American Society of Pharmacognosy

Vanguards of Natural Product Research 2021

All Times listed are EDT

Friday July 16, 2021

9:45 AM – 10:00 AM	Welcoming Remarks Co-Chairs: Robert Cichewicz, C. Benjamin Naman and Karen VanderMolen

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Session I

10:00 AM – 10:20 AM	C-001 **Taizong Wu** (The University of Queensland) *Highly Modified Deoxyamino C-glycosylated Polyketides from the Australian Pasture Plant-Derived Streptomyces sp. CMB-PB042*
10:20 AM – 10:40 AM	C-002 **Xinhui Wang** (Technical University Of Denmark) *Molecular Networking Reveals New Insights into the Chemodiversity of 28 Species in Aspergillus Section Flavi*
10:40 AM – 11:00 AM	C-003 **Thanet Pitakbut** (TU Dortmund University) *Antiviral Mechanisms of Cannabinoids Againts Sars-Cov2 Infection: A Scrceening Study*

11:00 AM – 12:00 PM	Break/Social Gathering

Friday July 16, 2021(cont.)

Session II

12:00 PM – 12:20 PM C-004
Amrita Salvi (University of Illinois at Chicago)
PHY34 Inhibits Autophagy Through V-Atpase V0A2 Subunit Inhibition and CAS/CSE1L Nuclear Cargo Trafficking in High Grade Serous Ovarian Cancer

12:20 PM – 12:40 PM C-005
Paul A. Price (Eastern Michigan University)
Using Complex Microbial Communities to Identify Silent Biosynthetic Gene Clusters

12:40 PM – 1:00 PM C-006
Tristan de Rond (Scripps Institution of Oceanography / University Of California, San Diego)
Co-Occurrence of Enzyme Domains Guides the Discovery of Oxazolone Natural Products and their Biosynthetic Machinery

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1:00 PM – 2:00 PM **Poster Session I**

Room A – Posters P-001 – P-025
Room B – Posters P-026 – P-050

2:00 PM – **Social Gathering**

Friday July 23, 2021

9:55 AM – 10:00 AM — Welcoming Remarks – Co-Chairs: Robert Cichewicz, C. Benjamin Naman and Karen VanderMolen

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Session III

10:00 AM – 10:20 AM — C-007
Michael Cowled (Macquarie University)
One is the Loneliest Number: Helping Fungi Reach their True Potential Through Co-Cultivation

10:20 AM – 10:40 AM — C-008
Maria Laura Bellone (University of Salerno)
EIF2A as Protein Target of Cannabidiolic Acid in Glioblastoma Cancer

10:40 AM – 11:00 AM — C-009
Thilini Peramuna (University of Oklahoma)
Semisynthetic Derivatization Studies of the Fungal Metabolite Phomasetin with Activity Against the Human Parasite Trichomonas Vaginalis

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11:00 AM – 12:00 PM — Break/Social Gathering

Session IV

12:00 PM – 12:20 PM — C-010
Aswad Khadilkar (University of California Santa Cruz)
Establishment of Biological Platforms for Botanical Natural Products Characterization for HIFAN Program

12:20 PM – 12:40 PM — C-011
Lydia Stariha (Duke Chemistry)
Discovery of the Class I Lasso Peptide Arcumycin

Friday July 23, 2021 (cont.)

12:40 PM – 1:00 PM C-012
Dulce Guillén (Scripps Institution of Oceanography/University of California San Diego)
The potential of specialized metabolites as chemotaxonomic markers in the marine actinobacteria Salinispora

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1:00 PM – 2:00 PM Poster Session II

Room A – Posters P-051 – P-075
Room B – Posters P-076 – P-100

2:00 PM – Social Gathering

Friday July 30, 2021

9:55 AM – 10:00 AM Welcoming Remarks – Co-Chairs: Robert Cichewicz, C. Benjamin Naman and Karen VanderMolen

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Session V

10:00 AM – 10:20 AM C-013
Marija Zacharova (University of St Andrews)
EQATA: Equitable Access to Quality Antibiotic Therapies in Africa

10:20 AM – 10:40 AM C-014
Alice Miral (Université Rennes 1)
Volatile organic compounds from a lichen-associated bacterium, Paenibacillus etheri, interact with plant-parasitic cyst nematodes

July 30, 2021 (cont.)

10:40 AM – 11:00 AM C-015
Liu Cao (Carnegie Mellon University)
MolDiscovery: Learning Mass Spectrometry Fragmentation of Small Molecules

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11:00 AM – 12:00 PM Break/Social Gathering

Session VI

12:00 PM – 12:20 PM C-016
Isaac Morrison (University Of The West Indies) *Uncovering the Potential chemopreventive and Anti-Cancer Effects of an Artocarpin Enriched Wood Extract of Artocarpus heterophyllus Lam.*

12:20 PM – 12:40 PM C-017
Robert Samples (University of Connecticut)
Integrated Mass Spectroscopy Data Analysis Facilitates Discovery of Specialized Metabolite Structural Diversification in Host-Associated Bacteria

12:40 PM – 1:00 PM C-018
Mary Popoola (University of Ibadan)
Silver nanoparticle biosynthesis, characterization, pharmacological activities and in-vivo toxicty study of Avicennia germinans leaf

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1:00 PM – 2:00 PM Poster Session III

Room A – Posters P-101 – P-125
Room B – Posters P-126 – P-151

2:00 PM - Social Gathering

We hope to see you next year in person at the ASP Annual Meeting in Charleston, SC! http://aspmeetings.pharmacognosy.us/

Vanguards of Natural Product Research 2021
Abstract Book

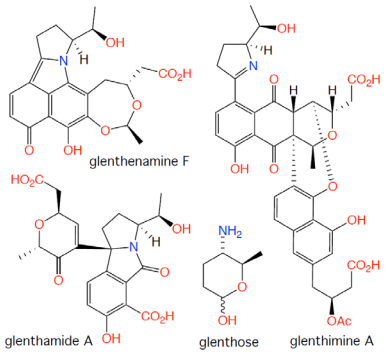
Contributed Speakers

C-001 – Taizong Wu

Highly Modified Deoxyamino *C*-glycosylated Polyketides from the Australian Pasture Plant-Derived *Streptomyces* sp. CMB-PB042

Taizong Wu,[1] Angela A. Salim,[1] Hui Cui,[2] Paul V. Bernhardt,[3] and Robert J. Capon [1]Institute for Molecular Bioscience, [3]School of Chemistry and Molecular Bioscience, The Universityof Queensland, Brisbane, QLD 4072, Australia, [2]School of Pharmaceutical Sciences, Guangzhou University of Chinese Medicine, Guangzhou, China

As part of our investigation into new antiparasitic natural products produced by Australian microbes, we selected *Streptomyces* sp. CMB-PB042 as a source of biologically and chemically interesting molecules. Bioassay-guided fractionation combined with GNPS molecular network analysis identified the antiparasitic agents as a mixture of known ionophoric polyethers (*e.g.* nigericin). Although our assessment was that such polyethers had little commercial potential, our investigations into CMB-PB042 also led to the discovery of an array of new pyranonaphthoquinones, glenthenamines A–F, glenthamineA, glenthimine A and glenthamide A. Recognizing the prospect of a common deoxyaminosugar *C*-glycoside precursor, we employed a Schiff base "fishing strategy" to detect (for the first time) the cryptic biosynthetic precursor glenthose (5-aminotetrahydro-6-methyl-2*H*-pyran-2-ol) in the culture extract. Single crystal X-ray analysis and biosynthetic considerations allowed us to resolve configurational ambiguities in the scientific literature, andassign absolute configurations to all new natural products.



C-002 – Xinhui Wang

Molecular Networking Reveals New Insights into the Chemodiversity of 28 Species in *Aspergillus* Section *Flavi*

Xinhui Wang[1], Karolina Subko[1], Sara Kildgaard[2], Francisca Vicente[3], Olga Genilloud[3], Jens C. Frisvad[1], and Thomas O. Larsen[1]. [1]Department of Biotechnology and Biomedicine, Technical University of Denmark, Søltofts Plads 221, DK-2800 Kgs. Lyngby, Denmark, [2]Present address: Section for Ecology and Evolution, Department of Biology, University of Copenhagen, Universitetsparken 15 Building 3, 2100, Copenhagen East, Denmark, [3]Fundación MEDINA, Parque Tecnológico de Ciencias de la Salud, 18016 Armilla, Granada, Spain.

Aspergillus section *Flavi* includes some of the most famous mycotoxin producing filamentous fungi known to mankind. In recent years, a number of new species have been included in section *Flavi*, however these species have been much less studied from a chemical point of view. In this study, we explored one representative strain of a total of 28 fungal species in section *Flavi* by systematically evaluating the relationship between taxonomy and secondary metabolites (SMs) with LC-MS/MS analysis. In addition, we did dereplication through an in-house database and the Global Natural Product Social Molecular Networking (GNPS) platform. This approach allowed the rapid identification of two new cyclopiazonic acid producers (*A. alliaceus* and *A. arachidicola*) and two new tenuazonic acid producers (*A. arachidicola* and *A. leporis*). Moreover, for the first time we report species from section *Flavi* to produce fumifungins and sphingofungins B-D. Finally, a following MS-guided isolation procedure yielded six new compounds, including asperazine D-H (**1-5**), aspergillicin H (**6**), which were further isolated and confirmed by NMR. Altogether, the approach used in this study was found to be very useful for rapid identification of species-specific or series-specific compounds that can be used as chemical markers for species identification and further highlights the metabolic diversity within section *Flavi*

C-003 – Thanet Pitakbut

Antiviral Mechanisms of Cannabinoids Against SARS-CoV2 Infection: a Screening Study

Thanet Pitakbut[1], Gia-Nam Nguyen[1,2] and Oliver Kayser[1]
[1]Technical Biochemistry Laboratory, Department of Biochemical and Chemical Engineering, TU Dortmund, Dortmund, Germany and [2]MINDbioscience GmbH, Dortmund, Germany

Plant secondary metabolites (PSMs) are well-accepted as a resource to develop anti-infective agents since plants evolved them to fight against a broad spectrum of pathogens, including viruses. Furthermore, cannabinoids are a unique group of PSMs with a wide range of biological activities, especially anti-inflammation mediated by cannabinoid receptors, especially the CB2 type. We tested THC, CBD, CBN, and CBT to evaluate antiviral SARS-CoV2 activity based on inhibition of virus entry to immune cells at concentration of 100 μg/ml. Two crucial SARS-CoV2 drug targets as human ACE2 and main viral protease (MPro), were selected. Remarkably, THC and CBD exhibit strong activity against SARS-CoV2 MPro by 100% inhibition while CBN and CBT inhibited less than 80%. In parallel, THC, CBD, and CBN inhibited human ACE2 activity by more than 89%, whereas CBT remained inactive. Further, we analyzed structure activity relationship for all tested cannabinoids. Remarkably, THC and CBN shared a similar structural feature. Only THC effectively inhibited human ACE2 and SARS-CoV2 MPro when CBN inhibited human ACE2 only. Based on our result here, we suggest to consider selected cannabinoids as interesting candidates for ongoing studies to fight against SARS-CoV2 infection.

C-004 – Amrita Salvi

PHY34 Inhibits Autophagy Through V-ATPase V0A2 Subunit Inhibition and CAS Nuclear Cargo Trafficking in High Grade Serous Ovarian Cancer

Amrita Salvi[1], Alexandria N. Young[1], Andrew C. Huntsman[2], Melissa Pergande[3], Melissa A. Korkmaz[3], Nicholas T. Cockroft[2], Brittney K. Mize[2], A. Douglas Kinghorn[2], Xiaolin Cheng[2], Mitch A. Phelps[4], Kiira Ratia[1], Markus Schirle[5], Jason R. Thomas[5], Leslie N. Aldrich[3], Stephanie M. Cologna[3], James R. Fuchs[2], Joanna E. Burdette[1]. [1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60607, [2]Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH, 43210, [3]Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, [4]Department of Pharmaceutics and Pharmaceutical Chemistry, College of Pharmacy, The Ohio State University, Columbus, OH, 43210, [5]Novartis Institutes for BioMedical Research, 250 Massachusetts Avenue, Cambridge, MA 02139, USA.

PHY34 is a synthetic small molecule, inspired by a natural compound in tropical plants of the *Phyllanthus* genus. PHY34 was developed to have potent *in vitro* and *in vivo* anti-cancer activity against high grade serous ovarian cancer (HGSOC) cells. PHY34 induced apoptosis in HGSOC cells by late-stage autophagy inhibition. PHY34 significantly reduced tumor burden in a xenograft model of ovarian cancer. To identify its molecular target/s, we utilized photo affinity labeling, pulldown, and mass spectrometry. Protein targetsfrom the nucleocytoplasmic transport pathway were identified from the pulldown assay with the cellular apoptosis susceptibility (CAS) protein, as the top hit. A tumor microarray confirmed data from mRNA expression data in public databases that CAS expression was elevated in HGSOC and correlated with worse clinical outcomes. Overexpression of CAS reduced PHY34 induced apoptosis in ovarian cancer cells. Compounds with a diphyllin structure similar to PHY34 inhibit the ATP6V0A2 subunit of V(vacuolar)-ATPase. ATP6V0A2 wild-type and ATP6V0A2 V823 mutant cell lines were tested with PHY34 and it induced cell death in the wild-type at 246 pM while the mutant cells were resistant up to 55.46 nM. Overall, our data demonstrates that PHY34 is a promising therapeutic molecule that targets theATP6V0A2 subunit to modulate autophagy and CAS to alter protein nuclear localization.

C-005 – Paul Price

Using Complex Microbial Communities to Identify Silent Biosynthetic Gene Clusters

Megan Steltz[1], Sadaf Dorandish[1], Maira Shoukat[1], Ifrah Shoukat[1], Hussein Chehade[1], Paul Price[1] [1]Biology Department, Eastern Michigan University, Ypsilanti, MI 48197.

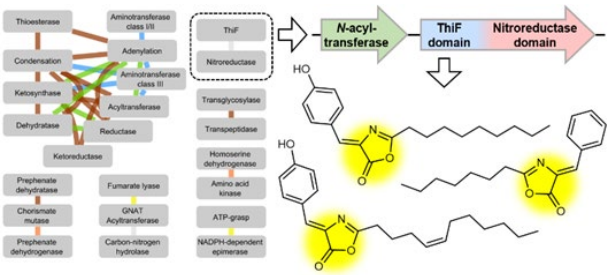
New antibiotics are desperately needed to combat infections caused by antibiotic-resistant bacteria, which now result in over 2 million infections and 35,000 deaths each year in the United States. Natural products hold the potential to deliver many new classes of antibiotics, but much of the biosynthetic potential encoded in bacterial genomes is not well expressed under traditional laboratory conditions. In contrast, microbes in their natural environments encounter many microbial partners and competitors that can elicit the production of different silent biosynthetic gene clusters (BGCs) including those that could produce antimicrobial compounds. We have recently determined that the simultaneous inoculation of soil microbes and target organisms results in very evident, although small, zones of inhibition over time, which we are calling the new modified crowded plate technique (mCPT). This method exploits the physiological concept that the prolonged exposure of bacteria to either bactericidal or bacteriostatic antibiotics will eventually result in death and lysis (i.e., the formation of a zone of inhibition) of bacteria due to the activity of autolysins in bacterial cell walls or direct killing of non-replicative cells. Importantly, the small zones of inhibition allow us to inoculate soil microbes at higher densities for longer time periods (months), providing more physical and/or chemical contacts that can induce the production of natural products from silent BGCs. Using the mCPT method during our Tiny Earth biology lab courses, students have isolated over 2800 antibiotic-producing microbes, most of which produce little to no antimicrobial compounds when grown axenically under more traditional laboratory conditions. This new methodology has greatly increased our ability to identify isolates that produce antimicrobial compounds effective against extensively-drug resistant Gram-negative and Gram-positive ESKAPE-TB pathogens.

C-006 – Tristan de Rond

Co-Occurrence of Enzyme Domains Guides the Discovery of Oxazolone Natural Products and Their Biosynthetic Machinery

Tristan de Rond[1], Julia E. Asay[1] and Bradley S. Moore[1,2], [1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, and [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego

Billions of years of evolution has provided immense genetic – and hence, biochemical – diversity. Some of this genetic diversity is starting to be explored through genome mining of biosynthetic gene clusters containing homologs of known core biosynthetic genes of established classes of natural products. We developed a contrasting genome mining approach for the discovery of biochemical transformations through the analysis of co-occurring enzyme domains (CO-ED) in a single protein. Guided by CO-ED, we targeted an unannotated predicted ThiF-nitroreductase di-domain enzyme found in more than 50 proteobacteria, leading to the discovery of a series of natural products containing the rare oxazolone heterocycle and the characterization of their biosynthesis. Notably, we identified the di-domain enzyme as an oxazolone synthetase, whose catalytic mechanism is currently under investigation. I will also present our ongoing studies into the distribution and possible ecological roles of these molecules.

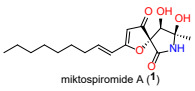


C-007 – Michael Cowled

One is the Loneliest Number: Helping Fungi Reach their True Potential Through Co-cultivation

Michael Cowled[1], John Kalaitzis[1,2], Ernest Lacey[1,2],and Andrew Piggott[1]. [1]Department of Molecular Sciences, Macquarie University, Sydney, Australia, 2109, [2]Microbial Screening Technologies; Smithfield, NSW, Australia, 2164.*

Elicitation of cryptic secondary metabolism by microbial co-culture is a powerful tool for generating new chemical diversity. However, the factors that mediate microbial interactions are complex and still poorly understood, with the success of co-cultivation experiments often being due to 'good luck' rather than 'good management'. To explore these factors in more detail, a systematic matrix of co-cultivation experiments was performed using a collection of talented fungi and compared to a collection of ecologically relevant fungal isolates obtained from the Northern Territory in Australia, with the specific aim of identifying secondary metabolite inductions, enhancements, and suppressions. A case study will also be presented involving the two fungi, *Aspergillus nomius* and *Penicillium brasilianum*, which respectively induce production of the novel secondary metabolites, miktospiromide A (**1**) and kitrinomycin A (**2**).



C-008 – Maria Laura Bellone

EIF2A as Protein Target of Cannabidiolic Acid in Glioblastoma Cancer

M.L. Bellone[1,4], G. Appendino[3], N. De Tommasi[1], F. Pollastro[3], F. Dal Piaz[2]. 1 Dipartimento di Farmacia, Università degli Studi di Salerno, 84084 Fisciano. [2]Dipartimento di Medicina e Chirurgia, Università degli Studi di Salerno, 84084 Fisciano. [3]Dipartimento di Scienze del Farmaco, Università del Piemonte Orientale, 28100 Novara, [4]Scuola di Dottorato in Scienze del Farmaco, Dipartimento di Farmacia, Università degli Studi di Salerno, 84084 Fisciano.*

Phytocannabinoids, the major secondary metabolites of cannabis plants, have been shown to exert a wide diversity of biological activities. The present study was focused on characterization of the bioactivity and identification of the molecular mechanism of action of cannabidiolic acid (CBDA), cannabigerolic acid (CBGA) and cannabidivarinic acid (CBDVA) in U87MG, glioblastoma cell lines. To identify the putative target(s) of CBDA, CBGA and CBDVA in that cell line, a mass spectrometry-based chemical-proteomic approach was carried out. This study allowed to indicate the eukaryotic initiation factor 2 (EIF2A) as a putative interactor of CBDA and CBDVA, whereas CBGA showed a treasurable affinity for it. This result was also confirmed by western blot analysis. Since proteomic data suggested CBDA as the most active molecule, it was regarded as the lead compound for the subsequent analyses. Therefore, to verify that the bioactive compound was actually able to interact with the target into the cell, CETSA experiments were performed. They revealed that EIF2A binding to CBDA induces its thermal stabilization, as inferred by an increase in the denaturation temperature of EIF2A following incubation of cancer cells with CBDA. The biological activity of three cannabinoids was studied also in 3D-cultured cells, showing a different cytotoxicity depending on the concentration of FBS in the upper- and lower-gel, thus confirming the critical role played by the molecule-FBS interaction. Based on these evidences, as future perspective both cell-based and cell-free techniques will be performed in 3D cell culture in order to confirm protein target of our molecules of interest.

C-009 – Thilini Peramuna

Semisynthetic Derivatization Studies of the Fungal Metabolite Phomasetin with Activity Against the Human Parasite *Trichomonas vaginalis*

Thilini Peramuna, Ziwei Hu, Karen Wendt, Adam S. Duerfeldt, Robert Cichewicz. Department of Chemistry and Biochemistry and Natural Products Discovery Group, University of Oklahoma, Norman, OK, USA.

Trichomonasis is the most prevalent sexually transmitted parasitic disease (STD) in the United States and is caused by *Trichomonas vaginalis*. The tetramate-containing natural product, phomasetin, has been identified as a promising candidate with good activity (EC_{50} = 0.35 μM) against this genitourinary tract parasite. A structure-activity study was undertaken to develop semi-synthetic derivatives of phomasetin with many of the derivatives containing modifications to the tetramate moiety using 'click' chemistry. The analogues containing triazole-linked phenol groups showed the most pronounced improvements in activity compared to the other structural modifications. The semisynthetic analogues of phomasetin hold promise to improve treatment options against *T. vaginalis* through the creation of compounds that exhibit improved activity and selectivity against the parasite.

C-010 – Aswad Khadilkar

Establishment of Biological Platforms for Botanical Natural Products Characterization for HIFAN Program

Aswad S Khadilkar[1], Akshar Lohith[1], Britney Hernandez[1], Tannia Lau[1], Lénaïg Défachelles[1], Susan Carpenter[1], Roger Linington[2], Nadja Cech[3], John MacMillan[1]. [1] University of California, Santa Cruz, CA. [2] Simon Fraser University, Burnaby, British Columbia, Canada, [3] University of North Carolina, Greensboro,NC.

While it is hypothesized that additive or synergistic activities of individual chemical constituents contribute to the biological effects of botanical extracts and other chemically complex natural products, this has been clearly demonstrated in only a few cases. Bottlenecks that contribute to slowing this research include the challenges of accurately defining the chemical composition of complex mixtures, and of elucidating the contributions of individual constituents and sets of constituents to the biological activity. Our program proposes to address these challenges through the integration of orthogonal assay systems using sophisticated informatics approaches, an approach that has been demonstrated to work with complex mixtures as well as with pure compounds. We are using gene expression-based (FUSION)and high content phenotypic screening (CP) in primary macrophages to provide agnostic and extensive coverage of critical biological pathways that are relevant to innate immune response during inflammation. Here I present our work to establish FUSION in BMDMs using Nanostring nCounter PlexSet gene expression analysis and CRISPR based genetic purturbations. Secondly, I will share our developments on cytological profiling in macrophages to study lipopolysaccharide stimulated inflammation and observe the effect of botanicals on their ability to modulate immune response.

C-011 – Lydia Stariha

Discovery of the Class I Lasso Peptide Arcumycin

Lydia Stariha, Duke University Chemistry Department Dr. Dewey McCafferty, Duke University Chemistry Department

Lasso peptides are a structurally diverse superfamily of conformationally-constrained peptide natural products, of which a subset exhibits broad antimicrobial activity. Although advances in bioinformatics have increased our knowledge of strains harboring the biosynthetic machinery for lasso peptide production, relating peptide sequence to bioactivity remains a continuous challenge with fewer than half of the members of this family isolated to date having been tested for biological activity. Towards this end, a structure-driven genome mining investigation of Actinobacteria-produced antimicrobial lasso peptides was performed to correlate predicted primary structure with antibiotic activity. Through this work a distinct relationship between phylogenetic lineage and structural class, as determined by the number and location of disulfide bonds, was observed. Further bioinformatic evaluation revealed eight putative novel class I lasso peptide sequences. This subset is predicted to possess antibiotic activity as characterized members of this class have both broad spectrum and potent activity against Gram-positive strains. Fermentation of one of these hits, *Streptomyces* NRRL F-5639, resulted in the production of a novel class I lasso peptide, arcumycin, named for the Latin word for bow or arch, arcumycin. The structure of arcumycin was elucidated using a mass spectrometry approach to confirm both sequence and topology. Arcumycin exhibited antibiotic activity against Gram-positive bacteria including *Bacillus subtilis* (4 μg/mL), *Staphylococcus aureus* (8 μg/mL), and *Micrococcus luteus* (8 μg/mL). Arcumycin treatment of *B. subtilis liaI-β-gal* promoter fusion reporter strain resulted in upregulation of the system *liaRS* by the promoter *liaI*, indicating arcumycin interferes with lipid II biosynthesis. The results from this assay present a conserved mechanism of action among Actinobacteria-produced lasso peptides that had not previously been elucidated. Cumulatively, the results illustrate the relationship between phylogenetically related lasso peptides and their bioactivity as validated through the isolation, structural determination, and evaluation of bioactivity of the novel class I antimicrobial lasso peptide arcumycin.

C-012 – Dulce Guillen

The Potential of Specialized Metabolites as Chemotaxonomic Markers in the Marine actinobacteria *Salinispora*

Dulce G. Guillén Matus[1], Paul R. Jensen[1] [1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA, USA

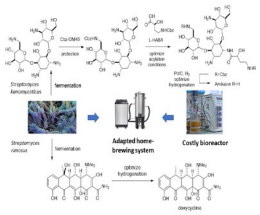
Bacterial species are defined using the polyphasic approach, which combines phenotypic and genotypic characters, including genomic information, morphology, physiology and chemotaxonomy. Many bacterial taxa are prolific producers of specialized metabolites; surprisingly, these molecules are rarely used as taxonomic markers despite numerous studies showing strong correlations between phylogeny and specialized metabolism. For example, the marine actinobacteria *Salinispora* exhibits species-specific patterns of biosynthetic gene cluster distribution and a few examples of known compounds fixed at the species levels. In fact, only a few gene clusters are shared among all the nine *Salinispora* species. These findings suggest that specialized metabolism may be an important phenotypic difference among *Salinispora* species. The main goal of this research is to explore the correlations between specialized metabolism and species phylogeny. We apply these findings to the chemotaxonomy of *Salinispora* spp. which will provide insight into the potential role of specialized metabolism in speciation.

C-013 – Marija Zacharova

EQATA: Equitable Access to Quality Antibiotic Therapies in Africa

Marija K. Zacharova, Yunpeng Wang, Viktorija Štikonaitė, Rebecca J. M. Goss, Gordon J. Florence School of Chemistry, University of St Andrews, St Andrews, United Kingdom*

Antibiotic treatable infections are still a global health and mortality burden, causing 5.7 million deaths annually, the majority of which occur in low- and middle-income countries (LMICS). In Africa, mortality rate from lower respiratory infections and diarrhoeal diseases outnumbers that from HIV/AIDS, TB and malaria combined,[1,2] and rising antimicrobial resistance will further increase the mortality rates associated with bacterial diseases. CCDEP identified a number of barriers to treating infectious diseases LMICS face which include low antibiotic affordability and unreliable supply chains, which in combination with poor quality control, counterfeit pharmaceuticals entering the market, and poor stewardship lead to widespread misuse and overuse of antibiotics, further compounding the emergence of antimicrobial resistance.[1] To tackle these challenges, two strategies have been proposed: Sustainable and supply chain-safeguarded fermentative production of Access antibiotics **-** A robust yet simple and cost-efficient fermentation rig constructed from an adapted commercially available home brewing system will be developed for the fermentative production of precursors to two Access antibiotics[3] – amikacin and doxycycline, followed by optimization of their semi-synthesis to be cost-efficient and suitable for semi-industrial scale. Drug discovery capacity building via community-driven discovery of novel bioactive molecules - In collaboration with our partners with Kenya, Tanzania and Nigeria, a citizen science-driven microbial discovery project will be launched. Run in collaboration with Tiny Earth,[4] the project will involve community-driven sampling soil and water and screening for presence of microorganisms producing novel, promising bioactive molecules. References: 1. Access Barriers to Antibiotics, CDDEP, April 2019. 2. WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation, WHO, 2018 3. The State of the World's Antibiotics 2021: A Global Analysis of Antimicrobial Resistance and Its Drivers, CDDEP, 2021 4.https://tinyearth.wisc.edu/



C-014 – Alice Miral

Volatile Organic Compounds from a Lichen-Associated Bacterium, *Paenibacillus etheri,* Interact with Plant-Parasitic Cyst Nematodes

A. Miral[1], C. Porte[2], A. Sauvager[1], S. Fournet[2], J. Montarry[2], S. Tranchimand[1] and S. Tomasi[1] [1]Univ Rennes, CNRS, ISCR-UMR 6226, Rennes, France. [2]INRAE, IGEPP, Le Rheu, France.

Healthy food is one of the major challenges to develop in this century. Plant parasitic nematodes cause important damage to many crops worldwide and till now, the use of chemical nematicides wasthe main means to control their populations. These chemical products must be replaced by more environmental friendly control methods. Biocontrol agents seem to be one promising option and thenumber of biopesticides derived from living organisms has increased in the last decades. To developnew plant protection products, we have decided to combine our skills, in chemical and nematology, and to focus on lichen microecosystem as underexploited ecological niches of microorganisms. We will present herein an efficient method to evaluate the potential of lichen-associated bacterialsuspensions, the supernatant of their culture and their metabolites as nematicides against the beet cyst nematode *Heterodera schachtii* and the potato cyst nematode *Globodera pallida*. Analytical approaches such as LC-UV-DEDL-MS have been carried out in order to analyze the chemical profileof crude extracts derived from these strains. A GC-MS analysis was also performed to determine thevolatile organic compounds (VOC) produced by these bacteria and which seem responsible to the effect on the tested cyst nematodes.

C-015– Liu Cao

MolDiscovery: Learning Mass Spectrometry Fragmentation of Small Molecules

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Recent advances in mass spectrometry have enabled the collection of tandem mass spectra of small molecules from hundreds of thousands of environments. To identify which molecules are present in a sample, one can search mass spectra collected from the sample against millions of molecular structures in small molecule databases. The existing approaches are based on chemistry domain knowledge, and they fail to explain many of the peaks in mass spectra of small molecules. Here, we present molDiscovery, a mass spectral database search method that improves both efficiency and accuracy of small molecule identification by learning a probabilistic model to match small molecules with their mass spectra. A search of over 8 million spectra from the Global Natural Product Social (GNPS) molecular networking infrastructure shows that molDiscovery correctly identifies six times more unique small molecules than previous methods. On a subset of the GNPS repository with known genomes, molDiscovery correctly links 19 known and three novel biosynthetic gene clusters to their molecular products.

C-016 – Isaac Morrison

Uncovering the Potential Chemopreventive and Anti-Cancer Effects of an Artocarpin Enriched Wood Extract of *Artocarpus heterophyllus* Lam.

Isaac J. Morrison[1,2ǂ], Jianan Zhang[3ǂ] , Jingwen Lin[3], JeAnn E. Murray[1], Roy Porter[4], Moses K. Langat[5], Nicholas J. Sadgrove[5], James Barker[6], Guodong Zhang[3] and Rupika Delgoda[1]*
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Colorectal cancer ranks second among the leading cause of global cancer-related fatalities, necessitating greater treatment and prevention options. Following bioactive guided evaluations, the crude wood methanol extract of *Artocarpus heterophyllus* was found to be the most potent extract against malignant cells[ǂ]. An enriched preparation of this extract containing 84% artocarpin (as determined by HPLC-MS-DAD) demonstrated time- and concentration-dependent cytotoxicity against human HCT116 malignant cells with an IC50 value of 4.23 mg/L following 72 h treatment. Further *in vitro* evaluations demonstrated that the enriched extract displayed irreversible inhibition of the activity of human cytochrome CYP2C9 enzyme, with an IC50 value of 0.46 μg/mL Human CYP2C9 had previously been shown to be over-expressed in colon cancer models. Following exposure to the enriched extract, there was a reduction in tumor multiplicity, proliferating cell nuclear antigen expression and proinflammatory cytokines (*Il-6* and *Ifn-γ*) and protumorigenic markers (*Pcna*, *Axin2*, *Vegf*, and I) gene expressions in the azoxymethane (AOM)/dextran sodium sulfate (DSS) colitis-induced model in C57BL/6 mice. Gene expression of murine *Cyp2c37*, an enzyme homologous to the human CYP2C9 enzyme was also significantly reduced. These chemopreventive, cytotoxic, anti-cancer and anti-inflammatory responses, combined with an absence of toxicity, validate further evaluation of the promising *A. heterophyllus* extract as a therapeutic agent. #Part of this work can be found at DOI: 10.1038/s41598-021-86040-5

C-017 – Robert Samples

Integrated Mass Spectroscopy Data Analysis Facilitates Discovery of Specialized Metabolite Structural Diversification in Host-Associated Bacteria

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Untargeted metabolomics is a powerful tool for investigating complex biological systems, but its utility is compromised by the presence of uninformative features which complicates statistical testing and prioritization by exacerbating issues related to multiple hypothesis testing. Here, we propose a new approach mass spectrometry metabolomics data analysis, employing filtering based on multiple modalities, statistical techniques incorporating hierarchal replication, and interactive data visualization tools. We demonstrate application of this approach to uncover hidden effects of metabolite induction with a tunicate-associated bacterium, *Streptomyces* sp. PTY087I2. Using this method, we have identified key metabolites involved in these interactions as well as three new granaticins with multiple novel structural alterations not previously seen in this class of metabolites.

C-018 – Mary Popoola

Silver Nanoparticle Biosynthesis, Characterization, Pharmacological Activities and in-vivo Toxicty Study of Avicennia Germinans Leaf

Mary C. Popoola and Bolanle A. Adeniyi. Department of Pharmaceutical Microbiology, University of Ibadan, Ibadan, Oyo State, Nigeria.

This investigation addresses the green synthesis of silver nanoparticles (AgNPs) using *Avicennia germinans* (Black Mangrove) leaf extract and investigates the antimicrobial, antioxidant activity and *in-vivo* toxicity. The *Avicennia germinans* (Ag) mediated green synthesized AgNPs (Ag-AgNPs) was characterized by ultraviolet⊙visible (UV⊙VIS.) spectrophotometry, Fourier transform-infrared (FT-IR) spectroscopy, X-ray diffractometry (XRD), transmission electron microscopy (TEM), scanning electron microscopy (SEM) and energy dispersive X-ray (EDX) spectroscopy. The mice model *in-vivo* was used to determine the toxicity of the extract and Ag-AgNPs, while the antimicrobial study was done on different strains of *Acinectobacter baumanii*, some dermatophytes (*Microsporum canis, Trichophyton rubrum, Candida parasilopsis* and *Meyerozyma canis), Staphylococcus aureus* and *Pseudomonas aeruginosa*. The results showed that the material was formed in nano-dimension with particle size in the range between 10–50 nm. The nanoparticles (NPs) were spherical in shape and demonstrated excellent material stability. The results showed that the extracts and its NPs did not induce any toxicity at 500 mg per kg body weight. Moreover, Ag-AgNPs demonstrated good antimicrobial activity against the tested microorganisms. Thus, this study may make a significant synthetic route for the production of green-AgNPs and their safe usages, and may also be used to augment the bioactivities of the material with minimum toxicity.

Poster Presentations

P-001 - New Lipopeptides from the Saprotrophic Fungus Myrothecium inundatum

Annika Jagels[1], Donovon A. Adpressa[2], Elizabeth Kaweesa[1], and Sandra Loesgen[1], [1]Department of Chemistry, University of Florida, Whitney Laboratory for Marine Bioscience, St. Augustine, FL 32080, [2]Merck Research Laboratories, Boston, MA 02115

Many microorganisms produce secondary metabolites that are believed to have critical roles in intra- and inter-species communication, competition for resources, or their specific lifestyles. Despite the importance of these metabolites, it is estimated that only a small fraction of fungal secondary metabolites has been identified, and a much smaller fraction of known secondary metabolites have well-established ecological functions. The saprotrophic filamentous fungus *Myrothecium inundatum* (Hypocreales, *Stachybotrys*-clade) represents a chemically underexplored species despite the large number of putative biosynthetic gene clusters found in its genome. Most fungi do not express their full secondary metabolome as respective gene clusters remain silent under standard laboratory culture conditions. Here we present new fungal metabolites from non-genetic gene activation experiments using nutrient and salt variations. We employed LC-MS-based metabolomics to rapidly identify new metabolites and leveraged a panel of assays to assess their biological function. We will present the isolation and structure elucidation of potent antimicrobial and cytotoxic lipopeptides. Four structures were established by analysis of NMR and HRMS data, their absolute configuration established by Marfey's analysis, and their helical behavior assessed by ECD. Moreover, we will give insights into their cellular mode of action.

P-002 - Identification of a Solo Acylhomoserine Lactone Synthase from the Myxobacterium Archangium gephyra (DSM 2261)

Hanan Albataineh, Maya Duke, Sandeep K. Misra, Joshua S. Sharp, and D. Cole Stevens Department of BioMolecular Sciences, University of Mississippi, Faser Hall, University, MS 38677

Considered a key taxon in soil and marine microbial communities, myxobacteria exist as coordinated swarms that utilize a combination of lytic enzymes and specialized metabolites to facilitate predation of microbes. This capacity to produce specialized metabolites and the associated abundance of biosynthetic pathways contained within their genomes have motivated continued drug discovery efforts from myxobacteria. Of all myxobacterial biosynthetic gene clusters deposited in the antiSMASH database, only one putative acylhomoserine lactone (AHL) synthase, *agpI*, was observed, in genome data from *Archangium gephyra*. Without an AHL receptor also apparent in the genome of *A. gephyra*, we sought to determine if AgpI was an uncommon example of an orphaned AHL synthase. Herein we report the bioinformatic assessment of AgpI and discovery of a second AHL synthase from *Vitiosangium* sp. During axenic cultivation conditions, no detectible AHL metabolites were observed in *A. gephyra* extracts. However, heterologous expression of each synthase in *Escherichia coli* provided detectible quantities of 3 AHL signals including 2 known AHLs, C8-AHL and C9-AHL. These results suggest that *A. gephyra* AHL production is dormant during axenic cultivation. The functional, orphaned AHL synthase, AgpI, is unique to *A. gephyra*, and its utility to the predatory myxobacterium remains unknown.

P-003 - Accelerated Solvent Extraction as a Viable Method For the Isolation of a Neurodegenerative Secondary Metabolite from *Streptomyces venezuelae*

Timothy J. Bushman, Jennifer L. Thies, Kim A. Caldwell, Łukasz Cieśla Department of Biological Sciences, University of Alabama, Tuscaloosa, AL, 35487

Members of the genus *Streptomyces* are well known for their ability to produce a wide range of secondary metabolites. It has been demonstrated that a secondary metabolite produced by *Streptomyces venezuelae* and isolated from spent media can induce dopaminergic neurodegeneration in a *Caenorhabditis elegans* model. Here we report a novel method for extraction and isolation of the metabolite of interest through the utilization of accelerated solvent extraction on the bacterial biomass itself. There is little to no published work utilizing accelerated solvent extraction in the isolation of bacterial metabolites, thus this project indicates a potential new and exciting way to maximize yield of bacterial specialized compounds for natural product discovery.

P-004 - Multi-Omics Analysis of Two Novel *Pseudonocardia* spp. Isolated from the Deep Southern Ocean

Jonathan Parra[1], Katherine R. Duncan[1]. [1]Strathclyde Institute of Pharmacy and Biomedical Sciences,University of Strathclyde, 161 Cathedral Street, Glasgow, G4 0RE, UK.

Multidrug-resistant pathogens have become a global threat. In this context, rare actinomycetes isolated from marine environments have been proposed as a potential source of yet untapped antimicrobial metabolites. In this study, two novel species, *Pseudonocardia abyssalis* sp. nov. and *Pseudonocardia oceani* sp. nov, isolated from deep Southern Ocean sediments are described. Furthermore, the genomic architecture, with a focus on Biosynthetic Gene Cluster (BGC), across eight strains belonging to the two novel species were investigated. A total of 13 Gene Cluster Families (GCF) were identified, of which sixGCFs comprise BGCs from both species, and seven were specific to each species. Following genome analysis, a comparative mass-spectrometry based metabolomics analysis was carried out, including phylogenetically closely related non-marine species, as well as other *Pseudonocardia* spp. strains isolated from different marine environments. Then, genomics and metabolomics data were correlated through NPLinker, an unsupervised method for integrating paired omics data. This metabolic-repertoire was found to be elicitated through the addition of *N*-acetyl glucosamine (GlcNAc), revealing chemically inducible bioactivity against the fungi *Candida albicas* and multidrug-resistant *Candida auris*. These results showcase the power of a combined genomic-metabolomics approach to investigate rare-actinomycetes from understudied locations and have uncovered a wealth of both biosynthetic and chemical diversity for further investigation.

P-005 - A New Perspective on Usnic Acid Biosynthesis in *Cladonia rangiferina*

Susan Egbert[1], Jordan Hoffman[2], James Lendemer[2], John L. Sorensen[1] [1]Department of Chemistry, University of Manitoba, Manitoba, MB, Canada, [2]Institute of Systematic Botany, New York Botanical Garden, Graduate Center, City University of New York, USA.

One of the most prevalent natural products in lichen fungi is usnic acid, which has been shown to possess a broad array of bioactivity. Although usnic acid was originally isolated from the lichens *Ramalina fraxinea* and *Usnea barbata*, the only putative biosynthetic gene cluster (BGC) was reported from the known producer *Cladonia uncialis*. This presentation will describe how we have used the gene cluster from *C. uncialis* as a guide to explore usnic acid biosynthesis in other *Cladonia spp.* We investigated strains of *C. rangiferina* and *C. stygia*, reported in the literature as lacking an ability to produce usnic acid. We first examined genomic data for several *C. rangiferina* strains and used genome annotation tools to identify the usnic acid BGC in these samples. A comparison of these BGC's to the usnic acid BGC's from a number of *C. unicalis* strains displayed high homology, suggesting that these genes should be functional. *Cladonia stygia* on the other hand lacked the usnic acid BGC entirely. Subsequent LC-MS analysis revealed readily detectable amounts of usnic acid in the *C. rangiferina* extracts.. The conclusions of this study demonstrate that the fundamental lack of knowledge on lichen secondary metabolism and biosynthesis represent a unique opportunity to discover new chemistry, evaluate phylogenetic relationships, and potential ecological functions of lichen chemistry.

P-006 - The Use of Cell Membrane Coated Magnetic Nanoclusters to Identify TrkB Receptor binders from Complex Matrices

Bishnu Adhikari,[1] Zekiye Ceren Arituluk,[1,2] Jesse Horne,[3a] Jeffrey Steltzner,[1] Shomit Mansur[3], Parmanand Ahirwar,[4] Sadanandan Velu,[4] Yuping Bao[3], and Lukasz Ciesla[1], [1] Department of Biological Sciences, The University of Alabama, Tuscaloosa, AL 345487.[2] Department of Pharmaceutical Botany, Hacettepe University, Ankara 06100, Turkey.[3] Chemical and Biological Engineering, The University of Alabama, Tuscaloosa, AL 345487.[4]Department of Chemistry, University of Alabama at Birmingham, 901 14th Street South, Birmingham, AL 35294. [3a] Current Address: Department of Chemical and Biomolecular Engineering, The University of Illinois at Urbana-Champaign, 114 Roger Adams Laboratory, MC 712 600 South Mathews Avenue, Urbana, IL 61801 USA

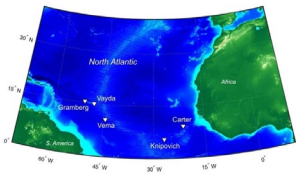
Tropomyosin-receptor kinase B (TrkB), one of the most widely distributed neurotrophic receptors in the central nervous system, is the key receptor for brain-derived neurotrophic factor (BDNF). BDNF signaling has a therapeutic prominence for the management of various neurodegenerative diseases including Alzheimer's and Parkinson's diseases. Due to its poor bioavailability, difficulties in crossing blood brain barriers, as well as side effects when consumed orally, BDNF is not considered a viable treatment option. While several phytochemicals show their neuroprotective effects by increasing the

expression of neurotrophins and their associated receptors, only a few compounds are able to mimic the effects of neurotrophins. In this study, we successfully developed a novel cell membrane encapsulated magnetic nanoclusters (CMMNs) containing functional TrkB receptors. The immobilized receptors were used to screen complex matrices, including plant extracts to identify novel TrkB agonists. Our research also attributes in the identification of potential TrkB agonists from Gotu kola, a commonly used herb in traditional Asian medicine for treating or managing different neurological diseases.

P-007 - Characterising and Bioprospecting the Atlantic Deep-Sea Sponge Microbiome

Sam E. Williams[1], Henry L Stennett[1], Catherine R Back[1], Jorge Ojeda Gomez[1], Katharine R Hendry[2], Christine L Willis[3], Paul R Race[1], Paul Curnow[1], [1]School of Biochemistry, University of Bristol, University Walk, Bristol BS8 1TD, UK, [2]School of Earth Sciences, University of Bristol, Queens Road, Bristol BS8 1RJ, UK, [3]School of Chemistry, University of Bristol, Cantock's Close, Bristol BS8 1TS, UK

Bioprospecting marine sponges has proved to be a productive source of novel bioactive metabolites, but this has been mainly limited to shallow waters. Here we present the establishment of the Bristol Sponge Microbiome Collection from 5 sites across the Atlantic. Characterisation of the microbiome has been conducted using 16S community analysis, providing in depth understanding of the microbial compositions of these unexplored communities. Culture based approaches and genome assembly has identified several novel species of gram positive and negative bacteria with antibiotic activity. To further maximise production of bioactive metabolites we've used ribosome engineering approaches to create talented producers.



P-008 - Genome Mining Guided Discovery of RiPP Biosynthetic Gene Cluster in *Streptococcus*

Keelie Butler[1], Jonathan R. Chekan[1], [1]University of North Carolina at Greensboro, Department of Chemistry and Biochemistry

Streptococcus species are often found as commensal bacteria within humans, but can also lead to illnesses. As an opportunistic pathogen, some *Streptococcus pneumoniae* strains can cause pneumococcal infections. Using genome mining strategies, a well conserved ribosomally synthesized and post-translationally modified peptide (RiPP) gene cluster was found within several commensals, pathogens, and common probiotic bacteria. In this study, we focused on *Streptococcus pneumoniae*, which is an important opportunistic pathogen in humans, as well as *Streptococcus uberis* which is a bovine pathogen. In this study, we aimed to express these gene clusters *in vitro*, identify and isolate the suspected product, and analyze the bioactivity of the product. Successful expression of the biosynthetic genes from *Streptococcus* species and LC-MS analysis revealed a putative new RiPP modification. These results have not only revealed a new enzymatic reaction but may give insight into the pathogenesis of clinically important *Streptococci*.

P-009 - Ethnobotany and the Role of Plant Natural Products in Antibiotic Drug Discovery

Gina Porras[1†], François Chassagne[1†], James T. Lyles[1†], Lewis Marquez[2], Micah Dettweiler[3], Akram M. Salam[2], Tharanga Samarakoon[4], Sarah Shabih[1], Darya Raschid Farrokhi[1], and Cassandra L. Quave[1,3,4], [1]Center for the Study of Human Health, Emory University. [2]Molecular and Systems Pharmacology Program, Emory University. [3]Department of Dermatology, Emory University School of Medicine. [4]Emory University Herbarium, Emory University, Atlanta, GA, USA. [†]Co-first authors.*

To date, the problem of drug-resistant bacterial infections has been gradually increasing, much faster than the development of new drugs, becoming a widespread problem in medical care. Therefore, it is imperative to develop new antimicrobial agents. Plant Natural Products (NPs) constitute a promising source of new and highly effective antibacterial agents that could help to counter increasing resistance and prevent the emergence of multidrug resistant bacteria. Historically, interest in plant NP's has been justified by their rich chemodiversity, worldwide distribution, accessibility, various antibacterial modes of action and effectiveness in clinical practice. In this work, the literature from 2012 to 2019 was systematically reviewed to highlight plant-derived compounds with antibacterial activity by focusing on their growth inhibitory activity. A total of 459 compounds are included in this review, of which 50.8% are phenolic derivatives, 26.6% are terpenoids, 5.7% are alkaloids, and

17% are classified as other metabolites. A selection of 183 compounds is further discussed regarding their antibacterial activity, biosynthesis, structure–activity relationship, mechanism of action, and potential as antibiotics. This review highlights the major findings on the antibacterial potential of plant NPs and their relevance in the development of next-generation antibiotic drugs.

P-010 - Evaluation of the heamostatic potentials of crude methanolic leaf extract of Persea americana in Wistar rats

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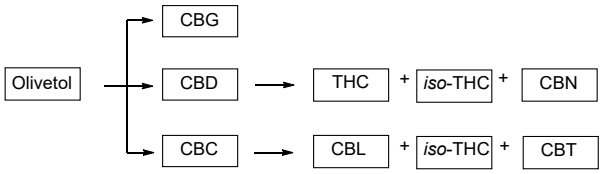
To date, there is limited information on the coagulative and possible haemostatic potentials of *Persea americana* extract. In light of this, the study was aimed to investigate the haemostatic potentials of crude methanolic leaf extract of *Persea americana* in Wistar rats using standard analytical methods. A total oftwenty-five adult male Wistar rats were arbitrarily distributed into five groups of five rats each and kept under suitable conditions for acclimatization and feeding. Group A was used as control and received feed and water only while various plant extracts (with concentrations 200, 400, 600 and 800 mg/kg) were orally administered on daily basis per body weight of animal in addition to normal feed and water for thirty days to the test groups B-E. After 4 weeks, the animals were sacrificed painlessly and blood samples were collected by retro-orbital plexus ofthe median canthus of the eyes. The prothrombin and activated partial thromboplastin times (PT and APTT), clotting and bleeding times (CT and BT) and plasma fibrinogen concentration were determined. Phytochemical screening of the leaf extract revealed substantial percentage of alkaloids, saponins, tannins, flavonoids, steroids and phenols. Results of the haemostatic potential showed a dose-dependent significant decrease ($P<0.05$) in the PT, APTT, CT, and BT and a slightly increase ($P<0.05$) in the plasma fibrinogen concentration when compared with the control. This study suggested that the leaf extract of *Persea Americana* had a stimulatory effect on intrinsic and extrinsic properties of the coagulation cascade.

P-011 - *One-step* synthesis of Cannabinoids from Resorcinol Derivatives as Starting Material

Gia-Nam Nguyen[1,2], Erin Jordan[1], Oliver Kayser[1]. [1]Technical Biochemistry Laboratory, Faculty of Biochemical and Chemical Engineering, Technical University Dortmund University, 44227, Dortmund, Germany. [2]MINDbioscience GmbH, Emil-Figge-Strasse 76a, 44227 Dortmund. *Corresponding Authors: Prof. Dr. Oliver Kayser. Technical Biochemistry Laboratory, Emil-Figge-Strasse 76a, 44227 Dortmund. Tel: +49 231 7557489.*

Efficient *one-step* synthesis of eight key cannabinoids was optimized and systematized. Main cannabinoids like Cannabigerol (CBG-C5) and Cannabidiol (CBD-C5) were prepared from olivetol via regioselective condensation. Further treatments of CBD-C5 led to Tetrahydrocannabinol (THC-C5), *iso*-THC-C5 and Cannabinol (CBN-C5). Alternatively, a *[3+3]* annulation between olivetol and citral yielded the minor cannabinoid Cannabichromene (CBC-C5), which was converted into two very rare polycycles Cannabicyclol (CBL-C5) and Cannabicitran (CBT-C5) in a *one-pot* reaction. Finally, all eight syntheses were extended by using resorcinol and two phenolic analogs, achieving a cannabinoid group with more than thirty compounds in a fast synthesis.

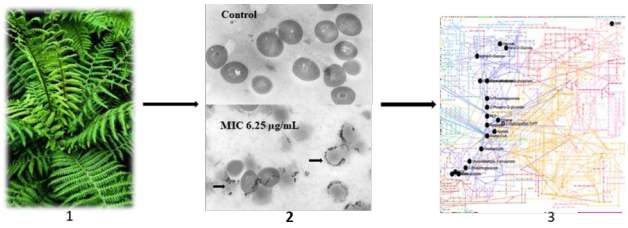


P-013 - Identifying Antimicrobial Phloroglucinol Derivatives from *Dryopteris crassirhizoma*

Sumana Bhowmick[1], Jianying Shen[2] and Luis A. J, Mur[1]. [1]Institute of Biological, Environmental andRural Studies, Aberystwyth University, Ceredigion, UK SY23 3DA, [2]Artemisinin Research Centre, Institute of Chinese Materia Medica, China Academy of Chinese MedicalSciences, Beijing, China

Our project aims on the isolation, purification of anti-Methicillin resistant *Staphylococcus aureus*.(MRSA) metabolites from *Dryopteris crassirhizoma* Nakai (1), a perennial herbaceous fern,. It is listed in Chinese Pharmacopoeia for treatment of viral diseases. Using chromatographic and identification methodologies, we performed assay-based isolation of fractions from *D. crassirhizoma*against MRSA. We have evaluated the anti

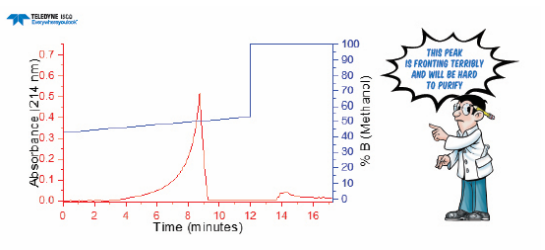
MRSA properties of the crude extracts and subsequent fractionation identified the active components (MIC 6.25 µg/mL(2)) using UHPLC-MS/MS. The potent active component was identified to be phloroglucinol derivatives. Metabolomic approaches were used to suggest the mode of action against MRSA in comparison to known antibiotics. Analysisof metabolite fingerprints suggested a novel mode of action that targeted the bioenergetic metabolism(3). The further study aims at validating mode of action studies using genomic analysis.

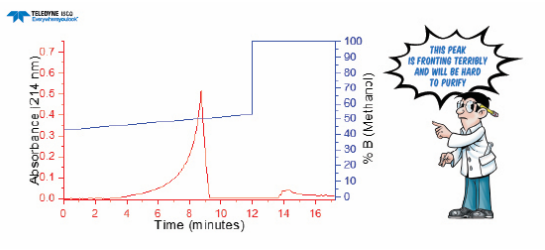


P-014 – Effects of Mobile Phase Solvents on Calculated Gradients

Jack Silver, Teledyne ISCO, 4700 Superior Street, Lincoln, NE 68504

This poster explores how the choice of elution solvents affects actual retention of compounds after the calculation of focused gradients. The use of calculated focused gradients saves time and solvent while maximizing resolution, thereby increasing loading capacity. Focused gradients are calculated from one or more scouting runs, which utilize a steep gradient encompassing the columns' applicable solvent range. There are instances in which the retention time differs from that expected from the calculation. Peaks eluting from focused gradients may also exhibit poor shape compared to the scouting run. The effects of pH, buffering, and solvent choice are explored as means to improve the chromatograms calculated for compounds. This poster will also describe compound features that can also lead to deviations from calculated gradient retention times. Calculated gradients in reverse phase chromatography are mainly affected by sample loading techniques and compound ionization as a function of pH. These effects apply to all types of gradient optimization techniques.





P-015 - Combining Genome Mining and Nitrogen NMR for Targeted Natural Product Discovery

Kalindi Morgan, University of British Columbia

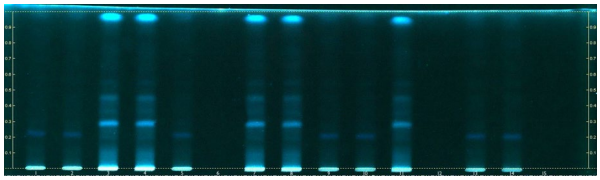
The discovery of novel natural products has widespread societal applications and is critical for developing new pharmaceuticals. Piperazic acid (Piz)-containing natural products were targeted through genome mining because this unique amino acid is often found in peptidic natural products with biological activity and impressive chemical structures. A method was sought to couple with genome mining that could guide the isolation of Piz-containing peptides produced in even the smallest of quantities. Piz was observed to display unique characteristics in nitrogen NMR spectroscopy. A nitrogen NMR-guided approach was thus developed to retrieve genetically predicted Piz-containing natural products from bacterial cultures. Very minor metabolites, with structural novelty and some with bioactivity, were obtained by applying this methodology. This approach employs chemical knowledge to access the information given by genomic sequences.

P-016 - Innovative Approaches to African Traditional Medicine in Analysis of Purity, Quality and Potency of New Phytopharmaceuticals

Jackson S. J[1]. 1. R&D Department, Modern Botany Ltd, Ardmanagh, Schull, Co. Cork, Ireland. P8IC564.

A proposed HPTLC technique of *Kigelia pinnata* fruit extract.

Commercial extracts of *Kigelia pinnata* HAB19F 30% EtOh was obtained from Company 1. and by commercial company 2. Using CAMAG HPTLC Automatic Sampler with HPTLC glass 20x10 cm, Si 60 F254 using solvent system of Ethanol, Chloroform and Ethyl Acetate, developed with 0.5% anisaldehyde reagent in methanol: acetic acid: sulphuric acid (85:10:5). For purposes of this experiment a known compound found in *Kigelia*, β-Bisobolol was used as a reference standard, the results shown in Plate 1. Indicatedifference in quality of extracts and purity from different commercial companies it also indicates that further chromatographic analysis needs to be undertaken to show better separation of active ingredients and identify a better reference compound. These results show that further modernisation work and HPTLC profiling needs to be undertaken before standardised commercial extracts and a standardised monograph can occur on extracts of *Kigelia pinnata.* Plate 1: HPTLC plate showing commercial extracts of 2 commercial extracts of *Kigelia pinnata* under 254nm Commercial extract No1 traces 3,4,7,8,11. Commercial extract No 2 traces 1,2,5,9,10,13,14. β-Bisobolol traces 6,12,15.

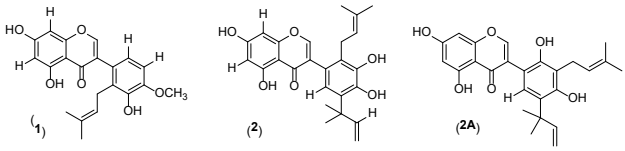


P-017 - Schottiin, a New Prenylated Isoflavone from *Psorothamnus schottii* and Antibacterial Synergism Studies between Methicillin and Fremontone against MRSA

Mallika Kumarihamy[1], Siddharth K. Tripathi[1], Shabana Khan[1,2], and Ilias Muhammad[1,1]National Center for Natural Products Research, [2]Department of Biomolecular Sciences, Researh Institute for Pharmaceutical Sciences, School of Pharmacy, The University of Mississippi, University, MS, 38677, USA.

Bioactivity guided isolation of an ethanol extract of the root of *Psoromanthus schottii* (Family Fabaceae) afforded a new prenylated isoflavone, named schottiin (1), together with four other isoflavones, including fremontone (2), 5,7,4′,5′-tetrahydroxy-2′-(3,3-dimethylallyl)-isoflavone (3), glycyrrhisoflavone (4) and fremontin (5), of which 3 and 4 identified as isomeric mixture. Structures of 1-5 were determined by full spectroscopic analyses. A comprehensive 2D NMR spectral data has allowed revising the structure of fremontone as 2 from previously reported 2A. Compound 2 showed weak *in-vitro* antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA). A combination study using a checkerboard assay between fremontone (2) and methicillin exhibited a synergistic activity with 8-fold decrease in MIC of methicillin, as well as an additive effect with vancomycin against MRSA ATCC 1708. Compounds 1 and 2 also showed moderate antiplasmodial activity against chloroquine-sensitive (D6) and -resistant (W2) strains of *Plasmodium falciparum* with no cytotoxicity to mammalian Vero cells.

Acknowledgement: This work is supported by USDA-ARS SCA # 58-6060-6-015.



P-019 - Diselaginellins Isolated from Roots of *Selaginella tamariscina* (Beauv.) Spring and Their Upregulating Activity on Low-Density Lipoprotein Receptor expression

Sunmin Woo[1,2], Hee-Sung Chae[1], Jinwoong Kim[1], Young-Won Chin[1, 1]College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 08826, Republic of Korea; [2]Center for the Study of Human Health, Emory University, Atlanta, GA 30033, USA

Plants within the genus *Selaginella* are widely distributed around the globe including more than 700 species. Hundreds of compounds including biflavonoids, selaginellins and terpenoids have been reported from *S. tamariscina*. Recently, several selaginellin-related compounds have been isolated and reported from *Selaginella* species. Despite their characteristic structures, the more diverse bioactivities of natural selaginellin derivatives have not been evaluated. Here the chemical diversity of naturally occurring selaginellin derivatives and their potential bioactivities were further explored. We report herein the phytochemical studies of roots of 90% ethanol extract of *S. tamariscina.* The EtOAc was fractionated to yield eight compounds: two new dimeric selaginellins, diselaginellins C and D (1 and 2), a new unusual derivative, selapiginellin A (4), a new selaginpulvilin U (5), and a known derivative, diselaginellin A (3). Among these compounds,

selapiginellin A (4) is the first naturally occurring compound comprising an ether-linked dimer of a selaginellin and a selaginpulvilin. Compound 5 was found to regulate mRNA expression of the low-density lipoprotein receptor (LDLR) gene and LDLR-related genes.

P-021 - Understanding Aurodox: A Type III Secretion System Inhibitor from Streptomyces goldiniensis

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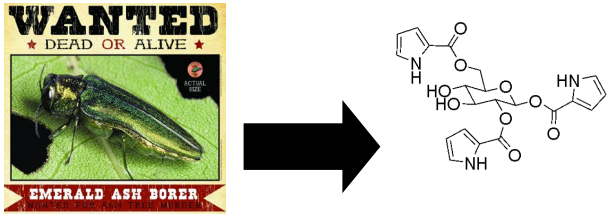
Aurodox, a specialised metabolite from the soil bacterium *Streptomyces goldiniensis* was discovered in 1972 and originally was investigated for its anti-staphylococcal and streptococcal properties. However, aurodox has been recently identified from large-scale compound screens as an inhibitor of the Enteropathogenic Escherichia coli (EPEC) Type III Secretion System (T3SS). Therefore to gain an understanding of its mechanism of action and to assess the suitability of this molecule for repurposing as an anti-virulence compound multidisciplinary approach to understanding aurodox was used. Whole transcriptome analysis, cell infection and GFP-reporter assays were used to demonstrate that Aurodox transcriptionally downregulates the expression of the Locus of Enterocyte Effacement (LEE) pathogenicity island- which encodes for the T3SS, acting via its master regulator, Ler. We have also observed these effects across other enteric pathogens carrying a homologous T3SS such as Enterohemorrhagic Escherichia coli (EHEC). Significantly, unlike traditional antibiotics, aurodox does not induce the production of shiga toxin. The biosynthesis of aurodox by *S. goldiniensis* was also investigated. Sequencing the whole genome of *S. goldiniensis* enabled the identification of the putative aurodox biosynthetic gene cluster (BGC). We have cloned and expressed this gene cluster in multiple heterologous hosts including Streptomyces coelicolor M1152 and can confirm this BGC is responsible for aurodox production. In-depth analysis of the BGC supports a model of a polyketide synthase pathway involving a combination of both cis and trans-Acyltransferases which synthesise the aurodox polyketide backbone. Furthermore, multiple aurodox resistance genes at distinct loci have been identified and their role in aurodox resistance has been explored.

P-022 - Defensive Chemistry of the Emerald Ash Borer (*Agrilus planipennis*)

Sarah M. Dauphin, Mackenzie J. Perpetua, Natalie C. Stagnitti, Stephen T. Deyrup. Department ofChemistry and Biochemistry, Siena College, Loudonville, NY 12211, USA.

The Emerald Ash Borer (EAB), *Agrilius planipennis*, is an invasive ecological pest in North America. Related jewel beetles are notable for their usage in traditional Chinese medicine for treatment of pruritus and as an insecticide. Although predators readily consume larval EAB, predation of adult EAB is rare. This, along with the aforementioned insecticidal uses of EAB relatives suggests that they are chemically protected. Chemical characterization using 1D and 2D NMR as well as UHPLC-HRMS has identified evidence of six buprestins present in EAB. Buprestins are acyl glucoside compounds which are known to be repellant to ants and mammals. This work provides evidence for the chemical protection EAB, which may play a role in allowing them to thrive as ecological pests outside their nativerange.



P-023 - Smooth Muscle Relaxant Effect of *Grewia asiatica* Extract is Mediated via Multiple Pathways

Muhammad Nabeel Ghayur[1,2], Saeed Ahmad[2], and Anwarul Hassan Gilani[2,3]. [1]University of Pikeville, Pikeville, KY, USA, [2]Aga Khan University, Karachi, Sind, Pakistan, [3]University of Haripur, Haripur, Khyber Pakhtunkhwa, Pakistan

Grewia asiatica is a commonly used edible fruit in South Asia. The fruit is employed in traditional medicine practice as a smooth muscle relaxant in different gastrointestinal and cardiovascular diseases. In this study we report its antispasmodic and vasodilator activities. Fruits were soaked in 70% aqueous-methanol and filtrate was dried to give the extract (Ga.Cr). Different isolated tissue segments were suspended in tissue baths. Ga.Cr dose-dependently (0.1-5 mg/ml) relaxed the spontaneously contracting rabbit jejunum. The extract only partially inhibited high K^+ (80 mM) induced

contractions in jejunum and ileum while completely suppressed (0.3-10 mg/ml) low K^+ (25 mM) induced contractions indicting a mechanism of action via opening K^+ channel (KCO) rather than blockade of Ca^{2+} channels (CCB). This suppressor effect was blocked in presence of glibenclamide, a K^+ channel blocker. Chromakalim, a standard KCO, also suppressed the low K^+-induced contractions at lower concentrations (this suppressor effect was blocked by glibenclamide similar to Ga.Cr). Verapamil, a CCB, was able to suppress K^+ 80 mM and 25 mM at similar concentrations. In endothelium-intact rat aorta, Ga.Cr inhibited phenylephrine (1 μM)-induced contractions (1-5 mg/ml). This relaxant effect was shifted to the right in presence of L-NAME, a nitric oxide (NO) synthase inhibitor, indicating effect mediated via release of NO from endothelium. These results indicate that the extract has antispasmodic and vasodilator activities mediated via opening of K^+ channels in the gut and release of NO from the vascular endothelium.

P-024 - Marine Algae Natural Products as Antiviral Agents for SARS-CoV-2

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Currently, there are no effective treatments for pre-exposure prophylaxis or active infection of SARS- CoV-2. As of May 2021, only 4.7% of the world's population is fully vaccinated while approximately 165 million cases of COVID-19 have produced nearly 3.5 million deaths worldwide. The discovery anddevelopment of small-molecule antiviral countermeasures has generally been challenged by the fast- evolving nature of viruses and the need to develop drugs or drug regimens that target multiple virus- dependent processes. Several recent reports have provided structural insights to key regulatory proteinsin SARS-CoV-2 and their susceptibility to be inhibited by compounds like those produced by marine algae. We hypothesize that redirecting a natural product and drug discovery effort to probe the chemical components of marine algae and other marine organisms unique to Puerto Rico's natural resources will reveal antiviral leads for COVID-19. Our research design encompasses a hypothesis-based expansion of a pre-existing marine natural product library and high throughput screening of this library for retroviralactivity against SARS-CoV-2 molecular targets. We present our initial results that show promising activity of several algae extracts to selectively inhibit the main protease (Mpro) of SARS-CoV-2 as wellas to disruptACE-2/Spike Protein interaction in vitro.

P-025 - Genomic and Metabolomic-Based Exploration of Biosynthetic Diversity in *Aspergillus nidulans*

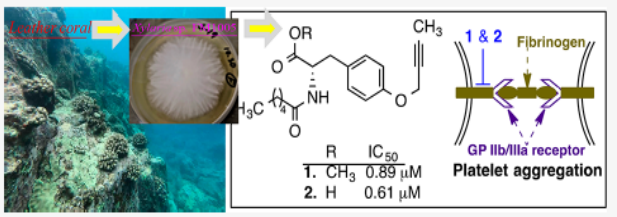
Lindsay K. Caesar[1], Milton T. Drott[2], Fatma A. Butun[3], Rafael W. Bastos,[4] Gustavo H. Goldman,[4] Neil L. Kelleher[1,3,5], Nancy P. Keller[2,6] , [1]Department of Chemistry, Northwestern University (NU) [2]Department of Medical Microbiology and Immunology, University of Wisconsin-Madison (UW), [3]Proteomics Center of Excellence, NU, [4]Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, [5]Department of Molecular Biosciences, NU, [6]Department of Bacteriology, UW.

In 1990, the first fungal natural product gene cluster was cloned in the model organism *Aspergillus nidulans*. Now, more than three decades later, over 30 biosynthetic gene clusters (BGCs) from *A. nidulans* have been linked to their encoded natural products. Nearly all of these discoveries were made using the *A. nidulans* A4 strain. However, recent studies have illustrated the remarkable biosynthetic diversity not only between fungal species, but also within them. Indeed, comparison of three *A. nidulans* strains has revealed not only chemical differences between the strains (which could result from differential expression of shared gene clusters), but also differences in BGC content. To explore this, we compared BGC content and metabolomics profiles of 20 *A. nidulans* isolates, revealing distinct BGCs that are not present in the A4 reference strain, as well as unknown metabolites that are only expressed in a subset of strains. Current work is underway to elucidate the structures and biosynthetic machinery of these unknown metabolites. In addition to facilitating discovery of novel metabolites and BGCs, this project highlights differences in BGC content and expression in different strains of the same organism.

P-026 - Secondary Metabolites from the Leather Coral-Derived Fungal Strain *Xylaria* sp. FM1005 and Their Glycoprotein IIb/IIIa Inhibitory Activity

KH Ahammad Uz Zaman[1], Jae Hyeon Park[2], Lela DeVine[1], Zhenquan Hu[3], Xiaohua Wu[1], Hyung Sik Kim[2], and Shugeng Cao[1]. [1] Department of Pharmaceutical Sciences, Daniel K. Inouye College of Pharmacy, University of Hawai'i at Hilo, Hawaii 96720, USA, [2] School of Pharmacy, Sungkyunkwan University, Gyeonggi-do 16419, Republic of Korea. [3] Warshel Institute for Computational Biology, The Chinese University of Hong Kong, Shenzhen 518172, People's Republic of China.

Five new tyrosine derivatives, one new phenylacetic acid derivative, two new quinazolinone analogues, one new naphthalenedicarboxylic acid, and one new 3,4-dihydroisocoumarin derivative, together with seven known compounds, were isolated from the fungus *Xylaria* sp. FM1005, which was isolated from *Sinularia densa* (leather coral) collected in the offshore region of the Big Island, Hawaii. The structures of compounds were elucidated by extensive analysis of NMR spectroscopy, HRESIMS, and ECD data. Due to their structure similarity to the antiplatelet drug tirofiban, tyrosin derivatives were investigated for their antithrombotic activities.

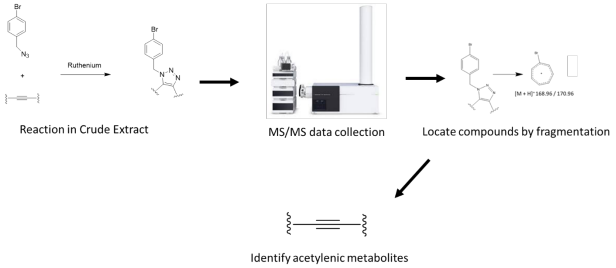


Compounds 1 and 2 strongly inhibited the binding of fibrinogen to purified integrin IIIb/IIa in a dose-dependent manner with the IC_{50} values of 0.89 and 0.61 μM, respectively.

P-027 - Ruthenium Mediated Click Chemistry for the Detection of Acetylenic Natural Products

Daniel Back, Benjamin Philmus, Department of Pharmaceutical Science, Oregon State University, Corvallis, OR

Copper mediated azide-alkyne cycloadditions (CuAAC) has played a vital role in the discovery and structure elucidation of acetylenic natural products, however it is limited to compounds possessing a terminal alkyne functional group. Ruthenium mediated azide-alkyne cycloadditions (RuAAC) have become increasingly popular for its ability to mediate the cycloaddition of azides with compounds possessing both terminal and internal alkyne moieties. Utilizing RuAAC, an LC-MS/MS method has been developed to aid in the *de novo* identification of natural products harboring carbon-carbon triple



bonds in crude extracts. This method has proved successful in identifying both known and new natural products containing both terminal and internal alkyne functionalities.

P-028 - MOAST: Mechanism of Action Similarity Tool, Automating Mechanism of Action Hypotheses

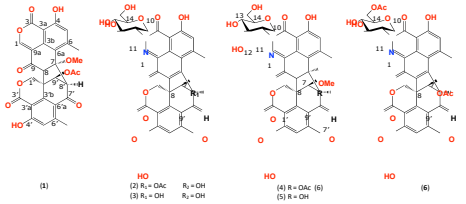
Akshar Lohith[1,2], John B. MacMillan, R. Scott Lokey[1]. [1]Department of Chemistry and Biochemistry, University of California, Santa Cruz, Santa Cruz, CA 95064, [2]Department of Biomolecular Engineering, University of California, Santa Cruz, Santa Cruz, CA 95064

In the field of phenotypic screening, 'guilt-by-association' analyses are used to hypothesize mechanism of action by linking the similarity in the phenotypic response of known treatments with unknown treatments. In order to achieve this, it is standard to have a large cohort or library of compound treatments to represent a number of phenotypes and leverage sophisticated models and mining techniques to extract subtle features and process them into relationships among the various treatments to discern and hypothesize mechanism of action. Here I present the construction of an automated method to take the pairwise similarities of an unknown treatment phenotypic profile to aset of annotated treatments and query a database in order to hypothesize the mechanism of action ofthe unknown treatment.

P-029 - Glyclauxins A-E: *N*-deoxyglycosides from an Australian Mud Dauber Wasp Nest Fungus

Kaumadi Samarasekera, Angela Salim and Rob Capon. Institute for Molecular Bioscience, TheUniversity of Queensland, St Lucia, Queensland 4072, Australia.

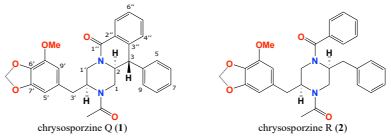
Molecular networking guided analysis of multiple fungal isolates from an Australian mud-dauber wasp nest drew our attention to *Talaromyces* sp. CMB-MW102, which was the only isolate to producenew examples of a rare class of metabolites of the duclauxin (1) class. These included five new *N*- glycosides, glyclauxins A–E (2–6), whose structures were assigned by detailed spectroscopic analysis and biosynthetic considerations. Of particular note, the glyclauxins incorporate a rare 1-deoxy-D- glucosamine moiety, that has only been prior reported in the natural products literature once. While glyclauxins C–D (4–5) are sensitive to mild heating (40 °C), undergoing a loss of MeOH to yield glyclauxins A–B (2–3), on exposure to MeOH 2–3 do not undergo a Michael addition to yield 4–5. All of 1–5 were detected in fresh culture extracts are designated as natural products.



P-030 - Chrysosporazines from Australian Marine Fish Gut-Derived Fungus, *Aspergillus* sp. CMB-F661

Amila Agampodi Dewa, Zeinab G. Khalil, Robert J. Capon. Division of Chemistry and Structural Biology, Institute for Molecular Bioscience, The University of Queensland, St Lucia 4072, Australia

During our investigations into secondary metabolites from Australian *Mugil* mullet gastrointestinal-derived fungi we reported on a rare class of phenylpropanoid piperazines, chrysosporazine A–M, produced by two *Chrysosporium* sp. CMB-F214 and CMB-F294. Our ongoing interest in thechrysosporazines was prompted as they were non-cytotoxic to mammalian cells, but selectedexamples were exceptionally potent inhibitors of the multidrug resistance efflux pump P-glycoprotein(P-gp). As a result, we set out to detect other members of this rare class of natural product from otherfish gut fungi. Remarkably, chemical analysis of the *Aspergillus* sp. CMB-F661 yielded two new exemplars of this structure class, chrysosporazines Q–R. These new examples will be used in structural activity relationship studies to better define the P-gp inhibitory pharmacophore.



P-031 - Multi-informational Molecular Networks to Identify New Microbial Natural Products

Viviene Santiago, Zeinab G. Khalil, Robert J. Capon, Institute for Molecular Bioscience, University of Queensland, St Lucia, QLD, Australia

The current challenge in the field of microbial natural products lies in developing strategies to prevent the rediscovery of known chemistry while at the same time identifying new biologically relevant molecules. While larger collections can increase the probability to identify new bioactive scaffolds, it also increases the time and effort needed to analyze all existing data for effective prioritization.

In this study, we propose the use of multi-informational molecular networks paired with in silico annotation tools to streamline the prioritization of strains containing selectively antimicrobial scaffolds and/or compounds within the chemical diversity of extract collections. A total of 345 microbes isolated from soils collected as part of the Soils for Science (https://soilsforscience.org.au) citizen science project was used to generate molecular networks using the Global Natural Product Molecular Networking (GNPS) platform. Antimicrobial data against a panel of pathogenic microbes, cytotoxicity data against human colon and lung carcinoma cells, and morphological analysis, were integrated and used to prioritize 18 isolates, with four progressing to detailed chemical analysis.

P-032 - Improved Accramycin Production by Deletion of Multiple Antibiotic Resistance Regulator in *Streptomyces* sp. MA37

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The genus *Streptomyces* represents one of the largest producers of diverse molecules with antibiotic activity. Continued search for potentially antibiotic-producing *Streptomyces* in our laboratory led to the isolation of a talent soil bacterium, *Streptomyces* sp. MA37, a prolific producer of pyrrolizidines, carbazoles, fluorinated metabolites, siderophores, and polyketides. From this strain, we isolated an antibacterial aromatic polyketide, accramycin A in trace amounts. Herein, we show that deletion of a single regulatory gene (*accJ*) in the accramycin biosynthetic gene cluster encoding for multiple antibiotic resistance regulator (MarR), resulted in improved production titre of accramycin A by 330-fold as well as production of ten more accramycin analogues, B-K not previously identified in the wild type strain. Furthermore, Type III polyketide metabolites were also isolated and characterized from the mutant extract. All accramycin metabolites showed remarkable activity against Gram-positive bacteria and clinical isolates of *Enterococcus* and *Staphylococcus* strains (MIC = 3.1–25 μg mL^{-1}). Our results highlight the importance of identifying the roles of regulatory genes in natural product discovery.

P-033 - Isolation and Structure Elucidation of Novel Triterpene Saponins from *Wisteria Sinensis* Roots.

Samir Hobloss[1], Tomofumi Miyamoto[2], Marie-Aleth Lacaille-Dubois[1], Anne-Claire Mitaine-Offer[1] [1]PEPITE EA 4267, Laboratoire de Pharmacognosie, UFR des Sciences de Santé, Université de Bourgogne Franche-Comté BP 87900, 21079 Dijon cedex, France, [2]Graduate school of pharmaceutical Sciences, Kyushu University, Fukuoka 812-8582, Japan

Wisteria sinensis (Sims) Sweet (Fabaceae), commonly known as the Chinese Wisteria, is an ornamental woody vine, distributed all over China. Its flowers and leaves are used by Orientals as food or tea substitute for treating gastric and breast cancer or rheumatoid arthritis patients[1]. Previousphytochemical studies have shown that *Wisteria* species are a rich source of triterpene saponins, as are *W. frutescens*[2] and *W. floribunda*[2]. Chromatographic separation of an aqueous EtOH extract of *W.sinensis* roots yielded three triterpene saponins. Their structures were elucidated by an extensive 600MHz NMR analysis including 1D and 2D NMR (^{1}H, ^{13}C, COSY, TOCSY, ROESY, HSQC, HMBC) experiments as well as ESI-MS analyses. All three compounds are oleanane-type saponins with glucuronic acid linked at the C-3 position. Two of them have never been reported before. One consistsof a soyasapogenol H aglycone (subprogenin A), whereas the other shows a novel genin. Mohamed, MA.; Hamed, MM.; Abdou, AM.; Wafaa, S.; Saad, AM. Antioxidant and cytotoxic constituents from *Wisteria sinensis*. *Molecules*, **2011**, *16*, 4020-4030. Champy, AS.; Mitaine-Offer, AC.; Paululat, T.; Papini, AM. And Lacaille-Dubois, MA.Triterpene saponins from *Wisteria floribunda. Natural Product Communications*, **2019**, *12* (10).

P-034 - Aurodox: Repurposing Old Drugs for Bad Bugs

Braes, R. E.[1], McHugh, R. E.[1], Hoskisson, P. A.[1] & Roe, A. J.[2] [1]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom. [2]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom.

Aurodox is an Elfamycin antibiotic produced by *Streptomyces goldiniensis* that exhibits antibiotic activity against Gram-positive bacteria, through inhibition of translation via elongation factor EF-Tu.Recently, a novel mode of action was discovered for aurodox, where it inhibits the Type III SecretionSystems of Enteropathogenic and Enterohemorrhagic *Escherichia coli*. To understand this novel mode of action, we sequenced the genome of *S. goldiniensis* and identified the putative biosyntheticgene cluster (BGC) responsible for the production of aurodox. We cloned and heterologously expressed this putative BGC in *Streptomyces coelicolor* M1152, confirming it was responsible for the production of aurodox. BGC analysis revealed a multimodular polyketide synthase pathway similar to the closely related kirromycin BGC. We hypothesised that the final step of biosynthesis was the conversion of kirromycin, to aurodox via a SAM-dependent *O*-methyltransferase on the pyridone moeity, catalysed by the BGC encoded AurM*. Cloning and expression of AurM* in the kirromycin producer, *S. collinus*, resulted in the production of aurodox. The aurodox BGC containsa Major-Facilitator Superfamily protein (AurT), thought to confer self-resistance, through

efflux of aurodox. Expression of the aurodox BGC in *S. coelicolor* M1152, indicated that *aurT* alone was insufficient for resistance. An additional Elfamycin-resistant copy of EF-Tu (*tuf2*) was identified in the genome of *S. goldiniensis*. Cloning of *tuf2* and expression in *S. coelicolor* M1152, with the aurodox BGC indicated that both *tuf2* and *aurT* are required for aurodox self-resistance.

P-035 - Chemical Diversity of Antimicrobial Metabolites Produced by Marine Eukaryotic Microalgae

Alison H. Hughes, Katherine R. Duncan.

Eukaryotic microalgae remain an untapped source of bioactive metabolites. Specialised metabolites are often produced in response to environmental triggers and thus the One Strain Many Compounds (OSMAC) approach is often used in the laboratory to elicit the production of these metabolites which can be utilised for human health and biotechnology. An example of this is the industrial production of β-carotene from *Dunaliella salina* which requires high salinity (up to 5 M NaCl) for maximum yield. This study investigates the response of three phylogenetically diverse marine microalgae from British waters (*Dunaliella primolecta* CCAP 11/34, *Phaeodactylum tricornutum* CCAP 1055/15, and *Nannochloropsis oculata* CCAP 849/1) to varying abiotic stress including salinity (Aquil synthetic seawater), sodium chloride concentration, sodium nitrate concentration, and pH. The use of Global Natural Products Social (GNPS) feature based molecular networking, coupled with antimicrobial bioassay screening against human pathogenic bacteria and fungi, afforded classification and prioritisation of bioactive metabolites produced in response to specific stress conditions. In the case of *Nannochloropsis oculata* CCAP 849/1, 208 metabolites were only produced under low salinity (4.3 ppt Aquil synthetic seawater) condition compared to 70 produced under low (0-12 g/L) sodium chloride concentration. Small organic metabolites produced by marine microalgae remain underexplored and this study not only provides insight into the chemical space of these microalgal strains but also their potential as pharmaceuticals.

P-036 - Daphnane-type Diterpenoids are Both Selective Inhibitors of the Basal-like 2 Subtype of Triple-Negative Breast Cancer and Activators of Innate Immunity.

Charles S. Fermaintt[1,2], Thilini Peramuna[3,4], Shengxin Cai[3,4], Leila Takahashi-Ruiz[1], Jacob N. Essif[1],Corena V. Grant[1], Barry R. O'Keefe[5,6], Robert H. Cichewicz[3,4], Susan L. Mooberry[1,2], and April L. Risinger[1,2], [1]Department of Pharmacology and [2]Mays Cancer Center, University of Texas Health Science Center atSan Antonio, San Antonio, TX, USA, [3]Department of Chemistry and Biochemistry and [4]Natural Products Discovery Group, University of Oklahoma, Norman, OK, USA, [5]Natural Products Branch, Division of Cancer Treatment and Diagnosis, and [6]Molecular Targets Laboratory, Center for Cancer Research, National Cancer Institute, Frederick, MD, USA.

Triple-negative breast cancer (TNBC) is devoid of targeted therapy treatment due to the absence of estrogen, progesterone, and HER2 receptors. While efforts are currently being undertaken to uncover molecular liabilities that could serve as pharmacological targets, on the clinical front immunotherapy has emerged as a promising therapeutic alternative for the treatment of TNBC. However, many metastatic TNBC patients remain unresponsive to this treatment regimen, suggesting that new approaches are needed. To this end, we introduced a new immunogenicity screening strategy to our ongoing search of TNBC subtype-selective natural product extracts that can also promote the differentiation of THP-1 human monocytes into macrophages as an immune activation readout. We identified several daphnane-type diterpenoids including yuahuacine that caused THP-1 differentiation, upregulated expression of antitumor cytokines in immune cells, and displayed potent and selective cytotoxicity towards cell lines belonging to the basal-like 2 (BL2) subtype of TNBC both in vitro and in vivo. Structure-activity relationships studies among these compounds revealed that the C6-7 epoxide contributes toward the potency of these compounds for both activities. Moreover, we determined that both activities were mediated by protein kinase C. In summary, we have implemented a multipronged screening strategy that has led to the identification of compounds that possess both selective in vitro and in vivo cytotoxicity against the BL2 subtype of TNBC and the ability to induce antitumor immunogenic signaling.

P-037 - Cytotoxicity of Essential Oils from Six *Baccharis* subgenus *Coridifoliae* Species

Valter P. Almeida[1], Sara E. L. Tolouei[2], Shabana I. Khan[3], Gustavo Heiden[4], Ikhlas A. Khan[3] and Jane Manfron[1]. [1]Pharmaceutical Science Graduate Program, State University of Ponta Grossa, Brazil, [2]Department of Pharmacology, Federal University of Paraná, Brazil, [3]National Center for Natural Products Research, University of Mississippi, USA, [4]Embrapa Clima Temperado, Pelotas, Brazil.

Table 1. Half-maximal inhibitory concentration (IC_{50}) of essential oils from six types of *Baccharis* against cancer and normal cell lines.

Samples	SK-MEL IC_{50} µg/mL	KB IC_{50} µg/mL	BT-549 IC_{50} µg/mL	SK-OV-3 IC_{50} µg/mL	LLC-PK1 IC_{50} µg/mL	Vero IC_{50} µg/mL
B. albilanosa	70	80	63	61	43	70
B. coridifolia	52	62	47	39	37	60
B. erigeroides	NC	NC	NC	NC	78	NC
B. napaea	50	57	50	43	40	60
B. ochracea	43	90	51	47	73	70
B. pluricapitulata	81	71	75	70	42	70

[1]Budel, J.M. *et al*. Essential oils of five *Baccharis* species: investigations on the chemical composition and biological activities. *Molecules* 23, 2620. Doi: 10.3390/ molecules23102620.

P-039 - NPOmix: A Machine Learning Approach to Systematically Connect Natural Products to their Biosynthetic Gene Clusters

Tiago F. Leao[1], Mingxun Wang[1,2], Ricardo da Silva[3], Justin J.J. van der Hooft[4], Anelize Bauermeister[1], Alexey Gurevich[5], Asker Brejnrod[1], Evgenia Glukhov[6], Robert Rex[6], Lena Gerwick[6], William H. Gerwick[1,6], Nuno Bandeira[1,2,], Pieter C. Dorrestein[1,7,]*.1 – Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, California, USA. 2 – Center for Computational Mass Spectrometry, University of California San Diego, La Jolla, California, USA. 3 – NPPNS, Physic and Chemistry Department, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil. 4 – Bioinformatics Group, Wageningen University, Wageningen, the Netherlands. 5 – Center for Algorithmic Biotechnology, St. Petersburg State University, St. Petersburg 199004, Russia. 6 – Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, California, USA. 7 – Center for Microbiome Innovation, University of California San Diego, La Jolla, California, USA. * Corresponding authors.*

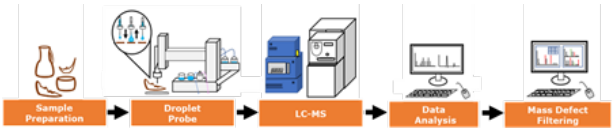
Microbial natural products, in particular secondary or specialized metabolites, are an important source and inspiration for many pharmaceutical and biotechnological products. The traditional bioactivity-guided methods widely employed in natural product discovery programs do not explore the full biosynthetic potential of the microorganisms and they usually oversee metabolites expressed at low concentrations. The use of genome mining in natural product research has facilitated the discovery of novel natural products with potentially new bioactivities. Additionally, rediscovery rates continue to be high, and the use of multi-omics approaches would help to make smarter prioritizations toward novel chemistry and their producers. However, most existing genome mining solutions to connect biosynthetic genes with metabolites tend to be low-throughput or selective to a specific type of biosynthetic genes (for example, ribosomal or non-ribosomal peptides). Here, we provide an unprecedented machine learning approach for systematically connecting metabolite spectra to the biosynthetic genes that encode their production. This fast and reproducible pipeline offers a good solution for annotating the biosynthetic genes for known, analogous to known and cryptic metabolites observed via mass spectrometry. We demonstrate our approach by the automated connection of five different metabolites and analogs to their corresponding biosynthetic genes in a dataset of 1,006 microbial genomes and experimental MS/MS spectra containing 5,421 biosynthetic gene clusters and 18 known reference MS/MS spectra (from the GNPS library). Our approach accepts bacterial, fungal, algal and plant paired genomes and MS/MS spectra.

P-040 - Droplet Probe: A Non-Destructive Chemical Residue Analysis of Wari Ceramics

Kristof B. Cank[1], Joshua M. Henkin[2], Anita G. Cook[3], Nicholas H. Oberlies[1]. [1]Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, Greensboro, NC, 27407, USA, [2]Department of Science and Education, Field Museum of Natural History, Chicago, IL, 60605, USA, [3]The Catholic University of America, Washington, DC, 20064, USA

Analyzing ceramics from ancient cultures can be challenging to researchers due to these materials being degraded or damaged over thousands of years of weathering. Most analytical techniques currently in use for residue analysis cause at least some amount of destruction of the artifacts during their preparation or sampling phase. We present here a test case of using a non-destructive LC-MS technique, termed the droplet-liquid microjunction-surface sampling probe (i.e., droplet probe), for studying the chemistry of ancient Andean ceramics. Three secondary metabolites, aurantiamide acetate, aurantiamide benzoate, and aurantiamide, were

identified on the surface of a vessel and a spoon sherd from the central highlands of Peru. The findings of these compounds could provide insight on the potential use of such items in the ancient Wari Empire.



P-041 - Verticillins: A Streamlined Approach to Purification

Herma C. Pierre[1], Huzefa A. Raja[1], Tyler N. Graf[1], Cedric J. Pierce[2], Nicholas H. Oberlies[1]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, 27412, [2]Mycosynthetix, Inc. Hillsborough, NC, 27278.

Verticillin A is a pharmacologically active dimeric epipolythiodioxopiperazine (ETP) alkaloid that exhibits potent *in vitro* cytotoxicity against ovarian cancer cell lines in cultures. Three separate *in vivo* studies of verticillin A, one of which was on a murine model of ovarian cancer, have also demonstrated significant activity of this compound. While there is an increased interest in further studying the activity and mode of action of verticillin A, the supply remains low (mg scale). This is due to (1) sample processing methods that need optimizations for verticillin-class compounds and to (2) low production (mg scale) of this compound in *Clonostachys rogersoniana* (strain MSX59553). Thus, the goal of the present study was to mitigate the first cause of low verticillin A yields (*i.e.* sample processing method) by optimizing current extraction and isolation protocols. Incorporating clean-up steps and optimizing flash and preparative chromatography conditions resulted in a smoother, simpler workflow that was greener (~75% decrease in solvent usage) and faster (15 days *vs* 45 days) than the current protocols with reproducible baseline resolutions of verticillin-class compounds at the final purification step (preparative HPLC). Results are discussed.

P-042 - Using Molecular Networking to Dereplicate Complex Biotransformations from a Surfactant Chemical Elicitor study with Marine *Streptomyces*

Zacharie Maw[1], Bradley Haltli[1,2], and Russell Kerr[1,2,3]. [1]Department of Biomedical Science, University of Prince Edward Island, Charlottetown, PEI, Canada, [2]Nautilus Biosciences CRODA, Charlottetown, PEI Canada, [3]Department of Chemistry, University of Prince Edward Island, Charlottetown, PEI, Canada.

Streptomyces have proved an unmatchable resource for bioactive natural products. As such, novel *Streptomyces* isolated from the under-explored marine ecosystems present great potential for new natural product discovery. Many natural products are deemed silent or cryptic, requiring environmental cues or stimuli not present under standard cultivation conditions. Through a combination of untargeted metabolomics strategies and the addition of chemical elicitor stressors, we can explore a broad group of strains for the production of silent natural products. Surfactants have the potential to induce silent natural products because they are regularly produced by many types of microorganisms, therefor *Streptomyces* would frequently interact with these molecules in nature. Molecular networking is being employed to help mitigate the discovery of simple biotransformations and degradation products from the added elicitors. The molecular networks also create basic structural groups of all molecules found in each extract, useful for putative identifications. This research provides insight into the effectiveness of using molecular networking to identify new silent natural products produced from exposure to surfactants.

P-043 - New Experimental Design to Identify Bioactive Peptides of Spirulina and Evaluate their Bioavailability

Giuliana Donadio[1], Valentina Santoro[1], Fabrizio Dal Piaz[2] and Nunziatina De Tommasi[1], [1]Department of Pharmacy, University of Salerno, 84084 Fisciano, Italy; gdonadio@unisa.it, [2]Department of Medicine and Surgery, University of Salerno, 84082 Baronissi, Italy

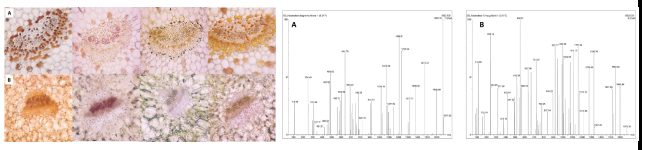
Spirulina platensis is a cyanobacteria used as food for centuries. Several studies demonstrated the primary role played by the proteins and peptides from this microalga that, after being released by digestive processes, exert different health benefit.

Immunomodulation, angiotensin converting enzyme inhibitors, anti-oxidative effects are just some examples of the different biological activities displayed by peptides from *Spirulina.* Few studies have been conducted to evaluate the real bioavailability of the bioactive molecules from spirulina. The purpose of this research was to evaluate the level of peptide production in the gastrointestinal digestion process of foods functionalized with *Spirulina* and to compare it with that observed for pure microalga, in order to verify the effectiveness of these products as a source of bioactive peptides. Therefore, a protocol was developed and optimized to simulate the enzymatic degradation that occurs in the gastrointestinal tract and the simulated digestion products were quantized through a mass spectrometry based analytical method.

P-044 – Chemical Differentiation of Two Species Known as "Mother of Thousands"

Evelyn A. Andrade[1], Isadora Machinski[2], Ana Carolina T. Ventura[2], Valter P. Almeida[1], Jane Manfron[1], and Flávio L. Beltrame[1]. [1]Pharmaceutical Science Graduate Program. State University of Ponta Grossa, PR, Brazil, [2]Department of Pharmaceutical Science, State University of Ponta Grossa, PR, Brazil.

Kalanchoe daigremontiana and *Kalanchoe* x *houghtonii* are commonly called "mother of thousands" and have similar morphologies. In folk medicine, *K. daigremontiana* leaves are used as anti-inflammatory and antiseptic, as well as in the treatment of cardiovascular dysfunction, diabetes, and cancer[1]; on the other hand, there is no information about the popular uses of *K.* x *houghtonii.* Trying to identify and differentiate the species, the present study was carried out; histochemical and LC-MS analysis contributed to distinguish the composition of these species, as shown in Figure 1. **Figure 1** – Histochemical and chromatography analysis of *K. daigremontiana* (A) and *K.* x *houghtonii* (B).



[1]Zawirska-Wojtasiak, R. et al. Vitamin C and aroma composition of fresh leaves from K. pinnata and K. daigremontiana. Sci. Rep. 9, 19786 (2019). Doi: 10.1038/s41598-019-56359-1.

P-045 – New Cyclic Octapeptides from a Fungicolous Isolate of *Sphaerostilbella broomeana*

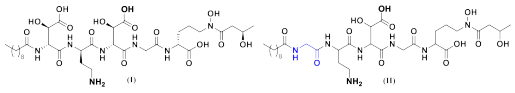
Dulamini I. Ekanayake,[1] Bruno Perlatti,[2] Dale C. Swenson,[1] Kadri Põldmaa,[3] Gerald F. Bills,[2] and James B. Gloer[1]. [1]Department of Chemistry, University of Iowa, Iowa City, IA 52242, United States, [2]Texas Therapeutic Institute, The Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center, 1881 East Road, Houston, TX 77054, United States, [3]Department of Botany, Institute of Ecology and Earth Sciences, University of Tartu, Lai 40, EE-51005 Tartu, Estonia

Sphaerostilbella broomeana is a fungicolous fungus that has been identified as a colonist of the basidiomata of forest pathogens. We have targeted fungicolous and mycoparasitic fungi as sources of antifungal agents with some success, indicating that studies of such colonists can prove fruitful. However, the chemistry of this genus is relatively unexplored. Studies of fermentation cultures of an isolate of *S. broomeana* (TFC201724) originally collected in Dehradun, India led to the isolation and identification of a new antifungal cyclic octapeptide, two closely related analogues, and four dioxopiperazines. The structure of the lead compound, broomeanamide A, was determined by analysis of 2D NMR and HRESIMS data. The structure consisted of one unit each of *N*-MeVal, Ala, *N*-MePhe, Pro, Val, and Ile, and two *N*-MeLeu units. HMBC and HRESIMS/MS fragmentation data were used to determine the amino acid sequence. According to NMR and HRMS data, the other two new peptides have the same amino acid composition, except that the Ile unit was replaced with Val in one and the *N*-MeVal unit was replaced with Val in the other. The absolute configuration of broomeanamide A was determined by applying Marfey's method to the acid hydrolyzate using both C_{18} and C_3 bonded-phase columns. Among the four dioxopiperazines encountered, two do not appear to have been previously encountered from a natural source. These metabolites were identified by analysis of ^{1}H NMR, ^{13}C NMR, and MS data, and by comparison to literature data. Two of the dioxopiperazine structures were confirmed and found to be racemic by X-ray crystallographic analysis. Broomeanamide A, the major cyclic peptide, had MIC values of 8.0 and 64 μg/mL against *Cryptococcus neoformans* and *Candida albicans*, respectively.

P-048 – Structure Characterization of New Cupriachelin Analogues from *Cupriavidus necator* B-4383

Mohammed M.A. Ahmed[1, 2] *and Paul D. Boudreau*[1], [1]*Department of BioMolecular Sciences, University of Mississippi, Oxford, MS, USA, 38677.* [2]*Department of Pharmacognosy, Al-Azhar University, Cairo, Egypt, 11371.*

Cupriavidus necator H16 is known to be a rich source of linear lipopeptide siderophores when grown under iron depleted conditions. Prior literature dubbed these compounds the "cupriachelins", these smallmolecules bear *β*-hydroxyaspartate moieties which contribute to a photoreductive reaction when bound as ferric cupriachelin. In our laboratory, we are interested in siderophores that have the capability to reduce metal centers and might be used in the bioremediation of heavy metals. Here, we present the structural assignment of new cupriachelin analogues from *C. necator* B-4383 grown under iron limitation. These new cupriachelin congeners present structural differences in not just the lipid tail but the amino acid residues of the peptide backbone. The characterization of those molecules structure was based on 1D and 2D NMR, MS-MS fragmentation analysis, and molecular networking (GNPS).



Cupriachelin (I) and cupriachelin congener (II)

P-049 – Phytofabrication of Silver Nanoparticles from *Newbouldia laevis* Root Extract and their Comparative Microbiological Activities

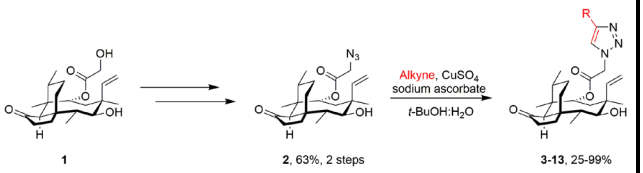
Onyekere P.F[1], *Ike-Onyishi U.E*[1], *Ozioko C.A*[3], *Ugwu C.E*[2], *Peculiar-Onyekere C.O*[3], *Chime S.A,*[2] *Okorie C.N*[3] *and Onyishi I.V*[2] [1]*Department of Pharmacognosy and Environmental Medicine, University of Nigeria, Nsukka. 410001. Enugu State, Nigeria.* [2]*Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka. 410001. Enugu State, Nigeria.* [3]*Department of Pharmaceutical Microbiology and Biotechnology, University of Nigeria, Nsukka. 410001. Enugu State, Nigeria.*

The peculiar physico-chemical and biological properties of biosynthesized silver nanoparticles (AgNPs) have proven to be comparatively more beneficial than conventional approaches. The root extract of *Newbouldia laevis* was qualitatively and quantitatively analyzed using standard procedures and used as reducing and stabilizing agent in the synthesis of AgNPs. The synthesized AgNPs, root extract, and the AgNPs dispersed in Neusilin US2[R] of *Newbouldia laevis* were characterized using FTIR spectroscopy. The antimicrobial properties were evaluated using agar diffusion method and the MIC determined. Phytochemical analysis revealed alkaloids, glycosides, tannins, flavonoids, saponins, proteins, at varying concentrations. The synthesized AgNPs and the dispersion of AgNPs in Neusilin US2[R] had good antimicrobial properties. The root extract can serve as stabilizing agent in the green synthesis of AgNPs.

P-050 – Semi-Synthetic Modification of the Antibiotic Natural Product Pleuromutilin: A Copper Catalyzed Azide-Alkyne Cycloaddition Approach

Logan M. Breiner[1], *Moriah Heifetz*[1], *Sophia Philbrook*[1], *Jennifer McCord*[1], *and Andrew N. Lowell*[1]. [1]*Department of Chemistry, Virginia Tech, Blacksburg, Virginia 24060, USA.*

Pleuromutilin thioether derivatives have found use in veterinary medicine and as topical and systemic antibiotics recently approved by the FDA.[1] These derivatives show enhanced pharmacodynamic and pharmacokinetic properties over the parent compound, namely improved binding and slow resistance development.[2] In the present work, azidation strategies have been employed to provide **3** which contains a convenient azide handle for rapid diversification using click chemistry. Utilizing green click-chemistry conditions, and commonly available alkynes, 3 can be regioselectively transformed into a diverse array of 1,4-disubstituted triazole counterparts 3-13. Triazole functionalities confer improved pharmacokinetic properties[3] and may increase binding affinity to the bacterial ribosome. The synthesis and biological activity of 3-13 will be discussed.



1. Goethe, O.; Heuer, A.; Ma, X.; Wang, Z.; Herzon, S. B., *Nat. Prod. Rep.* **2019**, *36*(1), 220-247. 2. Paukner, S.; Riedl, R., *Cold Spring Harb. Perspect. Med.* **2017**, *7*(1), a027110. 3. Jain, A.; Piplani, P., *Mini-Rev. Med. Chem.* **2019**, *19*(16), 1298-1368.

P-051 – Assessment of Evolutionary Relationships for Prioritization of Myxobacteria for Natural Product Discovery

Hanan Albataineh[1], Andrew Ahearne[1], Scot E. Dowd[2], and D. Cole Stevens[1]. [1]Department of BioMolecular Sciences, University of Mississippi, School of Pharmacy, University, MS 38677 [2] MR DNA, Molecular Research LP, Shallowater, Texas, USA

Discoveries of novel myxobacteria have started to unveil the potentially vast phylogenetic diversity within this group of bacteria. While traditional myxobacterial classification efforts relied on morphology, biochemistry, and conservation of 16S gene sequences, updated methods including whole-genome based taxonomy have provided an excellent preliminary taxonomic classification. Herein, we utilize long-read genome sequencing for 2 myxobacteria previously classified *Archangium primigenium* ATCC 29037 and *Chondrococcus macrosporus* ATCC 29039 as well as four environmental myxobacteria newly isolated for this study for the assessment of evolutionary relationships of myxobacteria. Average nucleotide identity and digital DNA-DNA hybridization scores suggest previously classified *A. primigenium* to instead be a novel member of the genus *Melittangium*, *C. macrosporus* to be a potentially novel member of the genus *Corallococcus*, and the 4 isolated myxobacteria to include a novel *Corallococcus* species, a novel *Pyxidicoccus* species, a strain of *C. exiguus*, and a novel *Myxococcus* species. We assess the biosynthetic potential of each sequenced myxobacterium and suggest that genus-level conservation of biosynthetic pathways support our preliminary taxonomic assignment. Altogether, we suggest that long-read genome sequencing benefits the classification of myxobacteria and improves the determination of biosynthetic potential for prioritization of natural product discovery.

P-052 – Gastrointestinal Relaxant Activity of 70% Methanolic Extract of Dried Ginger Rhizome

Muhammad Nabeel Ghayur[1,2], and Anwarul Hassan Gilani[2,3]. [1]University of Pikeville, Pikeville, KY, USA, [2]Aga Khan University, Karachi, Sind, Pakistan, [3]University of Haripur, Haripur, Khyber Pakhtunkhwa, Pakistan

Ginger (*Zingiber officinale*) is a popular plant used and known globally for its culinary and medicinal properties. Particularly in South Asia, the ginger rhizome is used in a number of gastrointestinal (GI) related ailments. In this study, we report preliminary findings on the GI relaxant activity of the dried variety of ginger rhizome. Ginger rhizome was soaked in 70% aqueous-methanol and dried to give the extract (Zo.Cr). Segments of different isolated smooth muscle preparations were suspended in tissue baths. Zo.Cr tested positive for presence of lipophilic & organic compounds, terpenoids, flavonoids, amines/secondary amines, phenols, and alkaloids. When tested for any possible spasmogenic activity on resting baseline of rabbit jejunum, guinea-pig ileum and colon and rat uterus, Zo.Cr did not show any effect till 10 mg/ml. Zo.Cr in bolus (0.3-5 mg/ml) and cumulative dosing (0.3-3 mg/ml), showed a spasmolytic effect on spontaneously contracting baseline of isolated rabbit jejunum. In guinea-pig colon, Zo.Cr showed a similar relaxant effect in bolus dosing (0.03-10 mg/ml). The extract was then tested against different standard GI stimulants like acetylcholine (ACh, 0.3 micM), histamine (1 micM) and potassium chloride (50 mM). Guinea-pig ileum was pre-treated with Zo.Cr (3 mg/ml) for 30 min which abolished the stimulant effect of standard agonists. Similar effect of Zo.Cr was seen in guinea-pig colon against ACh (0.3 micM). The study shows spasmolytic potential of dried ginger extract in different smooth muscle preparations and justifies the traditional use of ginger in hyperactive states of GI tract.

P-053 – Analysis of Lyophilized Hydroethanolic Extracts of *Mucuna pruriens* in a Restoration/ Recovery Murine Model of Parkinson's Disease (PD)

Tanya Denne[1], Lila C. Winfrey[4], Chase Whitner[1], Cindy Moore[4], Theresa D'Silva[4], Amala Soumyanath[2], Lynne Shinto[2], Amie Hiller[2,4], Charles K. Meshul[3,4] [1] Bastyr University, Kenmore, WA, USA [2] Department of Neurology, [3]Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR, USA[4] VA Portland Healthcare System, Portland, OR USA

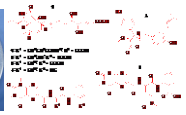
Decreased dopamine levels in the striatum are thought to contribute to symptoms of PD. Tyrosine hydroxylase (TH) is the rate limiting enzyme in the biosynthesis of L-dihydroxyphenylalanine (L-Dopa) and is a hallmark in PD. L-Dopa is a pharmaceutical commonly used to control the symptoms of PD. PD patients commonly use *M. pruriens* to treat PD as it is known to contain L-Dopa. To further understand the effects of *M. pruriens* extract we tested it in a 1-methyl-4-phenyl-1,2,3,6-tetrhydropyridine (MPTP) murine model of PD. To prepare the *M. pruriens* seed extract a hydroethanolic extract was rotovapped, lyophilized, and then resuspended in saline. In total there were 4 groups of mice; two of which were treated with MPTP to induce Parkinson like disease and the other two

were control groups treated with vehicle. One group of MPTP treated mice and one vehicle group were treated with orally administered *M. pruriens* extract. All groups were injected with carbidopa at a dose of 12 mg/kg, IP. In the MPTP group treated with *M. pruriens* the expression level of TH was found to be identical to that of the control group indicating that *M. pruriens* treatment, started after the establishment of significant dopamine loss in the MPTP experimental model, can result in recovery of TH protein expression. *M. pruriens* extract restored TH protein levels in the striatum where these levels have been depleted by the neurotoxin agent, MPTP. This suggests a novel neurorestorative property of this specific *M. pruriens* extract.

P-054 – Lumazine Peptides, Aspochalasin, ◎-Butyrolactone Derivatives and Cyclic Peptides with Antibacterial and NF-◎B Inhibitory Activities from a Hawaiian *Aspergillus flavipes*

Cong Wang[1,2], Xiaohua Wu[1], Helong Bai[3], KH Ahammad Uz Zaman[1], Shaobin Hou[4], Jennifer Saito[4], Supakit Wongwiwatthananukit[1], Kyung Sik Kim[5], Shugeng Cao[1]. [1]Department of Pharmaceutical Sciences, Daniel K. Inouye Colleg Pharmacy, University of Hawai'i at Hilo, United States. [2]Guangx Key Laboratory of Chemistry and Engineering of Forest Products, School of Chemistry and Chemica Engineering, Guangxi University for Nationalities, China. [3]Changchun Normal University, China. [4]University of Hawai'i at Manoa, United States. [5]Sungkyunkwan University, Republic of Korea.

Five new lumazine peptides, a new aspochalasin derivative a new γ-butyrolactone derivative, together with seven known compounds, were isolated from a Hawaiian fungal strain *Aspergillus flavipes* FS888. Compound **1** is an uncommon natural product containing an isocyano group. T structures of the new compounds were elucidated by NMR spectroscopy, HRESIMS, chemical derivatization and ECD analysis. Compounds **12**-**14** showed significant antibacterial activity against S. aureus when in combination with disulfiram. Additionally, compounds **9** and **13** showed NF-κB inhibitory activity with IC_{50} values of 3.1±1.0 and 10.3±2.0 μM, respectively.



P-055 – Synthesis and Evaluation of Aristoquinoline

Carolyn J. Straub, Dr. Malaika D. Argade, and Dr. Andrew P. Riley. Department of PharmaceuticalSciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612

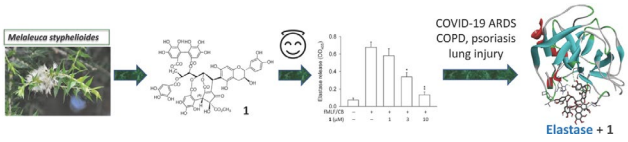
Selective antagonists of the α3β4 nicotinic acetylcholine receptor (nAChR) are reported to reduce psychostimulant-seeking and self-administration in rodent models, making α3β4 an attractive target for addiction therapy. However, the few agents that target the α3β4 nAChR suffer from suboptimal pharmacokinetics and poor target-selectivity. Aristoquinoline (ARQ), an alkaloid isolated from *Aristotelia chilensis*, was recently reported to inhibit human α3β4 nAChR preferentially over other neuronal nAChR subtypes, making it an attractive lead for designing and synthesizing a selective and potent α3β4 antagonist. In pursuit of this goal, we have established the first synthesis of ARQ employinga bridging Ritter reaction. Herein, the optimization of this bridging Ritter reaction is described. Additionally, to overcome limitations in this initial approach, a second synthetic route to access ARQ inhigh enantiopurity and an improved yield was developed. To complement our synthetic efforts, a cell- based receptor assay was employed to characterize the activity of ARQ at the α3β4 nAChR. Efforts are currently directed towards synthesizing structural analogs of ARQ to elucidate structure-activity relationships of ARQ at α3β4 nAChR.

P-056 – Anti-elastase Activity of *Melaleuca styphelioides* Ellagitannin *in Vitro* and *in Silico*

Michal Korinek[1,2], Eman Al-Sayed[3], Guan-Yu Chen[1], Pei-Wen Hsieh[2], Fang-Rong Chang[1], Bing-Hung Chen[1], Tsong-Long Hwang[2]. [1]Graduate Institute of Natural Products, Kaohsiung Medical University, Kaohsiung 80708, Taiwan. [2]Graduate Institute of Natural Products, Chang Gung University, Taoyuan 33302, Taiwan. [3]Department of Pharmacognosy, Ain-Shams University, 11566, Cairo, Egypt.

Previously undescribed ellagitannin **1** was isolated from *Melaleuca styphelioides*, a tree used as anti-inflammatory traditional medicine.

The structure of 1 was assessed by spectroscopic methods. Compound 1 inhibited fMLF/CB-induced elastase release in human neutrophils (IC_{50} 2.51 μM) and neutrophil elastase enzymatic activity in cell-free system (IC_{50} 2.58 μM). Further, 1 and its derivative (rhoipteleanin H) as well as approved elastase inhibitor (sivelestat) docked well and interacted with human neutrophil elastase binding sites *in silico* utilizing open-source software AutoDock 4.2. Therefore, ellagitannin 1 and its derivatives represent a promising class of anti-elastase agents against elastase-related inflammatory diseases such as asthma, psoriasis, but also COVID-19 associated ARDS.



P-057 – Pharmacognostic Evaluation and *in vitro* Hypoglycemic Activity of the Fruit Pulp of *Artocarpus odoratissimus* Blanco (Moraceae)

Querequincia, Joseph Mari B.[1, 2*], *Jonatas, Kay Ann .S.*[2,4], *Vasquez, Ross D.*[2, 3, 4, 1] *[1]Pharmacy Department, San Pedro College, Davao City, Philippines, 8000. [2]The Graduate School, University of Santo Tomas, Manila, Philippines, 1008. [3]Research Center for Natural and Applied Sciences, University of Santo Tomas, Manila, Philippines, 1008 [4]Faculty of Pharmacy, University of Santo Tomas, Manila, Philippines, 1008.*

Most of the plant species under the genus *Artocarpus* have phenolic phytochemical compounds and possess medicinal importance. *Artocarpus odoratissimus*, locally known as *marang* is an indigenous plant species in the Philippines. Currently, there are no scientific evidences about its potential medicinal value. Thus, this study sought to determine its pharmacognostic properties, biological activity such as hypoglycemic property through enzyme testing model and further characterize and quantify the compounds present in its fruit pulp extract. The plant sample showed minimal total ash, acid-insoluble ash and moisture contents were under minimal levels which is less than 1% and 10%, respectively. Polar solvents like ethanol have considerable affinities with the sample based from their extractive values. The crude extract was fractionated with increasing polarity solvents. Phytochemical screening revealed the presence of polyphenols and flavonoids. In the quantitative analysis of flavonoid and phenol compounds, the hexane fraction showed significant total flavonoid content 0.44 mg QE/ml. In the total phenol content assay, the crude extract, hexane and DCM fractions showed notable phenol equivalent contents with 0.36 mg GAE/ml. Among all of the sample extracts the semoipolar extract showed considerable inhibiting activity against α-glucosidase enzyme having an IC_{50} value of 26.42 mcg/mL. Based from the results of this study, *A. odoratissimus* can be a potential medicinal source having polyphenols. *Keywords*: *Artocarpus odoratissimus* Blanco, Hypoglycemic, Pharmacognostic, Polyphenols.

P-059 – Bromotyrosine Alkaloids from the Bahamas Marine Sponge *Pseudoceratina crassa*

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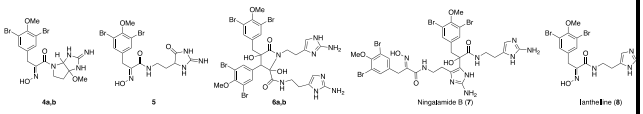

Bromotyrosine alkaloids (BTAs) are hallmark natural products of Verongida sponges characterized by modular structural assemblies. Here we present the most complex oxidative motif of BTAs discovered to date and reveal a new structural motif of selective butyrylcholinesterase (BuChE) inhibitors. Examination of a MeOH extract of the marine sponge *Pseudoceratina crassa* from the Bahamas that showed potent antifungal activity and inhibitory activity against BuChE revealed the presence of eight new BTAs (**1**–**6**). The planar structures of all eight compounds were obtained from analysis of MS, 1D and 2D NMR data. Each alkaloid, **4** and **6**, was isolated as a mixture of two diastereoisomers. The structures of **1**–**5** consist of an *O*-methy-2,6-dibromotyrosyl ketoxime (subunit A) amide linked to various groups (subunit B), whereas alkaloid **6** is a new oxidative motif in this family: it's a dimer of two units of *O*-methyl-2,6-dibromotyrosine 2-oxopropanamide linked to 2-aminohistamine through a five-membered lactam. Compounds **6**–**8** were responsible for the observed antifungal activity and inhibition of BuChE.

P-061 – SKINtegrated: Linking Metabolomics and *in silico* analysis in Screening Natural Products AgainstEmerging Skin Diseases

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Small molecule natural products from understudied Philippine plants can be explored as potential therapeutics against emerging tropical and autoimmune diseases related to skin. Beneficial cosmetic ingredients can be identified through metabolite profiling of plant extracts and assessing compatibility toskin *in silico*. In this study, metabolomics of endemic trees *Dillenia philippinensis*, *Dillenia luzoniensis*,and *Dillenia megalantha* was carried out using UHPLC-QTOF. Molecular networking in GNPS highlighted sulfated glucosides that were assessed to have general safety on skin based on QSAR predictions. Furthermore, the affinity of these compounds with receptors associated to leprosy, alopeciaareata, and rosacea was determined using molecular docking. The results suggest secondary metabolitesthat can be prioritized for antimicrobial, antioxidant, and enzymatic testing.

P-062 – Exploring the Metabolic Potential of Talaromyces sp. using OSMAC Strategy and Molecular Networking

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Expression of biosynthetic gene clusters (BGC) involved in secondary metabolites production may be modified according to culture conditions (One Strain Many Compounds, approach). In this regard, mixed culture fermentation, which consists of growing two or more microorganisms together, has demonstrated to be useful in triggering the biosynthesis of cryptic microbial secondary metabolites, and in some cases, enhancing the titers of specific molecules.[1] A robust technique that has allowed the analysis of metabolic differences between two different growth conditions and samples is the Liquid-Chromatography coupled to Mass Spectrometry (LC-MS).[2] This methodology allows for analyzing the chemical constellation of complex mixtures, and in combination with molecular networking, provides a visual representation of a sample's chemical space by detecting and correlating spectra sets from related molecules. Specifically, the GNPS (Global Natural Products Social Molecular Networking) platform can analyze data sets and compare the MS spectra to all available data.[3] In this scenario, the present research was conducted to explore the metabolic potential of *Talaromyces* sp., using a mixed fermentation approach (OSMAC strategy), LC-MS, and molecular networking. Furthermore, aiming to discover small organic molecules with inhibitory activity against protein tyrosine phosphatase 1B (PTP1B), an enzyme that negatively regulates the insulin and leptin pathways, and has gained significant interest from a pharmacological point of view since it is an emerging therapeutic target in the treatment of diabetes, obesity, and cancer.[4]

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P-063 – A Distinctive Stilbene Derivative from *Aspergillus flavus*-challenged *Arachis hypogaea* and a Novel Dimerization Product

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The peanut plant (*Arachis hypogaea*) is susceptible to attack by fungal pathogens, including *Aspergillus flavus*, which can attack peanuts both in the field and in storage and produces carcinogenic aflatoxins to which many people in developing countries are chronically exposed. Knowledge and exploitation of the plant's defenses against *A. flavus* infection could be important in helping to

control this problem. Our prior studies and others have afforded a number of stilbene derivatives that have been implicated as phytoalexins in peanut host defense. While studying *A. flavus*-challenged peanut plants, a further stilbenoid was isolated via RP-HPLC. However, NMR analysis proved difficult, as the sample readily decomposed upon collection. Several reactions were attempted in efforts to intercept this compound and obtain a stable product for analysis. Treatment of a freshly eluted sample with formic acid afforded a mixture that included a component having a subunit characteristic of cyclization between a prenyl side chain and an *ortho* phenolic OH. Treatment of another sample with BCl_3 gave a pseudodimeric product. Analysis of NMR data led to identification of this product as a Diel-Alder-type adduct constructed of two stilbenoid units. These results enabled proposal of the structure of the original metabolite as a stilbenoid containing a 3-methyl-1,3-butadienyl side-chain flanked by two phenolic OH groups. Previous studies had tentatively assigned this structure to an LCMS peak, but it had never been isolated or characterized. The structure of this side-chain and its placement appears to make it susceptible to facile oxidation and cyclization reactions.

P-064 – *Weeding* Out Small Molecules from *Euphorbia hirta* Herbal Supplements via LC/MS Metabolomics

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Teas and capsules made from the ubiquitous weed *Euphorbia hirta L.* have sprouted in the Philippine market, touted to have curative effect for dengue fever and asthma. However, information on the small molecule constituents of these supplements are insufficient to assess product efficacy and safety. To address this gap, profiling of ethanol and water extracts of fresh *E. hirta* leaves, capsules, and teas was done using LC/MS-based metabolomics. Analysis of MS and tandem MS data revealed the presence ofthe plant pigments, lipids, and flavonoids such as quercetin, kaempferol, myricetin, and isovitexin. Theseflavonoids are well-documented to have anti-viral and hemostatic effects, which could explain the benefits of *E. hirta* in folk medicine. Moreover, the impact of the type of supplement preparation on themetabolite content was explored through multivariate statistics. Quercetin was found to be highly abundant in spray-dried compared to air-dried capsules and teas. This elevated quercetin levels in spray-dried capsules could provide insights on the capsule's efficacy versus air-dried tea as well as the fresh *E.hirta* supplements.

P-065 – Isolation of Naturally Compounds Crocins from *Crocus Sativus* L. Stigma as Anticancer Agents

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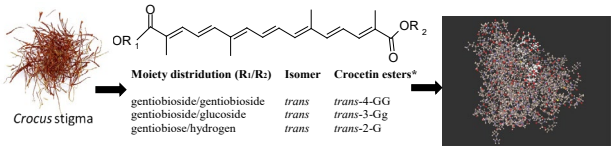
The current research demonstrates a simple method for *trans*-crocin 4, *trans*-crocin 3, and *trans*-crocin 2 isolation from the methanolic extract of *Crocus sativus* stigmas (saffron) using preparative chromatography. The analysis was performed using a Waters preparative HPLC Purification System with a Symmetry Prep C18 (300×19mm×7μm) column for isolation, using the mobile phase composition of a mixture of 0.1% acetic acid (A) and acetonitrile (B) solvents. The purity of compounds was studied using HPLC-DAD, UV-visible spectrophotometry and UHPLC-ESI-MS/MS and was more than 97%. The docking results showed that crocin exhibits a high affinity degree for the BRCA1 protein and has potential anti-cancer properties.



P-066 – Antioxidant and Antinociceptive Activity of Pterospartum tridentatum Methanolic Exctracts

Laranjeira, I.[1,2,3,4] *Vilasboas-Campos, D.*[1,2]*., Gonçalves, C.*[5]*, Teixeira-Castro, A..*[1,2]*, Almeida, A.,*[1,2] *Maciel., P..*[1,2]*, Dias, A.C.P.,*[3,4,6]*, Pinto-Ribeiro, F.,*[1,2,*] [1]*Life and Health Sciences Research Institute (ICVS), University of Minho;* [2]*ICVS/3B's - PT Government Associate Laboratory;* [3] *CITAB - Centre for the Research and Technology of Agro-Environmental and Biological Sciences, University of Trás-os-montes e Alto Douro;* [4]*Centre of Molecular and Environmental Biology (CBMA), University of Minho;* [5]*Department of Biology, University of Aveiro* [6]*Centre of Biological Engineering, University of Minho.* **filiparibeiro@med.uminho.pt*

Pterospartum tridendatum is an important source of active compounds with anti-inflammatory properties. After assessing the phytochemical profile of *Pterospartum tridentatum* leaves (PtL) by HPLC-DAD, its antioxidant activity was evaluated using several *in vitro* models: DPPH, iron chelating activity, NO and SO scavenging. Moreover, the toxicity of PtL extract was evaluated *in vivo* using *C. elegans*, in the food clearance assay. The ability of PtL extract in reversing OA-induced nociceptive impairments was studied in adult male rats using the kaolin/carrageenan (K/C) model of experimental OA. Two weeks after OA induction the pharmacological treatment started. Control animals (SHAM) were administered PBS while OA animals received either PtL 100mg/kg, 300 mg/kg or a commercial antiinflammatory (15mg/Kg, Brufen) via gavage, daily for three weeks. Nociceptive behaviour was evaluated weekly, using the Pressure Application Measurement test and locomotor behaviour was assessed using the catwalk and Open Field tests. Our phytochemical analysis showed the PtL extract mainly contains phenolic compounds which are in accordance with its significantly higher activity in scavenging NO and SO radicals. Our results indicate that the PtL extract was safe to *C. elegans* (up to 2 mg/mL). Treatment with PtL extract reversed OA-induced mechanical hyperalgesia in rats. Our work highlights the potential of PtL extracts as a source of compounds that can be used in oxidative stress-related diseases as well as adjuvants in the management of OA-induced pain.

P-067 – *Trachymyrmex septentrionalis* Ants Promote Fungus Garden Hygiene Using *Trichoderma*-Derived Metabolite Cues

Sara P. Puckett[1,†]*, Kathleen E. Kyle*[2,†]*, Andrés Mauricio Caraballo-Rodríguez*[3]*, Robert M. Samples*[1,4]*, Pieter C. Dorrestein*[3]*, Jonathan L. Klassen*[2,*]*, and Marcy J. Balunas*[1,*]*.* [1]*Division of Medicinal Chemistry, Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT, USA.* [2]*Department of Molecular and Cell Biology, University of Connecticut, Storrs, CT, USA.* [3]*Collaborative Mass Spectrometry Innovation Center, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, CA, USA.* [4]*Department of Chemistry, University of Connecticut, Storrs, CT, USA.* [†]*indicates equal contribution.*

Trachymyrmex septentrionalis ants are fungus-growing ants primarily located along the eastern seaboard of the United States. The ants are part of a multipartite symbiosis wherein ants bring leaves and/or other organic material to be digested by the fungus garden, and the garden, in turn, differentially grows gongylidia sacs the ants use as their main food source. Since this garden is crucial for ant survival, the ants have adopted various techniques to keep their gardens healthy, such as maintaining garden hygiene by physically removing pieces of compromised fungus garden known as weeding. However, how ants distinguish healthy from unhealthy garden is not known. The goal of this project was to determine if chemical cues induce weeding and if so, what metabolites contribute to this behavior. Using a combination of genomics, metabolomics, and infection analyses, *Trichoderma* fungi were determined to be present and potentially pathogenic in both field and laboratory experiments. Peptaibols, a class of common *Trichoderma* metabolites, were found to be highly abundant in bioactive fractions and purified peptaibols were confirmed to induce ant weeding behavior. Future experiments will explore if cues are sensed by the ants directly or if weeding behavior is the result of cues from infected fungus gardens.

P-068 – Investigating the Principle Rhode Island Secondary Metabolite (PRISM) Library for *E. coli* Quiescence Reversing Compounds

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Urinary tract infections (UTIs) are prevalent and pose significant clinical challenges, affecting between 50 and 80% of women at some point in their lifetimes. Of this population, up to 30% will experience a recurrent urinary tract infection (rUTI) within 3-12 months of the initial episode, with 77% of these recurrent infections attributed to the same uropathogenic *E. coli* (UPEC) strain which caused the initial infection. The high incidence rates of rUTIs call into question the characteristics of UPEC which are capable of forming quiescent intracellular reservoirs within the urothelium of the bladder, thus evading host immune response and antibiotic therapy. Utilizing the PRISM Library, a library of plant extracts derived from the URI Medicinal Garden, chemical extracts were screened against a novel quiescence assay to investigate quiescence reversing activity. Active extracts will be prioritized and analyzed using bioassay guided fractionation paired with LC-MS/MS-based molecular networking.

P-069 – Dereplication of Fungal Metabolites by Annotated Molecular Networking using MADByTE

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Strategies for dereplication are continually evolving, essentially in lock step with advances in MS and NMR techniques. MADByTE is a new platform that takes a less common approach, where NMR data are used to generate molecular networks with annotated spin systems that are often observed in well known compounds. This study used MADByTE for the dereplication of two classes of fungal metabolites, the resorcylic acid lactones (RALs) and spirobisnaphthalenes. A database was recreated using HSQC and TOCSY data of 19 RALs and ten spirobisnaphthalenes, and MADByTE was used to generate the networks with the annotated systems, and cluster the analogues based on common spin systems. Five fungal extracts were then dereplicated with MADByTE, demonstrating that the platform can be used for the detection of a specific structure or a structural core in the context of complex mixtures.

P-070 – Persuasive Strategy for Development of Synergistic Phytopharmaceutical Formulation for Multi Drug-Resistant Bacteria

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The synergic combination of antibiotics and phytochemicals represents a promising strategy with numerous clinical and developmental benefits. The activity of these plant molecules as inhibitors of microbial efflux pumps can act as restorers of antimicrobial susceptibility and open the door to combined antibiotic treatments, since these could exert their action more easily by not being expelled from the bacterial interior, allowing relive obsolete or discarded therapies due to this resistance mechanism. Some plant compounds have direct antimicrobial activity against antibiotic-resistant bacteria, while others can sensitize resistant bacteria against antibiotics, reversing the resistance. Some of these phytochemical compounds can enhance the effect of antibiotics by facilitating their entry into the cell by destabilizing the cytoplasmic membrane, inhibiting efflux pumps (EPs) in different pathogenic bacterial species or by dispersing biofilms. Some of the synergistic interactions between phytochemicals and antibiotics have following benefits include increased efficiency, lower antibiotic doses, reduced side effects, increased bioavailability and increased stability. The multidimensional and multifactorial activity of phytochemicals studied by network pharmacology is crucial for synergy with clinical antibiotics, opening the door to the process of research and development of new potential therapies.

P-071 – Expanding MADByTE Annotation with SHIMS (Substructure Hypothesis by Integration of MADByTE and SMART) and NMRShiftDB2 Shift Prediction

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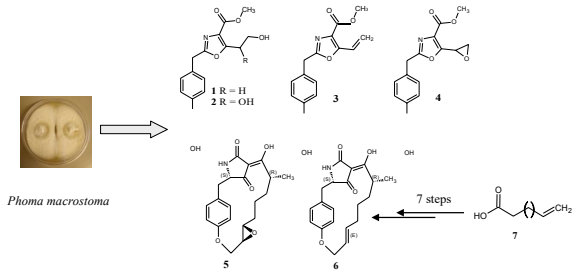
MADByTE, an NMR processing platform designed for metabolomics and dereplication using 2D NMR data was designed to integrate data from HSQC and TOCSY experiments to create contextual networks to annotate structural characteristics of unknown molecules in complex samples. MADByTE spin system features contain important structural information but can be challenging to interpret unless compared to a library of standard compounds. New methods for in-silico prediction of NMR chemical shifts could greatly alleviate this limitation. When the MADByTE comparison strategy is coupled to a molecular recognition platform (SMART) and an NMR shift prediction utility (NMRShiftDB2), substructures of molecules within complex samples can be proposed based on similarities in spectral profiles using the newly developed SHIMS module.

P-072 – Characterization and Biological Evaluation of Secondary Metabolites from the PlantPathogenic Fungus *Phoma macrostoma* (Ascomycetes)

Blondelle Matio Kemkuignou[1], Laura Treiber[2], Haoxuan Zeng[1], Schrey Hedda[1], Rainer Schobert[2], Marc Stadler[1]. [1]Department Microbial Drugs, Helmholtz Centre for Infection Research GmbH (HZI), Braunschweig, Germany. [2]Organic chemistry laboratory, University of Bayreuth, Universitaetsstrasse 30, 95447 Bayreuth, Germany.

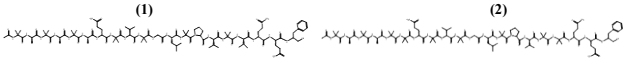
Investigation of the chemical components of the fermentation extract of the plant pathogenic fungus *Phoma macrostoma* led to the isolation of six compounds including four new oxazole carboxylic acid derivatives named macrooxazoles A-D (**1**-**4**) and two known tetramic acid derivatives named macrocidin A and Z (**5**-**6**). Their structures were elucidated based on high-resolution mass spectrometry (HR-MS) and nuclear magnetic resonance (NMR) spectroscopy. The hitherto unclear structure of macrocidin Z (**6**) was also confirmed by its first total synthesis by using compound **7** as the starting material. All the isolated compounds were evaluated in bioactivity assays against a panel of bacteria and fungi. The compounds exhibited weak activity against some of the organisms tested. However, the tetramic acid derivatives showed interesting anti-biofilm activity against *s. aureus* especially macrocidin A (**5**) which inhibited biofilm formation of *s. aureus* of 61% at 15.6 μg/mL. Cytotoxic activity of the isolates against two cancer cell lines KB3.1 and L929 was also assessed andthe compounds did not show any cytotoxic activity under test conditions.



P-073 – Antibacterial peptaibols Trilongin BII and Trilongin BIII from the *Trichoderma deliquescens* (Sopp) Jaklitsch Fungus Against Highly Drug-Resistant *Acinetobacter baumannii*

Heather L. Winter[1], Laura Flores Bocanegra[1], William J. Crandall[1], Fridah Rotich[1], Madeline Tillman[2], Kristof B. Cank[1], Huzefa A. Raja[1], Cedric J. Pearce[3], Nicholas H. Oberlies[1], Nadja B. Cech[1]. [1] Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27412, [2] Merck & Co inc. [3] Mycosynthetix, Inc, Hillsborough, NC, 27278.

A series of 2,500 fungal extracts derived from the Mycosynthetix collection were screened against the highly-drug resistant Gram-negative infectious bacterium *Acinetobacter baumannii* (strain AB5075). The compounds Trilongin BII **(1)** and Trilongin BIII **(2)** were isolated from an active fungal extract (MSX29608) of *Trichoderma deliquescens* (Sopp) Jaklitsch. Compounds **(1)** and **(2)** have been previously observed in *Trichoderma* sp. and are classified as peptaibols. The structures of the compounds were solved using mass-spectrometry based dereplication and nuclear magnetic resolution spectroscopy, and configuration was confirmed with Marfey's analyses. Cytotoxicity of the peptaibols is currently being assessed in a *Galleria mellonella* model.



P-074 – Antibacterial Activity Found in *Hypericum calycinum* (creeping St. John's Wort) Against Methicillin-Resistant *Staphylococcus aureus*

Colby M. Laws[1], Heather L. Winter[1], Madeline Tillman[2], Nadja B. Cech[1]. [1] Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27412, [2] Merck & Co inc.

Extracts from the aerial and root portions of *Hypericum calycinum* (creeping St. John's Wort) and *Hypericum perforatum* (St. John's Wort) as well as a commercial supplement of St. John's Wort were screened against the clinically relevant Gram-positive bacterium Methicillin-Resistant *Staphylococcus aureus* (strain AH1263). Antimicrobial activity was observed only for the *H. calycinum* extract. All samples were analyzed with ultraperformance liquid chromatography coupled to high resolution mass spectrometry on a Q Exactive mass spectrometer. Principal component analysis (PCA) was performed on the mass spectrometry datasets for all samples to generate scores and loadings plots. Influential features were annotated on the loadings plot. One feature unique to *H. calycinum* was found to match the accurate mass of the molecule chinesin I, which has previously been observed in *Hypericum chinense* and has reported antibacterial activity against *Staphylococcus aureus*. Further experiments are underway to isolate and confirm the presence of chinesin I in the *H. calycinum* specimen.

P-075 – Structure and Dentin Biomodification Activity Relationship of Oligomeric Proanthocyanidins

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Certain oligomeric proanthocyanidins (PACs) are capable of enhancing the mechanical properties of modified dentin and induce changes to the secondary structure of collagen. To enable exploration of structure-activity relationships (SARs), *Cinnamomum verum* was selected for scaled-up purification of A- and B-type PACs based on Diol-HPLC and LC-MS profiling. Ten PACs (DP 2~5) were isolated by a sequential separation including centrifugal partition (CPC) and Sephadex LH-20 column chromatography, followed by semi-prep HPLC. Among the isolates, the major *C. verum* trimer and tetramer were prepared at the gram-scale for extensive, pre-clinical dentin biomodification studies. Their structural characterization involving extensive spectral and chemical degradation approaches showed that epicatechin units are connected by either doubly-linked A- or the singly linked B-type interflavanyl linkages. In addition, an all-A-type PAC was obtained via chemical conversion of a B-type PAC. Moreover, to facilitate the communication of PAC structures in SARs studies, the PAC Block Arrays (PACBAR) system was developed as structural descriptors that capture PAC structural diversity. Dynamic mechanical analysis (DMA) and infrared spectroscopy were employed to evaluate the biomodification potency of PACs with collagen in a dentin model. The SARs studies revealed that the linear structure PACs (4→8) showed significantly higher activities in biomechanical assays than the branched structures (4→6). Aesculitannin E (EC=8EC-8EC-8EC) was the most potent PAC found so far to enhance the mechanical properties of dentin, showing a 14-fold modulus of viscoelasticity increase compared to control.

P-076 – Development and Application of an UHPLC-MS Method for Quantitative Analysis of Indole and Oxindole Alkaloids in Kratom [*Mitragyna speciosa* (Korth.) Havil.] Plants and Products

Preston K. Manwill, Laura Flores-Bocanegra, Manead Khin, Nadja B. Cech, Nicholas H. Oberlies, and Daniel A. Todd. Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27402, USA*

A growing population of Americans is turning to kratom [*Mitragyna speciosa* (Korth.) Havil (Rubiaceae)] to self-manage pain and opioid addiction. The tropical tree is native to Southeast Asia, where the fresh leaves are either brewed into a tea or chewed to combat fatigue and relieve pain. In the United States, a vast array of capsules, powders, and loose-leaf kratom products are readily available to consumers via online and local retailers. Additionally, several online sites supply live kratom plants, thus providing consumers access to unprocessed kratom material. Prerequisite to establishing quality control and quality assurance standards for the kratom industry or understanding how alkaloid levels effect clinical outcomes, is the identification and quantitation of major and minor alkaloid constituents within available products and preparations. To this end, an ultra-high performance liquid chromatography-mass spectrometry method was developed, validated, and used to quantify 14 kratom alkaloids in commercial kratom products, alkaloidal extracts, and living plant specimens. The findings demonstrate wide variability in alkaloid profiles for different plant materials all marketed as *M. speciosa*, with commercial products (purportedly from Southeast Asia) showing high levels of the indole alkaloid mitragynine and non-detectable amounts of the oxindole alkaloid isomitraphylline and North American grown kratom ("Rifat" clone) showing high levels of the indole

P-077 – Synthesis and Identification of Pericosine Analogues as Odor Neutralizing Agents: Computational and Experimental Studies

Aayushi Chatterji, Vardhan Satalkar, Yihan Shao, and Robert Cichewicz. Natural Products Discovery Group, Institute for Natural Products Applications and Research Technologies, Department of Chemistry & Biochemistry, Stephenson Life Science Research Center, University of Oklahoma, Norman, Oklahoma 73019, United States

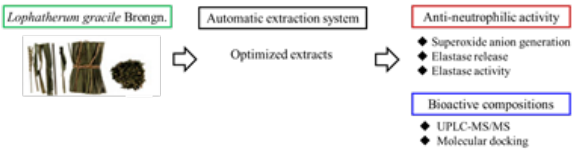
Skunk spray comprises several types of organosulfur compounds, mainly thiols and thioacetates.[1] The pungent odor of skunk thiols can be neutralized by a fungal metabolite called pericosine.[2] Conventional approaches to access pericosine involve expensive reagents and lengthy sequence of synthetic steps, which limit the commercial utility of these methods.[3] In this project, simplified analogues of pericosine were synthesized in an efficient and cost-effective manner. The analogues were tested against a variety of nucleophilic molecules including organosulfur compounds revealing their ability to effectively deodorize odoriferous compounds under aqueous conditions. Experimental and computational studies revealed thatthe presence of the Michael-acceptor group greatly promoted reactivity towards nucleophilic sulfur- containing compounds. The LCMS analysis and free solvation energy calculations showed that the aqueous solubilities of some of our analogues were relatively higher than the lead compound pericosine A. The studies to further understand the reaction mechanism are ongoing. References:

1. *J. Chem. Ecol.* 1991, *17*, 1415. 2. *J. Nat. Prod.* 2019, *82*,1989. 3. a) *Org. Lett.* 2010, *12*, 2206; b) *Org. Biomol. Chem.* 2009, *7*, 315; c) *J. Org. Chem.* 2007, *72*, 6127 d)*J. Nat. Prod.* 2011, *74*, 877; e) *Org. Lett.* 2009, *11*, 2699; f) *Synlett* 2006, 1598; g) *Chem. Lett.* 2005, *34*, 1062; h) *Synthesis* 2007, 3219; i) *Tetrahedron: Asymmetry* 2008, *19*, 1461.

P-078 – Preparation, Analysis, and Anti-Neutrophilic Activities of *Lophatherum gracile* Brongn

Yu-Li Chen[1], Kuei-Hung Lai[2], Yu-Chia Chang[1], and Tsong-long Hwang[1,3], [1]Research Center for Chinese Herbal Medicine, Graduate Institute of Health Industry Technology, College of Human Ecology, Chang Gung University of Science and Technology, Taoyuan, 33303, Taiwan. [2]Graduate Institute of Pharmacognosy, College of Pharmacy, Taipei Medical University, Taipei, 11031, Taiwan.[3]Graduate Institute of Natural Products, School of Traditional Chinese Medicine, Chang Gung University, Taoyuan, 33302, Taiwan.

Lophatherum gracile Brongn., a long used traditional Chinese medicine, was reported to inhibited inflammation through attenuating neutrophil activities. However, the relationship between chemical compositions and anti-neutrophilic activities remain unclear. In the current study, optimized bioactive extracts were prepared through an automatic and accelerating extraction system. The relationship between biological data and chemical



components will be presented.

P-079 – Microfractionation-based Bioactivity and Molecular Profiling Advances Antibiotic Discovery Screening

Shengnan Jin,[1,3,4] Gauri Shetye,[1,3,4] Sanghyun Cho,[1,3,4] Scott G. Franzblau[1,3,4] Guido F. Pauli,[1,2,3,4] Jonathan Bisson,[1,3,4], [1]Institute for Tuberculosis Research, [2]UIC Botanical Center, [3]Department of Pharmaceutical Sciences, and [4]College of Pharmacy; University of Illinois at Chicago, Chicago, IL, U.S.A.

Streptomyces has been one of the most prolific sources for antimicrobial agent discovery. Classical bioassay-guided fractionation typically leans favorably toward the most abundant components, and is associated with a substantial risk of reisolating known chemical entities. To advance this situation, it is essential to screen innovative antibiotics in parallel with dereplication of known compounds at the initial stage of drug discovery. Our newly developed strategy utilizes programmed, semi-preparative HPLC to generate 144 microfractions from active microbial extract in two deep 96-well plates. The collected microfractions were screened and assessed for growth inhibition of Mycobacterium tuberculosis (M.tb) H37Rv strain. Thereby, HPLC-bioactivity profiling can be established by aligning the LC chromatogram with the bioassay data, which enables highlighting bioactive constituents within complex crude mixtures. Additionally, LC-MS/MS is applied as a powerful dereplication tool to characterize and annotate known molecules in each micro fraction. Using high-resolution ESI-QTOF-MS/MS, we can construct a feature-based molecular network, which provides semi-quantitative

information, in silico and experimental annotation from databases and visualization of analogs of potential bioactives. The new approach is capable of integrating three-dimensional data sets (HPLC, bioactivity, LC-MS/MS) at high resolution (144 frs), adjustable biological dynamic range, and high chemical dynamic range (MS sensitivity), respectively. This enables efficient screening in the quest for new antibiotics using only a few milligram or less of crude microbial extract.

P-080 – Impurity or Isomer: What Exactly is in Your Rufomycin?

Jin Cao[a,b] Bin Zhou,[a,b] James B. McAlpine,[b] Shao-Nong Chen,[a,b] Jonathan Bisson,[a,b] Scott G. Franzblau[a,b] and Guido F. Pauli[,a,b].*
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Rufomycins are a group of cyclopeptides that contain seven amino acids and show promising activities against *M. tuberculosis*. Among them, rufomycin 4 (RUF 4, formerly RUF I) exhibited potent activity with a MIC value of 21 nM, and the C-32 epimer rufomycin 7 (RUF 7, formerly RUF II) showed MIC of 47 nM. Because of the difficulty of separation of these two compounds and their closed activities, a mixture of both has so far been employed for all biological studies. The achievable purity now reached 96.5% for the combined RUF 4/7 pair. Moreover, recent experiments indicated the remaining 3.5% "impurity gap" almost exclusively consists of their C-34 epimers, which are conversion products of RUF 4/7 that can be formed under aqueous conditions due to the lability of the hemi-aminal ring. This finding also led to the necessity of re-naming the RUF series of compounds: the four isomers were renamed now as RUF 4 (formerly RUF I, 32*S*,34*R*), RUF 5 (C-34 epimer of RUF 4, 32*S*,34*S*), RUF 6 (formerly RUF II, 32*R*,34*R*), and RUF 7 (C-34 epimer of RUF 6, 32*R*,34*S*). HPLC and qNMR analysis now established the ratio of these four isomers in the prior RUF I and II samples as containing RUFs 4/5/6/7 in the ratio 41.5% : 1.4% : 55.0% : 1.4%. This eventually allowed determination of the overall purity of the previous "RUF I and II" mixture isolates, now named as RUF 4–7, to be 99.3%. Considering the structural complexity of these cyclopeptides, this indicates the samples are highly suitable for biological studies and builds confidence in the extensive biological and SAR profiles of RUFs built in our laboratory.

P-081 – Molecular Docking of Phyto-Constituents from *Markhamia Tomentosa* Against Oncogene and Apoptotic Drug Targets

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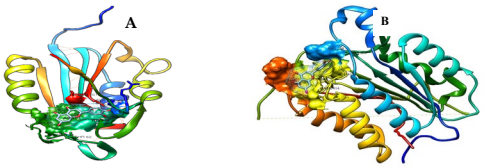
Hit compounds from *M. tomentosa* phyto-constituents which can be used to inhibit the growth of HPV16 E6 through induction of apoptosis were identified via an *in-silico* approach. Identified phyto-constituents from *Markhamia tomentosa* were retrieved from PubChem database and docked in predicted active sites of HPV 16 E6, caspase -3 and caspase -8 protein targets using AutoDock Vina from PyRx software. All tested phyto-constituents showed binding affinity for HPV 16. Luteolin, carnosol, ajugol, and phytol showed binding affinity with both caspases -3 and -8.



P-083 – A Targeted Metabolomics Evaluation of *Cannabis sativa* Compounds with Bioactivity Against *Methicillin-resistant Staphylococcus aureus* (MRSA)

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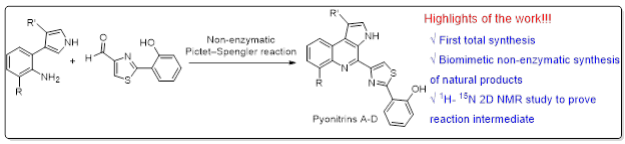
Infections that are resistant to available antibiotics are an increasing problem world-wide, responsible for an estimated 700,000 annual mortalities. Unfortunately, the use of antibiotics accelerates the development of resistance, which facilitated the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA). There is great need for the development of strategies to treat drug resistant infections such as MRSA. Hemp, a low-THC (< 0.3%) variety of the *Cannabis sativa* plant has recently been shown to possess antimicrobial activity against MRSA. According to Consumer Reports, in the US alone

one-third of adults have used low-THC containing products such as hemp or cannabidiol (CBD) oil, and the number of people 65 and older who used them has doubled in the past few years. Thus, hemp is both biologically active and readily available. With this project we combined bioassay-guided fractionation with high-resolution mass spectrometry with the goal of identifying antibacterial compounds from hemp. An extract from an authenticated hemp source material was prepared and fractionated, and the extract of several fractions displayed antimicrobial activity against a clinically relevant strain of MRSA. With this approach, we aim to identify compounds that inhibit the growth of MRSA and provide information about their structure. Experiments to elucidate the compounds associated with the antimicrobial activity are ongoing.

P-084 – Synthesis and Investigation of the Abiotic Formation of Pyonitrins A – D

Rahul D. Shingare,[a] Victor Aniebok,[a] Hsiau-Wei Lee,[a] John B. MacMillan[a] a. Department of Chemistry and Biochemistry, University of California, Santa Cruz, Santa Cruz, CA 95064.*



Pyonitrins A-D recently isolated natural product from the insect-associated *Pseudomonas protegens* strain exhibited impressive antifungal activity in an *in vivo* murine candidiasis assay. The genome studies of *Pseudomonas protegens* revels that pyonitrins A-D are formed by the spontaneous non-enzymatic reaction between biosynthetic intermediates of two well well-known natural products pyochelin and pyrrolnitrin. Here in this report we have accomplished the first biomimetic total synthesis of pyonitrins A-D in three steps and studied the non-enzymatic formation of the pyonitrins using ^{15}N labeled starting material. The continuous high sensitivity ^{1}H-^{15}N HMBC NMR spectroscopy used to understand the reaction mechanism by monitoring the reaction intermediates formed in real time.

P-086 – Genome Mining and Molecular Networking-Based Metabolomics of the Marine-Facultative *Aspergillus* sp. MEXU 27854

Anahí Martínez-Cárdenas and Mario Figueroa. Facultad de Química, Universidad Nacional Autónoma de México, CDMX, 04510, Mexico.

The marine-facultative *Aspergillus* sp. MEXU 27854, isolated form the Caleta Bay in Acapulco, Guerrero, Mexico, has provided an interesting diversity of secondary metabolites, including a series of rare dioxomorpholine derivatives and peptides. Its genome consists of 11 contings with a ~30.75 Mb total length of assembly, and its annotation resulted in the prediction of 10,822 putative genes. From the 67 BGC identified, ~60% belong to the NRPS and NRPS-classes. Functional annotation was accomplished by blasting protein sequences with different public databases. Of the predicted genes, 75% were assigned gene ontology terms. In addition, extensive genome mining allowed to predict a putative BGC for the dioxomorpholines. This work represents the first report of whole-genome sequencing and annotation from a marine-facultative fungal strain isolated from Mexico.

P-087 – Chemical Studies of Fungi from Cenotes of the Yucatan Peninsula

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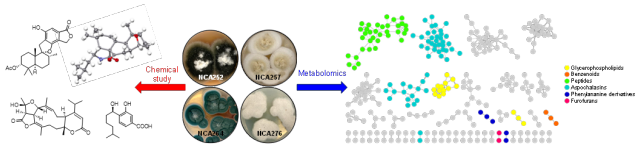
The Yucatan Peninsula has one of the most spectacular and developed karstic aquifers in the world. To expand the chemical knowledge of the microorganisms from this unique ecosystem, the organic extracts of four fungal strains obtained from sediments of the Kankirixché and Noh Mozón cenotes were subjected to chemical studies and metabolomic analysis. The isolated compounds, asterriquinols, penicillic acids, a bisabolene, phenylalanine derivatives, and aspochalasins from three *Aspergillus* spp. and melleins, atranones, and phenylspirodrimanes from a *Stachybotrys* sp., were annotated in the GNPS molecular network of each strain. In addition, the absolute configuration of the 17-desoxiaspergillin PZ was stablished by X-Ray analysis [Flack parameter 0.08(10)].

Some of these compounds were active against MRSA.



P-088 – Uncovering Molecular Cues That Drive a Unique Symbiotic Relationship Between *Biomphalariaglabrata* and *Capsaspora owczarzaki*: A Potential Agent Against Schistosomiasis

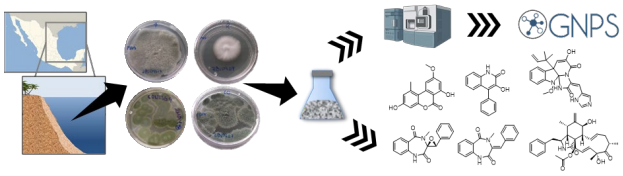
Ria Kidner[1], *Núria Ros-Rocher*[2], *Catherine Gerdt*[1], *Iñaki Ruiz-Trillo*[2], *J.P. Gerdt*[1]. [1]*Department of Chemistry, Indiana University, Bloomington, IN 47405, USA.* [2]*Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra), Passeig Marítim de la Barceloneta 37-49, 08003 Barcelona, Catalonia, Spain.*

Symbioses between diverse organisms are widespread and frequently underappreciated. An underexplored symbiosis between the freshwater snail *Biomphalaria glabrata* and the unicellular species *Capsaspora owczarzaki* presents a unique opportunity for the control of the neglected tropical disease schistosomiasis. The parasitic disease agent, *Schistosoma mansoni*, relies on *Biomphalaria* as anintermediate host in its parasitic lifecycle. In contrast, *Capsaspora*, which was originally isolated from the snail's hemolymph, swarms and kills *S. mansoni* parasites *in vitro*. Despite this interesting anti- parasitic activity, the relationship between *Capsaspora* and *Biomphalaria* is poorly understood. We havediscovered the first known phenotype *Capsaspora* displays in response to chemical cues released by its host: active cell aggregation. Our lab strives to understand the molecular cues behind *Capsaspora* aggregation in an effort to characterize its symbiosis with snails. Through activity-guided fractionation, we discovered lipoproteins to be the putative cue causing *Capsaspora* aggregation *in vitro* and have shown this behavior is likely dependent on receptor-mediated endocytosis involving the putative protein *Capsaspora* dynamin-1. Further work in uncovering signaling pathways between these organisms may help to develop *Capsaspora* as a biocontrol agent against schistosomiasis.

P-089 – Pharmacological Potential and Chemical Diversity of Marine Sediment Fungi of the Gulf of Mexico

Rodrigo Villanueva-Silva[1], *Patricia Velez*[2], *and Mario Figueroa*[1]. [1]*Facultad de Química and* [2]*Instituto de Biología, Universidad Nacional Autónoma de México, Ciudad de México 04510, México.*

As part of our investigations on the chemical diversity of organisms from unexplored marine habitats of Mexico, a series of 29 fungal strains isolated from deep-sea sediments (<600 m deep) from the Gulf of Mexico were investigated. The antimicrobial potential of their organic extracts from solid cultures grown under the *OSMAC* approach was assessed against a panel of ESKAPE bacteria and the yeast *C. albicans*. Chemical studies on the active scaled-up cultures and some small-scale cultures led to the isolation of benzochromenones from *Alternaria* sp. CIGOM4, benzodiazepines from *P. echinulatum* CONTIG4, a cytochalsin from *Biatriospora* sp. CIGOM2, and an imidazopyridoindole from *Penicillium* sp. CIGOM10. Molecular network analysis by GNPS combined with manual dereplication showed the enormous potential of these fungi to produce bioactive compounds.



P-090 – Anti-ESKAPE Potential of Endophytic Fungi from Mangroves in Tabasco, Mexico

Alejandra Arista-Romero[1], *María del Carmen Gonzalez*[2], *and Mario Figueroa*[1]. [1]*Facultad de Química and* [2]*Instituto de Biología, Universidad Nacional Autónoma de México, CDMX, 04510, Mexico.*

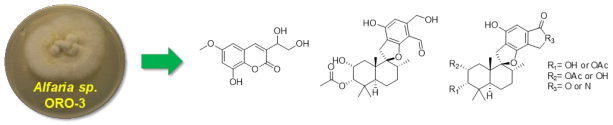
Mangroves are salt-tolerant forest ecosystems with a unique microbial diversity. The Pantanos de Centla Biosphere Reserve (PCBR) in Tabasco, Mexico, is an unexplored niche of unique fungal species with bioprospecting potential in medicine and agriculture. In this work, the organic extracts ($CHCl_3$-MeOH) from solid axenic cultures (moist rice) of 45 endophytic fungi isolated from mangroves of the PCBR were tested against a set of ESKAPE bacteria. From these, the strains with internal codes PC4 and PC5 showed significant activity at 20 and 200 μg/mL against *Staphylococcus aureus* ATCC

6538, *S. aureus* ATCC 25923, *S. aureus* ATCC 43300 (methicillin resistant), and *Enterococcus faecalis* ATCC 29212. Scaled-up (10◉) cultures of the active strains were submitted for bioactive compounds isolation.

P-091 – Chemical and anti-MRSA activity of *Alfaria sp* from the Oro Beach, Colima, Mexico

Marian A. López-Lobato[1], María del Carmen Gonzalez[2], and Mario Figueroa[1]. [1]Facultad de Química and [2]Instituto de Biología, Universidad Nacional Autónoma de México, CDMX, 04510, Mexico.

Microorganisms from marine habitats are a well-known source of biologically active compounds. From a series of marine-facultative fungal strains isolated in the Oro beach at Colima, Mexico, the organic ($CHCl_3$-MeOH) extract of species *Alfaria* sp. ORO-3 showed important antibacterial activity against methicillin resistant *Staphylococcus aureus* (MRSA). Bioactive-guided fractionation of the extract led to the isolation of a new coumarin derivative and the phenylspirodrimane derivatives stachybotrysin C stachyin A, and chartarlactam K, among others. Their structures were elucidated using NMR and HRMS analysis. To the best of our knowledge, this is the first report of chemical and biological studies of a species of the genera *Alfaria*.



P-092 – Multitarget Mechanisms of Antitumour Hybrid Combinations Integrating Terpenoids

Eva María Domínguez-Martín[1,2], Célia M. C. Faustino [3] , Patrícia Rijo [2,3*] Ana María Díaz-Lanza[1*1] University of Alcalá de Henares, Faculty of Pharmacy, Department of Biomedical Sciences, Pharmacology Area (Pharmacognosy Laboratory), New antitumor compounds: Toxic action on leukemia cells research group. Ctra. A2, Km 33.100 – Campus Universitario, 28805. Alcalá de Henares, Madrid, Spain. [2] Research Center for Biosciences & Health Technologies (CBIOS), Universidade Lusófona deHumanidades e Tecnologias, Campo Grande 376, 1749-024 Lisbon, Portugal. [3] iMed.ULisboa - Research Institute for Medicines, Faculty of Pharmacy, Universidade de Lisboa,Av. Prof. Gama Pinto, 1649-003 Lisbon, Portugal.*

Cancer comprises a group of diseases characterized by abnormal cell growth involving cell division without control. It is one of the main causes of morbidity and mortality worldwide, with approximately 14.1 million new cases diagnosed in 2012 and 8.2 million deaths, according to the World Health Organization (WHO) latest report on cancer. Different types of treatments are being employed to overcome cancer but their usually lack of selectivity and the development of resistanceresult in limited efficacy or ineffectiveness of the therapies. For these reasons, the seeking of new treatment options for this disease is necessary representing antitumour hybrid combinations apromising approach. This review aims to provide a synopsis into Anticancer Hybrid Combinations involving terpenoids, focusing on their multi-target mechanisms of action and synergistic effects. Antitumor hybrid combinations are the therapeutic combination of synthetic drugs with chemically defined constituents from plants (secondary metabolites) aiming to increase the pharmacological activity of the formulation and, simultaneously, reducing the toxic side-effects of the drugs, interaction known as synergy. The secondary metabolites used in these combinations are mainly plant-derived phenolic compounds and terpenoids, which are the focus of the present work. Their multitarget mechanisms are explained by some examples. Antitumour hybrid combinations are a hopeful therapeutic strategy to reduce cancer resistance todifferent treatments and minimize adverse effects, while simultaneously, showing selectivity to tumour cells and potentiate the activity of the drug that make them an interesting prospective optionto cure cancer.

P-093 – Development of Calcium-Independent Daptomycin Derivatives to Inhibit Antibiotic-ResistantBacteria

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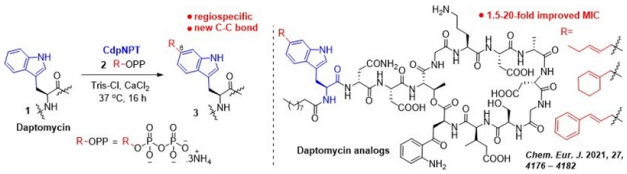
Daptomycin (1) is an FDA-approved calcium-dependent antibiotic for the treatment of skin and skin- structure infections. However, recent reports have shown rise in the resistance levels against daptomycin.The objective of this study is to develop daptomycin derivatives that are active against 1-resistant strainsusing a chemoenzymatic

method. Here, we synthesized and purified a library of diverse alkyl and aryl pyrophosphates 2. We used 2 to modify the tryptophan residue of daptomycin using a promiscuous prenyltransferase enzyme. Consequently, we achieved highly efficient regiospecific Trp-modified DAP analogues 3 with 1.5–20-fold improved activity against daptomycin-resistant strains. The new analogs seem to have a unique mechanism of action that is independent of calcium in contrast to the parent 1.



P-094 – Metabolomic Approach Using LC-MS/MS Analysis and Molecular Networking to Follow Upbioactive Constituents of *Calophyllum inophyllum* Nuts (*tamanu*) during Drying Process

Émilie Stierlin[1], Raimana Ho[1], Stéphane Greff[2], Gaëtan Herbette[3], and Phila Raharivelomanana[1]. [1]EIO,UMR 241, UPF, BP 6570, 98702 Faa'a, French Polynesia, [2]IMBE CNRS IRD, AMU-AU, rue de la Batterie des Lions, 13007 Marseille, France, [3]AMU, CNRS, Centrale Marseille, FSCM, Spectropole, 13013 Marseille, France.

Tamanu oil, obtained from the nuts of *Calophyllum inophyllum* L. (Calophyllaceae), was traditionallyused to cure various skin problems and ailments in French Polynesia. Nuts and containing oil are alsoused for skin care. Since the drying of nuts is an important stage for oil preparation, the objective of our study was to develop an analytical method to evaluate oil quality during nuts drying process following different drying parameters. Using a metabolomic approach combining LC-MS/MS analysisand molecular networking, the obtained data revealed differences in the metabolites chemical classes occurring in resulting oils. For the first time, our study provides new findings regarding the occurrenceand evolution of the metabolites in *tamanu* nuts during the drying process. The developed method provided a powerful analytical tool aiming a better identification of bioactive components formed in *tamanu* nuts during drying process and will be helpful to produce high quality oil for a natural active cosmetic ingredient. An efficient metabolomic approach was implemented to identify markers inducingvariability in chemical composition during drying process of nuts. Thus, this set-up analytical methodsuccessfully applied in *tamanu* could be used to the study of metabolites of a wide range of plants.

P-095 – Genome Mining for Novel Nucleosides in *Streptomyces*

Ola Pasternak[1] and David L. Zechel[1], [1]Department of Chemistry, Queen's University, Kingston, Ontario

The fluoronucleoside nucleocidin is a derivative of adenosine that contains biosynthetically rare 4′- fluorine and 5′-*O*-sulfamoyl substituents (1). The carbon-fluorine bond in nucleocidin is of interest froma biosynthetic perspective as this substitution requires an unusual sequence of abstraction of the C4′ hydrogen and stereospecific addition of fluoride ion. Both the mechanism and related enzyme(s) which catalyze this reaction are unknown. Moreover, the biosynthetic route to the 5′-*O*-sulfamoyl group has yetto be identified. Nucleocidin was discovered in 1952 in cultures of *Streptomyces calvus*. In 2015, a putative cluster containing 23 genes was identified (1). A genome mining approach using 16S rRNA sequences was used to identify new *Streptomyces* producers of nucleocidin and two additional unknown fluoronucleosides in 2019 (2). These new organisms produce fluoronucleosides at much higher titres, facilitating genetic studies. A sulfotransferase and two sulfatases are encoded within the gene cluster, andare hypothesized to play a role in biosynthesis of the sulfamate. Knockout studies of these genes, and several others within the cluster, were performed to determine their effect on biosynthesis. Furthermore, these genes and a glycosyltransferase encoded within the cluster were used as 'marker genes' to guide genome mining and discovery of novel glycosyl and sulfamate containing nucleosides. Recent work on characterizing the new nucleosides and secondary metabolite profiles of gene knockouts will be presented.References : (1) Zhu, X. M., *et al*. *ChemBioChem* 2015, *16*, 2498–2506. (2) Songya Zhang, A.R. Ola Pasternak, *et al*. *J. Biotechnol.* 2019, *292*, 23-31.

P-096 - Bioassay-Guided-Fractionation and MS/MS Molecular Networking of a Marine Cyanobacterial and Brown Algae Extract from Puerto Rico with SARS-CoV-2 Antiviral Activity.

Victoria M. Casimir-Montán[2], Marie L. Matos-Hernandez[1], Grayce Dyer[1], Chris Morales[2], Troy Messick[3], Ian Tietjen[3] and Eduardo J. E. Caro-Diaz[1]. [1]Department of Pharmaceutical Sciences, School of Pharmacy, University of Puerto Rico-Medical Sciences Campus, San Juan, PR 00935. [2]University of Puerto Rico, Rio Piedras. [3]The Wistar Institute, University of Pennsylvania 3601 Spruce St, Philadelphia, PA. 19104.

COVID-19 is an ongoing pandemic caused by severe acute respiratory syndrome (SARS-CoV-2) and, to date, there have been more than 165 million reported cases. Even though multiple vaccines have been developed, much attention is being devoted to developing small-molecule therapeutic agents to treat and/or prevent SARS-CoV-2 infection. We have recently embarked in a project that has identified several marine algae extracts that inhibit well-described molecular targets of SARS-CoV-2, specifically ACE-2/Spike interaction and the main protease (Mpro), providing potential antiviral leads for COVID-19 drug discovery and development. We report a bioassay-guided-fractionation of a cyanobacterial extract (yet to be identified) and brown algae (*Lobophora variegata*) along with chemical characterization via MS/MS molecular networking, to aid in isolation of natural products.

P-097 – Modeling Synergy in Natural Product Mixtures

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Antimicrobial and antiviral resistance remains to be one of the major health concerns to date, despite the development of several antibiotics and antivirals. Pathogens including some bacteria, fungi, and viruses have learned to resist existing therapies, making treatment very challenging. In many cases such as in rural areas, people may depend on alternative form of medicine, such as herbal remedies in the form of plant-based extracts or decoctions. Understanding the mechanisms of drug resistance opens an opportunity to find alternative ways of treatment. Use of combination therapy has been widely used against drug resistance and it is widely believed that complex mixtures contain constituents that work in concert (synergistically, additively, or antagonistically) to achieve their antimicrobial activity. However, it remains a challenge to predict synergy in complex mixtures using existing models. With this research, we seek to develop a multivaritate statistical model that can be applied to mass spectrometry metabolomics data to identify groups of compounds that exhibit combined biological effects. The model incorporates interaction terms to account for the possibility of synergistic effects. The model is being tested using a mixture that contains a known antimicrobial (berberine) and a known synergist (piperine) in the presence of multiple inactive compounds.

P-098 - An Obligate Peptidyl Brominase Underlies the Discovery of Highly Distributed Biosynthetic Gene Clusters in Marine Sponge Microbiomes

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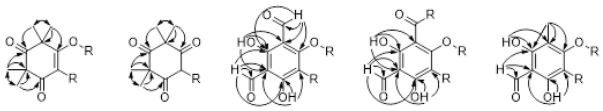
Mining for halogenating enzymes from metagenomes of phylogenetically and geographically dispersed sponges from the Pacific and Atlantic oceans leads to the discovery of a widespread conserved biosynthetic gene cluster (BGC). The BGC encodes a cryptic ribosomally synthesized and post-translationally modified peptide (RiPP) in the family of proteusin. Surprisingly, within a sponge microbiome, more than 50 copies of the BGC are detected in many different generalized bacterial taxa. This broad distribution is in contrast to the fact that bacteria symbionts-derived natural products and the specialized bacterial symbionts are specialized for a sponge host and not shared among phylogenetically distant hosts. To shed light on the cryptic, yet widely distributed proteusin RiPP, we demonstrate the bromination and cyclodehydration of cysteine residues to install azoline heterocycles in proteusin RiPPs by a tryptophan halogenase and a YcaO protein, respectively. This is the first demonstration of these modifications for proteusin RiPPs. The substrate scope of enzymes catalyzing these transformations was demonstrated to extent to other previously described proteusin peptides. The halogenase was found to be a broad-spectrum regiospecific peptidyl tryptophan-6-brominase which possessed no chlorination activity. This research shed light on the conservation of cryptic natural product biosynthetic potential in marine sponges that was not detected by traditional natural product-to-BGC (meta)genome mining.

P-100 - Application of non-uniform sampled HMBC for partial structure elucidation of chemotaxonomically pertinent and bioactive molecules in small sample extracts.

James R. Baxter[1,2], Anthony R. Carroll.[1,2]. [1] School of Environment and Science, Griffith University, Gold Coast, Qld 4222, Australia; [2] Griffith Institute for Drug Discovery, Griffith University, Brisbane, Qld 4111, Australia.

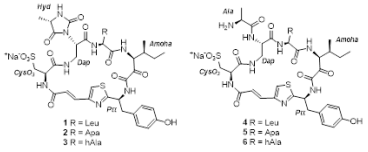
The application of NMR to chemotaxonomic research has been hampered by lower sensitivity and throughput resulting in chromatographic and mass spectrometric methodologies occupying the forefront of chemotaxonomic analyses. With the advancement of NMR field strength, cryogenic probes and the application of non-uniform sampled nD experimentation, these drawbacks have been reduced allowing for the non-destructive and non-discriminate benifits of NMR to be utilized. The application of non-uniformly sampled HMBC on small sample extracts (1.0 – 2.5 g) has allowed the elucidation of partial structures resulting in the identification of biologically active and chemotaxonomically pertinent classes of secondary metabolites between morphologically similar species of Australian eucalypts and Australian marine sponges.



P-101 - Cyclotheonellazoles D-I and DOSY NMR analysis of peptide mixtures from an Australian *Theonella sp.*

Darren C. Holland [1,2], Guy Kleks [1,2], Mark J. Calcott,[3] and Anthony R. Carroll.[1,2] [1] School of Environment and Science, Griffith University, Gold Coast, Qld 4222, Australia;[2] Griffith Institute for Drug Discovery, Griffith University, Brisbane, Qld 4111, Australia;[3] School of Biological Sciences, Victoria University of Wellington, Wellington, New Zealand

Six new thiazole-homologated cyclic peptides (THP) named the cyclotheonellazoles D-I (**1-6**), and the known compounds keramamides A and L, have been isolated from the EtOAc fraction of an Australian *Theonella* sponge species. The cyclotheonellazoles **1-6** have undergone a preliminary investigation into their bioactivities that has shown non-specific inhibition of the $3CL^{pro}$ SARS-CoV-2 protease (COVID-19). We also report the accurate MW prediction of peptides using our recently published diffusion-ordered NMR spectroscopy (DOSY) method, alongside exploration of pseudo 3D DOSY-COSY NMR to decrease signal overlap and provide extra structural information for the dereplication of complex NP mixtures.



P-102 - Exploring the Metabolome of Dietary Supplement Plant Microbiomes

Daniel Zagal[1,2,3], Stefan Green[5], James Graham[1,2,3], Jonathan Bisson[2,3,4], James B. McAlpine[2,3], David C. Lankin[1,2,3], Shao-Nong Chen[1,2,3] & Guido F. Pauli[1,2,3,4], [1]UIC Botanical Center; [2]Pharmacognosy Institute; [3]Department of Pharmaceutical Sciences; College of Pharmacy; [4] Institute for Tuberculosis Research; [5]Research Resource Center (RRC), Genomics Core, University of Illinois at Chicago, U.S.A.

The metabolome of plant microbiomes is undetectable or indiscernible when chemically characterizing entire plants or plant parts. The abundance of compounds produced by a single plant microbiota is below the achievable LOD and, even if detected, are often attributed to its host, the plant. Field collections in Alaska, Colorado and Pennsylvania produced 280 environmental DNA (eDNA) samples and over 300 mixed bacterial cultures. Endophytes and surface samples were collected from root, stem and leaf of popular dietary supplement plants (DSP) and congeners. Statistical analysis of metagenomic data of eDNA samples was performed to determine the presence of species and location-specific microbes. Over 500 plant-associated bacterial strains were isolated to establish a library. A small-scale extraction method is used to acquire LC/MS data from 2mL overnight bacterial cultures. These data allow us to mine the metabolome of bacterial isolates before further biological and phytochemical investigation. Feature analysis of acquired data will be used to prioritize isolates for chemical characterization. Bacterial isolates will be prioritized if they contain alkaloids, chemotaxonomic markers of the plant, or novel compounds. Analysis is carried out using custom and public MS databases.

P-103 - Chemical Diversity of *Streptomyces* sp. (PR35) from Cuatro Cienegas Basin, Coahuila, Mexico

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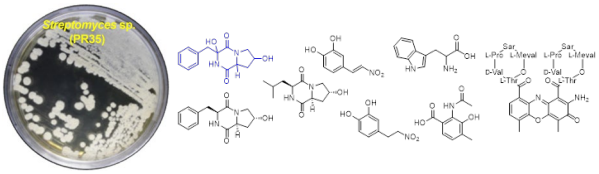
Due to its mosaic of environmental conditions, Cuatro Cienegas Basin (CCB), located in Coahuila, Mexico, concentrates a high number of endemic bacterial species. In our search for novel chemical entities, the study of *Streptomyces* sp. (PR35) led to the isolation of a new dipeptide derivative, cyclo-(4-hydroxyprolinyl)-2'-hydroxyphenylalanine, along with seven known compounds. All structures were stablished by NMR and HRMS analysis.



P-104 - Identification of Selective Cytotoxins for Non-Small Cell Lung Cancer Cell Lines

Sahar Hosseinzadeh[1], John B. MacMillan[1], [1] Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA

Non small cell lung cancer (NSCLC) is a leading cause of cancer related deaths in the United States. Diversity in the genetic lesions that cause NSCLC cancer is extreme. In consequence, a pressing challenge is the development of drugs that target patient-specific disease mechanisms. To address this challenge, we employed a chemistry-first discovery paradigm for de novo identification of druggable targets linked to robust patient selection hypotheses. In particular, chemical libraries comprised of 200,000 synthetic molecules and ~6500 natural product fractions were profiled across a heavily annotated test-bed of >100 cellular models representative of the diverse and characteristic somatic lesions for lung cancer. To identify novel therapeutic targets, we investigated marine microbial natural products that are cytotoxic against representative members of NSCLC cell lines came out from a high-throughput screen (HTS). We identified three marine bacteria harbor potential bioactive compounds against 27 NSCLC cell lines in the HTS. However, the mechanism of action (MoA) of these compounds is unknown. My initial efforts will be focused on the isolation, chemical and biological characterization and bioinformatic studies of the three marine bacteria. The goal of this project is to characterize MoA and identify molecular targets of the natural products in NSCLC cancer cell lines.

P-105 - Biocatalytical *cis*-Dihydroxylation of Aromatics Yields Relevant Enantiomerically Pure Synthons for Natural Products Preparation

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The dearomatizing *cis*-dihydroxylation of aromatics yield commonly employed synthons for the preparation of natural products and pharmaceuticals.[1] Though, up to day this fascinating reaction cannot be performed chemically in one single step. Actually, such limitation highlights the unique synthetic potential of Rieske non-heme iron dioxygenases, such as toluene dioxygenase (TDO), to circumvent the lack of chemical-driven synthetic strategies.[2] TDO is capable to perform the dearomatizing dihydroxylation of several aromatic substrates, incorporating molecular oxygen directly by harnessing the reductive power of NAD(P)H.[3–5] Herein, we report the enantioselective biosynthesis of cis-dihydroxylated synthons from facile aromatics, employing different TDO-based biocatalyst. Our results illustrate the striking TDO capability to employ readily available substrates such as benzene, naphthalene, 1,2,3,4-tetrahydroquinoline, and 2-phenylpyridine to generate pursued synthons, which can be further employed for the total synthesis of valuable natural products displaying sough-after pharmacological activities. [1] T. Hudlicky, *ACS Omega* 2018, 3, 17326–17340. [2] T. Hudlicky, D. Gonzalez, D. T. Gibson, *Aldrichimica Acta* 1999, 32, 35–62. [3] J. L. Wissner, W. Escobedo-Hinojosa, A. Vogel, B. Hauer, *J. Biotechnol.* 2021, 326, 37–39. [4] J. L. Wissner, J. T. Schelle, W. Escobedo-Hinojosa, A. Vogel, B. Hauer, *Adv. Synth. Catal.* 2021, DOI 10.1002/adsc.202100296. [5] J. L. Wissner, J. Ludwig, W. Escobedo-Hinojosa, B. Hauer, *J. Biotechnol.* 2020, 325, 380–388.

P-106 - A ^{31}P-NMR-Based Method for the Detection of Phosphonate-Type Natural Products

Wendy Escobedo- Hinojosa[1], Alejandra Prieto-Davó[1], Julian L. Wissner[2], Bernhard Hauer[2]. [1]Laboratorio de Ecología Microbiana y Productos Naturales Marinos, Unidad de Química en Sisal, Facultad de Química, Universidad Nacional Autónoma de México, Sisal,Yucatán, México, [2]Department of Technical Biochemistry, Instituto of Biochemistry and*

Technical Biochemistry, University of Stuttgart, Stuttgart, Germany.

Actinomycetes have been recently studied for its genetic potential to synthetize phosphonic acids, a class of natural products with a broad range of sought-after activities [1]. Genomic sequencing approaches have identified a diverse collection of phosphonate biosynthetic gene clusters in several actinomycetes strains [2-3]. In this sense, our aim is to employ genome mining tools to explore the presence of such gene clusters in isolated actinomycetes strains obtained from sinkholes located in the Yucatan's peninsula. Thus, in order to further verify the functionality of the encoded information we need to establish precise and suitable analytic approaches for the analysis of the key phosphonate intermediates occurring along the biosynthetic pathway, leading to phosphonic acids. ^{31}P-NMR is a powerful spectroscopic tool to undoubtedly detect phosphor-containing compounds [4]. An additional advantage is that an external supplementation source of the NMR active isotope is not required, since ^{31}P is highly abundant in nature. Moreover, ^{31}P-NMR spectroscopy has proven more reliable than MS-based analytics for the detection of phosphonates displaying novel structure. Herein, we report a suitable ^{31}P-NMR-based method customized for the direct detection of molecules harboring a phosphonate (P-C bond). [1] Metcalf WW, van der Donk WA. Annu Rev Biochem. 2009;78:65-94. [2] Ju KS, Doroghazi JR, Metcalf WW. J Ind Microbiol Biotechnol. 2014;41(2):345-56. [3] Ju KS, Gao J, Doroghazi JR, Wang KK, Thibodeaux CJ, Li S, Metzger E, Fudala J, Su J, Zhang JK, Lee J, Cioni JP, Evans BS, Hirota R, Labeda DP, van der Donk WA, Metcalf WW. Proc Natl Acad Sci U S A. 2015;112(39):12175-80. [4] Escobedo-Hinojosa, W., Wissner, J. L., Hauer, B. MethodsX, 8, 101285 (2021).

P-107 - Exploring a New Pathway of Exogenous Fatty Acid Incorporation In Cyanobacteria

A. Kahn [1], S. A. C. Figueiredo [1], A. Vieira [1], M. Cuau [1], J. P. A. Reis [1], P.N. Leão [1].[1]Interdisciplinary Centre of Marine and Environmental Research (CIIMAR/CIIMAR), University of Porto, Matosinhos, Portugal.

Fatty acids (FAs) are involved in multiple biological processes and are key metabolites in living organisms. Due to the high energetic cost of FAs biosynthesis, most organisms have evolved mechanisms to incorporate exogenous FAs (eFAs). By doing so, organisms reduce the energetic burden of FAs synthesis and increase their plasticity as to FAs source. Until recently, all characterized FA incorporation mechanisms were reported to involve activation of the FAs by the acyl-acyl carrier protein (Aas). However, our group recently reported a new cyanobacterial enzyme – BrtB – that directly esterifies free FAs with alkyl halide moieties found in the bartolosides. These are a group of abundant dialkylresorcinol glycolipids, whose biosynthesis is encoded by the *brt* gene cluster. We hypothesize that bartoloside esters represent a new system of eFAs scavenging and/or storage. Using cultures of the bartoloside producer *Synechocystis salina* LEGE 06099 supplemented with $^{18}O_2$-labeled FAs, we showed that BrtB esterifies the eFAs without prior activation. Additional experiments showed that perdeuterated eFAs are esterified with the pool of available bartolosides and are not incorporated into membrane lipids in early growth stages. In contrast, the closely related *Synechocystis* sp. PCC 6803, lacking the *brt* cluster, incorporated the deuterium labels into membrane lipids. Knocking out Aas in PCC 6803 abolished this incorporation. These observations confirm that i) the *brt* system indeed has a role in eFA capture and ii) its action precedes that of Aas. However, the role of the esterified bartolosides, the regulation of the *brt* system and its associated cellular locations remain unclear and will be the focus of our future work.

P-108 - Selective α-glucose Inhibition Activity from Taxus Mairei Leaves Polar Extracts

Mon-Der Cho1, Ho-Ni Cheng1, Yang-Chang Wu2,3, Tsong-Long Hwang4,5,6, Fang-Rong Chang1,7. 1Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University, Kaohsiung 807, Taiwan, 2Graduate Institute of Integrated Medicine, China Medical University, Taichung 404, Taiwan, 3Chinese Medicine Research and Development Center, China Medical University Hospital, Taichung 404, Taiwan, 4Graduate Institute of Natural Products, College of Medicine, Chang Gung University, Taoyuan 333, Taiwan, 5Research Center for Chinese Herbal Medicine, Research Center for Food and Cosmetic Safety, and Graduate Institute of Health Industry Technology, College of Human Ecology, Chang Gung University of Science and Technology, Taoyuan 333, Taiwan, 6Department of Anesthesiology, Chang Gung Memorial Hospital, Taoyuan 333, Taiwan, 7Drug Development and Value Creation Research Center, Kaohsiung Medical University, Kaohsiung 807, Taiwan.

Taxus has functions in treatment of diuresis, kidney disease and diabetes in ancient records. *Taxus mairei* (Taiwan yew) branches and leaves are also commonly used in the treatment of diabetes. We use polar extracts to hypothesis the potential active compounds and bioactivities similar as ancient use, water extract. And found the selective anti α-glucosidase activity compared

to Acrabose®, which means the ability to reduce breaks down of starch and disaccharides to glucose. Potential roles to help people cannot avoid carbohydrate use during diet control plan.

Inhibitory effects of compounds on α-glucosidase activity			Inhibitory effects of compounds on α-amylase activity	
Compound	IC_{50} (µg/ml)	Inhibition %	IC_{50} (µg/ml)	Inhibition %
BuOH crude	3.23 ± 0.31	101.65 ± 0.05	30.94 ± 1.12	56.51 ± 3.28
Sotetsuflavone	1.10 ± 0.11	89.89 ± 2.26	>60	38.62 ± 2.17
7,7''-di-Omethylamentoflavone	0.93 ± 0.02	99.9 ± 0.86	>60	40.48 ± 1.45
Amentoflavone	0.96 ± 0.04	91.89 ± 8.87	>60	39.47 ± 0.39
Acarbose	118.70 ± 4.08	91.47 ± 0.19	7.09 ± 0.27	113.83 ± 1.66

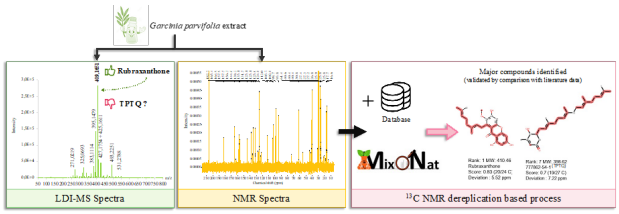
*Percentage of inhibition (Inhibition %) at 60 µg/ml concentration. Results are presented as mean±S.E.M. (n = 3).
*Concentration necessary for 50 % inhibition (IC_{50}).
*Percentage of inhibition (Inhibition %) at 1000 µg/ml concentration. Results are presented as mean±S.E.M. (n = 3).

*Percentage of inhibition (Inhibition %) at 60 µg/ml concentration. Results are presented as mean±S.E.M. (n = 3).
*Concentration necessary for 50 % inhibition (IC_{50}).

P-109 - Matrix-Free Laser Desorption Ionization Mass Spectrometry Assisted by ^{13}C NMR Based Dereplication Strategies Using MixONat Software to Annotate Complex Mixtures

Manon Meunier[1], Séverine Derbré[1], Dimitri Bréard[1], Khalijah Awang[2], Pascal Richomme[1], Andreas Schinkovitz[1]. [1]Univ Angers, SONAS, SFR QUASAV, Faculty of Health Sciences, Dpt Pharmacy, Angers, 49070 Beaucouzé, France. [2]Department of Chemistry, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia.

Comprehensive metabolite identification in complex mixtures is a central aspect in the field of natural products (NPs) research. Depending on the crude extract, long and expensive LC-MS experiments may be required to annotate known NPs[1]. To accelerate the dereplication process and link the advantages of MS and ^{13}C NMR, the authors propose to combine Matrix-Free Laser Desorption Ionization Mass Spectrometry (LDI-MS)[2] with ^{13}C-NMR linked to the MixONat software[3]. As a working example, the exhaustive LDI-MS based chemical fingerprint of *Garcinia parvifolia*, which was acquired within a few seconds, is presented. In a second step, ^{13}C-NMR facilitated the structural confirmation of major NPs (including isomers) as well as the detection of those compounds that were not ionizable by MS.



[1] M. Wang *et al.*, *Nat Biotechnol*, vol. 34, no. 8, 2016 [2] A. Schinkovitz *et al.*, *Anal Bioanal Chem*, vol. 410, no. 24, 2018 [3] A. Bruguière *et al.*, *Anal. Chem.*, vol. 92, no. 13, 2020, https://sourceforge.net/projects/mixonat/

P-110 - Arbuscular Mycorrhizal Fungi (AMF) Impact Metabolites Production by *Anchusa officinalis* L. Under Semi-Hydroponic Cultivation System

E. Tsiokanos[1], A. Cartabia[2], N. Tsafantakis[1], I. Lalaymia[2], A. Termentzi[3], K. Machera[3], S. Declerck[2], N. Fokialakis[1]. [1]Department of Pharmacognosy and Natural Product Chemistry, National and Kapodistrian University of Athens, Athens, Greece, [2]Applied Microbiology, Earth and Life Institute, Université catholique de Louvain, Louvain-la-Neuve, Belgium, [3] Department of Pesticides Control and Phytopharmacy, Benaki Phytopathological Institute, Kifissia, Greece.

In this study, two independent plant growth experiments, associating *A. officinalis* to the AMF *R. irregularis* MUCL 41833, were conducted in a semi-hydroponic (S-H) cultivation system to assess the AMF impact on primary and secondary metabolism during a 9 (Exp. 1) and 30 days (Exp. 2) period of growth. The total fresh weight as well as the AMF root colonization was assessed in both experiments and the differences in the content of primary (PMs) and secondary metabolites (SMs) in shoots and roots as well as in exudates of M (mycorrhized) and NM (non-mycorrhized) plants were evaluated by an untargeted UHPLC-HRMS metabolomics approach combined with multivariate data analysis. The increased plant fitness, in terms of growth rate, observed for M plants in Exp. 1, was followed by an enhance production of PMs, including organic acids and key amino acids. Similarly, SMs production has been significantly affected. 15 di-, tri- and tetra- meric C_6-C_3 derivatives of caffeic acid were mainly up-regulated in the roots of M plants while 4 oleanane-types saponins were overexpressed in the shoots. As a result of AMF symbiosis, herein, we describe for the first time two new salvianolic acid B derivatives and one new rosmarinic acid derivative, all presenting a common substitution pattern. An overexpression of methylated compounds was underlined in M plants suggesting that AMF has the potential to induce production of specific compounds.

P-111 - Screening for Tyrosinase Inhibitors from Actinomycetes; Identification of Trichostatin Derivatives from *Streptomyces* Sp. CA-129531 and Scale Up Production in Bioreactor

K. Georgousaki[1], N. Tsafantakis[1], S. Gumeni[2], I. Gonzalez[3], T. A. Mackenzie[3], F. Reyes[3], C. Lambert[4], I. P. Trougakos[2],

O. Genilloud[3], N. Fokialakis[1]. [1]Department of Pharmacognosy and Natural Products Chemistry, Faculty of Pharmacy, National and Kapodistrian University of Athens, Athens, Greece. [2]Department of Cell Biology and Biophysics, Faculty of Biology, National and Kapodistrian University of Athens, Athens, Greece. [3]Fundacion Medina, Granada, Spain. [4]Givaudan France, Active Beauty, route de Bazancourt 51110 Pomacle, France.

In the frame of MICROSMETICS EU project, 56 actinobacteria strains of global biodiversity were evaluated for their skin-whitening activity using the OSMAC strategy. Among the 614 generated extracts, the EtOAc extract of the strain *Streptomyces* sp. CA-129531 exhibited the most promising activity in cell free and cell-based assays. The scale-up production and chemical investigation of the extract led to the bio-guided isolation of one new trichostatic acid analogue, namely trichostatic acid B, along with six known trichostatin derivatives, four diketopiperazines, two butyrolactones and one hydroxamic acid siderophore. Among them, trichostatin A (TSA) showed six times stronger anti-tyrosinase activity (IC_{50} 2.18 μM) than kojic acid (IC_{50} 14.07μM) used as a positive control. Further kinetic studies, conducted based on the Lineweaver-Burk and Dixon plots revealed that TSA is a mixed-type inhibitor with a Ki value of 6.1 μM. In addition, TSA production started together with the exponential phase of growth of the strain (day 4) and the maximum concentration was reached at day 9 (2.67 ± 0.13 μg/mL). Despite the cytotoxicity of some individual components, the EtOAc extract resulted non-cytotoxic against a panel of cancer cell lines and in BG fibroblasts at the concentrations were it exerted the whitening effect, reassuring its safety and great tyrosinase inhibitory potential.

P-112 - Probing the Formation of the ClpC1/P2/P1 Complex by Anti-TB Ecumicins and Rufomycins

Nina M. Wolf[1,4,5] Hyun Lee[2,3,5] Bin Zhou[1,4,5] Celerino Abad-Zapatero[1,4,5] Gauri Shetye[1,4,5] Scott G. Franzblau[1,4,5] Guido F. Pauli[1,4,5] Sanghyun Cho[1,4,5] [1]Institute for Tuberculosis Research, [2]Biophysics Core at RRC, [3]Center for Biomolecular Sciences, [4]Department of Pharmaceutical Sciences, and [5]College of Pharmacy; University of Illinois at Chicago, Chicago, IL, U.S.A.

The protein degradation complex of ClpC1/P2/P1 is essential for homeostasis in *M. tuberculosis* cells. It is a three-layer complex (6-7-7) known to be disrupted by cyclic peptides (e.g., rufomycins, ecumicins) and acyldepsipeptides (e.g., ADEPs) that alter ClpC1 binding to ClpP2/P1. Earlier reports have shown that ecumicins and rufomycins have varying effects on the ATPase and protein degradation activities of ClpC1. We have now solved the structure of ClpC1-NTD in a complex with the rufomycin analog, RUF-But4, which also affects the ATPase activity. ClpC1-NTD co-crystal X-ray structures are limited to the *N*-terminal domain and do not allow conclusions about possible effects on the full length protein or the ClpC1/P2/P1 complex. This was addressed by developing a surface plasmon resonance assay to study the effects of these potential leads on the formation of the entire ClpC1/P2/P1 complex. While probing the modulation of the complex formation is challenging with such a large system, it is a viable path to gaining further insights on the mode of action of these cyclopeptides. It is necessary to form the complex on the SPR chip, immobilizating the diluted constituents due to the unstable nature of the components. The oligomerization of the full length ClpC1 protein is reduced by ecumicin but not by rufomycin. Using ADEP1 as a control for inhibition of ClpC1 and ClpP2/P1 binding, the interaction of rufomycin and ecumicin can be determined.

P-113 - Evaluation of the Anticancer Potential of a Library of Cyanobacterial Fractions by Combining Metabolomic Tools and Bioactivity Screening

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The Blue Biotechnology and Ecotoxicology Culture Collection from CIIMAR (LEGE-CC) holds 800 strains of cyanobacteria, offering an excellent opportunity for research in natural products. Such a vast biological collection makes it challenging to explore its full potential, so, a semi-automatic natural products library (LEGE-NPL) of cyanobacterial fractions was established. 512 fractions belonging to LEGE-NPL were screened against 2D and 3D cancer cell models, yielding 11 bioactive fractions. The LC-MS/MS data of the fractions of interest, was analysed using MZmine2, GNPS and MetaboAnalyst, for dereplication, annotation and statistical analysis. The combination of bioactivity and metabolomic tools proved to be key in selecting the most promising strains for the isolation of new compounds. Acknowledgments: This research was developed under CYANCAN project PTDC/MED-QUI/30944/2017, co-financed by NORTE 2020, Portugal 2020 and the European Union through the ERDF, and by FCT through national funds and was

additionally supported by the FCT strategic fund UID/Multi/04423/2019.

P-114 - Characterization of Leupeptin Biosynthesis in *Xenorhabdus* Species

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Leupeptin is a broad-spectrum serine/cysteine protease inhibitor isolated from multiple Streptomyces species used for protein purification and autophagy inhibition. Although several biochemical studies in the past suggested an NRPS-like biosynthetic pathway for leupeptin production, there has been no genetic evidence of this claim since then. *Xenorhabdus* and *Photorhabdus* are entomopathogenic nematode symbionts capable of producing various kinds of natural products for infection facilitation and bacterial competitions. After discovering several species of *Xenorhabdus* and *Photorhabdus* produce leupeptin, gene synteny analysis of known bacterial genomes was used, and a highly conserved gene cluster across all *Xenorhabdus* species was identified. Heterologous expression of this gene cluster in *E. coli* BL21 (DE3) successfully recapitulated the production of leupeptin and its intermediates in good yield. Further, we were able to discern the functions of individual genes and produce evidence against previous NRPS pathway claims. Additionally, more than 20 different leupeptin analogs were identified by tandem mass spectrometry including leupeptin B and leupeptin C, and we detected leupeptin in *C. violaceum* extract.

P-115 - Selection and Phytochemical Analysis of Medicinal Herb Crops and Comparison with the EUPharmacopeia Monographs

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The aim of this project is to investigate and select key medicinal herb plants for phytochemical study using a selection methodology and analyse the commercially grown extracts with Irish grown extracts compare and contrast with the EU Pharmacopeia standards[1,2]. Plants studied are German Chamomile *Matricaria recutita*,Roman Chamomile *Chamaemelum nobile* and Marigold, *Calendula officinalis*[2] they was grown and extracted by Modern Botany Ltd in Ireland using commercial seeds from years 2017 through to 2020. Commercial extracts were obtained in the same period, initial results indicate differences in purity, quality,efficacy and adulteration of commercial extracts. The results from the selection methodology[3,4] and phytochemical analysis highlighted further analysis onthese and other Irish grown traditional medicine needs to be undertaken before new forms and routes of active phytochemicals is taken forward for commercial use. [1] Heinrich, M., Kinghorn, A, Phillipson, J., Maizels, D. and Gibbons, S. Fundamentals of Pharmacognosyand Phytotherapy, Second Edition. Edinburgh: Elsevier, (2012) Ch4 p33-48. [2] Young M, Levielle G, Jackson S, In vitro antioxidant activity of Modern Botany™ products and selectednatural product ingredients, Planta Medica, Volume 85, December 2019, Page 1578. [3] S.J.Jackson, P.J.Houghton, S. Retsas, A. Photiou. (March 2000) In Vitro Cytotoxicity of Norviburtinal andIsopinnatal from Kigelia pinnata against Cancer cell lines. Planta Medica v66 (2000) p 758-761 S J Jackson (July 2012) Sausage tree (Kigelia pinnata): An Ethnobotanical and Scientific Review. Herbalgram –The Journal of the American Botanical Council Number 94 p48-p59.

P-116 - Microscopy of the Leaves of *Monteverdia ilicifolia* (Celastraceae) and its Adulterants

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Monteverdia ilicifolia (Mart. ex Reissek) Biral (syn. *Maytenus ilicifolia* Mart. ex Reissek), commonly known as "espinheira-santa", is a medicinal plant native to Brazil and also widely cultivated in the Southern region. Its leaves are popularly used in the traditional medicine to treat ulcers and gastric tumors. Due to similar morphologies, the leaves of several other species, including *Monteverdia aquifolia* (Celastraceae), *Citronella gongonha* (Cardiopteridaceae), *Jodina rhombifolia* (Santalaceae) and *Sorocea bonplandii* (Moraceae), are confused and frequently substituted in the herbal market. The leaves and petioles of the five species were studied by light microscopy and several features, especially the petiole shape and arrangement of its vascular bundles (Table 1), were found to be good anatomical markers for species identification and quality control of *M. ilicifolia*.

Table 1. Comparative anatomy of five species traded as "espinheira-santa".

Petiole anatomy	*Monteverdia ilicifolia*	*Monteverdia aquifolia*	*Citronella gongonha*	*Jodina rhombifolia*	*Sorocea bonplandii*
Shape in cross-section	Oval-shaped with a small convexity and two wings on the adaxial face	Concave-convex with rounded convexity on the abaxial side and with two wings on the adaxial face	Concave-convex with two conspicuous wings on the adaxial face	Flat-convex	Heart-shaped
Vasculation pattern	Medullated vascular cylinder (circular)	Medullated vascular cylinder (in arc)	Medullated vascular cylinder (flat-convex)	Many free bundles arranged in an open arc with three dorsal traces	Many traces arranged in a ring with two medullated bundles

P-117 - Diversity, Distribution and Genomic Context of Dimetal-Carboxylate Halogenases in Cyanobacteria

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Halogenated natural products are frequently isolated from marine organisms and have important applications in the pharmaceutical and agricultural fields. The introduction of halogen atoms is a frequent strategy to modify chemical scaffolds which can greatly modify their bioactivity, bioavailabity and metabolism. Accordingly, halogenating enzymes have the potential to become industrial biocatalysts. Recently, a new halogenase class was uncovered in cyanobacteria – its single biochemically characterized member is CylC, which halogenates unactivated carbon centers during cylindrocyclophane biosynthesis. In this study, we used both genome mining and a PCR-based screening to explore the genetic diversity and distribution of these cyanobacterial dimetal-carboxylate halogenases. We identified a large number of genes encoding CylC-like enzymes in Cyanobacteria but very few in other organisms. The vast majority of homologs were encoded in orphan biosynthetic gene clusters of different architectures and were often associated with type I or type III PKSs, dialkylresorcinol-generating enzymes, fatty-acid activation enzymes, 2-nitropropane dioxygenases or Rieske proteins. Therefore, most of the chemistry associated with CylC-like enzymes is yet uncharted and their BGCs can serve as a starting point for the discovery of new natural products scaffolds.

P-118 - A Tailor-Made NaDESs Development Strategy for the Enhanced Extraction of Hydroxynaphthoquinones from *Alkanna tinctoria* Roots

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The natural hydroxynaphthoquinone enantiomers, Alkannin-Shikonin are well-described pharmaceuticaland cosmeceutical agents. These potent molecules are present in many Boraginaceae roots, and especiallyin the European *Alkanna tinctoria* Tausch roots. Eco-friendly natural deep eutectic solvents (NaDESs) were used instead of organic solvents for the extraction of these metabolites. An extensive screening wasperformed with more than sixty NaDESs to have the best chance to discover one able to extract non- water-soluble compounds, as our target compounds. As a result of multivariate analysis, the most relevantdeep eutectic mixture with the highest extraction efficiency was composed of levulinic acid and glucose (LeG). A high extraction yield to hydroxynaphthoquinone enantiomers was obtained with a ratio of 5:1 (w/w) and 20% of water (w/w). The extraction parameters, including the extraction temperature, the extraction time, and the solid-to-liquid ratio, were statistically optimized using response surface methodology (RSM). Finally, our results revealed the optimized LeG mixture as a remarkable valid greenalternative for the extraction of hydroxynaphthoquinones from *Alkanna tinctoria* Tausch root with an extraction efficiency of 41,72 ± 1, 04 mg/g of dried root powder.

P-119 - *In vivo* Modulatory Effects of Corchorusoside C on Zebrafish Molecular Targets

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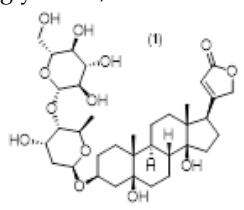
Corchorusoside C (1) is a cardiac glycoside, isolated from *Streptocalon juventas.* The preliminary mechanism of action that corchorusoside C (CC) exhibits in zebrafish has been investigated. The biochemical interactions on the Na^+/K^+-ATPase, NF-◎B and/or PARP signaling pathways were examined to confirm CC as a potential safe and effective drug lead for further studies. Western blot was used to analyze protein expression as indicators for pathway stimulation to



determine the predominant pathway in which CC exhibits its effects together with *in silico* studies. The analysis of protein expression levels of IKKα and IKKβ subunits and docking results suggested that CC acts on the non-canonical NF-◎B pathway in zebrafish. Also, the results of a wound healing assay indicated the ability of CC to suppress cell migration in DU-145 prostate cancer cells after 24 h of treatment. The decreased cell motility seen in this assay correlates with the potential ability of CC to reduce the risk of prostate cancer metastasis. Moreover, the results from a caspase-1 activity assay showed its activation in the presence of CC and indicated that enzyme activity leading to apoptosis can be attributed to caspase-1 activation, suggesting CC affects cytokines IL-1β and IL-18 as well as pyroptosis in DU-145 cancer cells. Thus, CC is showing great potential as a cancer drug lead.

P-120 - New Cyanobacterial Phenolate-type Siderophores with Anticancer Activity Against Cancer Multicellular Spheroid Cultures

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Cyanobacteria have been recognized on the past decades as fruitful producers of secondary metabolites that inspired 4 approved anticancer drugs. Herein, we will present the discovery of four new compounds with phenolate-type siderophore structure with anticancer activity. Thus, organic fractions derived from 27 cyanobacterial strains belonging to the Blue Biotechnology and Ecotoxicology Culture Collection, were screened against cancer multicellular spheroid cultures (MSC). The viability effects on MSC were assessed by acid phosphatase, and general morphology was monitored under fluorescence microscopy using fluorescent dyes (propidium iodide and calcein).One strain reduced MSC viability consistently in both methods. Metabolomic analysis with the Global Natural Product Social Molecular Networking showed the main content of the active fractionsto be a cluster of unknown compounds. Subsequent chromatographic fractionation steps, aided by HRLC-MS and NMR, yielded the isolation of the bioactive compounds. Acknowledgments: CYANCAN project PTDC/MED-QUI/30944/2017, co-financed by NORTE 2020, Portugal 2020 andEU through the ERDF, and by FCT and strategic funds UIDB/04423/2020 and UIDP/04423/2020.

P-121 - Chemometric Analysis for the Classification and Characterization of *Withania somnifera* Extracts Using LC-HRMS/MS

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Non-standardized plant extraction procedures create several challenges in confirming botanical integrity, achieving batch-to-batch reproducibility, and predicting biological activity of botanical supplements. The phytochemical composition of a plant extract will govern its bioactivity, potential health benefits and the outcome of clinical trials. Knowledge of chemical profiles of active extracts, and quantification of marker compounds for standardization purposes is necessary to minimize variability in biological response. *Withania somnifera* (WS) is a medicinal plant used to support resilience to neurological changes associated with aging. WS is receiving attention due to its cognitive, anti-stress, anti-depressant and anxiolytic effects found in preclinical and clinical studies. In this study, WS water and ethanolic extracts were fingerprinted and analyzed by combining liquid chromatography with high-resolution mass spectrometry. More than 10,000 *m/z* molecular features (deconvoluted detected ions) containing MS/MS data were recorded using positive electrospray ion mode acquisitions. The molecular features were used to establish similarities and differences between accessions and extracts using chemometric methods. These data will be helpful in understanding differences in biological activity between the extracts.

P-122 - Desmamides A and B, Novel Glycolipopeptides Isolated from the Cyanobacterium *DesmonostocMuscorum*

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Cyanobacteria are a highly diverse group of photosynthetic ancestral bacteria, which successfully adapted to all environments on Earth with light availability. This reflects their biological and lifestyle plasticity, including the production of a plethora of secondary metabolites, many with potentbioactivities and unique structures. From genome data, we now know that only a small fraction of cyanobacterial natural products has been isolated so far, and that therefore a vast chemical space remains to be discovered from this phylum. In this work, our efforts were directed to the chemical exploration of a group of Nostocalescyanobacteria isolated from cycad roots. Bioactivity screening, coupled with MS-guided isolation using GNPS molecular networking analysis, was used to prioritize strains for natural productisolation. Fractions derived from an organic extract of a *Desmonostoc* strain showed both antibacterial activity and a conspicuous molecular network cluster of MS features that was not found in other cyanobacteria extracts or in several natural products databases. From this strain, two novel glycolipopeptides – desmamides A and B – were isolated, along with several minor analogues. Theirstructures were elucidated using 2D NMR, HRESIMS/MS and chiral HPLC analyses. The compounds, which represent a new class of cyanobacterial glycolipopeptides, showed mild activity in antibacterial and anticancer assays.

P-123 - Discovery and Characterization of New Scytonemin Analogues with Strong UV Absorptionand Antimicrobial Activity

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Microorganisms have developed several protection strategies against the harmful effects of the UV radiation. Among these, cyanobacteria are recognized as a rich source of UV-protective compounds,producing the strong UV-absorbing scytonemins and mycosporine-like amino acids. Unlike mycosporines, scytonemins are exclusively found in cyanobacteria, absorb mainly in the UV-A rangeand form a very restrict family that currently frames only six molecules. In this work, we have identified, isolated and characterized a large number of new scytonemin analogsfrom a Moroccan cyanobacterial mat. The compounds present diverse blue light, UV-B and UV-A absorption properties. Used synergistically, they can strongly absorb in a broad spectrum range. Some of the new scytonemins present faint colors or are even colorless and possess interesting antimicrobialproperties against *B. subtilis*, which were never reported for any molecule of this family. Taking intoaccount their natural origin, high and broad UV absorption, organoleptic properties and bioactivity, these new scytonemins are good candidates for biotechnological applications, including the development of multifunctional sunscreens. Additionally, this work has significantly expanded the structural diversity of the a scytonemin family.

P-124 - Biosynthesis of Chlorosphaerolactylates, Natural Lactylates from Cyanobacteria

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Cyanobacteria produce many natural products (NPs) with potential for pharmacological and biotech-nological applications. Many of these secondary metabolites are synthetized by polyketide synthase (PKS) and non-ribosomal peptide synthetase (NRPS) assembly lines within biosynthetic gene clusters(BGCs). Despite recent advances in genome sequencing technologies, many compounds do not yet have a BGC associated and vice versa. Bridging this gap can reveal unique enzymes, promote com- pound discovery or enable heterologous production of NPs. Lactylates, consisting of a fatty acyl moi-ety and one or more α-keto acid moieties, are a group of emulsifiers widely used in the food and cosmetic industries. Recently, chlorosphaerolactylates, natural chlorinated 1-lactylates, have been re-ported from cyanobacteria. Here, we used stable isotope labelling and bioinformatics to identify a putative PKS-NRPS biosynthetic pathway for the chlorosphaerolactylates. A homology search with a known fatty acyl-halogenase led us to a single candidate BGC in the genome of the producing strain.Stable isotope incorporation experiments with fatty acids and α-keto acids confirmed label incorpo-ration of both putative building blocks into the chlorosphaerolactylates. We show, in silico, that the NRPS confers specificity for α-keto acids instead of amino acids, supporting the connection betweenthe BGC and the lactylates. The discovery of this putative biosynthetic pathway paves the way to microbial production of industrially relevant lactylates through pathway engineering.

P-126 - Metabolomic Investigation into the Cognitive-Enhancing Effects of Centella Asiatica in a 5xFAD Mouse Model of β-Amyloid Accumulation

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Centella asiatica (CAW) is an herb used in Ayurvedic and traditional Chinese medicine for its beneficial effects on brain health and cognition. Our group has previously shown that a water extract of *Centella asiatica* (CAW) elicits cognitive-enhancing effects in animal models of aging and Alzheimer's disease (AD). A recently published study by our group demonstrated a dose-related effect of CAW in the 5xFAD mouse model of β-amyloid (Aβ) accumulation. Here we endeavor to elucidate the mechanisms underlying the effects of CAW in the brain by conducting a metabolomic analysis of cortical tissue from these same 5xFAD mice treated with increasing concentrations of CAW. Tissue was collected from 8-month-old male and female 5xFAD and wild-type (WT) mice treated with CAW at 0, 200, 500, or 1000 mg/kg for 5 weeks and ultra-high-performance liquid chromatography coupled to high-resolution mass spectrometry metabolomics analyses were performed. We assessed relative levels of 120 metabolites in these samples. Our analyses revealed differences in pathway enrichment due to sex, genotype and CAW treatment. We found that pathways related to purine metabolism, nicotinate and nicotinamide metabolism, and glycerophospholipid metabolism were significantly altered by CAW administration. These results are in line with some of our previous findings, using other analytical techniques, regarding specific mechanisms of action of CAW and provide new information about other potential mechanisms of action of CAW in the brain.

P-127 - Structure-Activity Relationship Studies of Arylnaphthalene Lignan Lactones and MolecularDocking Visualization

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Arylnaphthalene lignan lactones, a class of natural products isolated from plants in the Phyllanthaceae family, have been found to display a diverse range of antitumor, anti-inflammatory, and antiviral properties. Through structural manipulation, efforts have been made to increase the potency and probe the mechanism of action of various members of this class, although a definitive protein target has remained somewhat elusive. Previously, the Kinghorn lab reported the isolation of two related series of arylnaphthalene lignan lactones, the phyllanthusmins and the acutissimalignans from *Phyllanthus poilanei* and *Phyllanthus songboiensis*, respectively. These natural products, which showed promising cytotoxicity in a number of cancer cell lines, served as lead compounds for a thorough structure-activityrelationship analysis that led to the development of the highly potent compound PHY-34. PHY-34 has shown low- to sub-nanomolar potency in several solid-tumor cell lines and promising *in vivo* data in an OVCAR8 xenograft model. Subsequent optimization of PHY-34 has focused on selective functionalization of the glycone portion of PHY-34 to probe cell line selectivity, increase stability, and develop mechanistic probes. Comparison of NCI 60 profiles and analysis of *in vitro* efficacy in a series of cell lines developed by Novartis has been carried out, suggesting that these compounds interact with the membrane-associated ATP6V0A2 subunit of the vacuolar ATPase (v-ATPase). Recent molecular docking studies have aided in the visualization of our natural product hit (PHY-D) and synthetic lead (PHY-34) interacting with v-ATPase.

P-128 - Absolute Configuration and Protein Tyrosine Phosphatase 1B Inhibitory Activity of Xanthoepocin, a Dimeric Naphtopyrone from *Penicillium* sp. IQ-429♦

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Protein tyrosine phosphatase 1B (PTP1B) is an active target for developing drugs to treat type II diabetes, obesity, and cancer. Accordingly, as part of a research program directed at findingnon-competitive inhibitors of *h*PTP1B$_{1\text{-}400}$ from Pezizomycotina, the extract of *Penicillium* sp. (IQ-429) was chemically investigated. This study led to xanthoepocin (**1**) isolation. The absolute configuration of **1** was determined to be 7*R*8*S*9*R*7'*R*8'S9'*R* by comparing the theoretical and experimental ECD spectra and by GIAO-NMR DP4+ statistical analysis. Xanthoepocin (**1**) inhibited the phosphatase activity of *h*PTP1B$_{1\text{-}400}$ (IC_{50} value of 8.8 ± 1.0 μM) in a mixed type fashion (docking xanthoepocin (**1**) with a homologated model of *h*PTP1B$_{1–400}$ and molecular dynamics simulations will be discussed). Furthermore, intrinsic quenching fluorescence experiments indicated that **1** behaves like a static quencher of *h*PTP1B$_{1\text{-}400}$ and binds to the enzymewith an affinity constant (k_a) of 3.7×10^5 M^{-1}. Finally, the drug-likeness and medicinal chemistryfriendliness of **1** were predicted with SwissADME.

P-129 - Seasonality Effect on the Yield and Physicochemical Features of Essential Oils of Six *Eucalyptus* Species

Izabel Pietczak Migacz, *Carolina Sabedotti and Jane Manfron. Pharmaceutical Science Graduate Program, State University of Ponta Grossa, Paraná, Brazil*

Eucalyptus is the most cultivated plant genus in the planet, due to its wide economic application. Essential oils of *Eucalyptus* are rich in monoterpenes and are extensively used in pharmaceuticals, perfumes, food flavorants and agrochemicals. This study provides the yield, density and index of refractionof essential oil from six species of *Eucalyptus*: *E. badjensis* Beuzev. & Welch, *E. benthamii* Maiden & Cambage, *E. dunnii* Maiden, *E. grandis* W.Hill, *E. globulus* Labill. and *E. saligna* Sm. The leaves were collected seasonally from the same agricultural environment. The essential oils were extracted by hydrodistillation. The lowest and highest essential oil yields were harvested, respectively, in winter and summer for all species. *Eucalyptus badjensis* showed the highest yield (2,43+/- 0,11%) in summer, whereas, *E. grandis* presented the lowest (0,7 +/-0,3 %) in winter.The density was higher for *E. grandis* (1,14 g/ml) collected in summer while it was lower for *E. badjensis* (0,89 g/ml) collected in summer. The index of refraction is the highest in *E. benthamii* (1,4745), whereas lowest in *E. badjensis* (1,4509). It was observed that the yield and the physicochemical characteristics have influence of seasonality, since this was variable throughout the year.
Reference: Migacz, Izabel Pietczak et al. Comparative leaf morpho-anatomy of six species of *Eucalyptus* cultivated in Brazil. Revista Brasileira de Farmacognosia. 2018, v. 28, n. 3.

P-130 - Daphne Members as Potential Myeloperoxidase Inhibitors

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Because several plants have provided useful anticancer drugs, we recently carried out a random screening for selective anticancer activity of plants collected in Andalusia (Spain). We found that the extract from the leaves of *Daphne laureola* L. (Thymelaeaceae) possesses a strong anticancer activity against two acute promyelocytic leukemia cell lines (NB4 and HL60), with IC50 values between 30 and 50 ng/mL. Because there is an interplay between cancer and inflammation, and anti-inflammatory drugs, such as NSAIDs, induce apoptosis in a variety of cancer cells, we decided to evaluate the anti-inflammatory activity of *Daphne laureola* L. In this study, we have evaluated the inhibitory activity of *Daphne laureola* L., and *Daphne gnidium* L. on the enzyme myeloperoxidase (MPO). MPO is a key enzyme in inflammation, and it is known that NB4 and HL60 cells constitutively have high levels of MPO protein and mRNA. HL60 cells were treated with the extracts or Indomethacin for 24 hours and, after cell lysis, MPO activity was determined by the ability to oxidize Orto-Dianisidine. Both plant extracts inhibited MPO activity in a dose-dependent manner, and the IC50 values were approximately 1 μg/mL. Our results suggest that the anticancer activity of these species may be related with their anti-inflammatory activity.

P-132 - Eupenifeldin Induces Differential Cell Death Events in High-Grade Serous Ovarian Cancer Cell Lines

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High-grade serous ovarian cancer is the most common and aggressive form of ovarian cancer. There is an urgent need to develop novel drugs that could improve patient outcomes. Eupenifeldin was recently produced in large yields by the Oberlies lab, which allowed for extensive biological characterization. In three high-grade serous ovarian cancer cell lines (OVCAR3, OVCAR5, OVCAR8), eupenifeldin was found to have an IC_{50} of less than 10 nM, with a therapeutic index 10X lower in fallopian tube secretory epithelial cell lines (FTSEC), indicating that there may be a specificity for tumor cells. In a clonogenic assay, incubation of 10 nM eupenifeldin for 8 hours was found to significantly hinder the ability of these cells to undergo expansion 5-fold suggesting cytotoxicity. Staining by annexin-V/propidium iodide assay was performed and showed eupenifeldin induced early apoptotic events. Western blot of OVCAR3 confirms cleavage of PARP; results for OVCAR5 and OVCAR8 did not exhibit these findings. OVCAR5, however, was found to induce autophagy as indicated by LC3B. Future studies will test the changes in the mitochondrial membrane potential as a factor of mitochondrial integrity in OVCAR3 as well proteomic sequencing to better understand how proteins are regulated to induce cell death in OVCAR3, OVCAR5, and OVCAR8 cells upon treatment with eupenifeldin. Natural products with nM activity that induce differential cell death may provide new therapies for ovarian cancer.

P-133 - Antiproliferative Isothiazolonapthaquinone Alkaloids from Freshwater Cyanobacterium *Nostoc* sp. UIC 10771 Induce Nuclear Accumulation of FOXO3a in Human Ovarian Cancer

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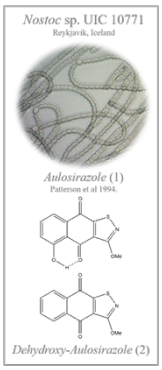
Aulosirazole (1), a previously described solid-tumor selective cytotoxin, was identified in the exometabolome of *Nostoc* sp. UIC 10771, a freshwater cyanobacterium isolated from soil collected in Reykjavik, Iceland. Bioassay and NMR-guided isolation led to the discovery of a novel, dehydroxylated analog of aulosirazole (2) within medium extracts. Both compounds have been evaluated against human ovarian cancer cell lines, demonstrating an IC_{50} of 0.304 and 0.585 μM against the OVCAR3 cell line, respectively. High grade serous ovarian cancer is characterized by low FOXO3a expression and currently lacks many therapeutic options. Here, aulosirazole (1) demonstrated strong nuclear accumulation of FOXO3a in the OVCAR3 cell line using Western blot analysis. This activity was visualized using fluorescent microscopy, where the accumulation of FOXO3a was observed in OVCAR3 using GFP-labeled reporters and DAPI staining. In the future, the bioactivity of (1) will be evaluated *in vivo* using a hollow fiber assay in transgenic mice. The novel analog (2) offers greater solubility while retaining bioactivity and therefore may provide a new avenue for drug lead development of this intriguing compound.



P-134 - Calcium Oxalate Crystals in Carquejas (Baccharis spp., Asteraceae)

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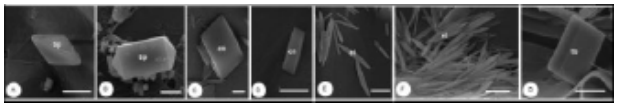
The occurrence and morphotype of calcium oxalate (CaOx) crystals in plants are taxon-specific and aid species identification. In a microscopy study of five Baccharis species commonly known as "carqueja", several morphotypes of CaOx crystals were observed. Bipyramidal crystals were found in Baccharis articulata, B. crispa, B. junciformis and B. milleflora. Whereas, cuneiform, styloid and tabular crystal were observed in B. articulata, B crispa, B. genistelloides and B. milleflora. This study provides an illustrated account of different types of CaOx crystals foundin carquejas.



(a, b) Bipyramidal; (c, d) cuneiform; (e, f) styloid; (g) tabular. [a: B. junciformis; b,c: B.milleflora; d,f: B. crispa; e,g: B. articulata. Scale bar: a, d-g: 5μm; b, c: 2μm]

P-135 -Mass Query Language - Mining Public Mass Spectrometry Repositories for New Natural Products

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Mass spectrometry is a technique to measure analytes in complex mixtures. It is sensitive, specific, and high throughput. Untargeted mass spectrometry techniques are able to capture thousands of molecules within minutes for a single analysis, with >150K MS files of samples from diverse environments and organisms publicly available. The current state of the art to minefor patterns in mass spectrometry data fall under two categories 1. User interfaces built into vendor or open source software, 2. Writing custom software to extract data. 1. Suffers from lackof portability and lack of expressiveness, 2. Suffers from inflexibility and accessibility. Further, there exist general query languages such as SQL that facilitate access of data in relational databases. Much previous work has helped to put mass spectrometry data into appropriate SQL formats, however, the primary limitation is the difficulty in framing massspectrometry questions into SQL and for the community that does not know the language. We introduce here a new language, the Mass Query Language, that aims to solve these concernsthat is 1. Powerful query abilities, 2. Concise, 3. Understandable by domain experts, 4. Scalablefrom single file up to repository scales. This language provides the ability for users to mine for distinctive tandem mass spectrometry fragmentation patterns, neutral losses, in-source fragmentation, and isotopic patterns to quickly find molecules of interest in complex and rich datasets. This tool empowers natural products researchers and mass spectrometrists alike to quickly sort through hundreds of thousands of samples and billions of spectra to aid in the discovery of novel molecules.

P-136 - Sesquiterpene Lactones and Flavonoids as α-Amylase Inhibitors from Asteraceae Plants

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Untargeted metabolomics has the potential to aid the determination of bioactive specialized metabolites from biological samples without the need for isolation, thereby fast-tracking the drug discovery process.
Of the Asteraceae plants investigated for α-amylase inhibition, 37 inhibited fungal α-amylase including *Silybum marianum*, *Acanthospermum hispidum* and *Tithonia diversifolia* and 12 inhibited porcine pancreatic α-amylase with the most active being *S. marianum*, *Baccharis gaudichaudiana* and *Eremanthus veadeiroensis*. All extracts were analyzed by LC/UV/MS and subjected to metabolomics analyses. These analyses indicated sesquiterpene lactones, tithonin and tagitinin C and flavonoids, isosilybin, rutin and tiliroside have potential for multiple mechanisms of antidiabetic action. Our study provided further evidence for application of metabolomics for the rapid determination of bioactive plant specialized metabolites, in this case, for modulating hyperglycaemia.

P-138 - MS/MS Molecular Networking Metabolomics Profiling, Diversity, and Bioactivities of the Bacteria Associated with the Fungus-Growing Ant *Acromyrmex echinatior* Ecosystem

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The fungus-growing ant-microbe symbiosis includes an intricate network of microbial partners (e.g. Basidiomycota, Actinobacteria, and Ascomycota).

The chemicals produced by microbial communities have several functions and are crucial to understanding the stability and ecology of these ecosystems, nevertheless, the information about the chemistry of fungus-growing ant-microbe symbiosis is limited. This study brings insights into the secondary metabolites produced by the bacterial community associated with the fungus-growing ant *Acromyrmex echinatior*. Moreover, we explore the diversity, composition, and biological activities of the culturable bacteria that are part of this ecosystem. Results of the taxonomic study indicated the presence of three phyla, eleven families, and fifteen genera. Antagonistic assays revealed that over 50% of the bacterial strains inhibit the specialized pathogen *Escovopsis weberi*, and 17% showed antibacterial activity including inhibition of the methicillin-resistant *Staphylococcus aureus* (MRSA). The metabolomic profile outcome with identification of several molecular families, belonging to the prodigiosins, indole, aromatics, siderophore, diketopiperazines, polyketides and lipopeptide chemotypes. We suggest that the rich diversity of secondary metabolites used to control *Escovopsis weberi* infections of the colony and to regulate the associated microbes in this ecosystem.

P-140 - Antagonistic Co-culture of *C. albicans* and Cyanobacteria *Moorena producens* Leads to the Upregulation of a Novel Linear Depsipeptide

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Candida albicans is the most prevalent fungal pathogen currently affecting humans through yeast infections and the thrush; the latter can be a painful opportunistic infection for patients living with HIV. Research into novel antifungals is critical to defending against the emergence of drug resistant strains, and natural product research can provide directed compounds perfected by nature for this problem. Cyanobacteria, commonly known as blue-green algae, are a rich source of biologically relevant molecules including compounds showing antifungal activity, such as tanikolide. The production of biologically relevant natural products has shown to be induced through antagonistic co-culture, such as in the case of the emericellamides A and B from the marine fungus *Emericella sp*. Performing a co-culture of *C. albicans* and the marine filamentous cyanobacteria *M. producens* JHB, a previously unreported secondary metabolite was upregulated, and was subsequently isolated and characterized. The complete biosynthetic gene cluster analysis of this linear depsipeptide was found in another strain of *M. producens* PAL, which is reported as annotated by antiSMASH with structural hints from NMR analysis. For the total synthesis I have optimized the peptide couplings, a diazotization, and methylations, and this will allow for further antimicrobial testing and determination of its absolute configuration.

P-142 - Exploring the Chemical Composition and Anticancer Potential of *Bellevalia longipes* Post. (Asparagaceae)

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Twenty-one compounds were isolated and identified from the bulbs of *Bellevalia longipes,* a wild plant that is commonly grow in Jordan. Of these, thirteen were known while eight were identified as new compounds in the homoisoflavonoids family. These were named as: 8-dehydroxy-5-*O*-demethyl-6-hydroxyscillapersicone (**7**), 6-methoxyscillapersicone (**9**), 5-*O*-demethyl-6-methoxyscillapersicone (**10**), 8-*O*-methylscillapersicone (**11**), 4'-*O*-methylscillapersicone (**14**), 4',8-*O,O*-dimethylscillapersicone (**15**), 3'-*O*-methylscillapersicone (**16**), and 8-demethoxy-3-hydroxyophiopogonanone A (**18**). The structure elucidation of these were determined via 1D and 2D NMR data analyses along with HRMS data. The absolute configuration was assigned using ECD data analysis. Out of the **21** compounds, six showed potent cytotoxic activities at the micromolar level against breast (MDA-MB-231), ovarian (OVCAR-3), and/or melanoma cancer cell lines (MDA-MB-435). Visualizing the cytotoxic properties exhibited by these compounds allow for better speculation of their structure-activity relationship (SAR map).

P-143 - Discovery of Novel Peptide Natural Products from Freshwater Sponge Associated Bacteria

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Marine sponges and their associated bacteria have long been a prolific source of biologically active natural products. However, freshwater sponges and their associated bacteria have seldom been explored for their ability to produce therapeutic leads. In this study we used SCUBA to collect 28 freshwater sponges from the Apostle Islands in Lake Superior. DNA sequencing was employed to classify the sponges into three different genera. Using the bioinformatics pipeline IDBac, we prioritized 127 freshwater sponge-associated bacteria to create a library with minimal taxonomic and chemical redundancy. To date, 23 of the prioritized 127 bacterial isolates have been screened in single dose assays against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Of the 23 isolates, 3 have displayed antibacterial activity. The active isolates were analyzed using UPLC-Q-TOF-MS which shows that peptidic molecules are present in the active fractions. 1D and 2D NMR experiments are required to elucidate and confirm the structure of these molecules.

P-144 - Discovery of Novel Natural Products from Anaerobic Gut Fungi

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Omics analyses have revealed a wealth of potential, novel natural products in four culturable anaerobic gut fungal species of class Neocallimastigomycetes: *A. robustus*, *C. churrovis*, *N. californiae*, and *P. finnis*. *In silico* predictive tools for genome mining identified 146 genes encoding biosynthetic enzymes for a variety of natural products, including nonribosomal peptides and polyketides. During standard laboratory growth, 26% of predicted core biosynthetic genes were transcribed, and 30% of predicted gene products were detected with proteomics across the four strains. Liquid chromatography-tandem mass spectrometry performed on fungal supernatants detected 72 potential natural products from *A. robustus* alone, with a putatively identified polyketide-like styrylpyrone (baumin) detected across all four strains. The corresponding data will be presented, as well as descriptions of current efforts to isolate gut fungal natural products and scale up production for characterization.

P-145 - Using Tripartite Communities to Identify Bacterial-Fungal Interactions in the Cheese Rind Microbiome

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Microbiomes have been linked to human health, and interest in how they function has increased recently. Within these microbial communities, many microbe-microbe interactions, such as bacterial-fungal interactions (BFIs), take place that can affect both he microbial community members and the host. For example, food contamination with the food borne pathogen *Escherichia coli* O157:H7 can lead to diarrheaand kidney failure. However, the genetic and molecular mechanisms of action of BFIs affecting the community remain understudied, especially in fermented food microbiomes. Therefore, a simplified modelsystem such as the cheese rind microbiome is important for the study of microbe-microbe interactions andprovides insight into potential health benefits associated with consumption of this highly popular fermentedfood. The cheese rind microbiome is comprised of 10-12 microbial species, most of which are well conserved across different geographic locations worldwide. They have also shown taxonomic similarity to microbes found in various human microbiomes and are easily cultured in a laboratory environment, makingthe cheese rind an ideal model system for studying BFIs. Previously, pairwise and large multi-species co- cultures have been used to identify BFIs in the cheese rind microbiome and benchmark microbial viability in the

cheese rind microbiome, respectively. However, BFIs in pairwise co-cultures may not be indicative of BFIs in more complex communities. Conversely, it is difficult to attribute interactions to species in large co-cultures due to the number of variables that could be taken into consideration. Therefore, I am using tripartite fungus-bacterium-bacterium co-cultures as the next step in community complexity to investigate specialized metabolites responsible for BFIs. Here, a native cheese rind fungus and bacterium is grown oncheese curd agar with a second native bacterium (i.e. *Pseudomonas psychrophila* JB418) or an analoguefor food borne pathogens (i.e. *Escherichia coli* K12). Metabolite profiles generated using matrix-assisted laser desorption/ionization-trapped ion mobility-time-of-flight imaging mass spectrometry (MALDI-TIMS- TOF IMS) and liquid chromatography-TIMS-tandem mass spectrometry (LC-TIMS-MS/MS) are used to identify secondary metabolites responsible for BFIs for further structure elucidation.

P-146 - Validation and Testing of the NaPDoS2 Webtool: Detecting and Classifying Ketosynthases in Genomic Space

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Advanced genomic sequencing approaches allow us to discover and identify novel microbial taxa without the need to cultivate them, as well as make predictions about their functional and chemical capabilities. Specialized metabolites, including polyketide synthases (PKSs) and nonribosomal peptide synthetases (NRPSs), are produced by a wide variety of microbes for ecological survival strategies. To synthesize these compounds, gene clusters containing the necessary ketosynthase (KS) and condensation (C) domain biosynthetic machinery are needed. NaPDoS ("Natural Product Domain Seeker") is a web-based analysis tool that (1) detects and extracts the key KS and C domains from sequencing data, (2) classifies the domains for broader predictions about the biosynthetic gene clusters in which they reside, and (3) provides phylogenetic context to help users identify new functional diversity and determine confidence of the classification. Here, we present the validation and testing of the updated NaPDoS2 webtool. The webtool has undergone major revisions including the classes of domains that can be detected and classified, as well as incredible improvements for users to analyze all types of genomic sequencing data. Our results highlight how the capabilities of NaPDoS2 support a wide variety of analyses. Future applications of NaPDoS2-mediated analyses will demonstrate how the tool can leverage an array of genomic data to provide further insight into the diversity of PKS specialized metabolism.

P-147 - Centella asiatica and Withania Somnifera Improve Resilience in Older Drosophila Melanogaster Flies

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Centella asiatica (CA) and *Withania somnifera* (WS) are botanicals reputed to promote resilience to neurological changes that occur during aging. Their efficacy was explored here in *Drosophila melanogaster* (DM) fruit flies. Plant material was authenticated and analyzed using chromatographic methods. DM were fed a water extract of CA (CAW; 10 mg/ml), a CAW fraction (A1; 1.15 mg/ml), or caffeoylquinic acids (CQA) or triterpenoid (TT) constituents of A1, or a water extract of WS (WSAq; 0.5 mg/g or 5.0 mg/g). CAW and A1 significantly improved phototaxis (an index of locomotion performance and reaction time) in both female and male DM aged 4 to 6-weeks-old. However, only female 4-week-old DM fed CQA or TT performed significantly better than controls. CAW improved phototaxis score deficits that occur during normal aging and at younger ages. Both TTs and CQAs contribute to CAW's activity in female DM. WSAq (0.5 mg/g, but not 5 mg/g) significantly improved phototaxis in 6-week-old female DM but significantly decreased phototaxis in 4-week-old DM of both sexes compared to controls. WSW (0.5 mg/g) may be beneficial for locomotion and reaction times in 6 weeks and older female DM but may not be beneficial when used in younger ages or in a higher dose.

P-148 - Discovery of the Non-Proteinogenic Amino Acid Homoarginine Provides a Key to Unlock Cryptic Natural Product Biosynthetic Pathway

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L-Homoarginine (hArg) is a non-proteinogenic basic amino acid with one additional main chain methylene (CH_2) group than the proteinogenic amino acid L-arginine (arg). The structural similarity of L-hArg to L-arg, makes this endogenous metabolite a surrogate substrate for Nitric Oxide Synthase (NOS) and leads to increased production of nitric oxide (NO), which facilitates vasodilation. Therefore, low serum concentrations of L-hArg in humans serves as a biomarker for increased cardiovascular risk and mortality.[1] In the marine organisms, hArg has so far evaded discovery. In our previous published work, we have provided evidence for the presence of hArg in marine sponges with natural products harboring the aminoimidazole propylamine moiety.[2] Our hypothesis for detecting hArg in the metabolomes of sponges with these natural products was based on previous reports of radiolabeled feeding experiments.[3] In this study we aim to assign the stereochemistry at the Cα position of hArg and provide its absolute quantification across phylogenetically and geographically disparate marine sponges. We have used Marfey's derivatized L- and D-hArg standards to compare against the hArg in sponge extracts. These derivatized hArg molecules are diastereomers and can be resolved by reserved phased column chromatography. To avoid matrix effects from leaching into quantitation data, we have used the in-house synthesized isotope labelled hArg as internal standard for LC-MS/MS analysis. References: 1.Pilz, S.; Meinitzer, A.; Gaksch, M.; Grübler, M.; Verheyen, N.; Drechsler, C.; Hartaigh, B. ó.; Lang, F.; Alesutan, I.; Voelkl, J.; März, W.; Tomaschitz, A., Homoarginine in the renal and cardiovascular systems. *Amino Acids* **2015,** *47* (9), 1703-1713. 2. Genta-Jouve, G.; Cachet, N.; Holderith, S.; Oberhänsli, F.; Teyssié, J. L.; Jeffree, R.; Al Mourabit, A.; Thomas, O. P., New insight into marine alkaloid metabolic pathways: revisiting oroidin biosynthesis. *Chembiochem : a European journal of chemical biology* 2011, *12* (15), 2298-2301.3.Genta-Jouve, G.; Thomas, O. P., Biosynthesis in marine sponges: the radiolabelling strikes back. *Phytochemistry Reviews* 2013, *12* (3), 425-434.

P-150 - Memory Enhancing and Metal Chelating Activities of Clerodane Diterpenoids Isolated from *Tinospora cordifolia* (Willd.) Miers ex Hook. F. & Thoms

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by cognitive impairment, which consequently leads to decrease in the quality of life. There are no effective drugs for the management of AD. Inhibition of acetylcholinesterase (AChE) is considered a promising strategy for AD management. This study, was therefore, aimed at isolating and identifying inhibitors of AChE from selected medicinal plants identified from Nigerian ethnomedicine. *Tinospora cordifolia* stem (FHI 112287) crude extract was successively partitioned into *n*-hexane, dichloromethane, ethyl acetate and aqueous fractions. Ethyl acetate fraction was subjected to chromatographic separations to isolate and purify bioactive compounds. The isolates were evaluated for AChE inhibitory activity using Ellman colorimetric *in vitro* assay using eserine as standard. *In vitro* analyses were used to evaluate the metal chelating potential of the compounds. Structures of isolated compounds were determined by spectroscopic analyses. Molecular docking was done using software (MOE 2015.010) to anticipate the binding affinity between drug candidates with protein targets using PDB ID: 10CE (Acetylcholinesterase). Data were analysed using One way ANOVA followed by Dunnet's Multiple Comparison test at $\alpha_{0.05}$ Three clerodane diterpenoid namely; 8-hydroxycolumbin, tinosporide and columbin were isolated. Columbin (IC_{50} of 1.29±0.17mg/mL) and 8-hydroxycolumbin (IC_{50} of 1.33±0.04 mg/mL) gave the promising AChE inhibitory activity at 1 mg/mL compared to eserine (IC_{50} of 0.53±0.34 mg/mL). 8-hydroxycolumbin also had the highest metal chelating potential (IC_{50} = 0.5672±0.00 mg/mL) compared to EDTA (IC_{50} of 0.05±0.11 mg/mL). Molecular docking revealed hydrophobic and hydrogen bonding interactions among tested compounds and the active site of AChE residue, which indicates their ability to mitigate symptoms associated with AD. Columbin and 8-hydroxycolumbin showed promising acetylcholinesterase inhibitory activities. The two biomolecules could serve as potential leads for novel drug development for the

for the management of Alzheimer's disease. Keywords: Alzheimer's disease, Acetylcholinesterase inhibition, Columbin, 8-hydroxycolumbin.

P-151 - Developing Blasticidin S and Other Peptidyl Nucleosides into a New Generation of Antibiotics to FightAntimicrobial Resistance

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Antimicrobial resistance has been declared one of the top 10 global public health threats facing humanity. In the U.S.alone, there are more than 2.8 million antibiotic-resistant infections and more than 35,000 deaths as a result of these infections each year and the occurrence of resistance is increasing. One approach to develop new antimicrobial agentsis to repurpose orphaned antibiotics – agents that were never developed for clinical use because they are toxic or possess non-drug-like qualities (i.e., poor pharmacokinetics). Resistance to these antibiotics is often less prevalent since there has been no widespread use. Altering the specificity and functionality of these antibiotics using semi- synthetic derivatization may lead to their development into effective antibiotics. Our approach is two-fold: derivatizecommercially available starting materials using standard organic synthesis techniques and using more novel chemoenzymatic routes.One particularly interesting orphan antibiotic is blasticidin S and it possesses broad-spectrumactivity. Blasticidin S belongs to the peptidyl nucleoside antibiotic family and features a beta amino acid and and amino sugar nucleoside. The proposed biosynthetic pathway for blasticidin S contains a ligase enzyme, BlsI, that couples the amino acid to the nucleoside, and ArgJ, is a peptidyl nucleoside in the arginomycin pathway. Currently, we are generating analogs of blasticidin S with a specific focus on the carboxylic acid of the amino nucleoside and the beta amino functionality on the amino acid, as this is predicted to increase selectivity towards the bacterial ribosome, thus decreasing mammalian toxicity.

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We look forward to seeing everyone at the 2022 ASP Annual Meeting in Charleston!
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