

# HFSP MATTERS

The Newsletter of the Human Frontier Science Program

## Altmetrics are everywhere: Citing HFSP support

By Guntram Bauer
Director of Scientific Affairs and Communications

All researchers are interested to see their work being downloaded, read and cited by other scientists. Beyond traditional citation counts, the impact of a research article can be gauged in different ways. The so-called altmetrics being one of them. Altmetrics gained a lot of momentum recently because they encompass important aspects such as digital use, data sharing, download reports and many more (for an overview see NATURE, 22 August 2013, Vol. 500: 491-492). As a funding organization, HFSP applies similar yard sticks to justify its use of governmental funds and to analyze the impact of the research that it supports.

It has become standard that manuscript submission systems allow the addition of the name of the funder and the award number in special fields that then appear in a separate section of the acknowledgments once the publication has been printed. Regrettably, not all HFSP awardees are aware of our interest and need for proper acknowledgment. We continue to spot many publications from HFSP awardees with incomplete or even without mention of the award (for example only "HFSP" is mentioned or only the award year).

HFSP Matters seems an appropriate medium to ask for your support in correctly referencing your HFSP award. What does this entail? Publications arising from work funded by HFSP should acknowledge the full name of the organization, "Human Frontier Science Program", rather than the acronym "HFSP". In addition, to effectively track the output of HFSP funded research, we require that you mention the full award number (e.g. LT000096/2011-C or RGP0012/2010). In the rare case that there is no specific award field, you could add a short sentence to your acknowledgements such as 'This work was supported by the Human Frontier Science Program [award number].'



## The 15th HFSP Awardees Meeting

12 -15 July 2015

The Salk Institute, La Jolla, San Diego, USA

As we prepare for the 2014 Awardees Meeting and the 25<sup>th</sup> anniversary event in Lugano, we are pleased to announce the venue of the 2015 meeting. We are very excited to be the guests of the Salk Institute in La Jolla, California. The institute is known for its outstanding research achievements and its laboratories are home to many grant and fellowship awardees, past and present.

The Salk Institute was established in the 1960s by Jonas Salk, M.D., the developer of the polio vaccine. He selected the world-renowned architect Louis I. Kahn to design the facility that he envisioned. Salk's distinctive vision saw the Institute's premises and laboratories as being adapted to the ever-changing demands of modern research. Yet, he wanted it to be simple and open. In the end Kahn succeeded in implementing an architectural marvel with the world renowned two mirror-image structure that flanks the courtyard giving an infinity view of the Pacific Ocean. The Salk Institute, a complex of 29 individual structures, was featured in the American Institute of Architects (AIA) exhibit "Structures of our Time (31 Buildings that Changed Modern Life)".

The HFSP Awardees Meeting will take place in the comfortable Salk Institute auditorium and the poster session and breaks will be organized in the adjacent foyer.

## Meet & Greet

## In this issue

Citing HFSP support	
The $15^{th}$ HFSP Awardees Meeting $1$	
HFSP alumni meetings	
HFSP awardees in the news	,
The Falling Walls conference6	, )
A Japanese PI in Switzerland8	•
Torsten Wiesel 9	)
Hind Medyouf wins the 2013 José	
Carreras Career Award	0
A message from Toru Nakahara 1	1
HFSP Council of Scientists1	1
Awardees' Articles	2
Prizes & Awards	2

## **Impressum**

The HFSP Newsletter is issued on behalf of the Human Frontier Science Program by the International Human Frontier Science Program Organization. It contains announcements of HFSP-related matters and other information of interest to the support of young scientists and to interdisciplinary research in general. Please tell your friends, colleagues, students, etc. about this mailing list. They can subscribe via a link on the HFSP home page.

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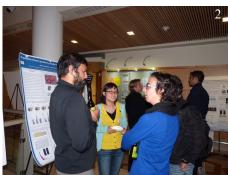
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## HFSP alumni meetings









1. Haim Garty, Vice-President of the Weizmann Institute and Ernst-Ludwig Winnacker, Secretary General HFSPO; 2. Poster session at UCSF; 3.The Koffler Accelerator, Weizmann Institute; 4. Guntram Bauer and Bruce Alberts

Early in 2014 we organized two more HFSP alumni meetings. The first took place in February immediately after the Annual Meeting of the Biophysical Society in San Francisco. HFSP alumna Katja Brückner was our host and helped us to organize the meeting at UCSF's Mission Bay Campus. We are very thankful to Bruce Alberts for giving a plenary lecture on "Biology past and biology future: Where have we been and where are we going?"

The meeting was successful in that it offered an opportunity for participants of the Biophysical Society meeting to

stay on and mingle with the local HFSP alumni community.

The second meeting in 2014 took us to a non-member country for the first time. In March the HFSP community in Israel gathered at the Weizmann Institute of Science in Rehovot. Some 50 alumni from all over the country attended. Israeli alumni were excited to have the first get-together in their country. We are very grateful to HFSP Cross-Disciplinary Fellow Benjamin Born for his suggestion to have a meeting in Israel and for his help with the local organization.



Prof. Haim Garty addresses HFSP alumni at the Weizmann Institute

## HFSP awardees in the news

We would like to congratulate all of our awardees whose work has recently been highlighted in scientific journals for their outstanding achievements.

HFSP grant awardees Roman

HFSP Cross-Disciplinary Fellow Gregory Sutton's insect work made the list of the "17 Important Things Science taught us in 2013" by BuzzFeed. Using grasshoppers as a model, Gregory Sutton showed that these insects have mechanical gears that connect the two hind legs with interconnecting teeth. http://www.buzzfeed.com/kellyoakes/17-important-things-science-taught-us-in-2013

The Nature publication "Elemental gesture dynamics are encoded by song premotor cortical neurons" by HFSP Cross-Disciplinary Fellow **Ana Amador** and colleagues was selected as one of the Editor's choices in 2013. <a href="http://www.nature.com/nature/journal/v504/n7480/full/504386a.html">http://www.nature.com/nature/journal/v504/n7480/full/504386a.html</a>

Stocker (MIT, Cambridge, USA) and Assaf Vardi (Weizmann Institute of Science, Rehovot, Israel), together with their postdocs Vicente Fernandez (MIT), Orr Shapiro (WIS) and Melissa Garren (MIT), won the NSF/AAAS International Science & Engineering Visualization Challenge in the photography category. Their sophisticated collage of a coral derived 'whirlpool' shows how coral polyps maintain their micro-environment. The winning image was selected for the cover of Science magazine: (7 February 2014, Vol. 343, #6171). http://www. sciencemag.org/content/343/6171. cover-expansion

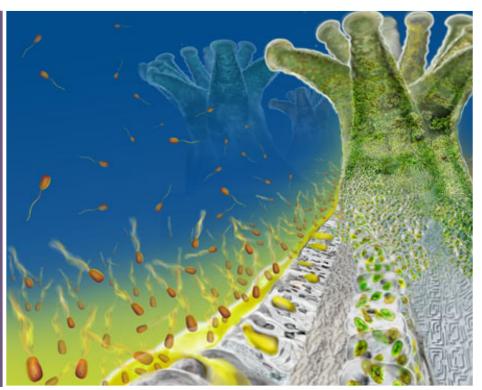
HFSP Fellow Fernando Garcia-Moreno of the University of Oxford and colleagues published a paper in Development reporting on CLoNe, a new method for clonal cell labelling in vivo, based on the combined electroporation into progenitor cells of plasmids encoding multiple fluorescent reporters, a Cre driver and a transposase. Their work was featured on the cover (2014, Development. 141(7):1589-98. doi: 10.1242/dev.105254). http://dev.biologists.org/content/141/7.cover-expansion

The May 2014 cover of Molecular & Cellular Proteomics shows a Mandelbrot fractal trace of the human hepatocellular carcinoma cell line, HC-04, at 24 hours following treatment with hepatocyte growth factor (HGF). It is a joint publication by HFSP Young Investigator Grant awardees **Justin Boddey, Rhoel Dinglasan** and **Phillip Jost** (doi: 10.1074/mcp.M113.035584; May 1, 2014 Molecular & Cellular Proteomics, 13, 1153-1164). http://www.mcponline.org/

content/13/5.cover-expansion

Coral reefs are threatened by disease. Using microfluidics and video microscopy to spy on the behavior of a coral pathogen, HFSP Young Investigator Grantees Roman Stocker and Justin Seymour and colleagues discovered that it follows gradients of chemical cues leaking from the coral surface and responds more strongly to those coming from heat-stressed hosts.

The figure corresponds to figure 4 in the ISME Journal, 2013 Dec 12, Garren et al., A bacterial pathogen uses dimethylsulfoniopropionate as a cue to target heat-stressed corals. Image by Melissa Garren, Glynn Gorick and Roman Stocker.



## Ending the grant on a high note By Miguel Vicente

In 2010 HFSP decided to fund a grant team that set out to reconstruct molecular complexes capable of reproducing functions of bacterial division in a test tube. At the centre of the team's interest was the question of how the so-called divisome would work. A synthetic biology approach seemed to be the best choice to support already existing conclusions derived from cellular and molecular analysis. Given the highly dynamic and membrane associated nature of this machine, and the difficulty of assaying its inputs and outputs, its reconstitution in vitro presented a daunting prospect. A risky idea but the project promised to really test the state of knowledge. The collaboration was born out of the combination of unique expertise in new technologies with a deep cellular, genetic, and biophysical understanding of the divisome. The Program Grant worked out tremendously well and below Miguel Vicente, the principal investigator, reports on the workshop that was organized on February 28, 2014.

During the course of this work we reproduced some mechanisms that bacterial cells use to determine their middle and to assemble a divisome. To conclude the project, we organised a workshop on "Cell Division Reconstruction" at the Centro Nacional de Biotecnología, attended by the project researchers and two additional invited speakers. In total, fifty nine scientists from Algeria, France, Germany, Italy, Spain, Sweden and the UK attended this workshop which attracted some fourteen posters.<sup>1</sup>

The question of how bacterial cells identify their middle has been investigated for over two decades. Placing the septum at midcell is important to ensure that cell division yields two equal daughters. This placement is mediated by proteins that are differentially distributed along the bacterial cell length and have a "measuring tape" function. Components of the Min and nucleoid occlusion (NO) systems of Escherichia coli have a spatial distribution compatible with this role. Both systems have one protein, MinC or SlmA respectively, that prevent assembly of FtsZ, a major structural component of the division apparatus at positions

other than midcell. The Min system works because of a cell pole to cell pole oscillation of its three components (MinC, D and E), allowing FtsZ polymers to form preferentially at the cell centre where the concentration of MinC is lowest.

In her talk, **Petra Schwille** (Max Planck Institute of Biochemistry, Martinsried), discussed results showing the co-reconstitution of FtsZ and Min proteins on flat lipid bilayers and in cell-shaped compartments. Results from her laboratory indicated that Min oscillations indeed position FtsZ filaments to a confined zone in the middle of an artificial cell-shaped compartment. Membrane-targeted FtsZ assembled into a static network of curved and staggered filaments, with GTP hydrolysis causing a constant exchange of monomers throughout. MinC and an end-capping variant of FtsZ, NZ, blocked the repolymerization, inhibiting FtsZ assembly on the membrane. MinC additionally increased the depolymerization rate of pre-assembled FtsZ filaments.

Miguel Vicente (Centro Nacional de Biotecnología-CSIC, Madrid) described how Min can be dissociated from NO using maxicells as containers. Maxicells are nucleoid-free cells in which protein synthesis is possible from genes encoded in plasmids. MinD and MinE, and therefore MinC (carried by MinD), retained their pole-to-pole oscillation in maxicells. ZipA and FtsA, two E. coli proteins that attach cytoplasmic FtsZ to the membrane, were stable in maxicells, but FtsZ and SlmA were proteolytically degraded. Notably, ZipA stabilized newly synthesized FtsZ from plasmids in maxicells via its interaction with the C-terminal end of FtsZ, a central hub for various protein-protein interactions.

Germán Rivas (Centro Nacional de Biotecnología-CSIC, Madrid) then followed with a report on how he and his colleagues used ZipA incorporated into nanodiscs to find that it bound to FtsZ oligomers and polymers with equal moderate strength. A minimal division machinery assembly was reconstructed in permeable giant vesicles containing FtsZ and ZipA. These vesicles shrank upon FtsZ polymerization, partly mimicking membrane constriction.

<sup>&</sup>lt;sup>1</sup>HFSP grant teams may organize small gatherings with all team members including students and post-docs involved in the work. For the meeting the team may invite a limited number of additional experts who are not part of the HFSP grant. Other than that, HFSP does not support scientific meetings or workshops.

**Daniel Daley** (Stockholm University) presented the work of his group using a combination of confocal fluorescence microscopy and "Fluorescence Recovery After Photobleaching" (FRAP) to determine if divisome proteins are present at the septum at the time of cytoplasmic compartmentalisation. His data suggested that many are, but that FtsZ and ZapA disassemble before the cytoplasm is sealed by constriction of the inner membrane. Miguel Vicente added that coinciding with FtsZ-ring disassembly, ZapA and ZapB migrated from midcell to the pole, taking FtsZ with them. The observations of Daniel Daley also imply that FtsZ cannot be a force generator during the final stages of envelope constriction in E. coli.

Martin Thanbichler (Max Planck Institute for Terrestrial Microbiology, Marburg) reported new insights into the function of MipZ, a key regulator of division site placement in Caulobacter crescentus, a bacterium that has a more complex division cycle than E. coli, involving differentiation. This FtsZinteracting ATPase also forms a bipolar gradient and can interact with ParB and the nucleoid. At the cell poles, ParB complexes stimulate the formation of ATP-bound MipZ dimers, which are then retained near the poles through association with the nucleoid. Their ATPase activity leads to dissociation into diffusible monomers, which are recaptured by ParB after spontaneous nucleotide exchange. This is an interesting variation to achieve a similar end.

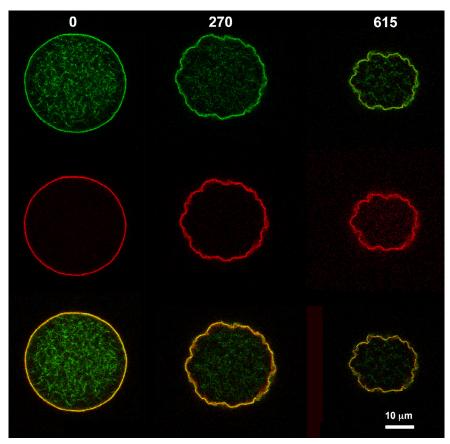


Figure 1 corresponds to figure 2 in Cabré et al., 2013, J. Biol. Chem. 288: 26625-26634. It shows the progressive shrinkage of a permeable vesicle containing FtsZ (green, top row) and ZipA (red, middle row) after the addition of a slowly hydrolizable nucleotide (GMP-CPP). Bottom row shows the merged images. Time in seconds.

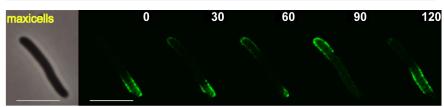


Figure 2 shows the pole to pole oscillation of a GFP-MinD fusion inside a maxicell. This image corresponds to part of figure 2 in Pazos et al., 2014, PLoS ONE 9(3): e91984. doi:10.1371/journal.pone.0091984. Time in seconds.

## **Chromatin and Epigenetics: From Omics to Single Cells**

October 14 - 15, 2014

IGBMC, Strasbourg, France

HFSP awardee Robert Schneider and his colleague, Maria-Elena Torres-Padilla (IGBMC, Strasbourg) are organizing a conference on chromatin and epigenetics on October 14-15, 2014 at the IGBMC in Strasbourg (France). The conference will highlight aspects of chromatin and epigenetic mechanisms that bring together genome-wide approaches with single cell and single molecule analyses. The aim is to link genome-wide epigenomics with recent advances in single cell approaches to better understand epigenetic mechanisms *in vivo*. The program is split into three sessions, the first of which will emphasize single cell approaches covering the main aspects of chromatin regulation. The second session will bridge these two areas, and focus on studies using single cell approaches to explain dynamics of epigenetic phenomena. The final session will concentrate on novel genome-wide analysis to understand the epigenome and its dynamic changes. Key note speakers are Tony Kouzarides and John Gurdon, University of Cambridge, UK. Registration ends on 22 September 2014 (early birds before 1 August).

Further information is available at: <a href="http://www.abcam.com/index.html?pageconfig=resource&rid=16178">http://www.abcam.com/index.html?pageconfig=resource&rid=16178</a>

## First HFSP fellows to attend the Falling Walls conference By Anne-Cécile Reymann and Benjamin Philipp Born

Which are the next "walls to fall"? On November 9, 2013 about 750 international attendees participated in the fifth Falling Walls Conference in commemoration of the fall of the Berlin Wall in 1989. In the Radialsystem V conference center on the banks of the River Spree, 20 experts discussed future breakthroughs in society, science and technology.

On the eve of the main meeting, 100 selected young scientists shared their breakthrough ideas before an international jury at the Falling Walls Lab. Among them two HFSP Long-Term Fellows, Falling Walls Lab-finalists and A.T. Kearney Scholars Anne-Cécile Reymann (Max-Planck-Institute of Molecular Cell Biology and Genetics, Dresden) and Benjamin Philipp Born (Weizmann Institute of Science, Israel). Sharing her concept of revealing the cortical architecture of cells in one of a hundred 3-minute presentations on stage and bridging the gap between different fields of science ranging from language studies to medicine and from engineering to philosophy in backstage discussions, gave Anne-Cécile "the peculiar feeling of knowing each other for much longer and being part of the same team, driven by the same enthusiasm for such a unique experience."

The winners of the Falling Walls Lab convinced the jury with their ideas of using computer simulations to improve stents for heart surgery (Katerina Spranger, University of Oxford) and how the lysis of red blood cells can be utilized for fast identification of bacteria in human blood by a self-made "2-Euro-device" (Klemens Wassermann, Austrian Institute of Technology). John Woodland from the University of Cape Town suggested a fluorescent marker for monitoring cellular free heme to investigate its function in pathology and Tarek Richard Besold from University Osnabrück proposed the implementation of artificial intelligence to innovative processes like composing music.

In a similar venue called Falling Walls Venture, representatives of start-up companies presented their work. The winning presenter was Tobias Grab from the Karlsruhe based start-up company Cynora for their concept of replacing the costly and rare metal iridium commonly used for organic light-emitting diodes (OLED) by copper. He envisioned "printing lights on flexible displays", windows that emit light when it gets dark, and OLED television.

The Falling Walls Conference was kicked-off by Germany's Minister for Education and Science, Johanna Wanka, who emphasized the importance of science communication to foster intercultural relations. An issue touched on by the live-broadcast of Chinese artist Ai Weiwei, who together with Olafur Eliasson from the Berlin Academy of Art, launched a sparkling internet art project named "moon" (http:// moonmoonmoon.com/) to which everybody can reach out and connect beyond the borders existing on our globe by leaving a comment on a digital whiteboard.



© Falling Walls Lab (2013) – HFSP fellow Anne-Cécile Reymann

Evolutionary biologist Mark Pagel, from the University of Reading, presented what he defined as collective stupidity: innovations are achieved by iterative and evolutionary improvements of concepts rather than by an individual spark of brilliance. Sophia Vinogradov considered computer games for training Schizophrenia patients to distinguish between real events and those made up in their mind. The neuroscientist from the University of California at San Francisco compared the effect of the video game exercise on a patient's brain function to that induced by the precise learning of the London city map which is a common exercise for London taxi drivers.

Michal Schwartz from the Weizmann Institute of Science introduced the concept of "protective auto-immunity", showing how the immune system supports healing of the brain.

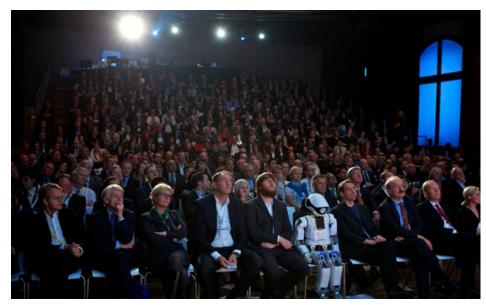


© Falling Walls Lab (2013) – HFSP fellow Benjamin Philipp Born

An open exchange platform on the internet for sharing and discussing biotechnology findings in a cooperative manner without being influenced by either academia or industry was presented by Steven Friend, President of non-profit organisation Sage Bionetworks.

Jagdish Bhagwati from Columbia University spoke in favor of globalization and how the Indian model for economic growth can be applied to other developing countries. Overcoming poverty in drought regions such as Africa could be achieved soon according to Jill Farrant from the University of Cape Town, who proposed the bioengineering of drought-tolerant crops based on natural desiccation mechanisms in resurrection plants. Benjamin Barber of City University of New York focused on the transition from states as geopolitical units to networks of interdependent cities which will govern future life as most people will be living in highly developed cities.

In the future, we will benefit from technologies like transparent electronics based on zinc oxide or fully-disposable cellulose-electronics as presented by Elvira Fortunato from University of Lisbon and from fuel-cells which will be operated by hydrogen and oxygen from artificial leaves performing watersplitting as introduced by Daniel Nocera from Harvard University. Luc Steels of the University of Brussels supported the



© Kay Herschelmann (2013) - Falling Walls conference in Berlin 2013

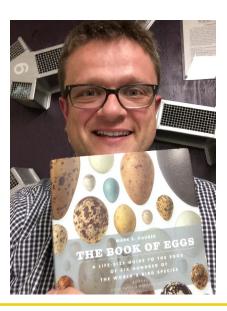
notion that science fiction is right among us by showing programmable kid-sized robots which are able to learn from robot-to-robot communication on the basis of trial-and-error. In a movie, Steel's robots were shown to prepare a pancake from scratch according to a recipe that one of the robots had downloaded from the internet.

Like the Falling Walls Lab, the Falling Walls Conference 2013 offered an atmosphere of interdisciplinary mingling allowing ideas to be exchanged with speakers and distinguished participants in the informal "non-breaks" between conference sessions when a panel of discussion sessions allowed everybody

to interact with the speakers, who were on stage a few minutes before, in a more direct manner.

Barriers between participants were as absent as the Berlin Wall itself in the spirit of a Conference specially intended to "tear down walls". In retrospect, Anne-Cécile Reymann reflects that the Falling Walls Conference gave the participants the opportunity to "broaden our perspective and to consider controversial topics with a high impact on society, such as civil rights, fair distribution of resources, or sustainability among others, stepping out of our own narrow subject of research."

#### The Book of Eggs - A life-size guide to the eggs of six hundred of the world's bird species



HFSP Young Investigator Grant PI, Prof. Mark E. Hauber of Hunter College at City University of New York, has written a new book entitled "The Book of Eggs" (<a href="www.tinyurl.com/eggbook">www.tinyurl.com/eggbook</a>), published by the University of Chicago Press. This is a life-size guide: all but the extinct elephant bird's eggs from Madagascar fit on the pages of the book! Prof. Hauber taps into the vast knowledge about bird eggs and the past 10 years of his own research, including his interdisciplinary studies as an HFSP investigator. He introduces readers to the diversity of avian eggs from structural, pigmentary, behavioral, ecological, and evolutionary perspectives, followed by detailed descriptions and analyses of six hundred bird species from around the world. The book is a generally accessible scientific journey told through individual stories that highlight the strategies employed by birds to successfully reproduce via the fragile structure that is the egg.

## A Japanese PI in Switzerland

### By Kentaro Shimizu, University of Zurich

One of the challenges of working in science is that you never know where you will live and I never imagined that I would live in Switzerland. During my undergraduate study at Kyoto University, Japan, I had the opportunity to attend a Summer Institute at the Weizmann Institute in Israel to study the EGF signaling pathway. I then traveled throughout Europe with a Eurail pass for 15 days. In Zurich, I became lost. I had no map but the people kindly told me how to take trams and trains. This was my first and very positive experience of life in Switzerland.

Towards the end of my postdoctoral training in the USA, I applied for Principal Investigator (PI) positions all over the world and was excited to accept an Assistant Professorship position at the University of Zurich for a new University Research Priority Program on Systems Biology/Functional Genomics. Except from my experience as a tourist, I did not know much about life in Switzerland or Swiss science at that time but I learned from a Nature column that Switzerland was recruiting young researchers from all over the world (Schiermeier, Nature 435, p. 532, 2005). The very first sentences were: 'Ursula Röthlisberger is in a minority at the Swiss Federal Institute of Technology in Lausanne (EPFL). That she is a woman and a young scientist leading her own independent group is not unusual. Rather, what makes her stand out is that she is Swiss.' I never felt out of place because I am Japanese and in my current institute there are over 20 nationalities just on my floor. The language at faculty meetings was changed from German to English to integrate all the foreign faculty members.

In Japan there is a growing concern that young scientists are no longer inclined to work abroad for a variety of reasons. After several years in Switzerland I know how important it is to experience life and work abroad. Therefore I was happy to accept an invitation to an HFSP luncheon seminar during the 35th Annual Meeting of the Molecular Biology Society of Japan, organized by Tadashi Uemura and Gohta Goshima,

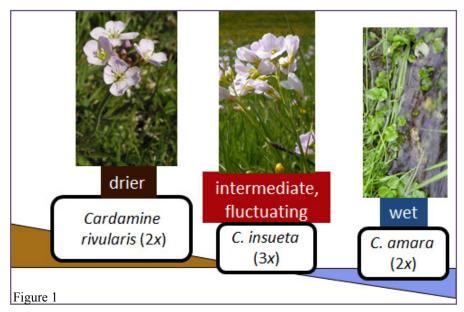
to speak to young Japanese scientists about my research experience in foreign countries. HFSP support is a rare and therefore unique funding mechanism to provide opportunities for intercontinental scientific collaboration. A Japanese saying can be applied to my situation: "Third time paid for all" – meaning two unsuccessful applications for an HFSP grant should not prevent trying again with a new team. Moreover, I am now in the privileged position of supervisor of Ulises Rosas, an HFSP fellow. I really would like to encourage young scientists to keep trying and not give up.

Sometimes the twists and turns of a career are marked by coincidence. At the time when I received the offer from Zurich I was a member of the orchestra at North Carolina State University and we were playing symphony no. 4 by the Swiss composer Arthur Honegger, a member of the famous "Les Six" whose portrait is featured on the 20 Francs note. And then I remember receiving a book from my postdoctoral supervisor, Prof. Purugganan: 'A PhD is not enough!' He gave this book to all postdocs and advised us that life as a PI would be exciting and also very different from postdoctoral work. As an established PI in Switzerland I agree with his advice and can honestly say that I have no regrets.



Kentaro Shimizu

In my research, I am interested in answering a fundamental question: how can some 20,000 genes generate the enormous biodiversity of millions of species? With the combination of the Swiss natural environment and an HFSP Young Investigator Grant, I am now enjoying my studies on the genetics of speciation. Speciation has been a central interest in biology since Darwin's 'Origin of Species', but a major difficulty in studying speciation is that it usually occurred a long time ago. Thus, little information is available about the molecular and population processes and the environment at the time of speciation. Notably, in Switzerland, a textbook example of contemporary speciation of Arabidopsis relatives has been described. Farmers created a new habitat by clearing forests in the small village of Urnerboden at the beginning of the 20th century. Then Cardamine amara (2x, diploid),



which lives in streams, hybridized with *C. rivularis* (2x), which lives in drier habitats. As a result, the new polyploid species *C. insueta* (3x) appeared in intermediate and fluctuating habitats such as hay meadows (Fig. 1) as well as another new polyploid, *C. schulzii* (6x). This is a rare example of a species that is known to have originated during the past 150 years around the world, and is probably the only one closely related to the model species *Arabidopsis*.

I started a collaboration with Dr. Jun Sese (Ochanomizu University and the Tokyo Institute of Technology) in network science and bioinformatics and with Dr. Angela Hay (University of Oxford, now Max Planck Institute for Plant Breeding Research in Cologne) in developmental and synthetic biology. We had the idea to investigate the question whether speciation by hybridization can be studied by analogy with network merging. Network merging is common in social networks, such as in the mergers & acquisitions (M&A) of companies. In M&A, a powerful leader could reorganize redundant components to increase efficiency. What happens in hybrid speciation, where two gene networks are merged by genome duplication? It somehow works well without external 'supervision' in a self-organized way, but very little is known about network merging in biology.

We were very excited that our interdisciplinary team was successful in securing an HFSP Young Investigator Grant. We started by establishing a new bioinformatic workflow to study the transcriptome in polyploid species. It has been very difficult to isolate and analyze duplicated genes (called homeologs) separately, because they are highly homologous by definition. We used next generation sequencing (NGS) to solve the issue, and Jun's group developed software named HomeoRoq (Homeolog Ratio and quantification). Using HomeoRoq, we suggest that subnetworks for stress responses that are unique to each parent may be safeguarded in polyploid species because of cisregulatory divergence, thus allowing them to exploit fluctuating habitats. We also reported that hybridization occurred recurrently in Urnerboden in collaboration with cytologists, taxonomists and colleagues from the Geography and Environmental Sciences Division in Zurich.

In many ways 2014 is a special year because it marks the 150th anniversary of diplomatic relations between Switzerland and Japan. One of the numerous commemorative events was the Swiss– Kyoto symposium in Zurich, which was attended by over 100 scientists from my alma mater, Kyoto University (Fig. 2). I am also very excited that the 25th anniversary of HFSP, a Program started on the initiative of Japanese Prime Minister Mr. Nakasone, will be held in Switzerland in 2014 and I look forward to attending the HFSP Awardees Meeting in Lugano.



Figure 2. 150th Anniversary of Diplomatic Relations between Switzerland and Japan: Plant and Environment Session

## Congratulations to Torsten Wiesel



On June 3rd, 2014, former HFSP Secretary General Torsten Wiesel will celebrate his 90th birthday. From all of us at the Secretariat but also from the wider HFSP community, our warmest wishes for happiness and continued good health.

## HFSP fellow Hind Medyouf wins the 2013 José Carreras Career Award



Hind Medyouf obtained her PhD at the Institut Curie (Paris), working under Jacques Ghysdael on the biology of pediatric T cell acute lymphoblastic leukemia (T-ALL) with emphasis on signal transduction and gene regulation. Her work was mostly centered on a signaling pathway that has been shown to play a critical role in normal T cell development, namely the calcineurin/ NFAT (Nuclear factor of activated T-cells) pathway. Using two different mouse models of T-ALL as well as primary patient samples, Hind was able to show that constitutive activation of this pathway was involved in hematologic malignancies and that calcineurin inhibitors, currently used as immunosuppressants in the context of organ transplantation, could have a therapeutic potential for lymphoid malignancies (ref. 1). After completion of her PhD, she joined Françoise Pflumio at the CEA (Commissariat à l'Energie Atomique) for a short period in order to gain insight into xenograft modeling, an expertise she planned to use in her next position.

In 2008 she was awarded an HFSP Long-Term Fellowship to work at the Terry Fox Laboratory (Vancouver, Canada) with Andrew Weng on Notch signaling-induced leukemogenic transformation of murine and human cells. Her research was very successful with two first author publications investigating the importance of key signaling pathways in T-ALL pathogenesis (refs. 2-3). Hind discovered that signaling downstream of a particular growth factor called IGF1 (Insulin like growth factor 1) was essential for T-ALL maintenance (ref. 3).

When this factor was blocked, blood cancer cells ceased to grow further. Moreover, the cancer stem cells, which are particularly dangerous and often the main source of relapse in patients, lost their ability to self-renew and so propagate disease in serial transplants. Inhibitors of this signaling pathway are already available and might help improve the treatment of this type of leukemia and also prevent recurrence.

For her third year as an HFSP fellow, Hind moved to the German Cancer Research Centre (DKFZ, Heidelberg) to work with Andreas Trumpp on the biology of myelodysplastic syndromes (MDS), a group of syndromes with ineffective production of mature blood cells and the propensity to evolve to acute myeloid leukemia. Studying the abnormal behavior of human MDS stem cells has so far been hampered by the fact that they could not be efficiently expanded in mice. Together with colleagues, Hind overcame this limitation by co-transplanting the MDS stem cells with their so-called "niche cells" and as such developed a unique in vivo model of human MDS (ref. 4). Niche cells from the bone marrow produce factors required for the

survival of hematopoietic stem cells thus providing a type of micro-environment in which stem cells flourish. Using their newly established model, Hind and her colleagues discovered that niche cells from MDS patients were much better than those from healthy donors in supporting MDS expansion in mice, thanks to their ability to overproduce factors that promoted the settling-in of transplanted MDS blood stem cells. Importantly, MDS cells triggered the expression of some of these factors by niche cells. The authors will now use the model to therapeutically target candidate factors involved in this bi-directional cross-talk between niche cells and MDS hematopoietic cells. Thus, there is hope to break the cycle and interfere with MDS early on in order to prevent progression.

Hind has recently been awarded the Jose Carreras Career Award to continue her work on MDS, and she is now taking the next step and preparing to establish her own laboratory. More information on the award is available at <a href="https://www.carreras-stiftung.de">www.carreras-stiftung.de</a>

#### References

- 1: Hind Medyouf, Héléne Alcalde, Caroline Berthier, Marie-Claude Guillemin, Nuno R Dos Santos, Anne Janin A, Pierre Decaudin, Hugues De Thé, Jacques Ghysdael: Targeting calcineurin activation as a therapeutic strategy for lymphoid malignancies. Nat Medicine. 2007. (13): 736-741.
- 2: Hind Medyouf et al.: High level IGF1R expression is required for leukemia-initiating cell activity in TALL and is supported by Notch signalling. Journal of Experimental Medicine, 2011, DOI:10.1084/jem.20110121.
- 3: Hind Medyouf, Gao X, Florence Armstrong, Samuel Gusscott S, Liu Q, Gedman AL, Larry H Matherly, Kirk R. Schultz, Francoise Pflumio F, James M. You, Andrew P. Weng: Acute T-cell leukemias remain dependent on Notch signaling despite PTEN and INK4A/ARF loss. Blood. 2010. 115(6): 1175-84.
- 4: Hind Medyouf et al: Myelodysplastic cells in patients re-program mesenchymal stromal cells to establish a transplantable stem cell-niche disease unit. Cell Stem Cell 2014, DOI: 10.1016/j.stem.2014.02.014.

## A message from former Deputy Secretary General of HFSPO Toru Nakahara



I came to HFSP in August 2009 and left in March 2014. Although my time in Strasbourg was less than 5 years, it was quite a delight to work in the Secretariat for the Program. Here, in the HFSP Newsletter, I would like to write a short message to HFSP and its scientists

As you may know, all governments have more or less financial problems now. As a result, it seems to me that every government comes to seek immediate or early returns for its expenditure. Unfortunately science is not an exception. Every government is very eager, when it invests in science, to get some result or something useful for innovation or for industrial application. I must say that this is very short-sighted and makes me worry very much. Although I came from the Japanese Government and was not a scientist, I came to recognize the importance of basic research, curiosity driven research, which is simply interesting and not necessarily useful in the short term. Real innovation comes from basic research, especially and very often when it is done by young scientists.

Picking up the best science and the best researchers from anywhere in the world has been the basic philosophy of the Program. I really hope the Program continues as now.

Lastly I want to thank all my colleagues in the Secretariat for their warm help. Without them, I could not have survived there. I cannot thank them enough.

"Picking up the best science and the best researchers from anywhere in the world has been the basic philosophy of the Program. I really hope the Program continues as now."

### HFSP welcomes three new members to its Council of Scientists

The Council of Scientists advises the HFSP Board of Trustees on a range of scientific and organizational matters, such as the evaluation of its current programs, the consideration of new ones, and the selection process for grants and fellowships. The Council also has the responsibility to select the annual winner of the HFSP Nakasone Award.

The HFSP Council meets on a regular basis on the day following the annual Awardees Meeting. HFSP awardees who participate at the Lugano meeting in July 2014 will have the chance to get acquainted with the new Council members and meet again with returning members.

COS members are chosen on the basis of their commitment to promoting international science as well as for their dedication to encouraging young scientists to pursue challenging problems. We would like to welcome three new colleagues to our scientific advisory body:

New York University biologist and Dean for Science **Michael Purugganan** is the new U.S. representative. <a href="http://puruggananlab.bio.nyu.edu/">http://puruggananlab.bio.nyu.edu/</a>

**Allan Herbison** is the Director of the Centre of Neuroendocrinology of the University of Otago in Dunedin, New Zealand.

http://www.neuroendocrinology.otago.ac.nz/labs/herbison.html



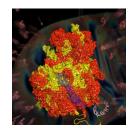




#### Breakthrough in mitochondrial ribosome structure

by HFSP Long-Term Fellow Alexey Amunts and colleagues and HFSP Program Grant holder Venki Ramakrishnan

Mitochondrial ribosomes are indispensable for living because they synthesize essential proteins, which constitute the catalytic core of the respiratory chain complexes embedded in the inner mitochondrial membrane. The aim of the HFSP fellowship awarded to Alexey Amunts was to reveal the atomic structure of mitoribosome. By the end of the fellowship, it was revealed that the structure of yeast mitochondrial large ribosomal subunit is composed of 40 proteins and ~3000 nucleotides using cryo-EM to an overall resolution of 3.2 Å. This currently represents the highest resolution limit reported by cryo-EM, better than most ribosomal structures determined by X-ray crystallography. It is also the first time that the atomic structure of a large asymmetric complex has been obtained without crystallization.



#### Spiders and sodium channels

by HFSP Young Investigator Grant holders Frank Bosmans and Filip Van Petegem and colleagues

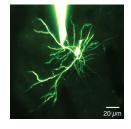
The voltage-gated sodium channel enables fast electrical signaling in the human body and forms the target for various toxins found in predatory species that can paralyze their prey. The first high-resolution structure of an essential subunit allows this complex machine to be dissected. The component partakes in a molecular tug-of-war with a tarantula toxin.



#### Neuronal dendrites are more than wiring, they compute

by HFSP Career Development Award holder Spencer Smith and colleagues

For the first time, scientists have obtained direct electrical recordings of dendrites processing visual information in awake mammals. They found that dendrites are far from passive wiring—they actively compute to support sensory processing.



Read more in the **Awardees' Articles section** of the HFSP website.

## **Prizes & Awards**

HFSP awardee listings continue to be a treasure trove for other organizations looking to bestow their prizes and awards on the very best. As always the complete list is too long to include in the newsletter. You will find a full list of prizes and awards in HFSP's Annual Reports (see HFSP website: <a href="http://www.hfsp.org/about-us/annual-reports">http://www.hfsp.org/about-us/annual-reports</a>)

Here are a few highlights from recent weeks:

- \* Congratulations to all HFSP awardees and alumni who have been elected as EMBO members. The HFSP contingent is almost 35% of the new members.
- \* Great honors for HFSP fellowship and CDA alumna Sophie Martin (University of Lausanne), who was awarded the 2014 EMBO Gold Medal.
- \* HFSP Program Grant awardee and former Council of Scientists member Pascale Cossart is the recipient of the 2014 FEBS-EMBO Women in Science Award.
- \* HFSP Program Grant awardee Allison Doupe received the 2014 Pradel Research Award from the National Academies of Sciences for her groundbreaking work using song birds to reveal important features of how neural circuits process information and are shaped by experience.
- \* HFSP grant awardee Titia de Lange is a recipient of one of the 2014 Canada Gairdner International Awards. She was honored for her discovery of the mechanisms by which mammalian telomeres are protected from deleterious DNA repair and damage responses.