, Chennai as partners. This database is being with the objective to integrate all major aspects of TB infection which allow simple submission of data as well as retrieval for exploratory analysis of information. This website provides links to the participating institutes and the databases/analytical tools developed by them. The whole genome sequences of a Mycobacterium smegmatis laboratory wild-type strain (MC(2) 155) and mutants (4XR1, 4XR2) resistant to isoniazid. The data is publicly available through the GEO database with accession number GSE64132. A prototype has also been developed

for the Tuberculosis pathway resource, in which we have identified 52 protein-protein interactions including 22 post-translational modification reactions between 21 unique enzymes in the pathways. Metabolic control analysis and flux balance analysis has been applied to specific and global pathways in M.Tb (RV Strain) pathways to assess various search of drug targets.

National Mango Database

Development of National Mango Database for providing information on following aspects:

The improved database schema has been developed for uploading all received data from the partner institutions. The information of GIS based analysis, vector layer and thematic maps were generated for mango database. 10 Mangifera species suitability map was generated for South East Asia including India Five hundred eighty two records updated with the details from different patent offices and 303 research based abstract reprints related to mango is also downloaded and updated on database. Details of 511 phytochemicals, 1200 EST, 10000 Nucleotides and 110 Proteins were updated in database. Also a database (<http://mangifera.res.in>) developed for custodian farmers and district information. For efficient management of mango phenology-data a web-based tool was developed in php. This tool provides an aid to the researchers for arranging the phenological data on timescale by decoding phenophases and depicting as images which helps in summarizing the data by generating frequency tables of different phenophases and thus makes interpretation easy. Mango variety 'Rumani' showed offseason bearing in Nagapattinam district of Tamilnadu. In Vellore, Kanchipuram districts, non-commercial mango sucking variety called 'Rasalu' is exclusively used for its juice in these area. Data on status of disease and pest occurrence on mango, production and postharvest technology and the Nutritional & Medicinal values of collected mango varieties

was updated in the database from various parts of India. Based on presence on *Mangifera* wild species, Maximum entropy approach (Maxent) was used for producing predictive maps of species occurrences both as image files and as raster output that can be further manipulated in a GIS. In our database the information included as, Geographical Distribution, Species, Varieties, Botany, Area Production and Productivity, Disease & Pest, IPR Issues and knowledgebase. In knowledgebase - Accession at Gene bank, Accessionbase, Literature base, Chemobase, Genes & Proteins, Technology base, On Farm Conservation, Reprints Paper, and Useful Links. Link for mango database is - <http://www.mangifera.org/litsearch.php>

National Rice Resource Database

Information documentation is key for utilization of genetic resources in crop improvement. The above project is an initiative to generate characterization and evaluation data of selected rice germplasm accessions and develop a user friendly interface to access such information. The project has two components. Component A- Development of database for rice genetic resources for which NBPGR is the lead institute; component B-Development of knowledge based database of rice genome with University of Delhi, South campus as lead institute.

Eight centers viz NBPGR, NRCPB, CRRI Cuttack, DRR Hyderabad, BHU Varanasi, CSSRI Karnal and IGKV Raipur, University of Delhi-South Campus (Text based curation) are partners in the project. So far 15000 accessions (3000 by each center) have been characterized for 30 descriptors (19 qualitative and 11 quantitative) during the last five years. Excellent variability for characters like leaf blade colour, stigma colour, seed coat colour and hull colour awns and panicle has been observed by various centers. From the data on characterization, a core of 1548 accessions has been developed and is being validated at

different centers for certain biotic and abiotic traits. Molecular characterization of core is in progress. NRRD database for accessions has been developed and implemented on server. It consists 15,000 records of rice passports, 3000 (Accessions) X 5 (Centers) X 3 (Years) characterization data and circulation data of accession among centers over the years. An NRRD website has also been developed. A text based database on rice has also been developed by UDSC, South Campus.



HUMAN RESOURCE DEVELOPMENT IN BIOINFORMATICS, COMPUTATIONAL AND SYSTEMS BIOLOGY

As an emerging interdisciplinary area of biotechnology, Bioinformatics is progressively attempting solving of biological research problems through systematic application of IT. Proteomics, genomics, combinatorial chemistry, nanotechnology, spectroscopy and structural and computational biology are having increasing applications of Bioinformatics for data acquisition and analysis. To handle biological research problems, it requires highly trained manpower to deal molecular biology and application of software tools. High priority has been accorded by the Department to this area and has introduced several innovative educational activities to meet

the present requirements including several long-term and short-term educational programs to address this gap. The details are as follows:

M. Sc. Network Program, M.Tech, Advanced P.G. Diploma Courses & Ph.D. Program in Bioinformatics:

The M.Sc. in Computational Biology is a two year Master's programme designed for students who have a good degree in the biological sciences or the physical sciences (computer science, mathematics, physics, engineering). The programme provides specialist skills in core systems biology (such as computing and biology) with a significant focus on the development of computational and mathematical research skills. The programme is ideal for students aiming for careers in industry or academia. This interdisciplinary programme is based in the MKU, Madurai, Pondicherry University, Pondicherry and Anna University, Chennai and has been initiated in a Network mode, on consortium basis two years back. The classes for these courses are being conducted through video conferencing and virtual class room approaches. The objective of the network programme is to share the expertise of teachers as well as the resources which are created by the BTISnet Centres. The program envisages creating of a strong computational and experimental basis to bioinformatics education at the post graduate level.

The other HRD programmes are i) M. Tech in Computational Biology at Centre for Computational Biology and Bioinformatics at JNU, New Delhi ii) M.Sc. in Bioinformatics at Department of Bioinformatics, Pune University, Pune and iii) Post Graduate Diploma course in bioinformatics Calcutta University, Kolkatta, respectively. This year more than 60 students have graduated from these programs this year. The six Centres of Excellence in Bioinformatics of BTISnet including the super-computing facility at IIT, New Delhi are running Ph.D. programs in

Bioinformatics to meet the huge requirement for high-end human resource in Bioinformatics and Computational Biology.

Training Calendar of Short Term Training Programs:

Bioinformatics being a multidisciplinary area, hands on experience to the researchers and students working in the areas of Biotechnology and Life Sciences is provided, by all the BTISnet Centres by conducting one or more short term training programmes each year. A schedule of the important training programmes conducted by BTISNet Centres all over India is published in the form of annual training calendar each year by the Department. This year the training calendar is distributed to all institutes through the btisnet website (http://www.btisnet.gov.in/trainingcalendar/TC_14-15.pdf). The BTISnet centres have organized more than 100 short-term training during the year 2015-16 with focus on a broad spectrum of areas such as knowledge discovery from Data, computational and structural Bioinformatics, network pathways and systems biology, genome and proteome analysis, Bioinformatics with respect to Medical, Agricultural, animal, aqua and Environmental Sciences.

DeLCON Consortium:

The DBT's Electronic Library Consortium (DeLCON) is a significant initiative of the Department of Biotechnology (DBT), Govt. of India, to enhance information resources in its research Institution. It was launched in January, 2009 with the ten DBT member-Institutions with large number prominent handpicked online journals. It is a topical endeavor for providing access to scholarly electronic resources including full-text and bibliographic databases in all the life science subject disciplines to the DBT Institutional community across the country. It facilitates access to high quality e-resources to research Institutions to enhance research, teaching and learning.

The access has now been extended to new 17 more DBT Institutions in 2nd phase of extension in this year 2010 and further 07 members added in the 3rd phase of extension in the Year 2011. In the year 2012 there emerged the enlarged DeLCON Consortium with 33 members. In the year 2013 total members of DeLCON Consortium were 33 Institution. Besides the DBT Institutions, an emphasis has been given to incorporate institutions and universities (both in the state and central government sectors) across the states in North Eastern India. DeLCON provides current as well as archival access to more than 1000+ core peer-reviewed journals and a bibliographic database (SCOPUS) in different disciplines from 22 overseas publishers and aggregators. Presently there are 28 members and 21 publishers in this consortium.

The Faculties, Scientists, Research Scholars, Students and Project Assistants of Institutions covered under DeLCON are the primary beneficiaries. DBT sponsored the entire expenses for DBT organizations for providing e-Journals access through 'DeLCON Consortium'. This consortium has given value addition to the member scientific institutions in terms of access to more number of journals and saving of time

as compared to the print version. The consortium has an excellent usage pattern. For more details log on to <http://www.delcon.gov.in>

Indo-Japan Collaboration:

The Bioinformatics Division is also handling this programme in which four projects were supported in the Bioinformatics area and subsequently four in the Cell Engineering area so far. The bioinformatics projects focus mainly focus on drug development and delivery systems. Four projects supported in the area of Biomedicine and Cell engineering focus mainly on senescence and cell proliferation, with the aim to understand cancers and develop novel ways for intervention using Ashwagandha.

In order to promote close and effective collaboration, AIST and DBT have set up DAILAB [DBT-AIST International Laboratory for Advanced Biomedicine] at the Biomedical Research Institute of AIST in Tsukuba (Japan) on October 3, 2013. In another effort to promote research in the field of biology, life science and materials science, the Ministry of Science & Technology, Govt. of India (DST and DBT) and RIKEN, Japan signed an MoU at NII, New Delhi on 14th Sept, 2013.



Dignitaries releasing the Proceedings of the 26th Annual BTISNet Coordinators Meeting

BIOTECHNOLOGY PARKS AND INCUBATORS

The Department of Biotechnology promotes Biotech research and helps to translate research into products and services. One of the means by which new commercial products was proposed to be achieved was through the setting up the Biotechnology Parks, where facilities for technology incubation, technology demonstration and pilot plant studies are provided for accelerated commercial development of Biotechnology. The Department in partnership with State Governments/ State Government Organisations /Central Government Organisations establishes Biotechnology Parks and incubators in different parts of the country to facilitate biotech product development, entrepreneurship, research, innovation.

Biotech incubators provide entrepreneurs with a supportive environment to help establish and develop their projects. The idea behind incubators is about creating an environment to help new businesses grow. By providing all needed services on a 'one-stop basis', and enabling overhead costs to be reduced by sharing facilities, these incubators can significantly improve the survival and growth prospects of start-ups and small enterprises at an early stage of development. An incubator is a multitenant facility providing affordable lab space and common instrumentation and other shared facilities in an environment that promotes the growth of small companies. The major issues for many start-ups are cost control and access to good advice and information which is attempted to be provided at these incubators.

Department of Biotechnology has over the years been assisting in the setting up of Biotech Parks and clusters in different States. This involves getting a group of interrelated companies, top

academic universities/institutions and service providers, together at a location, generally in a public-private partnership mode to promote biotech development, technology transfer and partnerships between tenants. It is expected that a vibrant biotech community will provide new products, services, jobs, income and prosperity to the region. Following Biotech Park and Incubation Centres have been established and have become operational :

- i) Lucknow, Uttar Pradesh
 - i) Hyderabad BT Park, Hyderabad, Andhra Pradesh
 - iii) TICEL Bio Park, Chennai
 - iv) The Golden Jubilee Biotech Park for Women, Siruseri, Kanchipuram District, Tamilnadu
- Other Biotech Park/Incubator projects which have been approved and are at various stages of development include:
- i) Assam: Guwahati Biotech Park
 - ii) Karnataka: Bangalore Biotech Park
 - iii) Kerala: KINFRA Biotech Park
 - iv) Odisha: Bio Pharma-IT Park, Andharua, Bhubaneswar

A. FUNCTIONAL BIOTECHNOLOGY PARKS AND INCUBATION CENTRES

(i) BIOTECH PARK, LUCKNOW

Biotech Park set up jointly by the Department of Biotechnology, Government of India and Department of Science & Technology, Government of Uttar Pradesh continues to provide an enabling environment for upcoming

entrepreneur to set up their R&D units in Park by providing incubator facilities. Biotech Park through its operational linkages with local CSIR and other institutions which are centers of excellence in their domain, is promoting bio-entrepreneurship in Uttar Pradesh. In a short time, it has fulfilled not only dreams the country had in 2002 when Lucknow was declared as "Biotechnology City" but also has enabled the state to provide a platform for "Make In India" Mission.

The Biotech Park is providing useful services to society by providing Bio-agriculture products like tissue culture banana plants, biofertilizers, biopesticides and Human Resource. The production capacity of Biofertilizers and Biopesticides (both liquid and solid) has also been increased. The Biocontrol Laboratory of Biotech Park has been certified for food safety management system under ISO 2200:2008 and also obtained manufacturing license of registered Biopesticides strains *Trichoderma harzianum* and *Pseudomonas fluorescens* (License No- 277/UP/LKO) and has started production. The NABL Accreditation of the Analytical and Quality Assurance Laboratory has been renewed with enlarged scope. Accordingly, the laboratory is now able to perform analyses of oils (essential and vegetable), soil, water (drinking, ground and surface water), herbals, pharmaceuticals and nutraceuticals. The Park provided its analytical and other support service to its present 17 incubates, local industries and R& D institutions. The Testing and Analytical facility of Biotech Park continues to undertake analyses of heavy metals, aflatoxin and other contaminants as well as of active molecules for the entrepreneurs located on the Park and helping other biotech companies/institutions and research students. In addition Park provided extraction facility to new venture business for agri-business, pharmaceutical, biochemical, nutraceuticals,

healthcare and other micro-manufacturing companies.

The park has brought in a culture of tissue culture in the state and price of tissue culture raised banana plantlets reduced from Rs. 22 to Rs. 14 per plant leading to increase in banana cultivation in the state. This season, Biotech Park has stepped the production of tissue culture 'grand naine' banana plants to 22 lacs and supplied 18 lacs net pot plants and 4 Lac hardened plants to farmers.

This year, an ex- Senior Scientist of CDRI, Lucknow has established her company M/s NexteLifesciences Pvt. Ltd. and other new company join hands with Biotech Park is M/s Pirinc Pharmaceuticals Pvt. Ltd. set up their R & D unit for the production of Herbal products (pain relieving - oil, gel) with the technology of CIMAP. Now Park hold hands of 17 companies out of which 2 are in biopharma, 3 in bioinformatics & bioservices, 10 in health area (diagnostics, herbal cosmetics, nutraceuticals) and 2 in Bio-agri area (two being run in PPP mode). These companies have made capital investment of approximately 24 crores and created number of jobs. Three companies have taken land on lease. M/s. Lifecare Innovations, a Biopharma Company, located in the Park is now producing liposome products- Fungisome I.V, Fungisome Gel, Psorisome Gel, Coltar S and Coltar SS. The Fungisome I.V is their most effective and least toxic product world wide for treatment of fungal infections. Recently, the facility has been successfully inspected by Columbia Regulatory Agencies and Lifecare Innovations looks forward to supply its products to Columbia. M/s Chandan diagnostics, another company in biopharma sector is fully functional. The third company Amor Herbals Pvt. Ltd, which has constructed their own building, is in process of installing equipments and will go into production and its R & D work has started.

The Park continued to impart training to B.Tech

and M.Tech Biotechnology students. The Park has been registered as Government training partner under Uttar Pradesh Skill Development Mission Program for providing training in the field of agriculture, perfume, flavor & fragrances. About 250 graduates and postgraduates students received short-term & long-term training in different areas of biotechnology. The seventh batch of Biotechnology Finishing School will be starting from January 1, 2016. Most of the pass-outs have been able to get placements. The Park continues to collaborate with Lucknow University and Integral University as per the MOU.

Biotech Park has also signed a MOU with Babasaheb Bhimrao Ambedkar University, Lucknow for sharing facility for Research & Development and Human Resource Development. Another MOU has been signed with SIDBI Innovation and Incubation Center (SSIC) of IIT, Kanpur. This will provide a platform to facilitate Biotechnology Business and entrepreneurship development in the state.

Three DBT sponsored training workshops entitled: Application of Molecular Dynamics Simulations in Molecular Modeling and Drug Designing; Recent Advances in Bioinformatics, Agri-informatics and Biomedical and; Bioinformatics and Cheminformatics Approaches in Computational Aided Drug Designing were organized in which total 86 students from different institutions from Lucknow and other places were trained.



Biotech Park, Lucknow

(ii) Biotechnology Incubation Centre, Hyderabad, Andhra Pradesh

This Incubation Centre has been established by CSIR-IICT and Govt. of AP with support from DBT and is owned by the Society for Biotechnology Incubation Centre (SBTIC). SBTIC has selected Alexandria for operating and managing the facility. This Incubation Centre is being run by Alexandria as Alexandria Innovation Centre, Hyderabad after extensive remodelling into a State-of-the-Art Research Facility for Start Up / Early Stage Companies.

World class facilities have been created for use by entrepreneurs on use and pay basis. There are 12 plug and play modular labs of 350 sq. ft each which is given out to companies. Business centre approach is being used in this Park and 9 companies are operating, 74 scientists are working there at present. The Park has office spaces supported by wide range of shared scientific equipment, amenities and support services which are accessible by the client tenants without making any substantial upfront investment.

BT has provided support for current good manufacturing practices (cGMP) compliance for Pilot plant facilities, required for quality manufacturing and for minimizing contamination. State-of-the-art cGMP Pilot Plant facilities are being set up with the following specifications:

- Cell Culture Fermentation System (30 Ltr)
- Microbial Fermentation System (20 Ltr)
- Microbial Fermentation System (200 Ltr)



Alexandria Innovation Centre, Hyderabad

**(iii) TIDCO Centre for Life Sciences (TICEL)
Bio Park, Chennai, Tamil Nadu**



The Park was established by Tamil Nadu Industrial Development Corporation Ltd. (TIDCO, an undertaking of the TN State Government with support from DBT. This Park has created infrastructure for Biotech R&D, on 5 acres of land in Chennai at a capital outlay of Rs.62.5 Cr. It has now achieved 100% occupancy with National and International clients. The tenancy area has 74 modules of 1525 sq.ft. each, available for clients to develop their own customized R&D labs of BSL2 standards, upgradeable to BSL3, in accordance with GLP standards. Clients can install their facilities appropriate to perform their independent research.

DBT had sanctioned grant for purchasing equipment towards establishing a Biotechnology Core Instrumentation Facility (BTCIF). The BTCIF will be located in TICEL II which is a new tower.

The Higher Education Department, GOTN has released grant towards establishing Training Centre at TICEL - II for providing training programmes in collaboration with the Universities. Laboratory facilities at BTCIF include Microbiology, Molecular Biology, Fermentation, Downstream Processing, Purification, Analytical Support, Animal Cell Culture Facilities and Utilities. The sources of income include Sample analysis services, Hands

on training for students/ trainers, Lease rentals from equipped laboratories. The park is fully funded by TIDCO and savings are being invested for new buildings while the equipment for the BTCIF is being supported by DBT.

(iv) The Golden Jubilee Biotech Park for Women, Siruseri, Chennai

The park was established by Govt. of Tamilnadu at Siruseri, Kanchipuram District with support from DBT and is fully functional since 2001. The park was registered as a Society under the Tamil Nadu Society's Registration Act 1975. It is a joint project of the Government of Tamil Nadu and DBT.

The Park has a Lab facility for providing Quality testing and Training programs for providing hands-on experience and to generate revenue streams for the Park. It is an entrepreneurial facility for women Scientists aided with managerial skills and capable of making small-scale investment, to independently take up the functioning of the lab. At present the park is fully occupied. 80% comprises of 1st generation entrepreneurs. All entrepreneurs are women. In all there are 150 workers which includes 50-60% of women both skilled/unskilled. The total annual turnover is Rs. 5 Cr. The production units that have been set up are for herbal cosmetics, bio-pesticides, bio-fertilizers, spice fortified with herbs, and essential oil, ready to eat snacks etc.



Bio-based Products



Women labour at work

ONGOING PROJECTS: BIOTECHNOLOGY PARKS & INCUBATION CENTRES

(i) GUWAHATI BIOTECH PARK TECHNOLOGY INCUBATION CENTRE

The project for the setting up of Guwahati Biotech Park Technology Incubation Centre submitted by the Govt. of Assam has been sanctioned by the DBT. An interim facility for the Incubation Centre has been built in an existing building of IIT Guwahati. This facility now has 8 Modular Laboratories, Specialized & Support Facilities ready to be used. A common instrumentation facility is being equipped with sophisticated instruments. The progress of the development of the Park is regularly monitored by GBPIC Management Committee and Technical Advisory Committee. This incubator is now trying to attract companies and incubates to develop commercial products based on the rich natural products of the region.

Govt. of Assam has recently allotted a land measuring 17 acres to Guwahati Biotech Park in proximity to IIT Guwahati for setting up of GBPIC. Assam Govt. has extended budgetary support for procurement of land and for construction of

perimeter fencing and land development cost for the permanent campus of Guwahati Biotech Park in the F.Y. 2013-14. The Incubation Centre in the interim facility will be shifted to this permanent location.



Modular laboratory



Common Instrumentation Facility

(ii) BANGALORE BIOTECHNOLOGY PARK

The project was sanctioned in the year 2005 and set up began with combined efforts of KBITS and DBT. The project has been extended to 2014-15.

Civil Construction (Nirmithi Kendra) is ~80% complete with 25 Incubation suites ranging

from 200 sft to 700 sft. Also includes Common Instrumentation facility, Mammalian and Plant tissue culture, Dark room/Cold room/Utilities, Animal house/Chemical store, Cafeteria/ Meeting rooms/Conference rooms etc.

Services including Plug and Play modular laboratories, Common equipments facilities, High End Equipments and Facilities, Mentorship, Funding, Networking, Branding, Legal, Finance/ Accounting will be made available to incubates and startup companies. This Park will assist in Cluster Development by-

- i) Facilitating Bio Helix Park Development by attracting Big/Medium Sized companies
- ii) Having linkages with Public R&D and Academic Institutions- IBAB, CHG
- iii) Advocacy and Policy Research
- iv) Creation of Value Networks



Bangalore Biotechnology Incubator

(iii) KINFRA BIOTECH PARK, KALAMASSERY, KOCHI, KERALA:

The proposal for setting up of a Biotechnology Incubator at Kerala Biotechnology Park was sanctioned in March 2005. Biotechnology Incubation Centre (BTIC) in 4 acres of land with

a total built up area of 50,000sq.ft is the key attraction of Biotechnology Park . It has been set up for accelerating and supporting the research process of entrepreneurs. M/s BCIL was the consultant for setting up of BTIC. A common facility lab in an area of 8000Sq.ft also set up for the entrepreneurs as well as incubates in the biotechnology park. M/S Rajeev Gandhi centre for Biotechnology is the Institutional Partner of KINFRA for operating the Lab.

The ground floor facility is provided with six Incubation modules for allotment. Entrance lobby has been cordoned off with two conference rooms and the reception area. The mezzanine



Chief Minister of Kerala, Mr Oommen Chandy, unveils a plaque after laying the foundation for the Kinfra biotech park at Kalamassery near Kochi

Since the BTIC was made operational in the year 2009, 5 incubatees have hired the space namely M/s. UBIO Biotechnology Systems Private Limited, M/s. Biosix Peptides, M/s. InnoBreez, M/s. Bipha Drug Laboratory and M/s. Ayurker. Due Care Herbals and Orion have applied for allotment of one module each. Out of these, UBIO has graduated in the Business Enterprise Zone (BEZ).

(iv) Odisha Biotechnology Park

The Govt. of Odisha proposal for setting up of a Biotech Park and Incubation Centre at Andharua,



Bhubaneswar was approved by DBT in 2009-10. The facility is being developed in Bhubaneswar on a land parcel of 64.61 Acres, which include Bio Tech Incubation Centre with 9.75 Acres, Bio-Tech Corridor - 25 Acres, IT Corridor - 15 Acres and Residential/Commercial space - 14.86 Acres

The Biotech Incubation Centre with 10 Incubator modules to be structured in the Park and will function under control of the Society for Development of Biotechnology in Odisha. The Park is to be developed in Public Private Partnership mode and M/s Bharat Biotech International Limited has been selected as Project Developer. The Industrial and Infrastructural

Development Corporation (IIDCO) will be implementing the project on behalf of the Orissa Govt. The Park shall be developed in two phases. The Park has sought extension for execution of the project.

NEW PROPOSALS: BIOTECHNOLOGY PARKS & INCUBATION CENTRES

Proposals for setting up of new Incubators/Parks have also been received from the states of Jammu & Kashmir, Gujarat, Chhindwara, West Bengal & Chattisgarh. These park proposals have been evaluated and Expert Committee has advised them to revise and improve upon the proposals.

INTERNATIONAL COLLABORATION

“Without effective international collaboration we would have limited access to breakthrough scientific knowledge generated by researchers in other countries; the quality of the scientific knowledge generated locally would decline and; our industries would be unable to obtain innovative technological information and knowledge needed to maintain their competitive edge. The future of our health system depends on having a critical mass of health scientists with the international knowledge and intercultural skills necessary to meet globalization’s challenges.”, quote unquote Canadian Institutes of Health Research.

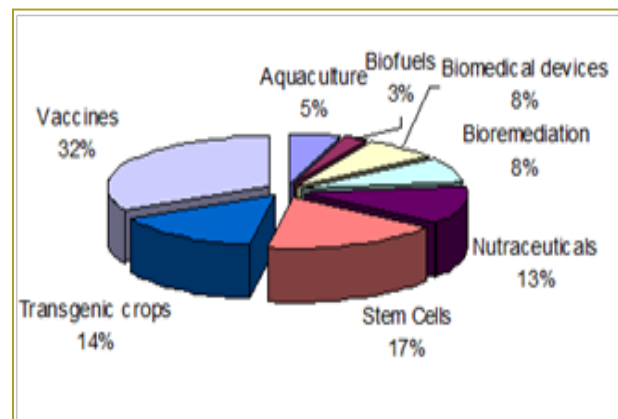
With climate change impacting global agriculture, marine and aquatic life and the threat of new emerging pandemic diseases; international collaborations become exigent. The Department of Biotechnology has in this year not just expanded International Collaborations but have developed partnerships which address the most challenging issues in marine biology, agriculture, health or human resources.

Australia

Under the Indo-Australian Biotechnology fund a ninth round of joint call of proposal was announced. The priority areas of the call were Food and agribusiness and Clean energy technologies. Twenty three proposals were received under the call and are being assessed and ranked by the IABF Advisory Panel.

The support under the programme led by more than 100 principal and co-investigators, with many postdoctoral researchers and students working along side them has been analyzed and

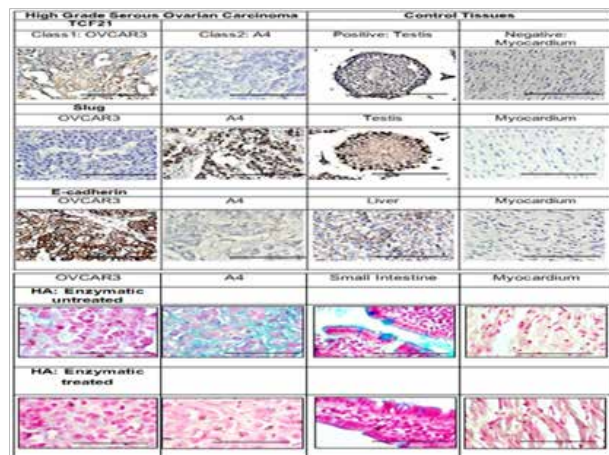
graphically presented e.g. area wise distribution of projects etc. Hundred and Seven exchange visits by the Scientists and Forty by students have taken place. One Hundred and Forty one students have been trained so far.



Researchers at Centre for Nanoscience and Molecular Medicine, Amrita Institute of Medical Sciences, Cochin in association with Australian counterparts have developed antigen conjugated nano-particles which suppress clinical symptoms of multiple sclerosis. These nanoparticles have potential to be developed into a therapy. In association with Australian Counterparts using immuno-modulatory peptide conjugated nanoparticles have confirmed that antigen conjugated silica nanoparticles were able to suppress the EAE clinical symptoms and has potential in developing a therapy in the dreaded disease multiple sclerosis.

In an attempt to identify key regulatory molecules governing migratory properties in High Grade Serous Ovarian Carcinoma (HGSC), the tight intra-modular correlation amongst the genes was initially demonstrated from the expression profiles of the TCGA class specific samples at

National Centre for Cell Science, Pune. Network analysis coupled with transcription factor (TF) binding site prediction identified 11 TFs which exhibited a molecular class-specific expression profiles. Several TFs exhibit cross- interactive capabilities that facilitated derivation of an underlying TF network. Understanding these expression profiles will provide insight into cancer development and progress.



Representative Immunohistochemical stained images for TCF21 (Row1), Slug (Row2), E-cadherin (Row3), and histochemical stained images for Hyaluronic acid (HA) untreated with enzyme (Row4) and enzymatically treated (Row5) sections. TCF21 and E-cadherin expressed is observed in OVCAR3 xenografts and not in A4 xenografts whereas Slug is expressed in A4 xenografts. The positive expression controls for TCF21 and Slug is testis tissue and negative expression tissue is myocardium.

Brazil

Under Indo-Brazil cooperation, a second Joint call for Proposals was announced in priority area of Agricultural biotechnology of Sugarcane, Biofuels and Red & White Biotechnology. Out of the 51 proposals received, 36 proposals were reviewed. After completion of the evaluation process, 6 proposals are recommended for

support from both sides.

Canada

Department has ramped up its collaboration with different Canadian agencies. A major initiative was announced during the visit of Hon'ble Prime Minister of India to Canada in April, 2015. In this initiative, five health innovations in India will be funded by Department and Grand Challenges, Canada, funded by the Government of Canada. An investment of \$2.5 million each from both sides was agreed upon.

Department in collaboration with IC IMPACTS (the India-Canada Centre for Innovative Multidisciplinary Partnerships to Accelerate Community Transformation and Sustainability), Canada under the ongoing programme "Water for Health" have funded four projects. In order to further collaboration with IC -IMPACTS a joint call in the area of "Portable Diagnostics and Analyzers" was announced. Under the joint call collaborative research projects focused on the development and evaluation of new diagnostics and analyzers for Infectious Diseases, Maternal and Infant Health, Nutritional Deficiency and Interdisciplinary Approaches and Platform Technologies will be supported.

A paper based device for testing water quality for *E. coli* load have been developed under project "Remote Sensing Network for Water Quality Management (SWQ)" jointly funded under DBT-ISTP, Canada collaboration. Researchers within institutions from India (IIT, Mumbai) and Canada (University of Alberta) have developed device based on flow characteristics. The device is easy to fabricate, cost effective and is suitable for resource limited settings.

Denmark

Department in collaboration with Innovation Fund Denmark (previously Danish Council

for Strategic Research) announced a call for proposals inviting Strategic Research Projects within Human Health Biotechnology. Under the call one project was jointly recommended for funding.

The ongoing collaborative project entitled “MicrobDiab” with institutional partners from India (Madras Diabetes Research Foundation, Chennai; THSTI, Faridabad and TCS, Pune) and Denmark (University of Copenhagen, Denmark) is expected to unravel the holistic status of pancreatic hormones viz., insulin, c-peptide, amylin and glucagon at the interface of type 2 diabetes pathogenesis and gut microbiome connectivity. Under the project 400 subjects have been recruited. The subjects are clinically well characterized for normal glucose tolerance (NGT), impaired glucose tolerance (IGT) and type 2 diabetes (T2D) and subjected to state-of-the-art metagenomics profiling to unravel the diversity, richness, abundance and functional repertoires of the gut microbiota. The metagenomics data along with the systemic levels of inflammation, gut metabolites and gut metabolite activity, their relationship to the receptor and non-receptor mechanisms, and clinical correlates of insulin secretion and insulin action are expected to unravel novel drug targets directed towards development of new therapeutic measures.

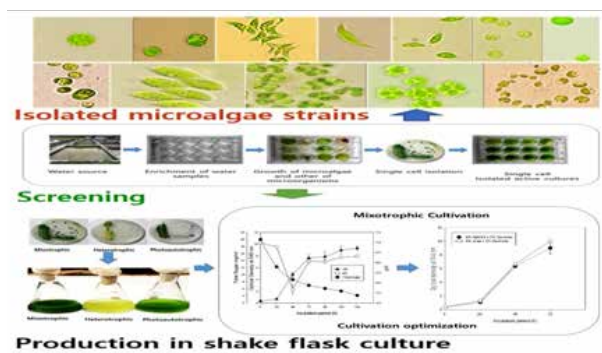
Finland

Department in partnership with TEKES, Finland (a funding agency for technology, innovation and industry collaboration) invited proposals in the area of “Innovative health and well-being solutions for all” through joint call. Under the joint call, two proposals have been recommended for funding.

Project “Finnish-Indian Ingredients for Improving Food Safety and Health” supported under DBT-TEKES collaboration is aimed to develop bio-insecticides for storage insects. Researchers from

CSIR-CFTRI, Mysore and University of Turku, Finland have successfully demonstrated that the oils (Clove leaf, Cumin, Caraway, Nutmeg, Ajwain, Oregano, Basil, Lemon, Thyme, and Mint) can be used as fumigant compounds against storage insects as exhibited by LC50 and LC90 mortality of storage insects. These oils are biologically safe and can be used as food.

Researchers have isolated 15 new strains of fresh water microalgae which show high lipid accumulation rates and have standardized protocols for the isolation and cultivation for range of fresh water microalgae for the production of omega-3 under the project entitled “Health promoting food and feed micro-algal omega-3 fatty acids, pigments and bioactive peptides produced on food industry side streams (ALGOMEG)”. Partnering institution in the project are GBPUAT, Pantnagar and University of Turku, Finland.



France

Department has signed a Memorandum of Understanding (MoU) The University Pierre ET Marie Curie (UPMC) and The Centre National DE LA RechercheScientifique (CNRS) for the establishment of a National Institute of Marine Biology and Biotechnology in India. The MoU was signed by Secretary, DBT, in the presence of Hon’ble Prime Minister of India and the Hon’ble President of France during the Prime Minister’s visit to France in April, 2015.



Memorandum of Understanding being signed by Prof K. Vijay Raghavan, Secretary, DBT, Prof. Jean Chambaz, President UPMC and Prof Alain Fuchs, President CNRS, in the presence of the Hon'ble Prime Minister of India Sh. Narendra Modi and the Hon'ble President of France Mr François Hollande on April 10, 2015

Germany

In collaboration with German Federal Ministry, Science Research and Technology (BMBF), the Department has agreed to participate in the joint call for proposals focusing on Biotechnology for reuse of biodegradable urban solid waste and Biotechnology for reuse of biogenic raw materials in agriculture. Joint call will be issued in February, 2016.

With Deutsche Forschungsgemeinschaft (DFG), Germany, DBT has agreed to establish the Research Unit for "Social-Ecological Systems in the Indian Rural-Urban Interface: Functions, Scales, and Dynamics of Transition" at UAS, Bangalore in collaboration with Kassel University and Goettingen University, Germany. The Research Unit has been established for a total funding period of six years.

Netherlands

Department and its subsidiary company the Bharat Immunologicals and Biologicals Ltd (BIBCOL) has signed a Memorandum of Understanding with the Institute for Translational Vaccinology (Intravacc) of the Kingdom of Netherlands on

"Development of Vaccines". The MoU was signed during the visit of the Prime Minister of Netherlands to India on 05th June, 2015. Intravacc and BIBCOL have agreed to partner with the aim of setting up of a measles-rubella vaccine plant for BIBCOL.

In collaboration with Netherlands Organization for Scientific Research (NWO), Netherlands Department announced a joint call for proposals in the area of "Crop sciences: improved tolerance to heat and drought". Three joint proposals in crop sciences were funded.

Department in association with NWO/STW, Netherlands organized an expert group meeting with thematic focus on "Water and Health". In the expert group meeting it was decided to announce a call for proposals focusing on Demonstration project for treating waste water in Delhi. Call will be announced in March, 2016.

Russia

Under the 'Programme of Co-operation' (PoC) between and Russian Ministry of Education and Science, Russian Federation in the area of Biotechnology five joint proposals in area of Nano-biotechnology, Affordable diagnostics and devices in Human Health and Bioenergy have been supported.

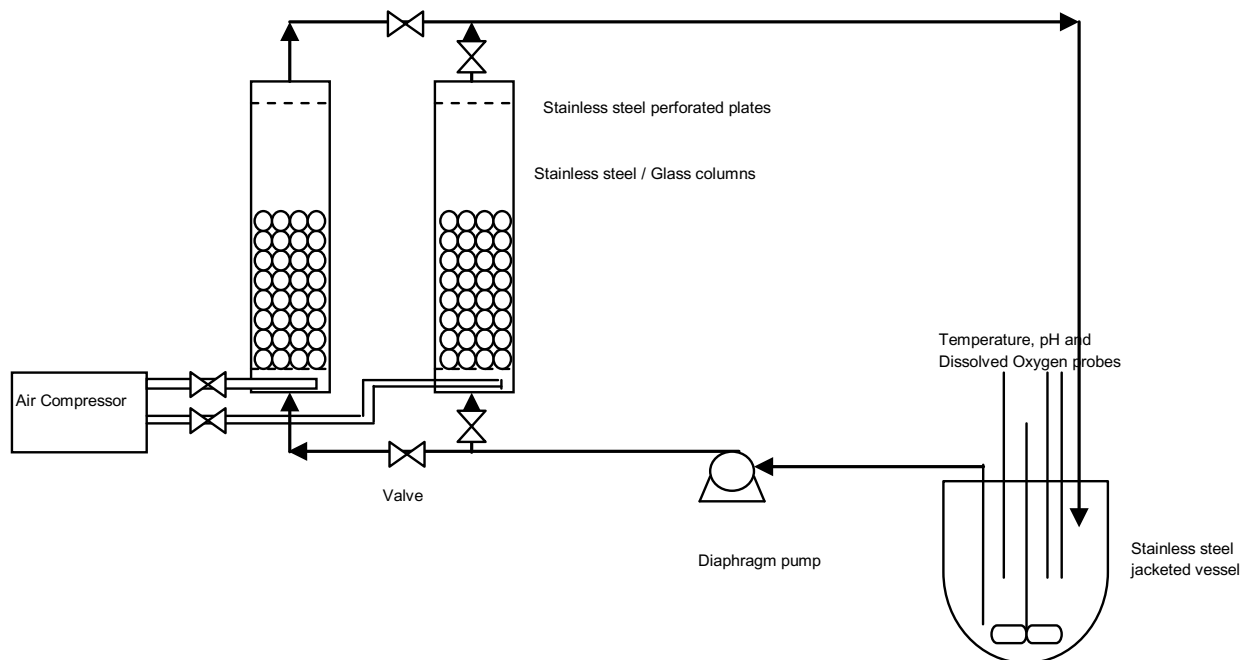
Spain

Department has collaborated with CDTI, Spain (The Centre for Industrial Technological Development) an enterprise of Ministry of Economy and Competitiveness, Spain for technological development and innovation of Spanish companies. Under the third DBT-CDTI joint call for proposals in the field of Biotechnology three proposals were recommended for funding.

Loyola College, Chennai; MDRF, Chennai; TVN Food Products, Salem and Spain (The University

of Valencia Science Park, Spain) have developed an industrial and household fermenter, for sugar free and non-alcoholic pomegranate juice for diabetics using immobilized yeast cell technology

Feed trials of the juice on *C. elegans* show marked reduction in fat content of the worms.



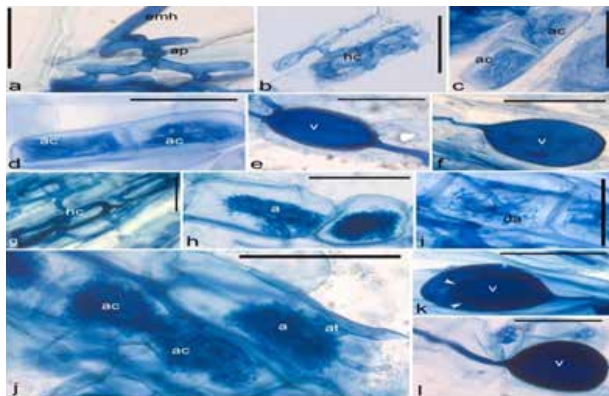
Process flow chart for the production of sugar free non-alcoholic pomegranate juice using immobilized *Saccharomyces cerevisiae* employing continuous fluidized bed reactor

Switzerland

ISCB is a flagship programme of the Department initiated in 1974 and entered into the 4th phase wherein food security issues taking into account the farmers' perspective have been given priority. The programme remains exemplary with respect to mission, vision, outcomes and outputs, in particular with the socio-economic dimension and taking forward the research leads along the participatory value chain. During the 4th phase, four network projects have been initiated after signing the joint multiple party agreements by the investigators from both countries. The crops identified in this phase include Cassava, Finger millet and Pigeon pea which have the potential to transform the agriculture in volume and quality.

A new collaborative network project titled "Improvement of pigeon pea for plant type, pod borer resistance and moisture stress tolerance" was initiated with Indian investigators from National Research Centre on Plant Biotechnology (NRCPB), Indian Agricultural Research Institute (IARI) and National Bureau of Plant Genetic resources (NBPGR), New Delhi; and Swiss investigators from Swiss Federal Institute of Technology (ETH), Zurich, and School of Agricultural, Forest and Food Sciences (HAFL), Zollikofen with the objective to develop pigeon pea varieties with improved productivity and resistance to pod borer which can be marketed, processed and priced in line with cereals and competing crops.

In the Biofertilization & Bioirrigation (BIOFI) project for sustainable mixed cropping of pigeon pea and finger millet, field trial of pigeon pea and finger millet in mixed cropping was done and the extent of arbuscular mycorrhizal (AM) fungal colonization and spore density were assessed from the root & soil samples collected from the experimental plots in Bangalore and Kolli Hills, at two different time intervals .



Arbuscular mycorrhizal fungal colonization in finger millet (a-f) and pigeon pea (g-l) from Kolli Hills and GKVK, Bangalore. a, Appressorium (ap) and hyphal entry into root; b, hyphal coils (hc); c, d, arbusculate coils (ac); e, intercalary vesicle (v); f, intercellular vesicle; g, hyphal coils (hc) in roots of pigeon pea; h, Arum type arbuscule (a); i, degenerating arbuscule (da); j, Arum type arbuscule (a) with arbuscular trunk (at) and arbusculate coils (ac); k, vesicle (v) showing internal proliferation (white arrow heads); l, intracellular vesicle (v). Scale bars = 50 µm.

The Ragi network project is envisaged to adopt genomic approaches for genetic enhancement

of ragi for improving yield potential, stress resilience with increased bioavailability of nutrients. It is expected that improved ragi cultivars enhances the socio-economic and health status of both marginal farmers and general public. Molecular diversity of the germplasm accessions is being screened using genomic simple sequence repeat (SSR) markers. High throughput

protocols for the estimation of phytic acid and mineral nutrients have been established. Growth trends in ragi cultivation and productivity has been accomplished .



Genetic diversity in ear head among finger millet germplasm

Sweden

Swedish Governmental Agency for Innovation Systems (VINNOVA) is partnering with Department. Under the partnership three joint calls for proposals have been successfully accomplished. In the current year, a call for proposals partnering DBT, India and VINNOVA, Swedish Research Council was announced in the area of Biotechnology. Under the call proposals were received and proposals were recommended for funding.

Research partners from IIT, Madras; IITM's Rural Technology and Business Incubator (RTBI), Chennai, Blekinge Institute of Technology (BTH), Sweden; BCC (BlekingeCountry Council) have developed antenatal and infant monitoring system (AIM). System is an innovative solution designed to support pregnant women and new mothers in rural India. This system s regularly sent out advisories (as automated phone calls) on the beneficiary mobile phones. It has also successfully captured feedback & health status information from the beneficiary directly, through "Automatic Speech Recognition" (ASR), is a simple yet powerful solution.

Tunisia

Under the joint programme of cooperation, Project entitled “Assessment of the protective effect against Tuberculosis, of a new vaccine composition” has been sanctioned at ICGEB. Major focus of the project is on development of a novel method of vaccination, against tuberculosis (TB), based on enhancement of BCG-mediated apoptosis through FOXO3 activation. The aim of the study is to use a novel vaccine composition made of the classical BCG mixed to FOXO3 activators (Commercially available chemicals and/or drugs capable to strongly activate FOXO3). Such composition would induce higher apoptosis of infected cells than the classical BCG alone and may confer a higher protection against TB.

U.K.

Department in collaboration with U.K partners (BBSRC, NERC, MRC, AMS, British council, DFID, Newton fund, INNOVATE) has launched programmes which touch upon an array of Global challenges which are relevant in local Indian context. Flagship programmes initiated in partnership with U.K are directed to address key issues of health, environment (atmospheric pollution), Climate Change and Agriculture, Antimicrobial Resistance, Vaccine Development and tackling loss of farm produce. Programmes also address underpinning need of improving upon quality of research through bilateral student exchange programmes.

The D.B.T and the Research Councils, UK signed RCUK- DBT letter of intent to work together in Climate Change and Agriculture, Antimicrobial Resistance and Vaccine Development as part of their joint grand challenges. This new initiative was announced during the November 2015 visit of the Hon’ble Prime Minister of India to UK and was endorsed by Prime Minister of UK.

Department and U.K partners (Medical Research Council and DFID) in their ongoing Global Research Programme “Addressing the health needs of women and children in the most disadvantaged populations globally” have funded seven projects. In another ongoing programme “Global Research Partnership in Aquaculture” with partnering agencies BBSRC and DFID, UK; four projects were recommended for funding.

Air pollution in cities is an emerging challenge and key health hazard. In order to address the same Department in collaboration with Earth System Science Organization, Ministry of Earth Sciences (ESSO-MoES), India and U.K partners (Natural Environment Research Council (NERC) and the Medical Research Council (MRC), UK have announced a call for proposals on “Atmospheric Pollution and Human Health in an Indian Megacity-Delhi”.

Department has announced Newton-Bhabha PhD placement programme in collaboration with British Council, U.K. under aegis of Newton-Bhabha agreement. Under the programme PhD students will have an opportunity for international exchange and will enable them to learn valuable new skills or techniques, access facilities or resources and build relationships with potential new collaborators, including industry partners where relevant. DBT and BC, on behalf of Department of Business Innovation and skills will support exchange of 35 students each on respective sides.

The Department has announced Joint call of proposals with the Innovate, UK on tackling challenges in agriculture food sector with particular reference to post-harvest losses. The aim of the call is to form collaborative partnerships with Indian counterparts and translate the outputs of excellent research into new solutions. These solutions being in the form of commercial

products, processes and services fit for the Indian market.

Under the project entitled “A genomics-assisted synthetic hexaploid wheat gene isolation and pre-breeding platform for improved heat tolerance and sustainable production” jointly executed by Punjab Agricultural University, Ludhiana; National Agri-Food Biotechnology Institute (NABI), Mohali and National Institute of Agricultural Botany (NIAB), Cambridge five *Aegilops tauschii* accessions were selected based on stay green and heat tolerance trait. *Aegilopstauschii* accessions were crossed with *Triticum durum* var. PBW114 to generate synthetic hexaploid wheats. Generated synthetics were screened by electrophoresis of seed storage proteins and chromosome count and five synthetics were selected (*Aegilops tauschii* acc. pau14102, 14170, 9809, 14576 and 14128) for their heat tolerance traits.

Partnering institution from India (International Centre for Genetic Engineering and Biotechnology, New Delhi, Jawaharlal Nehru University, New Delhi, Madurai Kamraj University, Madurai, Institute of Chemical Technology, Mumbai) and U.K (University of Nottingham, Nottingham, University of York, York, Newcastle University, Newcastle, Oxford Brookes University, Oxford) are jointly executing project entitled “RICEFUEL: Engineering enzymes, bacteria and bioconversion processes for advanced biofuels from waste grain straw”. Researchers have identified 326 proteins related to biomass degrading enzymes from microbial symbionts present in gut of rice stem borer. Based on their potential role in biomass hydrolysis 20 target enzymes were selected for their further heterologous expression and characterization. Apart from this 24 thermostable enzymes for alkane pathway were mined from metagenome data of hot spring microbial community, their genes were codon-optimized

for expression in *Geobacillus* and commercially synthesized.

In the project entitled “Sustainable bioenergy from microalgae – A systems perspective” research groups from India (Bharthidasan University, Tiruchirapalli; Lady Doak College, Madurai) and U.K (University of Sheffield) have identified algal strains with high lipid content. Strains are one marine microalgae *Chlorella sp.* BDU G91771 with 25% lipid and three fresh water microalgal strains *Monoraphidium contortum*, *Pseudomuriella sp.* and *Chlamydomonas sp* with 65% lipid.

Under the project entitled “Development of recombinant BCG vaccine and complimentary diagnostics for TB control in cattle” researchers from TRPV, Chennai and University of Surrey, U.K have developed an improved Diagnostic method for rapid Detection of antibodies specific for pathogenic *Mycobacteria* in cattle.

Joint India-UK collaboration programme in crop science:

A Memorandum of Understanding was signed on 24 February between D.B.T Ministry of Science and Technology, and a consortium of top UK research institutions for the establishment of a joint Indo-UK collaboration programme on crop science. The aim of the agreement is to enhance collaborative research, promote knowledge exchange, and support capacity building to develop resilience in food security. The agreement was signed by Prof. K. VijayRaghavan, Secretary, D.B.T Prof. Sir Leszek Borysiewicz, Vice-Chancellor Cambridge University and by Dr. Nafees Meah on behalf of the Biotechnology and Biological Sciences Research Council (BBSRC). It will also signed by representatives from the National Institute for Agricultural Botany (NIAB), in Cambridge; the John Innes Centre and the University of East Anglia, in Norwich; and Rothamsted Research.



Prof. K. Vijay Raghavan, Secretary, Department of Biotechnology and Prof Sir Leszek Borysiewicz, Vice-Chancellor Cambridge University ink the MoU on a joint Indo-UK collaboration programme on crop science.

USA

A Statement of Intent was signed between (DBT). and Prakash Lab, Stanford University, USA for 'Development and Deployment of Products from Prakash Lab'. The Statement was signed by Secretary, DBT in the presence of Hon'ble Prime Minister of India on his visit to USA during the India-US STARTUP Konnect event. DBT and Prakash Lab have agreed to enter into an agreement for a pilot programme through the DBT Star Colleges scheme, where the Foldscope will be used as an educational and training tool to understand physics, chemistry, biology and instrumentation. Workshops and training programmes will run by Prakash lab in collaboration with Indian laboratories.



Dr Manu Prakash of Prakash Lab, Stanford University demonstrating the wide applicability of Foldscope to the Hon'ble Prime Minister of India Shri Narendra Modi, at the Indo-US Startup Konnect, September 27, 2015

A series of Foldscope (a foldable; origami paper microscope costing about 50 cents; a great example of frugal science) workshops and talks in India were held. The "India-Prakash Lab Stanford Foldscope training camp: North eastern region twining was held at Delhi, Guwahati and Kaziranga National Park from 16th-21st December 2015



A training camp on Foldscope in progress in Venkateshwara College, Delhi
December 16, 2015

A joint India - U.S working group on Agriculture Biotechnology was set up.

Japan

DAILAB (DBT-AIST International Laboratory for Advanced Biomedicine) at the Biomedical

Research Institute (BMRI), Tsukuba campus of the National Institute of Advanced Industrial Science & Technology (AIST), Japan is the first International laboratory in Life Sciences & Biotechnology. Emerged as a step up from bilateral MoU and aimed to promote close and effective research collaboration and networking, it was established on Oct 3, 2013. DAILAB-TENJI (Training for Technology Exhibit & Networking to Jump for Innovation and Industrialization) B has been participating in industrial trade fairs held in the India and Japan to skill technology exhibiting and networking for innovation and industrialization. Some of these included (i) India-Japan Science Seminar at IIT-Delhi on Feb 26, 2015 Organized by Department of Science & Technology, Government of India and Ministry of Educational Culture, Sports, Science & Technology (MEXT), Japan and Japan Science & Technology Agency, (ii) "Amazing!! State-of-the-art Technology of Japan for Creating Future" seminar and exhibition organized by the MEXT, Japan on Feb 27, 2015 at the 21st International Engineering & Technology Fair (IETF) 2015 at Pragati Maidan, New Delhi, India and (iii) DBT Indian Pavilion at the BioTech Japan 2015 (May 13-15, 2015 held at Tokyo Big Sight represented by DBT, BIRAC (New Delhi) and C-CAMP (Bangalore) and Bharat Bio-Tech(P) Ltd.



DAILAB-SISTERS: DAILAB has initiated SISTER (Satellite Institutes for Special Training Education and Research) labs to further promote joint research and training programs. First SISTER DAILAB was launched at the Indian

Institute of Technology Delhi (IIT Delhi) on November 04, 2015 by Dr. Renu Swarup, Senior Adviser, Department of Biotechnology (DBT), Government of India, in the presence of Prof. R. Chidambaram, Principal Scientific Advisor to Govt. of India and AIST delegation <http://web.iitd.ac.in/~sundar/meeting/piknikh2015-2/>. On the same day November 04, 2015, an Indian delegation under the leadership of Dr. Harsh Vardhan, Hon'ble Union Minister for Science and Technology along with officials from Ministry of Science & Technology, Govt. of India and from the Embassy of India to Japan, visited the DAILAB at AIST in Tsukuba, Japan. The Union Minister for Science and Technology launched the DAILAB website on the occasion, which is available from the URL <http://web.iitd.ac.in/~sundar/dailab>

MULTILATERAL COOPERATION

EU

Department in order to foster multi country relations is partnering in fourth joint transnational call for in the area of 'Human infectious disease research' under Infect-EraNet. Under ongoing initiative with geographical era-net INNO INDIGO, Department has funded five proposals in area of "Clean Water and Health".

Under the project "Integrating Bio-treated Wastewater Reuse with Enhanced Water Use Efficiency to Support the Green Economy in EU and India (India side)". A consortium of 11 research and development partners from India and 22 partners from European Union countries are working in collaboration with a goal to enhance the safe use of treated wastewater in agriculture through valorization and improved water use efficiency through genetic enhancement as well as management practices. Partners have adopted and implemented constructed wetlands (CWs) as low-cost technology for treatment for industrial and municipal wastewater. The constructed wetlands were able to reduce Chemical Oxygen Demand (COD) by 30-92% and developed agro-aqua system as well as emitters for irrigation.

Apart from wastewater treatment and reuse of treated wastewater, partners are also conducting field scale experiments to reclaim degraded land (land degradation due to long-term use of waterwater for irrigation). In case of crop improvement package, drought tolerant traits were introgressed in chickpea and tomato.



Constructed wetland facility developed at KCP Sugar Industries to treat effluent from distillery

Under the project entitled “An attractive and promising strategy for early cancer diagnosis through the assembly of the human cancer volatome” supported under DBT-NEW INDIGO programme collaborating partner institutions from India (NCCS, Pune; CDFD, Hyderabad) and University of Madeira, Portugal; University of Rostock, Germany) are developing non-invasive approach for cancer diagnostics. In an effort in the direction to diagnose lung cancer eleven volatile organic metabolites (VOMs) unique to lung cancer patients have been identified.

European Molecular Biology Organization (EMBO)

Department of Biotechnology, Ministry of Science and Technology has signed aMemorandum of agreement with European Molecular Biology Organization (EMBO) and European Molecular Biology Conference (EMBC) on November 9, 2015. The objective of the co-operation between India, EMBC and EMBO is aimed at increasing scientific exchange between India and EMBC Member States. EMBO/EMBC being a

leadership group will help India with research transnational resources, capacity building, training and leadership & brand building. The EMBO membership includes some of the leading researchers in Europe and represents a dynamic cross-section of the life sciences community. Within EMBO is also European Molecular Biology Conference (EMBC). EMBC is an intergovernmental organization comprising 27 Member States, which are: Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom. EMBC promotes a strong transnational approach to improve quality research in life sciences. EMBC supports a wide range of EMBO activities. EMBC was founded in 1969 to support and finance the actions of EMBO and to give Member States more structured access to the expertise to EMBO Members.

In order to tap and avail this rich pool of scientific excellence, India has become a EMBC Associate Member. By being the Associate member State, DBT would provide nominal fees to be member state which will in turn provide access to core capacity and expertise of EMBO with very well laid out activities. More concretely, in EMBC India could apply to all of EMBO’s programme including:

- Post-doctoral fellowships; within EMBC and Associate EMBC Member States or cooperation states;
- Short-term fellowships; gaining access to high-level co-operation partners and the latest technologies; Courses and workshops; to host scientific events in India;
- Young investigators; gaining access to the network of the best young scientists in Europe and cooperation states;
- Installation grants, attracting scientists to establish research groups in India.

NATIONAL INSTITUTE OF IMMUNOLOGY (NII), NEW DELHI

The programmes of the National Institute of Immunology are focused to study frontier areas of modern biology pertaining to disease processes with special emphasis on the functional aspects of the immune system. During the reporting period the Institute continued expansion of scientific programmes in a multi investigator driven mode to ask challenging questions in biology for improvement of healthcare. The scientific findings have so far been published in 93 reputed journals. More publications of discovery science in reputed high-end journals are expected.

Intellectual Property

The knowledge generated has been patented for application which embodies translational aspects of the on-going research in the Institute and can be considered major outputs during this period. International patent on RECQL4, the DNA helicase mutated in rothmund-thomson syndrome, regulated mitochondrial function has been granted. Another international patent on 'a recombinant vaccine against *Clostridium perfringens* infection and Epsilon (ϵ) toxin intoxication' has been granted and validated in UK. National patent on 'process for obtaining bioactive recombinant protein from inclusion bodies' has been granted and new application has been made for national patent on 'Depletion of *M. tuberculosis* GlmU from infected murine lung affects the clearance of the pathogen'. Another national patent on 'a novel typhoid vaccine comprising of conjugate of Vi polysaccharide with flagellin' is ready for filing.

Technology Transfer

On the innovation front one technology on 'high cell density fermentation' has been transferred to IMGENEX India Private Limited, Bhubaneswar, Orissa. Two important technologies are in the pipeline for transfer. One is 'depletion of *M. tuberculosis* GlmU from infected murine lung effects the clearance of the pathogen', and the other is 'hemoglobin receptor as a novel vaccine for leishmaniasis'. Another noteworthy translational achievement is Memorandum of Understanding with Cancer Institute (WIA) Adyar, Chennai to undertake human clinical trials for cervical cancer employing dendritic cell based cancer vaccine using recombinant SPAG9 protein discovered at NII. This is a direct outcome of basic research to translational medicine. The DCGI approval and RCGM clearance for DC based cervical cancer vaccine trials using recombinant SPAG9 protein have been granted.

Agreements

Seven significant MoUs were signed during the reporting period by NII with various academic institutes/universities for exploring collaborative research. MoU was signed with Singapore Immunology Network (Biomedical Sciences Institutes); Regional Centre for Biotechnology; Licence agreement with IMGENEX India Pvt. Ltd. for transferring technology on 'high cell density fermentation'; CSIR-IMTECH; Birla Institute of Science-Pilani (Hyderabad) and National Institute for Research in Reproductive Health (NIRRH). A multilateral agreement was signed among National Institute of Immunology, University of Toronto (Canada), Regional Centre

for Biotechnology and Translational Health Science and Technology Institute for developing collaborative relationships.

Collaborations

Other major scientific collaborations of interdisciplinary nature initiated in the reporting periods which are expected to encourage innovative and groundbreaking strategies in investigating increasingly novel, complex and convoluted areas for research in cancer and tuberculosis which have societal benefits are:

- (i) Centre for Excellence in Cancer Biology would promote large scale collaboration in cancer research which is the leading cause of morbidity and mortality worldwide
- (ii) Centre for Excellence in Malaria Research - Signaling and trafficking pathways of malaria parasite, protein and lipid kinases, autophagy, proteases, apicoplast, trafficking, Proteases, ligand-receptor interaction, trafficking, ubiquitin proteasome system. The collaboration would accelerate the development of new and effective drugs for wider societal benefits.
- (iii) Centre for Excellence in Vaccine and Drug Delivery using biodegradable polymeric particles is expected to promote novel formulation for vaccines.
- (iv) SysTB: A Network Program for resolving the intracellular dynamics of host-pathogen interaction in TB infection (DBT) - Tuberculosis is a top infectious disease killer worldwide and the collaboration is expected to search for novel anti-TB drugs.
- (v) Indo-French collaboration - Deciphering the role of *Mycobacterium tuberculosis* Serine/Threonine protein phosphatase PstP (CEFIPRA). The collaboration is expected to provide mechanisms usable for drug

targeting.

- (vi) Indo-French collaboration- The institute is one of the participating Institutes in Systems Immunology and Genetics of Infectious Diseases (SIGID) consortium at Institute Pasteur de Lille, France which aims to integrate dedicated multidisciplinary teams in India and France to study the Immunology and Genetics of infectious diseases with a particular focus on Malaria, Filariasis and Leishmaniasis and is expected to lead to potential breakthrough in the design of more effective therapies and development of new generation of vaccines.

New Initiatives

A new academic initiative was undertaken towards fostering young and innovative scientific minds and maintain the level of productivity by encouraging three Canadian Queen Elizabeth Scholars under the 'Canadian Queen Elizabeth II Diamond Jubilee Scholarships' programme to carry out their summer internship at NII. The Institute's Ph.D. Scholars would also participate in the exchange programme. Besides this, training Program of Medical doctors in basic research laboratories under 'Long term Fellowship in Indian institutions under HRD Scheme of Department of Health Research under ICMR' has also been initiated. 'Science setu' which was conceptualized in 2014-15 to enable connectivity between Institute scientists and undergraduate students of 13 colleges of Delhi University, bloomed during the reporting period.

Other notable achievements

The Institute along with Wellcome Trust/DBT India Alliance and Department of Biotechnology co-organized a lecture on "Recent Developments in Cancer Research" by Nobel Laureate, Dr Harold Varmus, recognized for his research



on retroviruses and the genetic basis of cancer. His lecture largely gave an overview of the recent developments, challenges and the future directions in the field of cancer research, which included the current research of his group in this area. The foundation day lecture delivered by Dr. Alan Cowman, The Walter and Eliza Hall, Institute of Medical Research, Melbourne, Australia, was stimulating. In addition, the Institute continues to present enlightening and inspiring seminars from faculty from various scientific organizations regularly.

NATIONAL CENTRE FOR CELL SCIENCE (NCCS), PUNE

The National Centre for Cell Science (NCCS) was established with a mandate of three main functions:

- i. National Cell Repository
- ii. Research & Development
- iii. Human Resource Development.

In keeping with the vision of NCCS to expand into newer research areas, new initiatives were undertaken through two new faculty members

During the year 2014-15, NCCS provided four thousand five hundred and eight cell lines to four hundred organizations as a part of its commitment to supporting research in cell biology across the country. Towards nurturing young scientific talent, NCCS admitted 27 research scholars into its PhD programme, and 15 research scholars of NCCS registered as Ph.D. students with the University, bringing the total number of research scholars who are registered for a Ph.D. to 133 during this year. NCCS also trained 21 summer trainees and 44 project trainees.

Research Achievements

Cancer research group has shown that tumor

suppressor, FBXO31 gets stabilized in the cells upon exposure to known cancer therapy regimens, including chemo- and radio-therapy. The resultant increase in the levels of FBXO31 is then able to effectively degrade the oncoprotein MDM2 through a proteasome-mediated pathway, leading to the restoration of p53 activity. These findings, which reveal for the first time the missing link in the p53 activation pathway operative upon the administration of cancer therapy, were published in PNAS in July, 2015. The activation of p53 could enhance the response of cancerous cells to chemo- and radiotherapy.

Using an animal model of multiple sclerosis (MS), research group investigated how inflammation that is induced by cytokines and chemokines produced in the peripheral tissues can affect the BBB endothelial cells. Their findings revealed that the Th1-specific cytokine, IFN- γ , increased the expression of cell adhesion molecules like ICAM-1, VCAM-1, PECAM, and redistributed the tight-junction molecules, VE-Cadherin, zonula occludens-1 (ZO-1), occludins and claudin molecules, at the endothelial junction in a STAT-1 dependent manner. They found that blocking these molecules or downstream signals prevented the transmigration of CD4 T cells across the endothelial barrier. Further understanding the cellular and molecular mechanisms involved in BBB breakdown could help design novel therapeutic strategies to control neuronal inflammation and autoimmunity.

The role of free radicals in biology and medicine is being studied by a research group. Their current research is focused on elucidating the mechanisms that underlie the pathogenic processes occurring in the heart, which lead to diabetic cardiomyopathy (DCM). Mitochondrial redox regulation provides valuable insights into the molecular mechanisms responsible for altered cardiac function in diabetes. This group is

therefore studying the mitochondrial sources of reactive oxygen species (ROS) and the antioxidant mechanisms involved in DCM. Having earlier reported that the mitochondrial flavoenzyme, monoamine oxidase A (MAO A) is an important source of oxidative stress in the myocardium, this group sought to further determine whether MAO A plays a major role in modulating DCM. Their findings revealed that it promotes cardiac dysfunction, apoptosis, and fibrosis in DCM. These findings were published in Free Radical Biology & Medicine, in June, 2015. Discerning the operative molecular mechanisms could provide useful insights for improving therapy for DCM.

NCCS continues to uphold its legacy of carrying out frontline research in major areas of modern Cell Biology and supplying cell lines to researchers across the country, while also providing training to develop high quality manpower in cell biology. The research at NCCS, which is dedicated to understanding the functioning of the cellular machinery in health and disease, has resulted in several publications in the last year in leading journals like PNAS, Oncogene and Cell Metabolism. The research carried out by the students and scientists of NCCS has also received recognition through several awards and honours. With the expertise of new faculty members, NCCS continues to expand into newer, cutting-edge research areas such as those dealing with deciphering the role of RNA in biological control processes and the cellular and molecular basis of memory. During the year one patent application entitled 'Identification, quantification, monitoring and analysis of intratumor heterogeneity' PCT Application Number: PCT/IB2015/050358 has been filed by NCCS.

List of Bilateral/ Multilateral Agreements with other agencies, if any

NCCS signed a memorandum of understanding

(MoU) with the Venture Center, a not-for-profit technology business incubator, on 18th September 2015, for scanning and showcasing the technology, know-how and capabilities of NCCS for entrepreneurs and potential partners in the industry. The Venture Center will thus assist NCCS in advancing its R&D towards commercialization objectives and in promoting entrepreneurial activities.

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS (CDFD), HYDERABAD

CDFD provides services in the areas of DNA fingerprinting, diagnostic tests for human genetic disorders and analysis of basmati rice for purity, and is also engaged in basic research activities in different disciplines of modern biology. The Centre has witnessed significant growth in all phases of activities, and several new frontiers of research have been initiated.

SERVICES:

DNA Fingerprinting Services: In DNA profiling services, CDFD is identified as the premier organization in the country for referrals of complex and sensitive cases from various law enforcing agencies of Federal and State Governments, investigation agencies and the judiciary. The Laboratory analyzed the samples received in more than 550 cases in the year 2015.

Several prominent cases such as sexual assault and homicide case of a research scholar in Agra; cousin sisters rape and murder case from Badaun; identification of victims in Burdwan blast case; identification of unknown human skeletal remains in army firing in Kistwar; identification of unknown human skeletal remains from Democratic Republic of Timor-Leste, etc have been forwarded to CDFD for examination and reporting. CDFD has also entered into MoU with



various State Governments to promote and train the FSLs in undertaking such activities.

The CDFD in association with DBT, is piloting the Human DNA Profiling Bill which envisages creation of the DNA Profiling Advisory Board as an authority inter alia to establish standards and to implement quality control measures in laboratories undertaking DNA profiling services and establishment of a National DNA Data Bank for detection of, and to serve as deterrents against, repeat offenders.

Genetic Diagnostic Services: The Centre provides modern diagnostic and counseling services to children and families with inherited genetic disorders. The Diagnostics Division of the Centre has conducted approximately 4800 tests in the year 2015 in the areas of molecular cytogenetics and biochemical genetics. Further, the division is also involved in research towards identification of novel genes and mutations in families with genetic disorders.

Basmati DNA Testing: Based on one of the DNA inventions that was developed and patented by the Centre, the Agricultural Products Export Development Authority (APEDA) of the Govt. of India has entrusted to the Centre the task of certifying the quality and authenticity of basmati rice. More than 200 basmati rice samples have been examined for certification, a majority of which were forwarded to the Centre by Export Inspection Council (EIC) of India during the year 2015. In view of the complexities and challenges arising in Basmati adulteration testing, efforts are being made by the Centre to further expand adulteration testing protocol. Towards this direction, the Centre extended the method of multiplexed eight markers panel for identification of all notified Basmati varieties to generate a comprehensive database. The Centre has also standardized single grain analysis for varietal identification of Basmati rice which acts

as an effective deterrent against adulteration.

RESEARCH ACTIVITIES:

The Centre undertakes research in several frontier areas of modern biology, with a group of twenty two faculty members. The major thrust areas include genetics and epigenetics, silkworm genomics, computational and structural biology, cancer and stem cell biology, cell signaling, immunology, molecular and cellular biology, bioinformatics, fundamental studies on transcription and signal transduction, fungal pathogenesis, plant biology etc. The Centre has identified the first non-Wnt (12-gene) signature for early onset sporadic rectal cancer in humans. The role of DNA methyltransferases Dnmt3l and Dnmt2 have been dissected out in carcinogenesis and development. The Centre also identified novel mycobacterial proteins that interact with host genome and modulate immune response which has a potential to be used as biomarker and patent has been filed. Further, it has also been established that high affinity iron acquisition mechanism are critical virulence determinants in *Candida* pathogenesis and also identified principal constituents of the iron transport metabolism. Formal permission has been received by the Centre for the conduct of multi-locational trials in contained facilities of genetically engineered silkworm strains.

The ongoing research studies and knowledge base in epigenetics in the Centre has led to the discovery of a mycobacterial protein which regulates host response by gaining understanding of the interaction of pathogenic mycobacteria with the human cell during infection. This identification augurs well not only for it to be a potential target for therapy against mycobacterial infection but also developing a new biomarker for identification of *M. tuberculosis* infection in human. An Indian patent application has been filed by the Centre towards this discovery.

The Centre has achieved an impressive record of publications in international peer-reviewed journals such as Nucleic Acids Research, PLoS Genetics, Nature Communications, Nature Scientific Reports, Microbiology, Biochemical Journal, Cellular Signalling, Journal of Bacteriology, Bioinformatics, Journal of Biosciences, Molecular Microbiology, Molecular Carcinogenesis, etc.

During the year CDFD has published more than 50 research publications in peer reviewed scientific journals.

NATIONAL BRAIN RESEARCH CENTRE (NBRC), MANESAR

The National Brain Research Centre (NBRC) continues to work arduously towards reducing the burden of brain disorders in the country. The research carried out by NBRC has been greatly valued worldwide. NBRC's research contribution in understanding healthy and diseased brain has placed India at par with international laboratories engaged in brain research. At NBRC, molecular biologists, physicists, computational neurobiologists and clinicians work together towards reducing the burden of brain diseases in Indian population in future. The institutional focus is three folds - 1) Pursue research to understand brain function in health and disease, 2) To generate trained human resources with the capability to carry out interdisciplinary research in neuroscience (NBRC is a deemed university) and, 3) Promote neuroscience in India through networking among institutions across the country. In an attempt to make the neuroscience research performed at NBRC applicable for human population, NBRC is extending its reach to the people in India in various ways. Some important ones are mentioned below. A screening tool for children with learning disorders or dyslexia that was initially developed in four Indian languages will be expanded to some other languages,

including Gujarati in near future. NBRC has a major initiative in the area of identifying novel therapeutics for brain inflammation, infection and degenerative damage. Among the new initiatives is the development of a model for peripheral nerve injuries, with the possibility of screening drugs for improving their outcome.

Scientific Achievements

Understanding basic biology of neuroinflammation -Scientists at NBRC have delineated cellular and molecular intricacies of several brain disorders ranging from Learning and memory, Alzheimer's disease, Huntington's disease, Brain and Spinal Cord injury, virus induced neurodegeneration to glioblastoma multiforme, a highly aggressive form of brain cancer.

Dyslexia Assessment for Languages of India (DALI) -In a landmark achievement, a screening / assessment and amelioration package for dyslexia (learning disability) in Indian languages (Hindi, Kannada, Marathi and also in English) was released by Hon'ble Minister of Science and Technology and Earth Sciences, Dr. Harsh Vardhan, on 15 October 2015, after an extensive validation across the country. This application of Educational Neuroscience Research at NBRC would connect science to the society and pave way for teachers to help in identifying and assisting children with learning disabilities.

Early detection of Alzheimer's disease - Another application of neuroscience in clinical research was finding on the levels of glutathione (a molecule that lowers oxidative stress), which was reduced in people with Alzheimer's disease (AD). Research aimed at identification of early diagnostic marker for AD using magnetic resonance spectroscopy (MRS), found that healthy aged person turn into mild cognitive impairment (MCI) when their glutathione level depleted significantly in the left hippocampus



area. This is an important discovery as measuring glutathione level in various brain regions can help us to identify people that may turn from normal healthy individual to MCI.

Taking non-invasive diagnosis to another level -The MagnetoEncephaloGram (MEG) facility, a component of the centre for excellence in research (jointly by AIIMS and NBRC) was inaugurated by the Hon'ble Minister of Science and Technology and Earth Sciences, Dr. Harsh Vardhan on 5 June, 2015. The MEG which detects minute electromagnetic activity in precise regions of the brain would identify the specific regions to be surgically removed in drug resistant epilepsy. The centre is also carrying out basic and applied research in epilepsy, especially looking into their causation. This may lead to identifying new therapeutic targets and development of new anti-epileptic drugs.

Creating vibrant brain researchers in India - NBRC, being a Deemed University, has now institutionalised its multidisciplinary character as a Neuroscience teaching institution by widening its admission criteria to include students with diverse background, like physics, chemistry, computer sciences, mathematics and engineering sciences. In addition to regular course work, which includes molecular and cellular neurosciences, systems neuroscience and computational neuroscience, it has commenced teaching a clinical neuroscience module to sensitise basic neuroscience researchers to clinical implications of their research.

During the year NBRC has published more than 45 research publications in peer reviewed scientific journals. This year has been extraordinary in the number of research leads that have been shown to be ready for implementation on a large scale. These include dyslexia screening in four Indian languages and a marker for Alzheimer's disease and the possible use of the same as a therapeutic target.

INSTITUTE OF LIFE SCIENCE (ILS), BHUBNESHWAR

The Institute of Life Sciences (ILS), an autonomous institute has been brought under the fold of the Department of Biotechnology, Government of India in 2002. The mandate of ILS is to undertake basic and translational research in frontier areas of life sciences. Major research areas of the institute are Infectious Disease Biology, Gene Function and Regulation and Translation Research and Technology Development.

Research Highlights

Infectious disease biology:

Clinical severity in malaria was shown earlier to be increased by co-infection with *Salmonella typhimurium*. Investigations conducted this year have indicated that mice with chronic malaria (post recovery from *P.chaubudi* infection) were tolerant to LPS challenge and were also partially resistant to challenge infection with *Salmonella typhimurium*. These findings suggest that subjects in malaria endemic areas displaying asymptomatic infections could be resistant to other bacterial pathogens.

Studies on role of host factors for Chikungunya virus infection is one of the main focuses of the molecular virology laboratory. It was demonstrated that up-regulation of Hsp70 protein by thermal shock or PGA1 treatment has a deleterious effect on CHIKV infection as it enhances viral protein levels but ultimately decreases viral titers. Additionally, in 2013 in a hospital based cross sectional study in Odisha and Maharashtra during Dengue outbreak, it was observed that around 43 (44.8%) patients were co-infected with DENV and CHIKV which emphasizes the need of a continuous surveillance system for early and proper recognition of infecting pathogen for better patient care on time.

Interaction of the bacterial cell division protein FtsZ with MinD were studied using yeast two hybrid system and pull down assay. Yeast two hybrid assay shows MinD alone is able to interact with FtsZ. Results from Pull down assay shows FtsZ is pulling down along with MinD suggesting FtsZ is interacting with MinD and confirms the yeast two hybrid assay. This group further found out that C-terminus of FtsZ is important for the interaction with MinD.

Gene regulation and function:

Understanding the role of different genes and their post-translational modification in the development Chronic Myeloid Leukemia (CML) was addressed. The studies revealed that the expression levels of two genes viz., MEF2C and CEBP α are negatively correlated in the accelerated and blast crisis stages of CML. Moreover, MEF2C directly targets CEBP α and down-regulates its expression. Imatinib treatment down-regulates both the mRNA and the protein expression of MEF2C in CML patient sample. Statistical profiling shows that MEF2C, CEBP α and CSF3R expression levels are enough to molecularly discriminate different clinical stages of CML.

Several novel extremophilic organisms have been isolated and identified - among them, microbes like Pannonibacter indicus can be used as a model to develop arsenate bio-sensor. Besides, Photobacterium panuliri a marine bacterium is under trial for the large scale production of cellulose.

Studies have been initiated to most comprehensive list of so called uncharacterized proteins present in human, zebra fish and other major vertebrate model organisms. The initial analysis suggests that, although the mRNA of the majority of these uncharacterized proteins are expressed ubiquitously, some of these also show tissue specific expression during zebra fish

development. This would be the foundation for functional annotation of zebra fish genome.

Translational Research and Technology Development:

A High Throughput Virtual screening approach to identify bioactive compounds against DDX3 from ZINC natural database was attempted to address issues on oral squamous cell carcinoma. DDX3 belongs to DEAD box RNA helicase family and is involved in the progression of several types of cancer. Ketorolac salt was selected based on its binding free energy less than or equals to -5 Kcal/mol with reference to existing synthetic DDX3 inhibitors and strong hydrogen bond interactions as similar to crystallized DDX3 protein (2I4I). The anti-cancer activity of Ketorolac salt against DDX3 was tested using OSCC cell lines. This compound significantly down regulated the expression of DDX3 in human OSCC line (H357) and inhibited growth and proliferation of OSCC cells.

The research on prostate cancer revealed that bacterial LPS enhance survival of prostate cancer cells under conditions of nutrient stress through TLR4 activation. Moreover, LPS induces overexpression of CCL2 involved in the suppression of starvation-induced macroautophagy in Prostate Cancer cells, and enhanced macrophage population in prostate tumors in vivo.

REGIONAL CENTRE FOR BIOTECHNOLOGY (RCB), FARIDABAD

The Centre is an institution of international importance for biotechnology education, training and research and shall, in due course, be constituted as an autonomous body under an Act of the Parliament. It is regarded as a "Category 2 Centre" in terms of the principles and guidelines for the establishment and functioning of



UNESCO Institutes and Centres. The mandate of the Regional Centre for Biotechnology (RCB) is to provide an environment for research, education and training in biology and biotechnology.

Inter-institutional initiatives:-

- 1) BM14 Project:- In late 2008 an agreement was signed between Department of Biotechnology, European Molecular Biology Laboratory (EMBL) and European Synchrotron Radiation Facility (ESRF) that enabled Indian scientists to visit the BM14 beamline located in ESRF to collect X-ray diffraction data.
- 2) Multi-institutional Preterm Birth Programme (PTB):- A national level innovative multi-institutional study is implemented through RCB, which is an important partner on the pre-term birth involving a very large cohort. The basic aim of the project is to understand the epidemiology of PTB, its genetic and environmental interactions, and changes in vaginal microbial landscape.
- 3) International Networking: AIST, Japan:- The Regional Centre for Biotechnology (RCB) and the National Institute of Advanced Industrial Science & Technology (AIST), Japan entered into a partnership for capacity building initiatives in bio-imaging and biotechnology in the year 2014.
- 4) Biotech Science Cluster, Faridabad: RCB is an important component of and principal co-ordinator for construction of buildings and infrastructure facilities of the NCR Biotech Science Cluster, Faridabad. The cluster aims to facilitate public-private partnerships for the development of biotechnology business incubators and parks, including creative partnerships with Biotech & Pharma entrepreneurs and distributors.

Education & Training

- i) Multidisciplinary PhD Programme:

Multidisciplinary doctoral programme has been instituted for students who have completed Masters to carry out scientific research in RCB in the areas of cell, chemical, computational, developmental, plant and structural biology, tissue engineering, analysis of complex diseases for identification of intervention points, host-pathogen interactions and development of knowledge-based drug discovery strategies.

- ii) Young Investigator (YI) & Post Doctoral Fellowship Awards Programme: YI Awards scheme has been initiated to nurture outstanding recent PhD fellows with the aim to pursue novel discoveries under the mentorship of the RCB Faculty.

- iii) Short-term Training:- Post-graduate students have the opportunity to conduct short research projects and/or dissertation work towards partial fulfillment of their degrees.

- iv) Master's Degree in Medical Science:- Integrated Masters' programme in Medical Biotechnology leading to a PhD degree is at the early stages of conceptualization with the overall aim to foster practical learning and research skills among medical and related graduates to enhance their overall educational experience for development of competent medical researchers. The programme is designed with the objective of providing knowledge in life sciences with emphasis on human biology, clinical and translational research.

Research Achievements:

In the study on fundamental molecular mechanisms regulating cell division and

intercellular communication has highlighted the role of the cytoplasm dyne in subunit Light Intermediate Chain 2 in regulating mitosis and also reported detailed biochemical characterization of a key protein involved in nanoconduit formation. The bio-nanotechnology group has successfully designed amphiphiles targeting important microbial pathogens and these efforts may lead to a new class of antimicrobial drugs.

The laboratory focused on transcription and gene regulation has obtained deep mechanistic insight regarding an antiactivator important for assembly of flagella in *Pseudomonas aeruginosa*. The research programme addressing pathophysiology of thrombosis in disease conditions have acquired interesting insights regarding hemoglobin (Hb) mediated platelet activation, Hb mediated macrophage activity, Hb mediated stem cell differentiation and dengue virus induced thrombocytopenia. The laboratory interrogating the role of ubiquitin mediated signaling in cellular processes has highlighted the role of Ubiquitin-C terminal hydrolase 1 (UCHL1) in regulating Parkinson's disease pathology.

The research group investigating intrinsic signals that regulate skeletal muscle development and function has discovered the effect of loss of myosin heavy chain embryonic on muscle differentiation and mouse development. The recently initiated programmes in the area of plant biotechnology have progressed well in the past year. The group addressing modulation of plant host immunity and nutrient allocation by an obligate biotroph has optimized a tissue preparation method for infection site-specific expression profiling via laser microdissection microscopy and obtained preliminary evidence for a role for plant SWEET transporters in powdery mildew nutrition.

During the year 23 research articles and 12 reviews were published by RCB in peer reviewed scientific journals.

Regional Centre for Biotechnology is also taking care of the following important programmes:

1. Advanced Technology Platform Centre (ATPC): RCB is playing a key role in the setting up of a state-of-the-art Advanced Technology Platform Centre (ATPC). The ATPC would act as a catalyst for multidisciplinary basic and translational research and development by providing relevant instrumentation, training and professional services for the stakeholders and others alike on behalf of the Biotech Science Cluster in Faridabad.
2. Biotechnology Business Incubator: The biotechnology business Incubator is being established as part of the Biotech Science Cluster in partnership with BIRAC. This state of the art facility would provide new and emerging companies with a compatible environment to support their start-up phase and increase their likelihood of success.
3. Technology Advancement Unit: Technology Advancement Unit (TAU) is a joint initiative of the Swiss Agency for Development and Collaboration and the Department of Biotechnology. The Technology Advancement Unit is being set up with the aim to create a conducive environment for the planning and implementation of R&D projects focussed on product development and technology transfer.
4. Biosafety Support Unit: The Department of Biotechnology, Ministry of Science and Technology, has entrusted RCB with the responsibility of establishing a Biosafety Support Unit (BSU), which will develop guidelines and protocols for generating biosafety data to address the challenges raised by the emerging areas of biotechnology.
5. Centre for Molecular Medicine of the

Karolinska Institute, Sweden:- The Department of Biotechnology (DBT), Ministry of Science and Technology, supports 13 Research Institutes in India and extends research grants in the areas of Biotechnology, Bio-medicine and Translational medicine.

6. Collaboration with University of Toronto, Canada:- Regional Centre for Biotechnology along with partner institutions in the Biotech Science Cluster has initiated collaboration with the Department of Immunology, University of Toronto in the area of immunology and human health. The aim of such a partnership is to offer basic education and training to scientific personnel within participating institutes using traditional and modern methods.

NATIONAL INSTITUTE OF BIOMEDICAL GENOMICS (NIBMG), KALYANI

National Institute of Biomedical Genomics (NIBMG) is engaged in accelerating genomics for health and disease. NIBMG engages in discovering genomic evidence that underpins disease and health-related traits. NIBMG is the nodal institution for conduct of the India project on oral cancer under the aegis of the International Cancer Genome Consortium. The Institute has two program projects (a) to discover the biological and environmental correlates of pre-term birth - a multi-institutional project anchored in the DBT-aided institute, THSTI in Faridabad - and (b) a population cohort study, the Kalyani Cohort Study, to study natural histories of diseases and health-related traits. The Institute has a vibrant short-term training program and an outreach program.

Research Highlights

Oral Cancer: NIBMG has generated the mutational landscape of oral cancer and has

identified ten genes that drive oral cancer. When the driver mutations were mapped on to biological pathways, the arachidonic acid metabolism pathway was found to be significantly enriched. The arachidonic acid metabolism (AAM) pathway promotes tumour progression. Chemical inhibitors of AAM pathway prolong post-treatment survival of cancer patients. Amino-acid altering somatic mutations in genes of this pathway, acting as natural inhibitors, increased post-treatment survival; patients with mutations had a significantly ($p=0.003$) longer median disease-free survival (24 months) than those without (13 months). This inference was strengthened when data of this study were pooled with those of The Cancer Genome Atlas (TCGA) data.

Cervical cancer: Human Papillomavirus (HPV) type 16 oncoprotein E7 plays a major role in cervical carcinogenesis by interacting with and functionally inactivating various host regulatory molecules. Long noncoding RNA (lncRNA) HOTAIR is one such regulator that recruits chromatin remodelling complex PRC2, creating gene silencing H3K27me3 marks. Hence, we hypothesized that HOTAIR is a potential target of E7, in HPV16 related cervical cancers (CaCx). A significant linear trend of progressive HOTAIR down-regulation was identified from HPV negative controls, through HPV16 positive non-malignants, to CaCx samples. Expression of HOTAIR and PRC2-complex members (EZH2 and SUZ12), showed significant positive correlation with E7 expression in CaCx cases, suggestive of interplay between E7 and HOTAIR. This study elucidated one of the causal mechanisms of cervical carcinogenesis by HPV16 E7, through modulation of HOTAIR expression and function.

Genetic history of extant Indian population groups: India, occupying the center-stage of Paleolithic and Neolithic migrations, has been under-represented in genomewide studies of

variation. Systematic analysis of genomewide data, using multiple robust statistical methods, on unrelated individuals drawn from 18 mainland and 2 island (Andaman and Nicobar islands) populations selected to represent geographic, linguistic and ethnic diversities, revealed four major ancestries in mainland India. This contrasts an earlier inference of two ancestries based on limited population sampling. A distinct ancestry of the populations of Andaman archipelago was identified and found to be co-ancestral to Oceanic populations. This finding has implications in the design of case-control studies and in the analyses of data, in addition to linking history with genetics.

Trainings and Workshops

The Institute initiated a three-year DNB programme on Medical Genetics under the aegis of the National Board of Examinations. This programme is supported by the Department of Biotechnology.

The Institute conducted a workshop, jointly with the Indian Statistical Institute, during February 25-27, 2015. About 60 students were trained.

NIBMG conducted a Winter School during March 2nd to 7th, 2015, on "Analysis of Massively Parallel Sequencing (NGS) Data." About 30 students from various institutions in India were trained.

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE (INSTEM), BANGALORE

The institute is dedicated to the study of stem cells and regenerative biology. inStem facilitates cross-disciplinary, multi-pronged approaches to research, straddling the divide between clinical and laboratory research in stem cell biology. In trying to answer challenging questions that face the field, inStem seeks to rewrite the paradigm of

the research institute: without barriers and across disciplines.

Major Initiatives and Salient Achievements:

Since its inception in 2013, the Centre for Chemical Biology and Therapeutics (CCBT) has established an extraordinarily high quality programme in uncovering new molecules targeting phosphopeptide protein interactions. This is a close knit team effort that will soon reach out to its environs as it creates scientific assets that will enhance the scientific efforts of the community.

The Centre for Brain Development and Repair (CBDR), has established a platform programme (Centre for Synaptic Neuropathies) for studying neurophysiological aspects of stem cells taken from patients carrying autism spectrum disorders (ASDs) as well as developing novel rodent models for drug discovery and disease characterization. Amongst its most recent achievement is the electrophysiological characterizations of specific perturbations in neurons generated from ASD patient-derived iPSCs (induced Pluripotent Stem Cells).

The Cardiovascular Biology and Disease (CCBD) theme has a new and ambitious programme, supported by a Wellcome Trust-DBT India Alliance intermediate fellowship awarded in 2015 to Minhaj Sirajuddin, to reconstitute the sarcomere – the basic unit of muscle – to investigate functional outcomes of newly described mutations underlying cardiac myopathies. The CCBD has grown to include a human geneticist interested in studying perturbations in signalling pathways in paediatric cardiomyopathies. With new international collaborations within the theme and a truly interdisciplinary programme, the CCBD is now focussing on all the scales involved in cardiomyopathy.

The overall objective of the Centre for Inflammation and Tissue Homeostasis (CITH) is to decipher the



regulation of tissue development, regeneration and repair and the increasingly critical role that inflammation plays in these processes. With a principle focus on repair following damage to the skin, the theme has begun to make inroads in understanding cellular behaviour following wounding and sterile inflammation in developing embryos. The elucidation of the molecular mechanisms underlying these processes is evident from the publications from this theme. The members of CITH theme are in a competitive position to make important contributions to this area of mechanobiology research based on their animal models and historical strengths of the member labs.

The Technologies for Advancement of Science (TAS) theme continues its exploration of new tools and technologies with exciting applications of an addressable chemical scaffold as a drug delivery device, making its way into clinical trials in large mammals. As a broad collaborative effort that includes scientists at the National Centre for Biological Sciences, inStem is part of a Cryo-EM installation on campus.

The nascent Regulation of Cell Fate (RCF) programme, started its activities in January 2015. An emerging focus of the theme's efforts is on an interconnected investigation of metabolic control of cell fate, using diverse models and experimental systems. The member labs are supported by Wellcome Trust-DBT India Alliance intermediate fellowship awarded to Sunil Laxman and an award of a Centre of Excellence grant (from the DBT) to three investigators in the theme in 2015.

The clinical translational unit run at the Christian Medical College (CMC), the Centre for Stem Cell Research (CSCR) is another endeavour where clinical translation is being honed into three main areas of focus. Two are founded on core interests in gene therapy for haemophilia (based on the recognition of underutilized AAV

vectors in collaboration with Amit Nathwani at UCL, London, UK and Arun Srivastava at UFL, Gainesville, USA) and thalassemia (based on lentiviral vectors in collaboration with Trent Spencer at Emory University, USA). The third is on a musculoskeletal regeneration programme led by Vrisha Madhuri. The outcome of this latter focus is currently undergoing clinical trials in articular and physal cartilage replacement, along with bone and muscle regeneration.

During the year InSTEM has published more than 15 research papers in peer reviewed scientific journals. In the short (six year) period of its existence, inStem has successfully attracted outstanding investigators, who have initiated theme driven programmes on campus. These have crystallized into six major programmes at Bangalore and the translational, clinical unit at Vellore. The research demonstrates the breath of enquiry – from atomic resolution work to animal models and the depth of understanding it generates in mechanisms of regeneration to use of stem cells as a model to understand disease pathophysiology. In the coming years, with the completion of the new building and the available expanded space and resources, the institute hopes to grow its science exponentially.

Centre for Stem Cell Research (CSCR), CMC, Vellore

The Centre for Stem Cell Research (CSCR) is the translational research unit of inStem, Bengaluru, to bring stem cell science to management of patients with unmet needs. This is achieved by developing research along clearly defined themes which will help enhance understanding of disease biology or help create innovative diagnostics and therapeutics that is relevant to the needs of the country. During the year 15 research publications came out from CSCR in peer reviewed scientific journals.

NATIONAL INSTITUTE OF AGRI-FOOD BIOTECHNOLOGY, MOHALI

National Agri-Food Biotechnology Institute has main objective of promoting and coordinating research of high caliber in basic and applied aspects at the interface of Agriculture, Food and Nutrition. The institute has expanded its research work along with initiation in collaboration with the neighbouring and international institutes.

The main focus of the NABI encompasses five major core areas that includes a) Improving Cereals for nutrition and processing quality; b) Improving fruits for post-harvest quality and nutrition; c) Basic Biology for crop improvement; d) Diet and health and e) Computational biology approach for marker and gene discovery. Additionally, one of the initiatives that the institute has taken is to develop efficient, functional genomics tool to access the function of the target genes. The institute has also developed multiple genomic resources, especially generating the transcriptome data of multiple crops like wheat, Annona and litchi that could be utilized by the researches to address the trait development based approaches. Another major initiative includes generating synthetic hexaploid wheat to develop pre-breeding platform in order to improve their heat tolerance and sustainable production.

Research Achievements

NABI is addressing the possible role of genes and their regulators underlying nutrition and processing related quality traits. Researchers at NABI have identified non-synonymous mutations in starch metabolic genes. Starch thermal properties and dough rheological properties were estimated on the subset of 50 wheat genotypes. An EMS induced M4 population that was developed earlier was characterized for variation in amylose content. Many mutant lines were identified showing variation from 3-76 % in amylose content. Advanced breeding material

for improvement of chapatti, biscuit and bread making quality has been generated. Additionally, polymorphism in the genes related to the grain hardness and softness was explored and an updated database was created, which would be beneficial for developing breeding material with improved processing quality traits. In an attempt to improve the micronutrient bioavailability, localization patterns of iron in contrasting wheat cultivars were studied and potential genes were identified. Wheat RNAi plants targeted to achieve low phytate acid were also developed. To develop pro-vitamin A (β -carotene) rich biofortified Indian banana, several rounds of genetic transformation experiments with four QUT gene constructs (Gen2) have been performed and the transgenics are currently growing. Dominant negative and root-scion approaches have been tested and now expanded to understand development or control of the seedlessness nature of fruit crops.

In the area of food and nutrition biotechnology, investigations related to over nutrition, such as obesity, are being carried out using in-vitro and in-vivo models. Millet, whole grain/bran shows potential in alleviating symptoms of high fat diet induced metabolic alterations such as serum cholesterol and glucose levels, modulating beneficial gut microflora and SCFA production. In-vitro findings suggested a modulatory role of cinnamaldehyde in adipogenesis via promoting lipolysis. Detailed studies have shown that cinnamaldehyde initiates lipolysis, increases expression level of thermogenesis related genes in BAT and decreases feed intake. Microarray based gene expression analysis of murine brown and subcutaneous adipose tissue was also performed.

Characterization of dietary components from Indian millet varieties and spices as well as probiotics and prebiotics based approaches are currently in progress. Soluble dietary fibers extracted from millet that includes hydroxycinnamic acid bound arabinoxylans (HCA-AXs)



showed the presence of arabinose and xylose as major constituents (~60-70%) along with glucose, galactose and mannose as minor constituents. Significant variation in the individual phenolic acid content (caffeic, para-coumaric and ferulic acid) and in-vitro antioxidant potential of the extracted millet HCA-AXs were observed. In the area of nanotechnology, functionalized gold nanorods as a potential biosensor to detect food borne pathogens are being developed. Alginate encapsulated ferric saccharate micro-emulsions were tested successfully to ameliorate iron deficiency in mice.

In bioinformatics, micro RNA expression atlas database has been developed to facilitate the data mining and network studies in food crops like wheat, rice and maize. PmiRExAt, the web based repository, comprises of miRNA expression profiles and query tools. Literature mining scripts have also been developed for new entity recognition. This year NABI has published more than 25 publications and applied for one patent.

CENTER OF INNOVATIVE AND APPLIED BIOPROCESSING, MOHALI

Center of Innovative and Applied Bioprocessing (CIAB) formerly Bioprocessing Unit (BPU) aim is "to be a nodal lead research & innovation linking bioprocess and bioproducts R&D system knowledge, technology, leads etc. with production system, and serve as incubatorial platform for agri-process and agri-food-product related entrepreneurship along with frontal role in translation, innovation, optimization and up-scaling of approaches and technologies for Bioprocessing products to catalyze agro-industrial growth through progressive functional linkages and networking/collaborations with institutions and industries nationally and globally. The main mission of the institute is "value addition to agri-food biomass for secondary agri culture products

(SAP)". The Institute has following R&D priority areas:

- Value addition to primary processing residue/wastes for edible products

This area entails projects and activities focused at developing and/or gainfully modifying processes or recruiting existing processes for up-scaling to obtain value added products of nutrition, nutraceutical potential, better substitutes to existing food additives, new products etc.

- Valorisation of crop wastes for specialty products and chemicals

This area aims to create value for the biomass that is left after crop harvest or residue(s) after farm operations of grain harvest but are either not significantly used or are under-utilized in terms of volume despite knowledge based inherent economic significance. Thus, it aims to assess and realize the profitable scope of their processing biologically and/or chemically to generate a secondary stream of technology application based products.

- Nutritionals, nutraceuticals, and upgradation of value/use of primary processing bioproducts

This area covers research projects and activities involving processes and products including formulation of products of nutritional or nutraceutical significance as well as specialty enzymes of processing use.

- Biosynthetic technology for low volume-high value products and industrial enzymes

This area entails with specific objectives of designing and producing enzymes for specific advantages of catalytic specificity and/or performance in a processing use perspective to break the barriers of their

natural availability amongst available/usable species. Also, it intends to take programs recruiting biosynthetic technology/synthetic biology for xenogeneic production of high value nutraceutical molecules, food and flavor additives, colors etc.

Scientific Achievement:

A process for the production of natural and scented tartaric acid from geranium biomass and biomass hydro-distillation residual water as a novel ingredients. Scented natural tartaric acid was recovered from rose-scented geranium biomass hydro-distillation residual water via percolation/hydro-distillation, centrifugation, concentration and crystallization with or without the use of alcohol.

Withania somnifera (Ashwagandha) biomass based production of solanesol and uses thereof. The extraction of solanesol from the foliage of *Withania somnifera* (Ashwagandha) has been established. Solanesol is precursor for the synthesis of the dietary supplements coenzyme Q10 and vitamin K. It forms an option to advance the use of complete plant of Ashwagandha, of which currently only roots are being used.

A green, non-inflammable volatile and biogenic solvent based solid-liquid extraction process of lycopene from tomato fruit or tomato fruit peel/pomace/pulp and other congener cells/tissues or bioresources or materials containing lycopene. The residual biomass after extraction of lycopene and other carotenoids using the biogenic solvents is free from the issues of environmental hazards and waste disposal.

Leads on the production of xylitol, a low calorie sugar alternative, from rice straw and corn cob through integrated chemical and is an important option to valorise these largely unused agro-bio-resources.

Following patent applications have been filed during the year:

- A process for the production of natural and scented tartaric acid from geranium (*Pelargonium graveolens*) biomass/geranium biomass hydro-distillation residual water (Patent Application No. 1487/DEL/2015).
- A Process of *Withania & Somnifera* (Ashwagandha) biomass based production of solanesol and uses thereof. (Patent Application No. 3201/DEL/2015).
- A green process of non-inflammable volatile biogenic solvents based extraction and isolation of lycopene and other carotenoids from bioresources and other materials and uses thereof. (Patent Application No. 3197/DEL/2015).
- A process of volatile biogenic solvent(s) aided enhancement of colour and stability of lycopene and other carotenoids in presence or absence of light and uses thereof. (Patent Application No. 3228/DEL/2015).
- Non-alcoholic and biogenic solvent based process for Production of lactose and whey proteins from whey. (Patent Application No. 2291/DEL/2014).

NATIONAL INSTITUTE OF ANIMAL BIOTECHNOLOGY, HYDERABAD (NIAB)

The research at NIAB is focused broadly on Infectious diseases, Reproductive Biology, Animal Genetics and Genomics, Bio-informatics and Nutrition Enrichment with respect to livestock and poultry animals. Scientists have initiated projects on Infectious diseases, Reproductive problems, Antibiotic resistance and Bioinformatics. Major infectious diseases



studied are Brucellosis, Theileriosis, Babesiosis, Newcastle disease virus (NDV), Leptospirosis, Toxoplasmosis, Mastitis, Peste des petits ruminants virus (PPR) and Foot and Mouth Disease (FMD) with focus on developing new tools for diagnosing and preventing the diseases. During the year NIAB published 8 research papers in the peer reviewed scientific journals. The thrust areas of research are:

Studies on the virulence mechanisms of the zoonotic pathogen, *Brucella* to develop improved vaccines and diagnostic tools for animal and human brucellosis: Brucellosis is a chronic infectious disease of human as well as domestic and wild animals, caused by bacteria of the genus *Brucella*. Our studies focus on understanding the mechanisms of *Brucella* pathogenicity and host immune responses to *Brucella* infection with the objectives of developing efficient vaccines and diagnostic assays for brucellosis. Ongoing projects include identification and characterization of immunodominant antigens of *Brucella*, development of improved live attenuated vaccine for brucellosis by combinatorial gene knockout approach and identification and characterization of novel virulence genes and host factors that support *Brucella* replication.

Molecular Evolution, Characterization and designing of New Vaccine against the viruses Peste des petits ruminants (PPR) and Foot and Mouth Disease (FMD): Molecular evolution and characterization of PPR viruses from India and abroad have been studied using Sangers method. Currently these PPR viruses are being sequenced by New Generation Sequencing (NGS). DBT-BBSRC FADH grant has been successful that aims to study the disease resistance of PPR in different breeds of sheep and goats and to develop a DIVA vaccine for the national control programme. Under the scope of FADH grant collaborating with the Pirbright Institute and using reverse

genetics technique, for the first time Indian PPR vaccine strain (Sungri 96) has been rescued from a full length c-DNA clone. Currently this vaccine strain is being manipulated to make it a DVIA (Differentiating Infection in Vaccinated Animals) vaccine. Recently a new international grant has been awarded by BBSRC, UK to study the duration of immunity FMD vaccine adjuvanted with TLR III. The project will be collaborated between The Pirbright Institute, NIAB and Indian Immunologicals.

Characterization and Development of effective tools against Newcastle disease virus (NDV): NDV strain Komarov, a mesogenic vaccinal strain has been completely sequenced by classical method and the same has been validated using RNAseq data. Currently working on establishing the reverse genetics tool for NDV strain Komarov. The same will be used to develop thermostable and multivalent *in vivo* deliverable vaccine for use in poultry industry.

Molecular and Phylogenetic characterization of *Theileria* parasites from India: Theileriosis is one of the important tick borne diseases mainly caused by *Theileria* species causing mortality and huge economic losses worldwide among the livestock animals. Our study revealed an overall molecular prevalence rate of 32.40 % for *T. annulata* and 4.8% of *T. orientalis* infection from Andhra Pradesh and Telangana states. The Phylogenetic analysis of the strains identified novel genotypes among the *T. annulata* and *T. orientalis* strains from India. The emergence of these new genotypes could be an explanation for the frequent outbreaks of bovine theileriosis. The findings of the current study will support in devising policy or designing strategy to control theileriosis transmission to cattle. Further, research is going on for identifying novel genes which can help in designing new tools for combating against the disease.

Host-Parasite Interactions against Bovine Theileriosis: Theileriosis is characterized by lympho-proliferative disease. Research is under way to identify the key molecules of parasite involved in the immortalization of the host cell. This research work will help in identifying key molecules which can help in designing new anti-theilerial drugs. **Tick biology:** Ticks and tick borne diseases are causative of huge economic losses. Digestion of host blood is critical for the survival of the tick. Studies are going on to understand the mechanism(s) involved in digestion of host blood in the mid-gut of the tick. The identified molecules will be used as novel drug targets.

Reproductive biology: In this project, kisspeptin regulation of female reproduction is being studied. Kisspeptin is a novel neuroendocrine regulator of reproductive axis upstream to GnRH. Kisspeptin administration advances puberty. In our study, we found that chronic high doses of kisspeptin delays puberty in rats. It is not known if this is a direct effect or mediated through suppression of feed intake and body weight gain as observed in the study. The expression levels of kisspeptin and its receptor in gonads are being analysed. To understand the role of kisspeptin during pregnancy, preliminary studies have been carried out to study the plasma level of kisspeptin and expression level of kisspeptin and its receptor in brain, gonads and placenta. The role of kisspeptin in neuropeptide Y induced augmentation of LH release will be studied shortly. In addition, the effect of kisspeptin on plasma reproductive hormones such as FSH and LH, in comparison with GnRH, will be studied in buffaloes.

Elucidating the role of cell cycle regulators in *Toxoplasma gondii*: implications for cell cycle progression and transcription: *Toxoplasma gondii* is an important obligate intracellular protozoan parasite responsible for abortion, still birth and

neonatal mortality in humans and animals alike. *Toxoplasma* exhibits a unique three-phase cell cycle with only G1, S and M phases and a missing G2 phase. In spite of being a relatively well studied model system, there is very little information available about its un-conventional cell cycle and its regulators. In eukaryotes both cell cycle and PolIII transcription are regulated by a trimeric complex, called the Cdk activating kinase (CAK) complex composed of Cdk7, Cyclin H and MAT1. CAK's role is well documented in the higher eukaryotes however, existence of such a complex and its role has not so far been investigated in the parasites. Therefore, we designed our study to identify and functionally examine the role of *T. gondii* CAK components in cell cycle regulation and transcription. In this study we have identified the functional homologs of CAK subunits in *T. gondii* using yeast complementation assays. Interaction between the CAK components has been demonstrated by yeast two hybrid and GST-pulldown assays. Heterodimeric combination of CDK 7 and cyclin H display kinase activity which is significantly enhanced in presence of assembly factor MAT1. The robust kinase activity of this complex is abrogated in presence of specific CDK7 inhibitors. Here we report for the first time the presence of an active CAK like complex in the apicomplexan parasite *T. gondii* with important implications in the process of transcription.

Understanding host immune response and development of subunit vaccine against *Leptospira*: Current research is focused on understanding host immune response and development of vaccine against *Leptospira* infection. Cloned and expressed several outer membrane proteins of *Leptospira* and in process of screening them for innate immune activity (TLR activity) on cell lines. Selected proteins will be further tested in animal challenge model to understand protective mechanism and develop subunit vaccines.

Bioinformatics: *Brucella melitensis* strain sequenced by NIAB were analysed with other available strains for various different aspects of comparative genomics and evolutionary relationship as well as informative SNPs were extracted. In another effort, the sequence of an organophosphate (OP) compounds degrading bacterium has been assembled with *de novo* approach, in a single chromosome of 4,147,822 bps. The bacterium has been taxonomically placed in Sphingopyxis genus.

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE (THSTI), FARIDABAD

Translational Health Science and Technology Institute (THSTI) is designed to be a dynamic and interactive organization with a mission to integrate the fields of medicine, science, engineering and technology into translational knowledge and make the resulting biomedical innovations accessible to public health. The institution strives to effectively enhance the quality of human life by inculcating a culture of shared excellence through amalgamation of various disciplines.

THSTI has the following niche centres of research in a number of interface areas relevant to human health. Vaccine and Infectious Disease Research Center (VIDRC) is armed with the mission to study infectious disease and pathogens and understand host-pathogen interactions at the molecular and cellular level with an aim to generate translational knowledge for developing prophylactic and therapeutic measures against diseases prevalent in India. The primary goal of Pediatric Biology Center (PBC) is to serve as an interdisciplinary research center where research on the biological basis of childhood health and disease leads to the creation of knowledge-driven interventions and technologies that can

be sustainably implemented. The major objective of Centre for Human Microbial Ecology (CHME) is to investigate the outstanding association between microorganisms and the human host and attempt to understand the role and effect of microorganisms in human health and disease. Centre for Bio-design (CBD) has the mission to create medical technology innovation in India for affordable health care utilizing the biodesign concept and support services that extend from strategic bench work to commercialization. Policy Centre for Biomedical Research (PCBR) aims to bridge the huge gap that exists between health researchers and those who implement and are impacted by that research by providing technology analysis that could guide strategic planning and ensure the dual goal of meeting local health needs and supply global health technologies. Drug Discovery Research Centre (DDRC) has the mission to combine multiple disciplines to generate a robust and versatile pipeline for drug discovery research including the capabilities for analyzing large-scale data to identify the most promising targets for further drug development. Clinical Development Services Agency (CDSA) is an extramural unit of THSTI to facilitate the development of affordable healthcare products for public health diseases. As a training academy, CDSA aims to build capacity and capability in the area of clinical development and translational research.

I. Vaccine and Infectious Disease Research Centre (VIDRC)

The scientists at Vaccine and Infectious Disease Research Centre (VIDRC) are conducting research on medically important viruses and viral infections to define the early biomarkers and predict the dengue disease severity in paediatric patients. Studies showed that the dengue viremia did not correlate with disease severity. However, patients with secondary

infections had prolonged viremia as compared to primary infections. Further screening of a library of pharmacologically active compounds has identified inhibitors that completely inhibit dengue virus production in cell culture. Using a siRNA library screen, c-terminal Src kinase (Csk) was identified as one of the kinases involved in dengue virus replication and a possible target of the identified inhibitor molecule. Future efforts will focus on understanding the mechanism of action of Csk in virus replication and how this knowledge could be exploited for dengue antiviral development.

In the area of hepatitis, VIDRC scientists have developed an EGFP based replicon model of HEV in human hepatoma cells. A new virus-encoded factor, which plays an essential role in genotype-1 HEV replication by modulating the viral RNA-dependent RNA polymerase (RdRp), has been identified. This will help in establishing a better cell culture model to study HEV replication. Additionally, HEV RdRp has been purified from bacterial and mammalian cells for the development of an assay to characterize viral RNA replication. This should help in development of novel direct-acting antivirals.

For tuberculosis research at VIDRC scientists have implemented the CRISPRi system in both fast-growing *Mycobacterium smegmatis* (Msm) and slow-growing Mtb-complex bacteria. By using this approach efficient repression of diverse sets of genes in both Msm and Mtb-complex to negligible levels was observed.

II. The Pediatric Biology Centre (PBC)

The Pediatric Biology Centre was established with a vision to serve as an interdisciplinary research center for childhood health & diseases and become a national catalyst in designing solutions for maternal, neonatal and infant care engaging multiple expertise groups in this endeavor. It aims to bridge the gap between classical clinical

and population epidemiology and mechanistic biology in order to develop a fascinating science driven approach to solving maternal and child health problems.

As a part of Inter Institutional Program for Maternal, Neonatal and Infant Sciences-A translational approach to studying Preterm Birth, PBC has established the cohort of pregnant women, who are followed from early in pregnancy to delivery for documenting clinical and biological markers that would predict adverse pregnancy outcome. A study undertaken at PBC has characterized phenotypes of 22 leukocyte subsets from umbilical cord blood in term neonates who are born small for gestational age and appropriate for gestational age. Another study involving randomized controlled trial for the role of vitamin D supplementation on development of the immune system over the first 6 months of life is being evaluated. So far this study has enrolled 611 of the proposed 900 infants. The role of CD80 in nephrological disorders has been explored and demonstrated that CD80 disrupts the kidney podocyte slit diaphragm, by interacting with SD proteins leading to protein loss and proteinuria associated with nephrotic syndrome. PBC has also initiated two new grand challenges funded projects; (i) Creation of a bio repository and imaging data bank for accelerating evidence generation to facilitate children to thrive, (ii) Stress outcomes on pregnancy, fetal growth and birth weight: Development of methods to identify mothers at risk of preterm birth and intrauterine growth restriction resulting from maternal stress

III. Centre for Human Microbial Ecology (CHME)

The research at the Centre for Human Microbial Ecology (CHME) objective of the Centre is to investigate the outstanding association between microorganisms and the human host and attempt to understand the role and effect of

microorganisms in human health and disease. At present, CHME research is directed to investigate the role and impact of human microbiome in certain health disorders, which are directly linked to microbial richness, dynamics, and functional repository of the microbial genome. Currently, the human microbiome group at CHME is working on structural and functional metagenomics of gut and vaginal microbial communities with following research activities Profiling and cataloguing of human microbiota in different body sites with major emphasis on the gut microbiome; Role and impact of gut microbial richness and functional repertoires in nutrient and energy assimilation in under - nourished and healthy children; Study associations between the microbiome and clinical outcomes w.r.t pregnancy outcomes and the vaginal microbiome; Small molecule signaling systems of human gut pathogens; Molecular insights into antibiotic resistance traits of enteric bacterial pathogens.

IV. Centre for Biodesign and in-vitro Diagnostics (CBD)

The Centre for Biodesign has focus on in-vitro diagnostics. This Centre has established collaboration with various Departments at AIIMS, New Delhi.

V. The Drug Discovery Research Centre (DDRC)

The Drug Discovery Research Centre (DDRC) is a multi-disciplinary research centre that integrates basic with translational research in the field of drug discovery. The emphasis is to apply systems-level approaches and perspectives for both understanding disease-specific perturbations, and for the development of therapeutic strategies. DDRC has initiated a research focus on the metabolic syndrome, a chronic progressive disorder that has become a global public health concern. Research on this

disease is being conducted to integrate both experimental and theoretical approaches that converge through collaborative participation of multiple investigators. DDRC has developed novel approaches for analyzing high-throughput experimental data in order to extract dynamic, disease-specific networks. These approaches are being further refined and they intend to exploit these for the purpose of drug target discovery for Metabolic Syndrome.

VI. Clinical Development Services Agency (CDSA)

The Clinical Development Services Agency (CDSA) is registered as a not-for profit research organization. It aims to develop an eco-system for training and learning and work with public sector institutions, and small and medium enterprises (SME) to translate innovative technologies into medical products for public good. CDSA supports investigators and SMEs on regulatory process encompassing product development, registration and consultation on regulatory dossier preparation (EC, IND, CTD, etc). CDSA advises on regulatory affairs on preclinical and clinical product development and registration in India. CDSA has conducted 58 trainings so far with 14 training programs during 2015-16. CDSA has also implemented good documentation practices that supported the fundamental principles of GCP. Better GCP compliance protects subject's rights, safety and well-being. CDSA has conducted Site and Investigator feasibility reviews across 10 sites in India for BIBCOL bivalent OPV study in 1000 newborns. CDSA is coordinating a phase 2 clinical study on verapamil in tuberculosis sponsored by NIRT, Chennai. In order to reach out to the investigators and innovators on wider scale, a quarterly "Newsletter" has been started by CDSA. CDSA with 5 Centers of Excellence (KEM Hospital, Pune; Society of Applied Sciences (SAS), New Delhi; Center for Chronic Disease Control

(CCDC), New Delhi; JSS University, Mysore and CMC Vellore) has formed a collegium of Centers of Clinical Research Excellence for collaboration in education, training and capacity building and for collaboration in research, innovation, and clinical development support services.

During the year more than 25 research publications came out from THSTI. Instituted has also filed following patent applications:

- Cleaved functional clade C envelope glycoprotein: U.S. provisional patent application Serial No. 62/068,202
- Native trimeric ENV immunogen design: U.S. Patent Application No. 62,155,673
- HIV-1 CLADE C ENVELOPE GLYCOPROTEINS: US provisional application. 62/189,418.
- 7-substituted 2-nitro 6,7- dihydroimidazo [2,1-b][1,3] oxazine derivatives of their optical isomers, pharmaceutical composition containing the same as an active ingredient. Korean application no.DP-201-40911-01.
- Bhatnagar S, Khanna N, Natchu UCM, Wadhwa N, Gupta S, Bagga A, Saini S. "A method and device for detection of anti-transglutaminase antibodies" (patent no. 1133/DEL/2011 dated 18-04-2011).
- Ashutosh Tiwari, Chandresh Sharma, Anurag Sankhyan, Tarang Sharma, Shinjini Bhatnagar, Navin Khanna. "Monoclonal Antibodies specific to Salmonella typhiflagellin, and use thereof" (patent no. 683/DEL/2015 dated 13 March 2015)
- Ashutosh Tiwari, Tarang Sharma, Chandresh Sharma, Anurag Sankhyan, Shinjini Bhatnagar, Navin Khanna. "Production of recombinant ATB protein and its uses as diagnostic tool thereof" (patent no. 1350/

DEL/2015 dated 14 May 2015)

- Ashutosh Tiwari, Anurag Sankhyan, Subrata Sinha. "Human monoclonal antibodies specific to preS1 domain of Hepatitis B virus, and use thereof" (patent no. 2291/DEL/2015 dated 28 July 2015)
- Rajat Anand, Srikanth Ravichandran, Samrat Chatterjee. "Drug Targeting" (patent no. 78/DEL/2015 dated 09.01.2015)
- RajatAnand, SamratChatterjee. "Computer Software for Drug Targeting" (patent no. 52951/2014-CO/SW dated 20.08.2014)
- Amit Sharma, ManickamYogavel, Kanury Rao, Varshneya. "Novel Autophagy-inducing Compounds" (patent no. 1055/DEL/2014 dated 17.04.2014)
- Amit Sharma, ManickamYogavel, Kanury Rao, Varshneya. "Compounds for Induction of Autophagy" (patent no. 1056/DEL/2014 dated 17.04.2014)
- Sundeep Dugar, Dinesh Mahajan, Kanury Rao, Varshneya. "Novel Compounds as anti-Tubercular Agents" (patent no. 1431/DEL/2014 dated 30.05.2014)

NATIONAL INSTITUTE OF PLANT GENOME RESEARCH (NIPGR), NEW DELHI

The National Institute of Plant Genome Research (NIPGR) has played an important role in the past 16 years in contributing to basic plant science and applied agricultural research in frontier areas of plant genomics. Overall, the Institute's motto has been to engage in research that has long term implication for the betterment of the society. In the past academic year, apart from core research, NIPGR has also made attempts to translate few of the technologies developed through basic research activities for their application



in agriculture. Some of the important findings covering research done in important crops namely, chickpea, tomato, rice, foxtail millet and mustard and other developments at the Institute, for the period under report are as follows:

The Institute has developed advanced version of chickpea draft genome and performed sequence alignment to the genetic map. Genotyping by sequencing technology has been utilized to simultaneously identify a large set of SNP markers and construct a high density inter-specific linkage map of chickpea. NIPGR has focused not only on development of these genomic resources but also on transcriptomic resources for gene discovery. One of the examples in this direction is profiling of root nodule transcriptome. Another important focus area of research at the Institute is genetic and molecular dissection of seed size and weight associated traits for seed quality and yield improvement in chickpea. Further, analyses of small RNA deep sequencing data sets generated from various tissues of chickpea identified large number of novel miRNAs. Such discovery of candidate genes has led to identification of function of root specific miRNAs and these outputs will be useful for improvement of various agronomic traits in chickpea in future. For tomato crop improvement, the Institute is focusing on two main areas, namely, development of thermotolerant plants and increasing shelf life of the harvested fruits. Three key heat stress response gene families and microRNAs targeting them are being studied to understand the thermotolerance. Also important genes regulating fruit ripening are being manipulated to delay the ripening with the aim to increase shelf life.

Institute is also interested in developing rice plants with better utilization of phosphorus, a critical but less abundant nutrient. Whole-genome sequencing of low phosphorous sensitive

and tolerant genotypes allowed identification of high resolution markers for low phosphorous tolerance. Further, few labs at the Institute are working to develop rice plants with better root system under stress, this is yet another focus at the Institute. Under abiotic stress tolerance research, functional characterization of OsSAP gene family has been one of the major focuses. NIPGR has also made progress in understanding gene regulatory networks during flower, anther, seed development and seed vigor/viability in rice. In foxtail millet, association mapping for few yield contributing traits and genome wide analysis for abiotic stress tolerance related traits has provided considerable insight in understanding these two complex agronomically related aspects.

On the product development, Institute is making steady progress in many fronts. Two such examples are: development of a simple and quick on-site early diagnostic kit for rice sheath blight pathogen and development of low glucosinolate Indian mustard lines and assessment of their agronomic performance under contained field conditions. This is expected to be a useful product because of its nutritive value.

Some of the basic biology research programmes that achieved significant progress during the year include, understanding glucose signaling, light dependent regulator networks, characterization of inositol metabolism and dissection of mediator protein complex. Various findings have also been made in the area of plant proteomics and immunity. Further, several important bioinformatics tools and databases were developed. Few important databases, namely, EssOilDB - a repository of plant essential oils, IGMAP - an integrative genome maps for plants, CGWR - chickpea genomics web resource and FmTEMDB - foxtail millet transposable element-based marker database, have utility for wide

spectrum of plant science researchers.

In the year 2015, researchers at the Institute have contributed 118 publications in various reputed international and national journals/books. In addition to this, 03 patents were filed/ granted. Many of NIPGR students and scientists have been recognized with various national/international honors, fellowships and awards. With the addition of three new faculties, thus taking total current strength to 25, and fully functional additional labs in the newly constructed block, expanding the laboratory space and core facilities, NIPGR is poised to take up widened research mandates. In addition to expansion of research programmes under the current thematic areas, the new areas of research recently initiated include understanding plant-herbivore interaction, nitric oxide signaling under flooding stress and shade tolerance of plants. Such research activities are expected to not only strengthen the 'basic plant biology' research in our country, but also contribute to Indian agriculture through crop improvement.

Technology/Products/Database processed/ developed

1. IGMAP: Interactive Genome Maps for Plants; a platform for mapping and clustering of genes and gene families. Available at <http://nipgr.res.in/igmap.html>.
2. CGWR: The Chickpea Genomics Web Resource. Available at <http://www.nipgr.res.in/CGWR/home.php>.
3. EssOilDB: A database of essential oils reflecting terpene composition and variability in the plant kingdom. Available at <http://nipgr.res.in/Essoildb/>.
4. An open access Foxtail millet Transposable Elements-based Marker Database has been

constructed for catering the developed marker resource to the global scientific community through the web address <http://59.163.192.83/ltrdb/index.html>.

5. Low glucosinolate Indian *B. juncea* line(s), having total seed-glucosinolate content less than the internationally acceptable limit (30 α moles g⁻¹ seed DW) are currently being analyzed for their agronomical performance under the containment field conditions.
6. Development of simple, quick and on site early diagnostic kit for *Rhizoctonia solani*, the causal of sheath blight disease of rice.

RAJIV GANDHI CENTRE FOR BIOTECHNOLOGY (RGCB) THIRUVANANTHAPURAM

Rajiv Gandhi Centre for Biotechnology (RGCB) major strategic goals are understanding the biology that defines basic mechanisms involved in the disease process and its implications for human health, turning research into technology innovation and on to business, trans-disciplinary health science to inform individual, clinical, and public health decision making to improve health and developing and retaining a sustainable pipeline of biotechnology professionals across a range of related disciplines including fundamental science, technology development, translation, policy and outreach through efforts in education, training, and career development.

During the year DBT has approved an SFC that will allow RGCB to create a specialized ecosystem called Bio-Innovation Center (BIC). This will be a unique knowledge center and hub for mid and high level innovation founded on deep and advanced level technical platforms, multidisciplinary cores that will seed growth and innovation. The transit



facility located at the KINFRA Film and Video Park in Thiruvananthapuram now houses the RGCB's Bio-Imaging, Genomics and Laboratory Medicine & Molecular Diagnostics core facilities in addition to laboratories for Chemical Biology and Tropical Disease Biology. This facility also hosts research programs of the Srinivasa Ramanujam Institute for Basic Sciences, an R&D institution of the Kerala State Council for Science, Technology and Environment (KSCSTE), Government of Kerala. RGCB has also started a major initiative on "Ayurveda Inspired Discovery". The program has clear objectives that include developing a center of excellence for generating knowledge on treatment response and effects on pathophysiological processes in response to Ayurveda based therapeutics

Significant Research Achievements

RGCB identified a phosphorylated residue, Serine 6 in the zinc finger domain of Star- PAP, a nuclear non-canonical poly(A) polymerase with specific mRNA targets. The intranuclear phosphorylation of S6 by CKI is necessary for the nuclear retention of Star- PAP and its eventual interaction with PIPKI. Unlike at the catalytic domain, the phosphorylation at ZF domain is independent of oxidative stress. This is suggestive of a signalmediated regulation of CKI activity. This conceptually paves way to novel roles for phosphorylation in determining Star-PAP target mRNA specificity.

Scientists at RGCB were quite successful in extracting a semi-purified fraction from the dichloromethane extract of *W. tinctoria* leaves named DW-F5. This chemical was proven to completely abolish MITF-M through BRAF, Wnt/ -catenin and Akt-NF B signaling pathways in *in vitro* and *in vivo* studies. Elucidating the

anticancer properties of the active principle of *W. tinctoria*, this study enriches the scope of developing potential drug formulations from natural resources.

RGCB deciphered the entire proteomic profile of the pathogen during dormancy and reactivation. Functional correlation between energy metabolism and the relative levels of different proteins during different stages of infectivity is giving us a whole new target for therapeutic intervention to prevent reactivation of latent infections. In this era of personalized medicine, stem cell therapeutics is gaining a strong foothold. Understanding the molecular mechanisms of cellular differentiation cannot be compromised at any level.

RGCB also worked in the less explored area of hematopoietic differentiation from hemogenic embryonic stem cells in depths. Identifying and analyzing the complex mechanisms of regulation of transcription factor RUNX1 by histone chaperone HIRA newly defined the RUNX1-HIRA axis during the developmental process of blood cells.

During the year RGCB published more than 80 research publications in peer reviewed scientific journals. Details of patents filed /technologies developed during the year are as follows:

Patents filed

- A method of detecting and quantifying the calcium conducting activity of calcium channel proteins
- A process for the preparation of plant extract that can inhibit neuronal ligand gated calcium channel

Patents granted

- Assay for detection of transient intracellular Ca²⁺ (European Patent Office)
- Novel porphyrin derivatives for photodynamic therapy (PDT): a process for the preparation thereof and their use as PDT agents and fluorescence probes for biological applications (European Patent Office)

Technologies developed

- A method of detecting and quantifying the calcium conducting activity of calcium channel proteins
- A process for the preparation of plant extract that can inhibit neuronal ligand gated calcium channel

Technologies commercialized

- Assay for detection of transient intracellular Ca²⁺

INSTITUTE OF BIORESOURCES AND SUSTAINABLE DEVELOPMENT (IBSD), IMPHAL

The main mandate of IBSD is conservation and sustainable utilization of bioresources for the socio-economic development of the North Eastern region. Research and Development activities are pursued under core areas such as medicinal plants, horticulture, algae, microbes, insects, fisheries, wildlife and other aquatic bioresources with emphasis on bioresources database development, bioresources education, Human Resources Development. During the year IBSD has published more than 25 research publications in peer-reviewed scientific journals.

Scientific Achievements:

In the Plant Resources programme, a beta-aminobutyric acid mediated drought stress alleviation pathway in maize has been described. Further, a disease-free Khasi Mandarin

production using *in vitro* microshoot tip grafting and its assessment using DAS-ELISA and RT-PCR has been developed.

In the Natural Product Chemistry programme, a novel series of flouoroarene derivatives of artemisinin have been synthesized. The anti-diabetic effects of *Cycas pectinata* have also been demonstrated. The essential oil of *Cephalotaxus griffithii* have also been shown to recruit mitochondria-initiated and death receptor-mediated apoptosis pathways in inhibiting the proliferation and migration of human cervical cancer cells.

In the Microbial Resources programme, bacterial dynamics have been characterized during the yearlong spontaneous fermentation of ngari, a dry fermented food product of Northeast India. Gut diversity of the tribes of India have also been compared with the worldwide data. The production of Angiotensin I Converting Ezyme Inhibitory (ACE-I) Peptides during milk fermentation and their role in reducing hypertension has been demonstrated. The characterization and optimization of Bio-flocculant exopolysaccharide by Cyanobacteria has also been published.

In the Animal Resources programme, the complete mitochondrial genome of the wild eri silkworm, *Samia canningi*, has been published. Further, a bioactive molecule has been isolated from the root stock of *Colocasia esculenta* (L.) and characterized it as 2, 3-dimethylmaleic anhydride (3, 4-dimethyl-2, 5-furandione) based on various physico-chemical and spectroscopic techniques (IR, ¹H NMR, ¹³C NMR and Mass)

During the year, IBSD has initiated several new programs. This started with bringing together leading experts from all over the country for



the 1st National Bioresources and Sustainable Development Summit that was held at IBSD, Imphal during February 19-20, 2015 and a key output of this summit was a focused “Imphal Declaration 2015”. As a follow up of IBSD efforts towards this declaration, IBSD has pioneered several initiatives. IBSD has also initiated research programs on Conservation of Siroi Lily (Manipur’s State Flower) and Black Rice Improvement Programme. IBSD launched India’s First Cherry Blossom Festival Initiative for Sustainable Eco-Tourism in Meghalaya. IBSD has also signed a Memorandum of Understanding (MoU) with CSIR-Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh for joint research, technology development and Human Resource Development through mutual sharing of infrastructure, laboratory, library facilities and logistic support. Efforts have been initiated to sign MOU with leading institutions from USA, France, Belgium, Korea and Japan soon.

BIOTECH SCIENCE CLUSTERS

The National Biotechnology Development Strategy approved by the Government of India envisions institutional cluster development as a key strategy to promote innovation and accelerated technology and product development, in an approach wherein facilities for promoting life science research bioengineering, translational biotech sciences, platform technological resources and biotech entrepreneurship are located together to nurture and promote innovation for building successful solutions and enterprises to maximize synergy and efficiency.

Bangalore Life Sciences Cluster for Multiscale Basic and Applied Research in Biological Sciences (B-Life):

Bangalore Life Sciences Cluster for multiscale basic and applied research in Biological Sciences (B-Life) has been established in January, 2015. The cluster partnering institutes are as follows: Institute for Stem Cell Science and Regenerative Medicine (inStem) Bangalore; National Centre for Biological Sciences (NCBS), Bangalore; Centre for Cellular and Molecular Platforms (C-CAMP), Bangalore; and Institute of Bioinformatics and Applied Biotechnology (IBAB), Bangalore. They have identified and setup a system to enable access to more than 20TB of cancer data placed by NCI under dbGaP (controlled access). They are developing a predictive mathematical model describing the role of cytokines in Rheumatoid arthritis. During the last year, they have developed and used automated pipelines using Bioconductor packages in R for analysing microarray data stored in the open source repositories line Gene Expression Omnibus (GEO). These pipelines can analyse the repository data from various microarray platforms like Affymetrix, Illumina and others. By modifying and combining these pipelines with MySQL libraries in R, they have the potential to realize a powerful tool for creating large curated microarray gene expression data towards big data. analytics. The R statistical package is becoming an important open source tool for data analytics in the field of business analytics as well as in life sciences. The basic use of the tool is a part of the regular curriculum in IBAB along with Biostatistics. They made special efforts to prepare specialized applications in R for high end data analytics.

NCR Biotech Science Cluster, Faridabad

NCR Biotech Science Cluster is being established involving five autonomous institutes of DBT (NII, NIPGR, NBRC, THSTI and RCB). The

mandate of the cluster is to support discovery of basic mechanisms in biology and development of novel technologies; to facilitate public-private partnerships for the development of biotechnology business incubators and parks; to network with the potential constituent institutions to create a synergistic ecosystem for accelerating discoveries and facilitating translational research and to provide, in terms of infrastructure, state-of-the-art technology platform center, animal facilities and bio safety containment laboratories. The cluster has initiated 'Advanced Technology Platform Centre (ATPC)' that would act as a catalyst for

multidisciplinary basic and translational research by providing relevant instrumentation, training and professional services for the stakeholders and others alike on behalf of the Biotech Science Cluster in Faridabad. Secondly a biotechnology Incubator is being established as part of the Biotech Science Cluster in partnership with BIRAC. This state of the art facility would provide new and emerging companies with a compatible environment to support their start-up phase and increase their likelihood of success. In addition, the incubator will also facilitate prototype to product conversion for devices and implants.



PUBLIC SECTOR UNDERTAKINGS

1. BHARAT IMMUNOLOGICALS AND BIOLOGICALS CORPORATION LIMITED (BIBCOL)

Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL) is Central Public Sector Unit (PSU), a listed company and having authorized and paid up capital of ₹ 43.18 crore under the administrative control of the Department of Biotechnology (DBT), Ministry of Science & Technology, Govt. of India. BIBCOL is a leading biotechnology company based in Uttar Pradesh India. The company has its OPV plant in state of Uttar Pradesh, India. BIBCOL was established in 1989 with the novel theme to achieve the country as polio free nation.

It started its commercial production in 1996 and since then has supplied billion of doses of oral polio vaccine to Ministry of Health & Family Welfare for its polio eradication program. In the year 2015-16 (up to Dec 15), BIBCOL has supplied about 136 million doses of oral polio vaccine and achieved a turnover of Rs 72.5 crore. Company is striving hard to diversify into other products for its long term sustainability and growth. In this endeavour company has signed MOU with a Dutch company for development of vaccines.

BIBCOL started its journey with single product (tOPV) but gradually added more products and now produces Diarrhoea Management Kit, Oral Polio Vaccine (mOPV, bOPV and tOPV), and Zinc Dispersible Tablet. BIBCOL is now continuously doing well and based on audited accounts its turnover for the financial year 2014-15 was 146.22 crores with Profit After Tax (PAT) of 1.54 crores and for the year 2013-14, the turnover was of ₹ 202.75 crores with PAT of ₹ 6.40 crores.



tOPV Vials with dropper



BIB Zinc dispersible Tablets



Combo kits (Zic tab + ORS)



Manufacturing area

2. INDIAN VACCINES CORPORATION LTD (IVCOL)

Indian Vaccines Corporation Limited was incorporated in March 1989 as a Joint Venture Company promoted by Govt. of India (Dept. of Biotechnology-DBT,) Pasteur Merieux Serum & Vaccines (PMSV) France and Indian Petrochemicals Corpn. Ltd. (IPCL- a PSU) with a paid up capital of Rs. 18.78 crores, with the objective of manufacturing vaccines based on Verocell Technology to be supplied by PMSV France. The company came into existence after a joint venture was signed on 1st February 1989.

The main objective of the company was to manufacture Injectable polio vaccines (IPV) to be incorporated in the mass immunization programme of Govt. of India. However, IPV was not approved by W.H.O as a result the project was put on "HOLD" in February 1992. Thereafter P.M.S.V. exited from the J.V. in 1998 by selling its shares to DBT. In the year 1999, National Brain Research Centre (NBRC) (An Autonomous Body) was given 38.78 acres of land on thirty years lease, at a nominal lease rent of Rs.10 lacs per annum. This is the only income of the company at present. The company has no

trading or commercial activity at present and is maintaining establishment to look after site and complying with the statutory obligations under the company's act 2013. IVCOL is presently being controlled by a board of Directors, with two Directors representing RIL and one Director representing GOI (DBT),

Company has been incurring losses for the last two years (Rs.165.36 lacs for 2013-14 and Rs.164.37 for 2014-15) and has accumulated losses of Rs.577.16 lacs as of 31.03.2015.

Share holding of IVCOL at percent is as under.

Govt. Of India (DBT)	66.67%
Reliance Industries Ltd	33.33%

3. BIOTECHNOLOGY INDUSTRY RESEARCH ASSISTANCE COUNCIL (BIRAC)

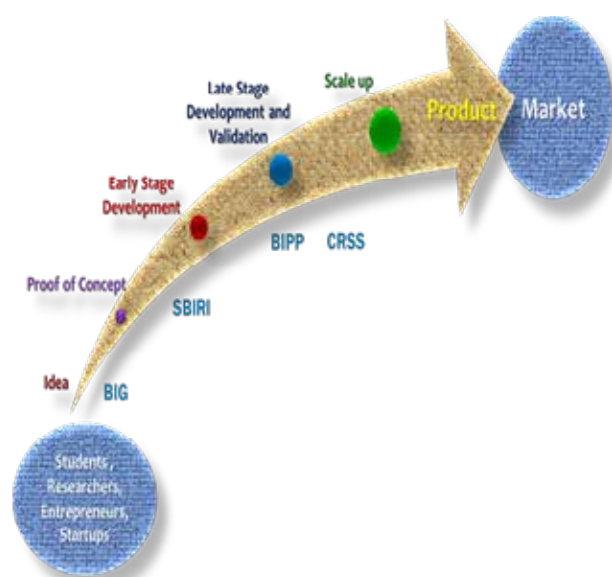
Biotechnology Industry Assistance Council (BIRAC), is a not-for-profit PSU under the aegis of Department of Biotechnology (DBT). BIRAC being a unique organization in the biotechnology ecosystem, works as an interface agency of the Department of Biotechnology, Ministry of Science & Technology, and has the mandate of fostering and nurturing the Biotech Enterprises specially start-ups and SME's for enhancing their innovation research capacities and promoting affordable product development. BIRAC supports Industry-Academia interaction, serve as a single window for the emerging biotech industry, helps establish connectivity with professional and institutional networks, and provides financial support for quality innovation targeted at affordable solutions and product development.

BIRAC is working towards providing enabling support and empowering the entire innovation ecosystem and today more than 310 companies

- large, small, medium and start-ups; and more than 170 entrepreneurs are a part of BIRAC's Innovators network. (BIRAC) has its registered office in the National Capital Territory of Delhi with an authorized capital of Rs. 1 crores divided into 10,000 equity shares of Rs. 1,000 each.

Empowering, Enabling & Driving the Indian Biotech Innovation Ecosystem for Affordable Product Development

BIRAC funding modalities recognise and evaluate the 'staged risks' and the 'innovativeness' of several product development proposals. The funding schemes cover all aspects of the innovation pipeline. New ideas that have a potential for commercialisation to bubble and grow are encouraged. Support is provided for Proof of concept, alpha prototype projects, late stage product development through clinical and field trials, pilot stage and scale up. Many of the funding schemes endeavour to bring together industry and academia to work in partnership underlying BIRAC's commitment to build strong bridges between these two important stakeholders of biotech ecosystem.



BIRAC Support at various stages of Product Development

BIRAC supports affordable product development by empowering and enabling Indian biotech innovation ecosystem. To encourage start ups and SMEs to take roots and bring affordable products to the market, BIRAC is funding the entire span of biotech arena through its pioneering schemes such as Biotechnology Ignition Grant (BIG), Small Business Innovation Research Initiative (SBIRI), Biotechnology Industry Partnership Programme (BIPP), Contract Research and Services Scheme (CRS) and Social Innovation programme for Products: Affordable & Relevant to Societal Health (SPARSH).

BIRAC's innovation funding schemes encourage collaboration between the two important stakeholders of biotech ecosystem i.e. industry and academia and provide a conducive environment for collaborative R&D. Out of all the projects supported, industry has been instrumental in taking forward 295 technologies/products through their own efforts as well as using viability funding from BIRAC. An early stage grant has been provided to more than 99 individuals for promoting entrepreneurship in biotechnology to help bridge the gap between idea and innovation. BIRAC has been actively involved in promoting collaborations and has supported 115 collaborative projects till date out of which 107 projects had Industry-Academia collaborations and 8 projects had Industry - Industry collaboration. These projects have delivered 23 affordable products/technologies and 19 early stage technologies in addition to generating 45 intellectual property and developing five facilities.

Fostering Innovation by Promoting Entrepreneurship

Entrepreneurship Development at BIRAC, focusses not only on the funding support, but also on making available the right infrastructure, mentoring and other networks for technology

transfer and licensing, IP and business mentoring including regulatory guidance.

In order to foster innovation, BIRAC has started several initiatives and has achieved considerable success in these. BIRAC has a strong belief that the “bio-innovation capital” of the nation would come from novel ideas which have a commercialisation potential and that evolve out from start-ups or academic spin-offs.

Biotechnology Ignition Grant

BIRAC’s strategy is to populate the start of the innovation funnel with numerous exciting ideas which have an unmet need for funding and mentorship. This strategy is fulfilled through a grant funding scheme called Biotechnology Ignition Grant (BIG) which is available to scientist entrepreneurs from research institutes, academia and start-ups. The scheme is designed to stimulate commercialization of research discoveries by providing very early stage grants to help bridge the gap between discovery and invention.

The BIG Innovators receive mentoring and networking help from five BIG Partners (C-CAMP, Bangalore, IKP Knowledge Park Hyderabad, FITT at IIT Delhi, NCL Venture Centre Pune and KIIT-TBI, Bhubaneswar) during the course of the project.

Presently, around 170 young entrepreneurs are being supported through BIG.

Bio-incubators

In order to foster techno entrepreneurship in biotechnology, BIRAC has initiated a scheme for strengthening and up-gradation of the existing bio-incubators and also to establish new world class bio-incubators in certain strategic locations. These Bio incubators provide incubation space and other required services to start-up companies for their initial growth. Fifteen existing incubators

across the country have been strengthened and over 150,000 Sq. ft of Bio-incubator space has been created to support start-ups. By strengthening these incubators, till now BIRAC has supported approximately 186 start-ups and individual entrepreneurs over three years either directly as resident incubatees or indirectly as associates through various services models.

BIRAC has supported skilled manpower for managing these incubators. A total of 59 jobs were generated through 13 incubators in FY 2015-2016. Another 13 jobs will be created by the end of 2016. A total of 72 skilled jobs were created through Bio-incubators Support.

Mentorship and Capacity Building

Ignite Boot Camp

BIRAC and Centre of Entrepreneurial Learning (CfEL) of Judge Business School, University of Cambridge had initiated a partnership that enables BIRAC supported applicants to take part in CfEL’s flagship intensive entrepreneurial boot-camp programme called “Ignite”, which is aimed at providing scientists and early Start Up’s to explore entrepreneurial opportunities of their innovative ideas and transform them into a business project. In the year 2015, BIRAC along with its Ignition Grant partners (C-CAMP, IKP Knowledge Park, FITT at IIT Delhi, NCL Venture Centre, Pune and KIIT-TBI, Bhubaneswar) selected 3rd batch of five candidates to attend the intensive programme at Cambridge. The third batch of 5 BIRAC supported IGNITE candidates underwent training at Cambridge for two weeks in July 2015 and have given positive feedback about the programme.

Apart from this, the five BIG partners regularly organize mentoring workshops for the Innovators incubated with them.

Roadshows and IP Management Workshops

BIRAC organized a series of Roadshows and IP Management Workshops at Kolkata, Bhopal and Chennai to enhance its outreach and make the stakeholders and potential innovators and entrepreneurs about the relevance and importance of securing and exploiting intellectual property. Two more such workshops are planned at Goa and Delhi.



Three Regulatory workshops for New Drug Approvals, Bio-pharmaceuticals and Phytopharmaceuticals were organized by BIRAC in collaboration with Clinical Development Services Agency (CDSA). BIRAC in collaboration with IIT Madras, conducted a hands-on Capacity Building Workshop on Downstream Processing of recombinant proteins and other biomolecules. 28 representatives from 22 different enterprises participated in the workshop. The primary objective of this workshop was to provide hands on training to participants from industries who are working in the area of bioprocess optimization, with a primary focus on recombinant systems.

Social Innovation

Sparsh is the social innovation program of BIRAC which is highlighting the need of Innovative solutions to society's most pressing social problems. The program since its inception on 15th Aug 2013, aims at investing in ideas and innovations that improve health care of all Indians and provide affordable product development in social sector. The first two calls of Sparsh are

aligned with the UN Millennium Development Goal 4 and 5 i.e. Reducing Child mortality and Improving Maternal Health.



Social innovation Immersion Program (SIIP) of Sparsh is a Knowledge Innovation platform available to "Social Innovators" for identifying and developing specific needs and gaps in healthcare arena. The programme is currently supporting 15 social innovators who are trying to develop solutions for most pressing problems in the MCH arena.

Maternal and Child Health (MCH) Cluster of SIIP is envisaged to be operationalised with partners who help provide a whole host of technical, business and Marketing mentoring to the fellows. Currently, it is managed by four Incubation Partners who provide the rural and clinical immersion to the innovators. These four partners are:

The SIIP Partners have recruited 15 social Innovators for the Immersion. These Innovators are provided rural Immersion and exposure to Clinical settings. They are mentored on process of systematic clinical & Community observations, needs assessment, refinement and affordable technology development. The Social Innovators will come out with detailed document on the 2-3 final ideas which will be narrowed down for prototype development.

BIRAC expects the Social innovators to reach a point where they either have a ready business plan to pitch to investors, or an advanced proposal with some preliminary results suitable for further funding.

Under the Affordable development mandate Sparsh has supported around 7 Individuals and

10 Small and Big Companies through two calls over duration of two years.

Few examples of the technologies which are supported under the Sparsh are:

1. Microfluidics based On chip Real Time PCR Device for Neonatal and Maternal
2. Noninvasive electrical device for transcutaneous iron replenishment
3. A point of Care (POC) device for detection of antibiotic sensitivity of uropathogens in human urine
4. Electricity Free Baby Incubator
5. A novel technique for monitoring of fetal growth through volume imaging of the fundus and estimating the gestational age, amniotic fluid index and intra uterine growth abnormalities of the fetus
6. Development of a point of care diagnostic tool for pre eclampsia screening
7. Implantable Scaffolds for Obstetric Fistula
8. Establishing proof of concept for recombinant Sinapultide A peptide for the treatment of respiratory distress

Building Strategic Alliances for Affordable Product Development

a. BIRAC-CEFIPRA-French Embassy in India

BIRAC forged a partnership with CEFIPRA and French Embassy in India to launch a call for proposals on 19th March 2014 in Red Biotechnology area providing funding support up to pre-commercialization stage. Continuing this collaboration a joint call with CEFIPRA and French Embassy was launched on 15 October 2015 for the thematic area:

- Molecular diagnostic for prediction of Alzheimer’s and other dementia
- New assisting technologies for mobility of physically challenged (including prosthesis and robotics applications)
- Biomaterials and cell engineering for health applications

Also, a joint call with CEFIPRA and Bpifrance Financement, a French Public Investment Bank was announced on 18 November 2015. The theme of the call focussed on development of industrial application oriented health technologies in the areas of:

Digital healthcare: ehealth, Tele-monitoring, Tele-care connected health, health IT, Big data, e-patients, internet of M-health things “m-IoT”, 4Ghealth.

Individualized medicine: Development of therapeutic solutions for individual patients, repaired human, pharmacogenetics

b. BIRAC-DeitY

BIRAC collaborated with Department of Electronics and Information Technology (DeitY), Ministry of Communications & IT, Government of India, to launch an Industry Innovation Programme for Medical Electronics. DeitY has pledged INR 10.50 crores for promoting innovation in Medical electronics, while BIRAC will manage the entire programme. The first call under the partnership was launched in May 2015, focusing on – Imaging & navigation, technologies for chronic diseases, convergence of medical devices and bioinformatics, and increasing the outreach through medical electronics.

c. BIRAC-USAID-IKP

BIRAC collaborated with USAID to fund a joint programme on TB Diagnostics which will be managed by IKP Knowledge Park, Hyderabad.



The programme call is planned to aim at supporting new diagnostics for TB in collaboration with BIRAC. IKP proposes to allot a total of USD 2.0 million for this call with a funding of USD 1.0 million each from BIRAC and USAID. The call was launched on December 1, 2015 focusing on the theme - Innovative Solutions from India to improve TB Detection, Case Notifications and Treatment Outcomes for Adapting in Developing Countries in Africa and South Asia and Scaling up in India.

d. BIRAC-BMGF-DBT Grand Challenges in Healthcare, Agriculture, Food & Nutrition

An umbrella Memorandum of Understanding was signed in June 2013 by BMGF with the Department of Biotechnology (DBT) in India to collaborate on health and development research. BIRAC is an implementing partner for initiatives under the MoU. A joint DBT-BMGF funded program management unit (PMU) is set up at BIRAC to implement the initiatives carried out under the MoU. The funding for the PMU was split 50% BMGF and 50% DBT. There are several specific initiatives in this partnership program

Grand Challenges India (GCI): The program also has funding support from USAID. 3 Calls have been announced so far.

- a. Ist Call: Achieving healthy growth through Agriculture and Nutrition in which 5 projects were awarded. The first round of monitoring & evaluation has been completed.
- b. IInd Call: Reinvent the Toilet Challenge in which 6 projects were awarded. The first round of monitoring & evaluation has been completed.
- c. III Call: All Children Thriving in which 7 projects got award in BIRAC's Innovator Meet 2015. Kick-off meeting is expected in April 2016.

e. BIRAC-UKTI (UK Trade & Investment)

BIRAC & UKTI entered into an MoU to be Knowledge Partners for boosting the innovation capabilities of the Indian and British biotech/life science industry and foster collaborations between the two countries through following modes:

- UKTI would provide BIRAC supported companies with relevant information (technical, markets & possible distribution channels) regarding the UK's S&T ecosystem especially the UK's life sciences industry
- UKTI would facilitate BIRAC supported companies to connect and network with relevant stakeholders in the UK (business, regulatory, academia)
- UKTI would seek BIRAC's support in connecting British biotech industry with Indian biotech industry
- BIRAC & UKTI would explore either creating new knowledge networks or exploring leveraging already existing networks for the benefit of biotech/lifescience industry in India and the UK

f. BIRAC-Lords Education and Health Society (LEHS), through its WISH Initiative

BIRAC entered into an MoU with LEHS to scale up the BIRAC supported innovations into the Primary Healthcare system through the SCALE initiative of LEHS.

The objectives of this partnership are to:

- a. Combine the focused efforts of BIRAC and LEHS towards accelerating innovation and enterprise scale up for sustainable healthcare delivery systems in primary health care.
- b. Handhold the start-ups'/entrepreneurs'/companies' innovations in healthcare

developed through the funding assistance of BIRAC, so as to culminate into affordable solutions for improved access and quality of primary healthcare.

Industry - Academic Interaction

a. BIRAC's Fourth Innovators Meet was organized on 15-16 September 2015 at New Delhi, over 200 participants from academia, industries, key stakeholders and policy makers. The theme of the event was - Prioritizing Innovation Research for Affordable Product Development.

It was attended by over 250 delegates from

Government, academia, industry, start-ups and budding entrepreneurs. The event witnessed the announcement of the prestigious BIRAC Innovator Awards and the Grand Challenges IndiaGrants - for the All Children Thriving Call, which is a collaborative initiative of DBT, Bill & Melinda Gates Foundation, managed by BIRAC.

Dr. R.A. Mashelkar, Chancellor, AcSIR & National Research Professor, National Chemical Laboratory was the esteemed guest of the meet. He gave his Plenary Talk entitled 'Building India as an Innovation Nation'.



Foundation day celebration of BIRAC



S.No	Applicant	Innovative Product/Technology/PoC/IP
Products/Technologies		
1	Shantani proteome	Validation of Small-molecule Target Identification Technology for its Versatility (SBIRI)
2	Celestial Biologicals	Scale-up of Plasma Fractionation Facility for High Value Products (BIPP) *Two products i.e. Albumin & Immunoglobulin have come out
3	Merkel Haptic Systems	Hi-fidelity affordable mannequin for effective CPR (Cardiopulmonary Resuscitation) Training (BIPP)
4	Sahajanand Medical Technologies Pvt. Ltd.,	Development & building indigenous capability for Balloon Catheter Manufacturing (BIPP)
5	Persistent Systems	SanGeniX: A comprehensive next generation sequence (NGS) data analysis solution (BIPP)
6	Embio Limited	Demonstration of conversion of Benzaldehyde to Phenylacetylcarbinol (PAC) with improved efficiency on scale of 4 KL (Phase-II) (SBIRI)
Early Stage Technologies (PoC)		
1.	Tran-Scell Biologics	Stem Cell Implant Bio-complexes for Periodontal Tissue Regeneration (SBIRI)
2.	Orbit Biotech	Development of Reuterin based biopreservative as an alternative to harmful sodium nitrite & sodium nitrate based chemical preservatives; for use in packaged meat food products (SBIRI)
3.	Hi Tech BioSciences India	Development of platform technology for nitrilase catalyzed biotransformation processes (Phase I) (SBIRI)
4.	Shantani proteome	Pre-clinical Development of First-in-class Glucose management of type-2-diabetes and related complications (SBIRI)
5.	Serum Institute of India	Development of HPV Vaccine (BIPP)
6.	Kumar Organic Product Ltd.,	Sustainable and versatile microbial polymers: a bio-based prospect for India (BIPP)
7.	Geo Biotechnologies	Association mapping and whole Genome marker assisted recurrent selection for development of Abiotic stress resilient Maize (BIPP)
8	Bug Works	Novel antibiotics for Gram negative bacteria: Structure based strategy to Ameliorate antibiotic efflux and enhance compound efficacy (BIPP)
9	Saveer Biotech	Commercial Scale Production of Nano-pesticides and Nano-fungicides for Indian Agro-industry (BIPP)

INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY (ICGEB)

In the year 2015, the centre has made a significant progress in the field of Molecular biology and Biotechnology. During the year one Indian Patent application entitled “a novel selectable marker system for transgenic plants” has been granted and three new Indian patent applications and one PCT have been filed. The Center has also conducted two training programs on a) Discovery of new Drugs against Malaria and b) MicroRNAs in Plant Development stress, respectively. The major focus of the Center is in two areas; Human Health and Plant Sciences. The research at the Centre can be broadly categorized in nine areas viz. Malaria, Virology, Immunology, Recombinant Gene Products, Structural and Computational Biology, Plant Molecular Biology, Insect Resistance, Plant Transformation and Synthetic Biology and Biofuels.

MALARIA

The primary focus of Malaria research at ICGEB is to understand the basic biology of blood stage plasmodium parasites and to develop drugs and vaccines for malaria. As a promising lead in the field of drug development, the group has identified specific inhibitors for falcipain-2 enzyme, a major hemoglobinase of *Plasmodium falciparum*, under joint Indo-Canada Program (Chakka et al, 2015).

An important development has been made in the field of Tuberculosis and Malaria. The scientists at ICGEB identified an 11-kDa synthetic protein, M5 that binds to human Intercellular adhesion molecules; ICAM-1 and ICAM-4. M5 greatly inhibits the invasion of macrophages and erythrocytes by *Mycobacterium tuberculosis* and

Plasmodium falciparum, respectively. This work helped to identify a unique host target which could be used against both tuberculosis and malaria. (Nat Commun, 2015, 14; 6:6049)

RECOMBINANT GENE PRODUCT

This group has continued its efforts towards development of a safe, inexpensive and efficacious tetravalent subunit Dengue vaccine. The animal studies are being conducted on the potential dengue vaccine candidates. An international patent on a designer dengue vaccine candidate has also been filed in August 2015. Several companies have also shown their interest for licensing of the know-how of this technology.

A new 5-year NIH supported project to study Dengue virus infections in India has also been initiated in 2015. ICGEB is the Indian Headquarter for this project with Emory University and Rockefeller University, USA. This project is being carried out in collaboration with AIIMS, CMC and NIV.

IMMUNOLOGY

The main focus of the research in the field of Immunology is on identification of bio-markers and novel drug targets for tuberculosis. The multidisciplinary work got good recognition through published study in a royal society press journal on analysis of the hierarchical structure of the *B. subtilis* transcriptional regulatory network (Molecular bioSystems11, 930-941). These published results also attracted international collaboration with an established lab in the Cambridge (Prof M. Vendruscolo). Important findings are depicted in the figure below.

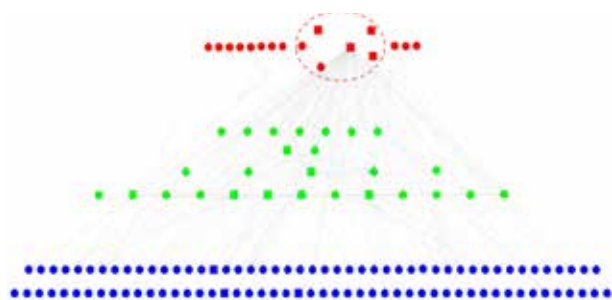


Figure 1: Hierarchical decomposition of transcriptional regulators into Top, Middle and Bottom levels in the TRN of *B. subtilis*-factors. The network of transcriptional regulators has a pyramidal structure, where the largest strongly connected component (LSCC) of 6 nodes (encircled with red dashed oval) lies at the Top level of the hierarchy. Transcriptional regulators in the Top, Middle and Bottom levels of hierarchy are shown in Red, Green and Blue, respectively; transcription factors (TFs) are depicted as circles and factors as squares. The network visualization was obtained by using Cytoscape

Under a separate study, sets of deregulated exhaled breath volatile organic compounds have been identified that could explain gender dimorphism and differentiate drug naïve active and non tuberculosis cases. Currently, these findings are being validating in independent patient population. These findings are planned to be translated later for development of an easy to use battery operated electronic nose as a point of care tuberculosis screening device.

STRUCTURAL AND COMPUTATIONAL BIOLOGY RESEARCH

The group has expertise of structural biology studies of malaria parasite proteins, membrane protein structure determination, NMR and Bioinformatics. The group is enthusiastically working towards understanding molecular mechanism of interactions between protein and RNA that exhibit a wide spectrum of sequence and shape specificity. The understanding of molecular mechanism of the interaction by highly conserved

and abundant proteins will help in formulation of a general code of RNA interaction. Efforts are being made to decipher the molecular mechanism of aa-tRNA synthases from Apicomplexa through comprehensive bioinformatics cum structure-function investigations and use the information for inhibitor discovery. The other important project of the group is to uncover the molecular mechanisms underlining the processes like metal-ion transport and virulent protein translocation in *Mycobacterium tuberculosis* (M. tb).

VIROLOGY

The major focus of virology is on chikungunya virus. The group is working currently on two aspects of chikungunya virus (CHIKV) - evolution of CHIKV in our country and its interaction with the vector and host.

With respect to studying CHIKV evolution, collaborations have been established with hospitals in Delhi and Mumbai to characterize the virus and studying the clinical aspects of the infection since the last five years. The initial observation showed that CHIKV exists as co-infection with Dengue (DENV) in almost 10% of reported cases (Londhe et al., in press).

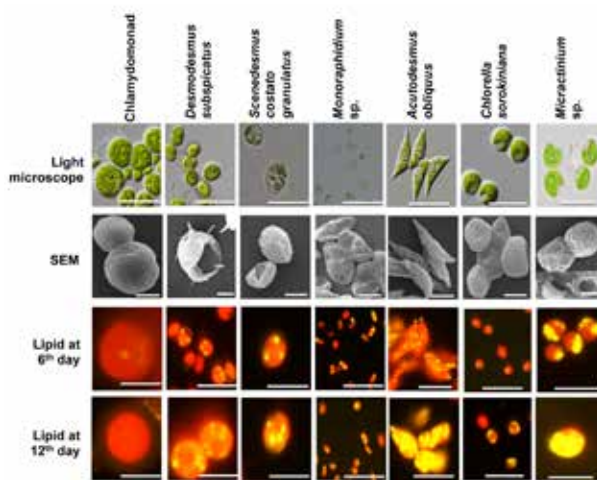
SYNTHETIC BIOLOGY AND BIOFUELS

The DBT supported center got success to generate a functional genome scale metabolic model (GSMM) of a biotechnologically important thermophilic bacterium. The analysis of this GSMM has provided novel insights into the metabolic capabilities and limitation of this organism. This model will be a great tool for biotechnologists working with this bacterium.

To supplement the metabolic modeling efforts, capabilities to knock-in and knock-out genes in cyanobacteria have been established. This includes expression of homologous and heterologous

genes, including codon optimization. We have also been able to match literature-reported values for polyhydroxybutyrate (PHB) production in cyanobacteria by manipulation of culture conditions.

In the area of Algal biofuel, few microalgae with higher biomass and lipid content (>15% dw) have been successfully screened and characterized for biofuel production that has potential industrial applications as shown in below picture.



PLANT SCIENCES

Efforts are being made to develop abiotic and biotic stress-tolerant crops by using genetic engineering techniques. Studies are being conducted to understand rice-gall midge interaction in particular and insect plant interaction in general.

Use of naturally occurring resistance in plants is an environment-friendly method to confer resistance against insect pests. However, to be able to do so one needs better understanding of this interaction.

In the area of research on weed control, a multisite-compensating mutations in rice EPSP synthase and acetolactate synthase (ALS) has been established. These mutations drastically decreased affinity for glyphosate and sulfonyleurea respectively without affecting their catalytic functions. Using these mutant genes transgenic lines have been developed that showed significant tolerance for glyphosate and sulfonyleurea for effective weed management in rice cultivation and to prevent the development of herbicide tolerant weed population.

Another group of scientists with expertise in plant transformation are actively working on chloroplast transformation, molecular farming and production of cellulolytic enzymes etc. A major project of the group is on cotton genomics. Scientists have validated four functionally promoters from cotton, over-expressing in boll/fiber tissue and also identified key genes involved in biotic stress tolerance in cotton

Publications: About 122 high-impact publications emanated from the research undertaken in the institute.

LIST OF PATENTS

Patent Granted to ICGEB, New Delhi in 2015:

S.No.	Patent Name	Group	Priority Date	Application status
1	A novel selectable marker system for transgenic plants	PMB	31.01.2005*	Indian patent GRANTED On 14th August,2015

Patents filed by ICGEB, New Delhi in 2015:

S.No.	Patent Name	Group	Priority Date	Application status
1	Over-expression of a rice-specific miRNA, MiR820 leads to plant and panicle vigour	PMB	10.02.15	Indian patent PENDING
2	A method for obtaining a composition for biomass hydrolysis	SBB	09.06.15	Indian patent PENDING
3	Dengue subunit vaccine quadrivalent candidate DSV against all four DENV serotypes	RGP	01.09.15	PCT patent PENDING
4	Method of Utilization of Carbon Concentration Mechanism in Micro-Algal Species to Increase Production of Lipids and Obtain Bio-Fuel	SBB	11.09.15	Indian patent PENDING

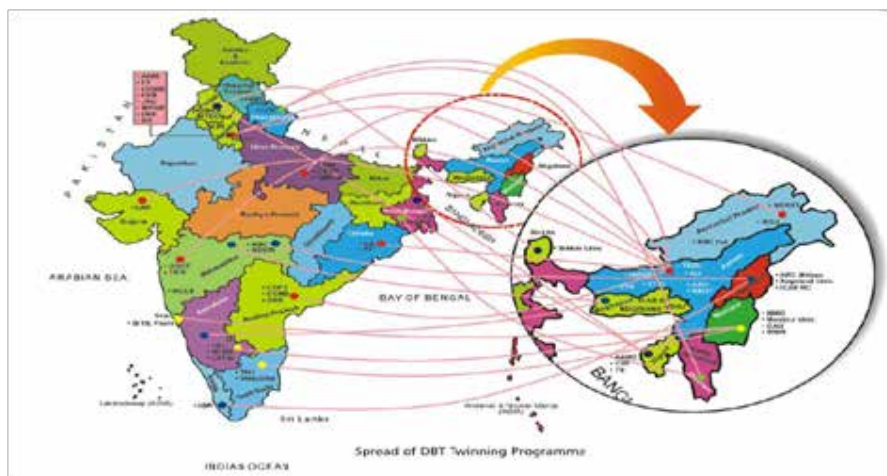
PROMOTION OF BIOTECHNOLOGY IN NORTH EASTERN REGION (NER) OF INDIA

The North East Region (NER), of India is a treasure house of exceptional natural beauty, floral and faunal biodiversity and abundant mineral, water and forest resources. It has been identified as one of the biodiversity hotspots of the world. Rich bioresources spread across NER's diverse ecosystems and nurtured by indigenous communities, provide ample opportunities for furthering economic development of the region. However, NER has remained arguably the most backward region of the country, prompting the Government of India to make unprecedented commitment to allocate 10% of its total budget for the development of NER. Accordingly, the Department of Biotechnology has earmarked 10% of its total annual budget towards biotechnology-backed development activities in the North Eastern Region of India.

Towards this commitment, DBT established the North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) in 2009-10, functioning through Biotech Consortium India Limited (BCIL), for implementation and monitoring of biotechnology programmes in the NER. The NER-BPMC is working in

close cooperation with various Government Ministries/ Departments/ Agencies at the Central and State level along with universities and Research and Development (R&D) institutions for development and implementation of various programmes.

Of the several programs launched by NER-BPMC since 2009-10, the R&D Twinning Programme has made a huge impact by catalysing vibrant collaborations between institutions from NER and those from the rest of India, evolving NER-specific projects and their implementation across all eight states of the region. More than 300 Twinning projects have been implemented, addressing issues in Healthcare (Medical biotechnology), Agriculture (Agri-biotechnology), Livestock & Fisheries (Animal and Aquaculture Biotechnology), and in the areas of Environment, Medicinal and Aromatic Plants (MAP) with specific relevance to developmental needs of the region; nearly 200 research papers have been published in peer-reviewed journals and more than 400 young scientists of NER have been trained in advanced biotechnology.



In the healthcare/ medical biotechnology sector, in order to enhance the quality of patient care and diagnostic services, DBT has provided substantially significant support towards strengthening & up-gradation of laboratory infrastructure in 11 medical colleges/institutions in NER, involving 21 principal investigators spread across Assam, Manipur, Nagaland, and Tripura. An impressive six-storey DBT Healthcare Laboratory established at the Naga Health Authority-Kohima (NHAK) is the first of its kind facility in Nagaland, bringing efficient diagnostic services to the door step of patients in the state.



DBT Healthcare laboratory & Research Centre

A “Comprehensive Facility for Diagnosis and Management of Genetic Disorders” has been established at the Assam Medical College & Hospital, Dibrugarh (Assam), facilitating studies in Biochemical Genetics, Molecular Genetics & Cytogenetics, as well as providing genetic counseling services to the families at risk. This facility will provide timely and accurate diagnosis of genetic diseases due to chromosomal aberrations, single gene mutations, haemoglobinopathies, etc. Hopefully, this facility will create a nucleus for the emergence of a centre of excellence for quality education and research in Medical Genetics in NER.

A “Molecular Diagnostic Laboratory” is being established at the Mizoram State Cancer Institute, Aizawl (Mizoram). Recognizing that accurate

and precise diagnosis is the cornerstone of any successful cancer treatment, DBT has established this molecular laboratory which will not only enhance the quality of comprehensive cancer care but will enable quality research to understand the factors underlying high incidence of cancer in the State. The initial focus of the research project would be on three cancer types commonly encountered in Mizoram: 1. Chronic myeloid leukemia (BCR-ABL translocation); 2. Breast cancer (HER2/neu), and 3. Lung cancer (EGFR).

DBT has provided crucial support for establishing sophisticated infrastructure for improved diagnostic services in pathology, hematology and genetics departments at the North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong (Meghalaya). The support is expected to significantly improve the efficiency of the diagnostic services of the institute, and help generate credible statistics about various diseases as well. These facilities will specifically help in establishing viral etiology of nasopharyngeal carcinoma (EBV), and oral squamous cell carcinoma (HPV); in unraveling pattern of neoplastic renal diseases and hematolymphoid neoplasma, and in molecular typing of minor blood group antigens in NER.

A programme to provide “Research Grants to MD-MS Thesis” has encouraged PG medical students in NER to learn and apply the biotechnology research strategies in their thesis projects; nearly 200 students have benefitted from this programme. Training workshops on the principles and practice of clinical epidemiology have been conducted in Assam, Manipur and Tripura; more of such training workshops are in the pipeline. Two short-term, hands-on training workshops on “Recent Technique in Infectious Disease Diagnostics, for Mid-career Scientists from NER” have been held at All India Institute of Medical Sciences, New Delhi. A programme

on a series of workshops on Good Clinical Practices, Good Laboratory Practices and Ethics in Biomedical Research, is being formulated to be launched soon.

Under the Agri-Biotechnology section, a Centre of Excellence (COE) named “DBT-AAU Centre for Agriculture Biotechnology in NER” has been established at the Assam Agriculture University, Jorhat (Assam). This Centre focuses on research in the areas of Gene technology, Allele mining, Molecular breeding and Microbial gene prospecting. It is engaged in developing skilled/trained human resource, generating bio-inputs to assist eco-farming in NER, and documentation and genetic cataloguing of bioresources for IP management of IP-related issues. All this will lead to establishment of an accredited laboratory for quality analysis of farm inputs and products. The Centre has successfully generated transgenic chickpeas and blackgram lines using Bt genes to confer protection against pod borers; 750 rice germplasm are genotyped using 120 SSR markers; Development of drought tolerant rice variety (Ranjit) is in progress; Seven acid tolerance genes are found to be up-regulated in *Bacillus megatarium*, Biofertilizers and biopesticides generated at headquarter and at satellite centres are being distributed to the farmers. Nine PhD students enrolled in Agri-biotechnology at Assam Agricultural University are awarded with fellowships. Centre has also funded 9 innovative projects to the PIs from various organizations at N E India and conducted 6 scientific workshops on biotechnology and several training workshops on bioinput production involving researchers of N E India as well as other parts of the country.

A multi-centric programme on value addition in jackfruit and commercialization of its processed products aims at identification of superior genotypes of jackfruit and their molecular characterization on the one hand, and validation

and commercialization of technologies for value added products from Jackfruit, on the other. Being implemented by University of Agricultural Sciences (UAS) GKVK, Bangalore; College of Home Science, Central Agricultural University (CAU), Tura, Meghalaya; Department of Horticulture, AAU, Jorhat; NGOs GRAMA (NGO), Kerala; Parivarthan (Women SHG), Karnataka; Kadamba Marketing Society, Karnataka; KVK, Tripura (Under ICAR-RC, Tripura Centre); KVK, Kamrup, Assam, (Under AAU, Jorhat), the programme has identified more than 40 elite jackfruit genotypes from Karnataka, Assam and Tripura for culinary or table purposes, organized training workshops for farmers for existing jackfruit technologies, and produced value added products like pickle, curry, bhaji, tikki, chips, squash, wine, jam, papad, etc. Marketing and supply chain is being developed through involvement of farmers and entrepreneurs.

Recently, a collaborative research programme on Chemical Ecology of North Eastern Region has been launched, with scientists from institutions in Bangalore (National Centre for Biological Sciences (NCBS), Indian Institute of Science (IISc), University of Agricultural Sciences) and those from NER institutions [IBSD, Imphal, (Manipur), Regional Centre of IBSD, Gangtok (Sikkim), NEHU, Shillong (Meghalaya), Nagaland S&T Council, Kohima (Nagaland), Rajiv Gandhi University, Itanagar, (Arunachal Pradesh)], being the partners in this programme. The programme will focus on identification of the origins and compositions of plant, insect and vertebrate pheromones and semio-chemicals; analysis and (re) engineering of chemical communication mechanisms; molecular and structural mechanisms; behavioral and neural mechanisms; biochemical, genetic and physiological mechanisms, governing interactions between flora and fauna of NER.

A multi-centric network programme has been implemented for promoting eco-friendly agriculture practices in 14 districts across all 8 NE states, with emphasis upon the application of bio-inputs (biopesticides, biofertilizers) for organic farming of key high value crops (HVCs) of NER, mass multiplication of required bio-inputs and evaluation of their efficacy. The programme has provided training to nearly 1400 farmers in the use of bio inputs in organic farming of 9 target crops (5 spices, 2 fruits and 2 vegetable crops). An area of 156 hectare was developed and certified for organic farming. The programme has shown success of technology in field demonstrations with some target crops such as Tomato, King Chilli, French Bean, Turmeric, Ginger, Pineapple and Mandarin Orange. Results from these field demonstrations have indicated high possibility of substituting chemical fertilizers and synthetic pesticides with safe and effective bio-inputs. A considerable yield increment has been reported during bio inputs under the project.



Another network programme on biotech-facilitated utilization and conservation of selected Medicinal & Aromatic Plants (MAP) focuses on molecular taxonomic characterization of important medicinal and aromatic plant (MAP) species, isolation and pharmacological evaluation of their bioactive extracts/ ingredients for specific medicinal value. The programme also promotes Good Agricultural Practices (GAP), and large scale production of planting material and post harvesting technologies. The programme is being implemented by Assam Agricultural University (AAU), Jorhat; College of Veterinary Sciences, AAU, Khanapara, Guwahati and North East Institute of Science and Technology (NEIST),

Jorhat, Assam. Under this programme, four plant species (*Homalomena aromatica*, *Clerodendrum indicum*, *Acorus calamus*, and *Piper longum*) have been selected for taxonomical studies, development of GAP, mass multiplication and post-harvest management. The contents of alkaloid, Tannin, Flavonoid and Riboflavin amongst the germplasm of *H. aromatica* have been determined. Distinct RAPD DNA sequences for 22 genotypes of the targeted plant species from different areas of NE states have been assigned distinct Accession numbers by the GenBank.

DBT has also supported a multicentric programme on assessment of impact of Jhum cultivation on soil microbiota and on restoration of diverse agro-ecosystem in NER. This programme is aimed at amelioration and eco-restoration of Jhum lands in North East India. Its specific objectives include estimating the genetic & biochemical diversity of untapped microbial pool, screening for heat and acidity tolerant microbes, bio-prospecting studies for stress tolerant genes and Allele mining, defining roles of hardy native plant spp. resilient to slash & burn practices in Jhum system, developing rapid multiplication technique for eco-restoration during fallow periods, and exploring the possibility of establishing symbiotic relationship between native plant species and potential microbes.

In the area of Animal Biotechnology, DBT has recently launched an ambitious programme on Advanced Diagnostics and Services in Animal Health and Disease (ADSAHD) for surveillance and control of trans-boundary, exotic and zoonotic pathogens. The programme, renamed as Advanced Animal Disease Diagnosis and Management Consortium (ADMaC), envisages establishing three core laboratories across the NER for carrying out research and training activities in trans-boundary and endemic animal diseases. It aims to impart training to the State

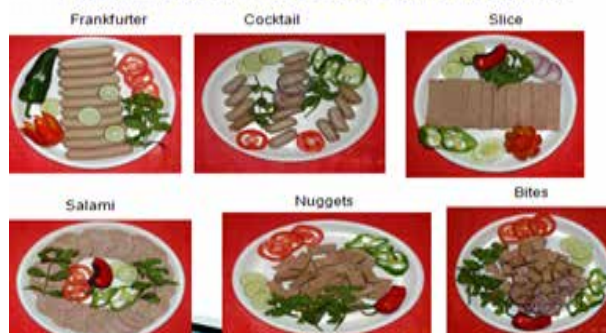


veterinary personnel in disease reporting, sample collection techniques and fostering public-public partnership module for effectively handling the animal-man-environment continuum chain. The North Eastern Region of India, owing to its unique geographical location sharing five international borders, bears constant threat of exotic trans-boundary diseases of our valuable livestock. This programme is aimed at strengthening regional infrastructure and capabilities for developing latest diagnostics and organizing rigorous surveillance for the highly contagious and ravaging diseases so that forecasting model on disease outbreaks in the region can be developed for a formidable defense to guard the territories against possible onslaught by exotic virulent pathogens.



A DBT-supported programme on Augmenting Clean Pork Production and Value Addition, being implemented at the National Research Centre for Pig, Guwahati, Assam, is designed to develop shelf stable pork products (namely nuggets and bites, sausages, patties, kebabs, samosa, momo, slices etc.) and to refine & standardize the technologies for producing a wide range of value added pork products to provide variety to the pork consumers. Production of pork sausages has already been initiated. With more than 75% non-vegetarian population (with special attraction towards pork and pork products) in the North-Eastern Region, the technologies developed herein could be taken up at commercial scale with possible turnover of

Value Added Processed Pork Products



For strengthening the Fisheries and Aquaculture Biotechnology (FAB) related R&D activity in the NER region, DBT has established a FAB-Centre of Excellence (FAB-COE) at College of Fisheries, Central Agricultural University, Lembucherra, Tripura. Its main objectives are to improve the yield of fish production in NER, to explore the fish biodiversity across all the eight North Eastern States, understand the lineage of species diversity, development of protocols for breeding, seed production and farming of economically viable species, fish resource management education and capacity building, and R&D on feed development.



Inauguration of Wet Laboratory set up under Centre of Excellence on Fisheries and Aquaculture Biotechnology by the Hon'ble Union Minister for Science & Technology

In addition, DBT has made intensive inputs in capacity building and human resource development (HRD) for the benefit of entire North Eastern Region of India, as follows:

- Sophisticated biotech infrastructural facilities have been created at National Research Centre on Yak at Dirang (Arunachal Pradesh), for strengthening research dynamics for desirable gains in Yak husbandry, and at National Research Centre on Mithun at Jharnapani, Medziphema (Nagaland) for improving research activities on Mithun husbandry, genomics and conservation.
- In order to give a strong fillip to research in experimental medical sciences and in herbal medicine, DBT has initiated establishment of a state-of-the-art, Regional Animal House Facility at Regional Medical Research Centre (RMRC), Dibrugarh. It will provide well-equipped and fully-functional lab space to the researchers from entire NER for carrying out critical experiments in disease biology, molecular medicine, immunology/vaccinology, drug development and molecular pharmacology. This facility will facilitate availability of specific-pathogen free (SPF) and genetically defined lab animals. Imparting training to the biomedical research staff in standard procedures in animal experimentation will be yet another important activity of this facility.
- DBT has established a network of 126 Biotech Hubs across NER, providing necessary infrastructure in universities/ colleges/ institutions and the required training in sophisticated technologies so as to support and promote biotechnology education and research. At this juncture, there are 6 State-Level and 120 Institutional Level vibrantly active Biotech Hubs spread across all the eight states of NER. Together these hubs have conducted more than 300 training programmes and supported more than 300

PG and PhD students. More than 30 research papers, published in peer reviewed journals, underline the quality of research being undertaken at some of the Biotech Hubs.

- DBT has established “X-Ray Crystallography Facility” at IIT Guwahati under one of the twinning projects, “Studies on structure of enzymes and their interaction with nanostructure materials for bioelectronics devices and other applications”. This facility created at Central Instrumentation Facility of IIT Guwahati is fully functional and available to all NER researchers for their experimental use.



- With a view to recognize promising mid-career scientists in NER, a programme of awarding Unit of Excellence (U-Excel) grant to them has been initiated so as to enable them to pursue their innovative research in frontier areas of biotechnology. So far, 20 Units of Excellence have been established.
- An Overseas Associateship Scheme for NER Scientists aims to promote capacity building in cutting edge areas of biotechnology and life sciences. The Award promotes and supports scientists of merit in their pursuit of skill enhancement in scientific research/training in Overseas laboratories for short term as well as long term. So far, 130 scientists have been awarded the Associateship. As of now, more than 100 scientists have availed this Associateship. This Overseas Associateship has resulted in more than 20 research papers in peer reviewed journals and has also enabled more than 10 laureates in getting

extra-mural funding for their R&D projects besides training in-house scientific human resource of NER.

- An unprecedented growth in the field of biotechnology makes it imperative to create awareness about it at the school level and also to provide an environment of access to a well-equipped laboratory. Recognizing this need, DBT has initiated a scheme for establishing “Biotechnology Labs in Senior Secondary schools (BLISS)” across all 8 states of NER. In the first round, 88 Senior Secondary Schools from NER have been selected by DBT for support under the BLISS scheme.
- DBT has also initiated a “Visiting Research Professorship (VRP)” Scheme to utilize the expertise of outstanding biotechnology professionals for bringing advancement in the Biotechnology and Life Science related activities in various institutions of research and higher learning in the NER States of India. Scientists/faculty from reputed institutions in India shown their interest in sharing their domain expertise with NER institutions through this scheme. In the first phase, 14 scientists/faculties have been selected for “VRP in NER” scheme.
- Twenty nine bioinformatics centers have been established in all the 8 states of the NER and are networked as the North Eastern Bioinformatics Network (NEBINet). These Bioinformatics centres are provided with latest IT equipment to support the research activities of the host institutions in NER. Two new bioinformatics centres were established during the current year at College of Fisheries, Central Agricultural University, Lembucherra, Tripura and National Research Centre on Mithun (ICAR), Nagaland.

- DBT’s e-Library Consortia for North Eastern Region (NER-DeLCON) was established in the year 2010 through which access to more than 900 High Impact e-journals were subscribed by DBT. The facility is being offered to 18 selected NER institutions free of cost; it is being extensively used by scientists, faculty and students of these 18 institutions. A separate website www.delcon.gov.in has been created for DeLCON.
- An online human resource repository of Biotechnology and Bioinformatics Resources of North East India (BABRONE) has been created and located at College of Veterinary Sciences (AAU), Khanapara, Guwahati (Assam). It is a freely accessible e-learning server developed as a common platform for uploading learning materials, sharing of information and as an online discussion forum at www.babrone.edu.in.



- Comprehensive “Entrepreneurship Development Programme (EDP) in Biotechnology” has been initiated by DBT through Biotech Consortium India Limited (BCIL) in NER, with the objective to assist budding entrepreneurs with guidance and technical support from concept to commissioning of their enterprises. Through this initiative, 2 entrepreneurs have setup their commercial ventures successfully
- Preparation of a “Digital Database of Bio Resources of NER” is under development. This database will cover all plant species

from NER having medicinal and nutritional properties and would be a useful database for researchers for identification of plant species for research work and preservation.

- Recently DBT has established a “DBT Biotechnology/Bioinformatics training centre for teachers & research scholars from the North Eastern Region of India” at ACTREC, Mumbai. This centre will provide high end hands on training to NER researchers on cancer biology. Presently 15 researchers from NER are being trained at ACTRECT.



- DBT has recently initiated a training programme through NIBMG, Kalyani, to provide comprehensive training to scientists, research students and clinicians belonging

to the North Eastern Region (NER) of India, who are engaged in “Biomedical Research”, to better equip them to undertake focused research leading towards understanding the molecular basis of diseases prevalent in NER of India. So far 30 researchers from NER (2 batches) have been trained

- In collaboration with the Govt of Assam, DBT has established a Biotech Park at Guwahati, Assam, as a meeting point of technological innovation for knowledge-based biotechnology enterprises and to provide sustainable linkages between the industry, research institutions and academia to boost the region’s competitiveness. Its main objectives are to encourage and support the startup, incubation and development of innovation led, high growth knowledge based business in the multidisciplinary area of biotechnology. The park will promote formal and operational links between centers of knowledge creation such as national R&D laboratories, Universities, Medical Institutions and research organizations in India and abroad and create a strong network.

ADMINISTRATION

Administration is responsible for providing a good and ambient working atmosphere for the in-house scientists, officers and staff. Logistic supports were given for organizing various Task force & Expert Committee meetings successfully. Modern office equipments like laptops, computers, multimedia projectors, photocopiers, etc. were made available within the Department to maximize the work output. Being a scientific department, a large number of meetings, interactions and quick referral with technical experts, specialists, academicians and scholars from far reaching places and across the world are held. Therefore, to obviate unnecessary travelling and to minimize expenditure on this account, an effective Video Conferencing System has been made operational in the Department. The System is widely used in the Department for such purpose.

Department housed in Block No.2, CGO Complex, New Delhi does not have its own building or campus and is facing shortage of office space. The Department has been allotted 11,000 sq. ft. additional office space in Block No.3, CGO Complex. This office space has been renovated through the Hindustan Prefab Limited, a PSU under the Ministry of Housing and Urban Poverty Alleviation. The office space is ready for possession and necessary furniture and logistics have been arranged by the Department.

12 Officers and staff participated actively in different segments of Inter-Ministry Badminton Tournament, Table Tennis, Basket Ball, Crickets etc. organized by the Central Civil Services Sports and Cultural Board, Department of Personnel & Training in 10 - 12 October, 2015.

Swachh Bharat Abhiyan

In consonance with the call of Hon'ble Prime Minister, the Department of Biotechnology (DBT) alongwith its 15 Autonomous Bodies and 2 PSUs decided to launch "Swachh Bharat Abhiyan" from its campuses in different parts of India from 2nd October, 2014. Also DBT geared up its employees to launch "Swachh Bharat Mission" from 25th September, 2015 to 31st October, 2015 and 18th December, 2015 to 27th December, 2015 with a 'Cleanliness drive' on the concept of Mahatma Gandhi's vision, "sanitation is more important than Independence". The Cabinet Secretary inspected DBT premises on 27th December, 2015 and appreciated the cleanliness and ambiance of the Department offices and Canteen facilities.

All DBT employees agreed to dedicate at least 100 hours every year towards 'Swachh Bharat Abhiyan'. It was decided that on the last Friday of every month, all DBT employees would earmark two hours between 3.30 & 5.30 for 'Swachha Abhiyan' at DBT to assist and voluntarily contribute for the maintenance of cleanliness of the office building and surroundings.

ESTABLISHMENT

Establishment Section in the Department is entrusted with the following functions:-

- a) Recruitment and promotion to various posts: During the period under report, two posts of Scientist 'H' to be filled up on deputation were revived with the approval of Department of Expenditure and one post of Scientist 'H' on direct recruitment fell vacant on account of retirement of Dr. T. S. Rao. The process to fill up these vacancies has been initiated and advertisements were

released in Employment News calling for applications. Similarly, the advertisements were also released in Employment News for filling up two vacant posts of Scientists 'C'.

- b) Ante-dating the date of promotion: In pursuance of the CAT's Order and ACC's approval, the ante-dating the promotion date was done in respect of two Scientists G in the Department with all consequential benefits.
- c) Recruitment Rules: The proposal for framing revised Recruitment Rules with regard to the technical staff in the department is being taken up with Department of Personnel & Training and Department of Expenditure.
- d) Modified Assured Career Progression Scheme: The cases for grant of Modified Assured Career Progression (MACP) Scheme to eligible officials are processed from time to time.
- e) Training: The officers and staff were deputed for various training programmes conducted by the Institute of Secretariat Training &

Management, IB Centre Training School and Indian Institute of Public Administration, Goa to enhance their skills in relevant fields.

- f) Grant of Advances and Reimbursements: The cases of grant of various advances, medical reimbursement and other allowances were processed as per rules in a time bound manner.
- g) Miscellaneous: In order to fill up seven vacant posts of Junior Technical Assistants, the Staff Selection Commission (SSC) has been requested to conduct open examination for selection of suitable candidates.

The category wise position of posts sanctioned and filled as on 31-12-2015 is as under:-

Category of posts	Posts sanctioned	Posts filled
Group 'A'	74	63
Group 'B'	89	55
Group 'C'	86+1 Plan	60+1 Plan
Total	249+1 Plan	178 + 1 Plan

Representation of SC/ST/OBC/PH: The number of SC/ST/OBC/PH employees in Grade 'A','B','C' and 'D' categories as on 31-12-2015 are as under:-

Group	Group 'A'	Group 'B'	Group 'C'	Total
Total Sanctioned Strength/Total filled	74	89	86+1 Plan	249+1 Plan
	63	55	60+ 1 Plan	178 + 1 Plan
Scheduled Castes	03	12	19	34
Scheduled Tribes	03	05	08	16
OBC	01	03	10	14
Physically Handicapped	02	02	-	04

Parliament Matters

The meeting of Parliamentary Standing Committee on Science and Technology, Environment & Forest was held on 06/04/2015 at Parliament House to consider the Department of Biotechnology's Demands for Grants (2015-16

GRIEVANCE REDRESSAL

Department has established an effective grievance redressal mechanism to deal with the public as well as staff grievance petitions. The department regularly updates progress, disposal and pendency of public grievance on the website

DARPG of Department of Administrative Reforms & Public Grievances.

VIGILANCE UNIT

A Vigilance Cell is functioning in the Department to handle vigilance and complaint cases expeditiously. Complaints received from various sources were processed timely. In pursuance of the instructions of the 'Central Vigilance Commission', a Vigilance Awareness Week was observed in the Department with taking Pledge on 16.11.2015.

PROGRESSIVE USE OF HINDI IN THE DEPARTMENT

Hindi division ensures progressive use of Hindi and implementation of Government policy on Official Language in the Department. An Official Language Implementation Committee, constituted under the chairmanship of the Joint Secretary (Admn.) in the Department reviews the progressive use of Hindi in every quarter and suggests corrective measures for promoting the use of Hindi. During the year, all documents issued under Section 3(3) of the Official Languages Act, 1963 were in bilingual form and the letters received in Hindi were replied to in Hindi only. In order to strengthen the monitoring system of progressive use of Hindi, the officers who sign the papers have been made the check-points. Under Rule 8(4) of the Official Language Rules, 1976, Establishment, Administration, PPVC, Cash sections and Library in the Department have been notified to do their 100% work in Hindi. During the year, 40 officers and employees were imparted training in Hindi workshop. Hindi fortnight was organized in the Department during 01-15th September 2015, in which 6 different competitions namely, Ashuchitra lekh, Noting & Drafting, Hindi Typing, Antakshari, General knowledge competition and Hindi Vyavahar competition were held. The competition for general knowledge

was especially held for encouraging the multi tasking staff. 55 officers/employees participated in various competition, out of which 42 officials won different prizes.

Successful participant of different competitions of Hindi fortnight were awarded in a prize distribution ceremony. The first prize of ₹5000/-, second prize of ₹3500/-, third prize of ₹2500/- and 5 consolation prizes of ₹1500/- each have been awarded. With a view to encourage writing of original books on biotechnology related subjects in Hindi, the Department has been implementing an award scheme namely "Dr. Jagadish Chandra Bose Hindi Granth Lekhan Puraskar Yojna" since 2002. Under this scheme, first prize of Rupees one lakh rupees, second prize of rupees fifty thousand, third prize of rupees twenty five thousand and two consolation prizes of rupees ten thousand each is given. Only one book was awarded during the competition for the scheme of 2014, wherein an award of rupees ten thousand was given.

FINANCE

Department of Biotechnology was allocated an Amount of Rs.1625.14 Crore (Rs. 1606.80 Crore under plan and Rs. 18.34 Crore under Non-plan) for the year 2015-16. This was revised to Rs. 1624.35 Crore (Rs.1606.80 Crore under plan and Rs. 17.55 Crore under Non-plan). The Financial Statement showing the details of actual expenditure during 2014-15, B.E. and R.E of 2015-16 in respect of various programmes/schemes are given in Annexure II.

Status of Audit Observations

In compliance with the instructions of Department of Expenditure, Ministry of Finance vide O.M.No.12(4)/E.Coord./2014 dated 15.04.2014, gist of audit observations made by C&AG for the year 2014-15 is placed at Annexure-III.



ANNEXURE-1

**COMPOSITION OF THE COMMITTEE CONSTITUTED FOR COMPILATION OF ANNUAL
REPORT 2015-16**

1.	Dr. Mohd. Aslam, Sc. 'G'	-	Chairman
2.	Dr. Shailja V Gupta, Sc. 'F'	-	Co-Chairperson
3.	Dr. Sangita M Kasture, Sc. 'E'	-	Member
4.	Dr. Kalaivani Ganesan, Sc. 'D'	-	Member Secretary
5.	Dr. O. N. Tiwari, Sc. 'D'	-	Member
6.	Dr. Jyoti M Logani, Sc. 'D'	-	Member
7.	Shri J.K. Dora, Under Secretary	-	Member
8.	Shri Vinay Kumar, Under Secretary	-	Member
9.	Shri Bhupal Singh, Asstt. Director (OL)	-	Member

S. NO.	Name of the Programmes/ Schemes	2014-15			BE 2015-16			RE 2015-16		
		ACTUAL EXPENDITURE			TOTAL	Plan	Non-Plan	TOTAL	Plan	Non-Plan
		Plan	Non-Plan	TOTAL						
1	2	3	4	5	6	7	8	12	13	14
	REVENUE SECTION	1327.39	19.59	1319.03	1606.80	18.34	1625.14	1606.80	17.55	1624.35
1	Secretariat Economic Services									
1.01	Secretariat	0.00	19.59	19.59	0.00	18.34	18.34	0.00	17.55	17.55
2.00	AUTONOMOUS R & D INSTITUTION	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2.01	National Institute of Immunology	53.43	0.00	53.43	0.00	0.00	0.00	0.00	0.00	0.00
2.02	National Centre for Cell Science	30.00	0.00	30.00	0.00	0.00	0.00	0.00	0.00	0.00
2.03	Centre for DNA Finger Printing and Diagnostics	41.00	0.00	41.00	0.00	0.00	0.00	0.00	0.00	0.00
2.04	National Brain Research Centre	20.93	0.00	20.93	0.00	0.00	0.00	0.00	0.00	0.00
2.05	National Centre for Plant Genome Research	14.00	0.00	14.00	0.00	0.00	0.00	0.00	0.00	0.00
2.06	Institute of Bioresources & Sustainable Development	28.23	0.00	28.23	0.00	0.00	0.00	0.00	0.00	0.00
2.07	Institute of Life Sciences	34.04	0.00	34.04	0.00	0.00	0.00	0.00	0.00	0.00
2.08	Translational Health Science & Technology Institute	22.44	0.00	22.44	0.00	0.00	0.00	0.00	0.00	0.00
2.09	Rajiv Gandhi Centre for Biotechnology	32.50	0.00	32.50	0.00	0.00	0.00	0.00	0.00	0.00
2.10	UNESCO Regional Centre for Education and Training, Faridabad	22.00	0.00	22.00	0.00	0.00	0.00	0.00	0.00	0.00
2.11	National Agri-Food Biotechnology Institute & Bioprocessing Unit, Mohali	35.90	0.00	35.90	0.00	0.00	0.00	0.00	0.00	0.00
2.12	Institute for Stem Cell Research & Regenerative Medicine, Bengaluru	45.32	0.00	45.32	0.00	0.00	0.00	0.00	0.00	0.00
2.13	National Institute of Biomedical Genomics, Kalyani	25.90	0.00	25.90	0.00	0.00	0.00	0.00	0.00	0.00
2.14	National Institute of Animal Biotechnology, Hyderabad	19.50	0.00	19.50	0.00	0.00	0.00	0.00	0.00	0.00



2.15	International Centre for Genetic Engineering and Biotechnology (ICGEB)	21.00	0.00	21.00	0.00	0.00	0.00	0.00	0.00	0.00
2.16	Biotechnology Industry Research Assistance (BIRAC)	15.00	0.00	15.00	20.00	0.00	20.00	20.00	0.00	20.00
2.17	Bio-clusters and Incubators	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2.18	Centre of Innovative and Applied Bioprocessing, Mohali	14.25	0.00	14.25	0.00	0.00	0.00	0.00		0.00
2.19	Support to Autonomous R&D Institutions	0.00	0.00	0.00	491.62	0.00	491.62	561.79	0.00	561.79
	Total = Autonomous R&D Institutions	475.44	19.59	495.03	511.62	18.34	529.96	581.79	17.55	599.34
3.00	Assistance to other Scientific Bodies									
3.01	HUMAN RESOURCE DEVELOPMENT	84.19	0.00	84.19	90.00	0.00	90.00	110.00	0.00	110.00
3.02	BIOINFORMATICS	20.38	0.00	25.00	43.50	0.00	43.50	43.50	0.00	43.50
3.03	RESEARCH & DEVELOPMENT	448.36	0.00	448.36	470.00	0.00	470.00	470.00	0.00	470.00
3.04	BIOTECHNOLOGY FOR SOCIETAL DEVELOPMENT	13.56	0.00	13.56	15.00	0.00	15.00	12.50	0.00	12.50
3.05	GRAND CHALLENGE PROGRAMMES	30.27	0.00	30.27	37.00	0.00	37.00	27.00	0.00	27.00
3.06	PROGRAMME FOR PROMOTION OF EXCELLENCE & INNOVATION	49.06	0.00	49.06	63.00	0.00	63.00	65.33	0.00	65.33
3.07	BIOTECH FACILITIES	60.00	0.00	60.00	57.00	0.00	57.00	57.00	0.00	57.00
4.01	I & M SECTOR - ASSISTANCE FOR TECH. INCU. PILOET PROJECT BIOTECH	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4.02	I&M Sector - Public Private Partneship	60.49	0.00	60.49	69.00	0.00	69.00	69.00	0.00	69.00
5.00	INTERNATIONAL COOPERATION	53.07	0.00	53.07	0.00	0.00	0.00	0.00	0.00	0.00
6.00	Biotechnology Clusters	32.57	0.00	0.00	90.00	0.00	90.00	10.00	0.00	10.00
7.00	Provisions for projects/schemes for the benefit of North Eastern Region and Sikkim	0.00	0.00	0.00	160.68	0.00	160.68	160.68	0.00	160.68
	TOTAL = Revenue Section	1327.39	19.59	1319.03	1606.80	18.34	1625.14	1606.80	17.55	1624.35

S. No.	Audit Observations for the year 2014-2015	Action Taken
Part-II (A)		
Para 1	Irregular expenditure of Rs. 49.18 crore for establishment of a Centre for Cellular and Molecular Platforms (C-CAMP)	Information from the Division is being sought
Part-II (B)		
Para 1	Heavy advance withdrawals – Rs. 12 crore lying unadjusted	Information from the Division is being sought
Para 2	Project titled Establishment of National Database on Tuberculosis (NDT)	Information from the Division is being sought
Para 3	Deficient Monitoring resulted in delay in Project (file No. BT/PR/101/BHU/08)	Information from the Division is being sought
Para 4	Irregularities in the implementation of Centres of Excellences Scheme in the Project title 'Centre of Excellence on Computational and system Biology	Information from the Division is being sought
Para 5	Renovation of office space of Department of Biotechnology at 5 th Floor in Block No. 3, CGO Complex, New Delhi	Information from the Division is being sought
Para 6	Hiring of data entry of operators and computer operators	Information from the Division is being sought
Para 7	Irregularities in Income Tax Calculations	Information from the Division is being sought
Para 8	Delay in remittance of Government Money leading to a minimum loss of interest of Rs. 5.29 lakhs to the exchequer in the year 2014-15	Information from the Division is being sought
Para 9	Non-disposal of vehicles	Information from the Division is being sought
Para 10	Non Production of records	Information from the Division is being sought
Part-III, Test Audit Note		
1	Irregularities in maintenance of Service Books	Information from the Division is being sought
2	Improper maintenance of Loan and Advance Registers	Information from the Division is being sought
3	Irregularities in maintenance of pay bill register	Information from the Division is being sought
4	Non reconciliation of accounts	Information from the Division is being sought
5	Internal Control Deficiencies in the Department	Information from the Division is being sought



ABBREVIATIONS

AAU	:	Anand Agricultural University
ACTREC	:	Advanced Centre for Treatment, Research and Education in Cancer
AFB1	:	Aflatoxin B1
AHPF	:	Augumented Home Prepared Food
AIIMS	:	All India Institute of Medical Sciences
BAC	:	Bacterial artificial chromosome
BHU	:	Banaras Hindu University
BLAST	:	Basic Local Alignment Sequence Tool
BMP	:	Bone morphogenetic proteins
CBD	:	Centre for Biodesign and in vitro diagnostics
CD	:	Cluster of Differentiation
Cdk1	:	Cyclin-dependent kinase 1
cDNA	:	Complementary deoxyribonucleic acid
CDS	:	Coding Sequences
CHO	:	Chinese hamster ovary
CIFA	:	Central Institute of Freshwater Aquaculture
CIFE	:	Central Institute of Fisheries Education
CiRA	:	Center for iPS Cell Research and Application
CO 1	:	cytochrome c oxidase I
COC	:	Cumulus ophorus complexes
COE	:	Centre of excellence
CRC	:	Colorectal Cancer
DBT	:	Department of Biotechnology
DCFR	:	Directorate of Coldwater Fisheries Research
DIGE	:	Difference Gel Electrophoresis
DNA	:	Deoxyribo Nucleic Acid
DNA	:	Deoxyribonucleic Acid
DUF	:	Domains of Unknown Functions
E.coli	:	Escherichia coli

EchAMP	:	Echidna anti-microbial Protein
EcpD	:	Escherichia coli Chaperone protein D
EGFP	:	Enhanced green fluorescent protein
ELISA	:	Enzyme Link Immuno Sorbent Assay
ELISA	:	Enzyme linked immune sorbent assay
ELISA	:	Enzyme-linked immunosorbent assay
ES-cells	:	Embryonic stem cells
ESR1	:	Estrogen Receptor 1
FAME	:	Fatty acid methyl ester
FSH	:	Follicle stimulating hormone
GO	:	Gene Ontology
HE	:	Human epidermal growth factor receptor-2 -enriched
hFSH β	:	Human follicle stimulating hormone beta
HIV	:	Human Immunodeficiency Virus
HSP	:	Heat Shock Proteins
HTIC	:	Healthcare Technology Innovation Centre
IACS	:	Indian Association for the Cultivation of Science
IASRI	:	Indian Agricultural Statistics Research Institute
IBD	:	Inflammatory Bowel Disease
IBDV	:	Infectious Bursal Disease virus
IBIN	:	Indian Bioresource Information Network
ICGEB	:	International Centre for Genetic Engineering and Biotechnology
ICMR	:	Indian Council of Medical Research
IC-SCR	:	Institutional Committee for Stem Cell Research
IDA	:	International Depositary Authority
IDRS	:	Intrinsic Disordered Regions
IFI16	:	Interferon-inducible
IISER	:	Indian Institute of Science Education and Research
IIT-D	:	Indian Institute of Technology, Delhi
IITK	:	Indian Institute of Technology, Kanpur
IIT-M	:	Indian Institute of Technology, Madras



IMTech	:	Institute of Microbial Technology
inStem	:	Institute for Stem Cell Biology and Regenerative Medicine
iPS	:	Induced pluripotent stem cells
iPSc	:	induced Pluripotent Stem cells
ISG15	:	Interferon-stimulated gene 15
iTRAQ	:	Isobaric tags for relative and absolute quantitation
ITS	:	Internal transcribed spacer
IVF	:	In vitro fertilization
IVRI	:	Indian Veterinary Research Institute
JNU	:	Jawaharlal Nehru University
L.rahamnosus	:	Lactobacillus rhamnosus
LAMP	:	Loop mediated isothermal amplification
LB	:	Luminal B
L-NAME	:	L-NG-Nitroarginine methyl ester
LPS	:	Lipopolysaccharide
M. tuberculosis	:	Mycobacterium tuberculosis
MAPK	:	Mitogen-activated protein kinase
MARK1	:	Microtubule Affinity-Regulating Kinase 1
MCC	:	Microbial Culture Collection
MCP-1	:	Macrophage Chemoattractant Protein-1
mFSH	:	Marmoset follicle stimulating hormone
M-II	:	Metaphase II
miRNA	:	Micro RNA
MPF	:	Maturation promoting factor
mRNA	:	Messenger RNA
NAC-SCRT	:	National Apex Committee for Stem Cell Research and Therapy
NBA	:	National Biodesign Alliance
NBDB	:	National Bioresource Development Board
NBFGR	:	National Bureau of Fish Genetic Resources
NCBI	:	National Center for Biotechnology Information
NCBS	:	National Centre for Biological Sciences

NCBS	:	National Centre for Biological Sciences
NCCS	:	National Centre For Cell Science
NCS-TCP	:	National Certification System for Tissue Culture Raised Plants
NEFA	:	Non-esterified fatty acids
NIMHANS	:	National Institute of Mental Health and Neurosciences
NIPGR	:	National Institute of Plant Genome Research
NMR	:	Nuclear magnetic resonance
OAS1	:	Oligoadenylatesynthetase 1
PBMC	:	Peripheral blood mononuclear cell
PCR	:	Polymerase Chain Reaction
pdk1	:	Phosphoinositide-dependent kinase-1
PDK1	:	Pyruvate Dehydrogenase Kinase, Isozyme 1
PEG	:	Poly Ethylene Glycol
PLA	:	Poly Lactic Acid
PPR	:	Peste des Petits Ruminants
PUFA	:	Poly unsaturated fatty acid
R & D	:	Research and development
R&D	:	Research and Development
RCB	:	Regional Centre for Biotechnology
RDA	:	Recommended Dietary Allowance
RGCB	:	Rajiv Gandhi Centre for Biotechnology
RNA	:	Ribo Nucleic Acid
RNA	:	Ribonucleic Acid
RNAi	:	RNA interference
RNAP	:	RNA polymerase
ROS	:	Reactive oxygen species
RT-PCR	:	Reverse Transcription- Polymerase Chain Reaction
Runx	:	Runt-related transcription factor
RUTF-C	:	Commercially procured ready to use therapeutic food
RUTF-L	:	Locally procured ready to use therapeutic food
SAM	:	Severe Acute Malnutrition



SAR	:	Systemic Acquired Resistance
SCD	:	Stearoyl-CoA Desaturase
SCFA	:	Short Chain fatty acid
SEA	:	Spontaneous egg alteration
SIB	:	School of International Biodesign
SLAMF	:	Signaling lymphocyte activation molecule family
SNAP	:	Strontium Nitrate Actone Peroxide
SpaA	:	Sortase-mediated pilin assembly A
SpaD	:	Sortase-mediated pilin assembly D
TB	:	Tuberculosis
TGF β	:	Transforming growth factor beta
TLR	:	Toll-like receptors
WBUAFS	:	West Bengal University of Animal and Fishery Science
WSSV	:	White Spot Syndrome Virus
β OHB	:	Beta-Hydroxybutyric acid

