American Society of Pharmacognosy

Annual Meeting

Natural Product Solutions to Global Challenges

North Charleston, SC
July 23 – 28, 2022

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By the 2022 ASP Organizing Committee

Dear Friends and Colleagues, The 2022 Organizing Committee of The American Society of Pharmacognosy (ASP) is delighted to welcome you to Charleston, South Carolina! The Embassy Suites North Charleston Hotel and Convention Center is just minutes from the Charleston International Airport and about 10-15 minutes by taxi to historic downtown Charleston. The sessions will be held in the Convention Center attached to the hotel. The committee has worked tirelessly to create a very unique and diverse ASP meeting with timely topics related to climate change responsiveness, emerging infectious diseases and new technologies, in addition to featuring presentations some of our younger members. A series of pre-meeting workshops on Saturday provide expert training in proteomics, MS, NMR and computational approaches. We would like to extend special thanks to NCCIH, Proctor and Gamble, Corteva Agriscience as well as our sponsors and exhibitors for their generous support for the program. After several years of Zoom meetings, we are looking forward to seeing all of you in person, reconnecting with colleagues and developing productive new relationships during the opening reception, an afternoon taking in the many sites Charleston has to offer and Tuesday evening at the SC Aquarium. Please enjoy an evening or two in Downtown Charleston, taking in the many historical sites as well as the local cuisine. We hope that you find the Charleston Conference intellectually stimulating, the rich history engaging and the local flavors unlike anything you have experienced before.

We want to hear from you #ASP2022

2022 ASP Annual Meeting

Organizing/Scientific Committee

Mark Hamann, Chair (Medical University of South Carolina)
Angela Calderón (Auburn University)
Guy Carter (Biosortia)
Jie Li (University of South Carolina)
Frank Mari (NIST)
Courtney Thomas (South Carolina State University)

Meeting Planner/Registration

Laura Stoll (The American Society of Pharmacognosy)

American Society of Pharmacognosy

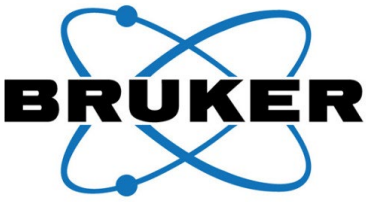
CODE OF CONDUCT

The American Society of Pharmacognosy (ASP) believes that the pursuit of scientific excellence is strengthened by the unique perspectives contributed by scientists from diverse backgrounds. The society strives for an inclusive environment that makes all our members feel included, welcomed and represented. We expect our members to interact with each other in a positive, professional manner, and to conduct themselves with kindness and courtesy. Members participating in discussions at our meetings should remain open-minded to different points of view and opinions and be professional and respectful when expressing dissent.

The ASP will not tolerate threatening, intimidating, or harassing behavior from any individual associated with the society or its events. For the purpose of this policy, harassment means unwelcome behavior directed at another person's sex, race, color, national origin, religion, sexual orientation, gender identity, disability, age, or other status protected under applicable law. For example, harassment can include comments or jokes that focus on gender differences or sexual topics, unwelcome advances or requests for dates or sexual activities, or the use of language or images that demean or degrade others.

Violations to this code of conduct may be reported to Laura Stoll, business manager for the American Society of Pharmacognosy (asphcog@ gmail.com) or Lesley-Ann Giddings (lgiddings@smith.edu) or Christine Salomon (csalomon@umn.edu) Co-Chairs of the ASP Diversity, Equity and Inclusion Committee. By registering for this conference, you have agreed to abide by the code of conduct. The ASP reserves the right to revoke the conference badge of any individual who violates the ASP code of conduct.

Thank you to the 2022 ASP Annual Meeting Sponsors!



Thank you to the 2022 ASP Annual Meeting Exhibitors!

ASP Award Winners

Norman R. Farnsworth Research Achievement Award -
Bradley Moore, University of California at San Diego (2021)
Hung-wen (Ben) Liu, University of Texas at Austin (2022)

Varro E. Tyler Prize
John H Cardellina II, ReevesGroup (2021)
Djaja Djendoel Soejarto, University of Illinois at Chicago (2022)

Matt Suffness Young Investigator Award
Jason Crawford, Yale University (2021)
Laura Sanchez, University of California, Santa Cruz (2022)

Undergraduate Research Award
Margaret Hill, University of Rhode Island
YanZhe Liu, University of CA, San Diego

Research Starter Grant
Jie Li, University of South Carolina

Active Member Travel Grant
Barbara Adaikpoh, University of Illinois at Chicago
Jeffrey Rudolf, University of Florida
Nassifatou Koko Tittikpina, University of Lome (Togo)

D. John Faulkner Travel Award
Carla Menegatti, Virgina Tech

Student Research Award
Ethan Older, University of South Carolina

David Carew Student Travel Award
Richard Tehan, Oregon State University

Jerry McLaughlin Student Travel Award
Hannah Fernandez, University of Illinois at Chicago
Jared Wood, University of North Carolina at Greensboro

Lynn Brady Student Travel Award
Margaret Paige Banks, Virginia Tech
Márcio Barczyszyn Weiss, University of São Paulo
Sandra Bennett, University of North Carolina Wilmington
Ama Boamah, University of Utah

Lynn Brady Student Travel Award Continued
Susan Egbert, University of Manitoba
Kelli McDonald, Auburn University
Zarna Atul Raichura, Auburn University
Emma Stowell, University of Florida **Alex Taylor Swystun,** University of North Carolina Wilmington
Kara Talbott, University of the Pacific

President's Travel Award
Sarah Barr, University of North Carolina Wilmington
Kabre Heck, Auburn University
Caitlin McCadden, University of Florida

Waqar Bhatti Student Travel Award
Erin Marshall, University of Florida

2022 Arthur E. Schwarting Award
An Integrated Strategy for the Detection, Dereplication, and Identification of DNA-Binding Biomolecules from Complex Natural Product Mixtures Hongyan Ma, Huiyun Liang, Shengxin Cai, Barry R. O'Keefe, Susan L. Mooberry, and **Robert H. Cichewicz** *J. Nat. Prod.* **2021**, *84*, 750–761.

2022 Jack L. Beal Award
April L. Risinger, Shayne D. Hastings, and Lin Du. Taccalonolide C-6 Analogues, Including Paclitaxel Hybrids, Demonstrate Improved Microtubule Polymerizing Activities. *J. Nat. Prod.* **2021**, *84*, 1799-1805.

American Society of Pharmacognosy

Annual Meeting
July 23 – 28, 2022
Charleston, SC

Natural Product Solutions to Global Challenges

Program Schedule

Saturday July 23, 2022

8:00 AM – 7:30 PM	**Registration** – *Ballroom Foyer*
9:00 AM – 4:00 PM	**Executive Committee Meeting (Invitation Only)** *Meeting Room 10 & 11*
9:00 AM – 12:00 PM	**WORKSHOPS – TICKETED – REGISTRATION REQUIRED**
AMWS1	**Exploration of the Natural Products Magnetic Resonance Database** *Meeting Room 6/7* Presenters: **Roger Linington**, **Tamara Jordan** and **Matthew Pin** (Simon Fraser University)

AMWS2	**Mass Spectrometry-Based Bioassays** *Off Site – MUSC Campus (Bioengineering Building) – 68 President St., Charleston, SC 29425 - Includes Tour of Mass Spectrometry Facility (Transportation on your own)* Presenters: **Angela Calderón** (Auburn University) and **Richard van Breemen**
12:00 PM – 1:30 PM	Lunch on your own
1:30 PM – 4:30 PM	**WORKSHOPS – TICKETED – REGISTRATION REQUIRED**
PMWS1	**NIH Grantsmanship for Natural Product Researchers** *Meeting Room 6/7* Presenters: **Michelle R. Bond** (NIH National Institute of General Medical Sciences), **Hye-Sook Kim** (NIH National Center for Complementary and Integrative Health), **Adam J. Kuszak** (NIH Office of Dietary Supplements), **Tawnya McKee** (NIH National Cancer Institute), **Barbara C. Sorkin** (NIH Office of Dietary Supplements) and **Patrick Still** (NIH National Center for Complementary and Integrative Health)
PMWS2	**Proteomics and Bioinformatics for Mechanism of Action Discovery** *Off Site – MUSC Campus (Bioengineering Building) – 68 President St., Charleston, SC 29425 - Includes tour of Proteomics Facility (Transportation on your own)* Presenter: **Nicholas J. Carruthers** (University of Michigan)
PMWS3	**Computational Chemistry Approaches Including DP4+ for NMR Predictions to Assist Assignment of Natural Product Structures** *Off Site – MUSC Campus (Bioengineering Building) – 68 President St., Charleston, SC 29425* Presenters: **Robert J. Doerksen** (University of Mississippi) and **Pankaj Pandey** (University of Mississippi)

6:00 PM – 9:00 PM **President's Opening Reception -** ***Ballroom A***
(Ticketed Event)
Supported by the American Society of Pharmacognosy Foundation through a generous donation from the Estate of Gerry and Lynn Brady

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Sunday July 24, 2022

7:00 AM – 5:00 PM Registration – ***Ballroom Foyer***

Welcoming Remarks and Announcements
Ballroom A

8:00 AM – 8:30 AM **Mark Hamann** (Medical University of South Carolina)
Kerry McPhail (ASP President/Oregon State University)

Symposium I – *Ballroom A*
Cryo-EM Drug Discovery
Chair: John Lemasters

8:30 AM – 9:15 AM PL-01 - **Alexis Rohou** (Genentech)
Supporting Drug Discovery and Research with Cryoem in Industry, with an Artisanal Touch

9:15 AM – 10:00 AM PL-02 - **Iain Mylchreest** (Thermo Fisher Scientific)
Impact of Advances in Cryo EM for Drug Discovery

10:00 AM – 10:30 AM Break – **Ballroom Foyer**

Symposium II – *Ballroom A*
NP and Drug Discovery for SARS-CoV2
Chair: Stefan Sarafianos

10:30 AM – 11:15 AM PL-03 - **Barry R. O'Keefe** (National Cancer Institute, National Institutes of Health)
Clinical Development of the Antiviral Protein Griffithsin

11:15 AM – 11:35 AM	I-01- **J Brent Friesen** (Dominican University) *Can Cannabidiol Help Prevent SARS-CoV-2 Infection?*
11:35 AM – 11:55 PM	I-02 - **Hendrik Luesch** (University of Florida) *Sec61 Inhibitor Apratoxin S4 Potently Inhibits SARS-CoV-2 and Exhibits Broad-Spectrum Antiviral Activity*
11:55 AM – 3:00 PM	Exhibitor Set Up – ***Ballroom Foyer***
11:55 AM – 1:45 PM	Lunch on your own
11:55 AM – 1:45 PM	Journal of Natural Products Editorial Board Meeting (Invitation Only) – ***Meeting Room 6 & 7***
1:15 PM – 3:00 PM	Presenters for Poster Session I Set up Posters ***Ballroom B***

Session S-PM1 – *Ballroom A*

Advances in Cannabinoids

Chair: Mahmoud Elsohly

1:45 PM – 2:15 PM	I-03 - **Mary Paine** (Washington State University) *Pharmacokinetic Cannabis-Drug Interactions: Weeding Mechanisms Using Translational Tools*
2:15 PM – 2:45 PM	I-04 - **Marilyn Huestis** (Thomas Jefferson University) *Cannabinoids Offer Unique Mechanisms of Action for New Therapeutics but also Impair Driving & Brain Development*
2:45 PM – 3:05 PM	C-01 - **Fridah Rotich** and **Joseph Mangun** (University of North Carolina at Greensboro) *Identifying Antimicrobial Constituents of Cannabis Sativa L. (Hemp) Against Methicillin-Resistant Staphylococcus Aureus (MRSA)*

3:05 PM – 3:25 PM C-02 - **Prakash Nagarkatti** (University of South Carolina)
Role of Epigenome and Microbiome in the Regulation of Inflammation by Cannabinoids

3:25 PM – 3:45 PM C-03 - **Robert P. Driscoll** (Rousselet Robatel Centrifugation)
Utilization of Centrifugal Partitioning Chromatography (CPC) for the Isolation of Cannabinoid Fractions from Cannabis Distillates

3:45 PM – 4:05 PM C-04 - **Emily R. Britton** (Waters Corporation)
Analytical Approaches for Characterizing Cannabinoids for Quality, Safety, and Research Applications

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Session S-PM2 – *Ballroom C1/C2*

Chemical Ecology
Chair: Melany Puglisi

Sponsored by:

1:45 PM – 2:10 PM I-05 - **Erik Sotka** (College of Charleston)
Marine Herbivore Offenses Against Algal Chemical Defenses

2:10 PM – 2:35 PM I-06 - **Marcy Balunas** (University of Michigan)
Trachymyrmex septentrionalis Fungus-growing Ants as a Model for Exploring Unique Aspects of Host-microbe Chemical Ecology

2:35 PM – 2:50 PM C-05 - **Monica Pupo** (University of São Paulo)
Uncovering Functions and Applications of Specialized Metabolites from Microbiomes of Brazilian Stingless Bees

2:50 PM – 3:05 PM C-06 - **Carla Menegatti** (Virigina Tech)
Novel Oxidized Alkaloids from the Millipede Ischnocybe plicata

3:05 PM – 3:20 PM C-07 - **Lesley-Ann Giddings** (Smith College)
Molecular indicators of environmental change in an Antarctic Polar Desert

3:20 PM – 3:35 PM C-08 - **Skylar Carlson** (University of the Pacific)
Understanding the Chemically Mediated Microbiome of Caulerpa spp.

3:35 PM – 3:50 PM C-09 - **Emily Brown** (Florida Gulf Coast University)
Predator Cues Target Signaling Pathways in Toxic Algal Metabolome

3:50 PM – 4:05 PM C-10 - **Shmuel Carmeli** (Tel Aviv University)
Studies Toward Understanding the Ecological Role of *Microcystis* spp. Modified Peptides

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4:05 PM – 6:30 PM **Poster Session I – Ballroom B**
Poster #'s P-001 – P-124
Chair: Mohamed Ali M. Ibrahim

Posters will remain up through Monday

All posters need to be picked up by Tuesday 9:00 AM
ASP is not responsible for lost or damaged posters

7:00 PM – 10:00 PM **Younger Members Event – Casino Night**
(Ticketed Event) - ***Ballroom A***

Monday July 25, 2022

8:15 AM – 1:00 PM Registration – ***Ballroom Foyer***

8:15 AM – 1:00 PM Exhibition – ***Ballroom Foyer***

Symposium III – *Ballroom A*
Carbon Dioxide Reduction and Utilization
Chair: Tadeusz Molinski

8:45 AM – 9:15 AM Chair Intro - **Tadeusz Molinski** (University of California, San Diego)
Chasing Carbon. Sequestration of CO2 to Save a Planet

9:15 AM – 10:00 AM	PL-05 – **Ming Yang** (Clemson University) *Design of Single-Site Heterogeneous Catalysts for Energy and Environmental Applications*
10:00 AM – 10:30 AM	Break – **Ballroom Foyer**

Session M-AM1 – *Ballroom A*

Botanicals and Resilience

Chair: Angela Calderón

10:30 AM – 11:00 AM	I-07 – **Craig Hopp** (Deputy Director, Division of Extramural Research National Center for Complementary and Integrative Health National Institutes of Health) *The NCCIH Natural Products Clinical Trials Resource: How to Communicate with the FDA About Your Study*
11:00 AM – 11:30 AM	I-08 - **Amala Soumyanath** (Oregon Health & Science University) *Towards Optimized Clinical Trials of Centella Asiatica, a Neurologically Active Botanical*
11:30 AM – 12:00 PM	I-09 - **Giulio Pasinetti** (Icahn School of Medicine and Mount Sinai) *Microbiota Metabolites Modulate the T helper 17 to Regulatory T cell (Th17/Treg) Imbalance Promoting Resilience to Stress-Induced Anxiety- and Depressive-Like Behaviors*
12:00 PM – 12:20 PM	C-11 - **Hellen A. Oketch-Rabah** (USP) *Ashwagandha Root Chemistry and Potential Liver Toxicity*
12:20 PM – 12:40 PM	C-12 – **Wendy Strangman** (University of North Carolina Wilmington) *Assessment of In Vitro ADME of Medicinal Plant Extracts*
12:40 PM – 1:00 PM	C-13 – **Amy Keller** (University of Colorado Denver) *(–)-Epicatechin Improves Vasoreactivity, Mitochondrial Respiration and Cellular Signaling in a Rat Model of Cardiovascular Disease*

Session M-AM2 – *Ballroom C1/C2*

Synthesis Methodologies

Chair: James Fuchs

10:30 AM – 11:15 AM	PL-05 - **Darren Dixon** (Oxford University) *New Broad Scope Catalytic Strategies for Simplifying Complex Natural Product Synthesis*
11:15 AM – 11:45 AM	I-10 - **Jeffrey Johnston** (Vanderbilt University) *New Chemical Tools and Strategies that Enable Discoveries in Natural Product-Based Therapeutic Development*
11:45 AM – 12:15 PM	I-11 - **Tadeusz Molinski** (University of California, San Diego) *Axinisoside-1. Complete Stereostructure of a Complex Glycolipid*
12:15 AM- 12:35 PM	C-14 - **Elizabeth Parkinson** (Purdue University) *Synthetic Natural Product Inspired Cyclic Peptides for Discovery of Bioactive Natural Products and Biocatalysts*
12:35 PM – 12:55 PM	C-15 - **Andrew Riley** (University of Illinois at Chicago) *Discovery of Potent Opioid Ligands Derived from Picralima nitida Alkaloids*

3:00 PM – 5:00 PM	**MWS – Workshop – *Meeting Room 3*** *Hands-On Training of IDBac, an Informatics Tool for Strain Prioritization* Presenters: **Brian Murphy** (University of Illinois at Chicago), **Laura Sanchez** (University of California, Santa Cruz) and **Chase Clark** (University of Wisconsin-Madison

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3:00 PM	Afternoon and Evening on your own

Tuesday July 26, 2022

7:15 AM – 4:00 PM	Registration – ***Ballroom Foyer***
7:15 AM – 4:00 PM	Exhibition – ***Ballroom Foyer***

Symposium IV – *Ballroom A*

Emerging Technologies

Chair: R. Thomas Williamson

7:45 AM – 8:25 AM	PL-06 - **Jonathan Goodman** (Cambridge University) *From Spectrum to Structure: DP4-AI and Data-Driven NMR Analysis*
8:25 AM – 8:55 AM	I-12 - **Clemens Anklin** (Bruker BioSpin Corp.) *Modern Advanced NMR Spectroscopy for non-NMR Experts*
8:55 AM – 9:25 AM	I-13 - **Roberto Gil** (Carnegie Mellon University) *Reference-Free Quantitative NOE and the Structural Value of Two-Bond Proton-Carbon ($^2J_{CH}$) Coupling Constants for Configurational Analysis Small Molecules*
9:25 AM – 9:45 AM	C-16 - **Hyunwoo Kim** (Dongguk University) *DeepSAT: Learning Molecular Structures from Nuclear Magnetic Resonance Spectroscopy*

9:45 AM – 10:15 AM	Break – **Ballroom Foyer**

Symposium V – *Ballroom A*

Biosynthesis

Chair: Bradley Moore

Sponsored by:

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10:15 AM – 11:00 AM	PL-07 - **Ben Shen** (Scripps Florida) *Leverage a Large Actinobacterial Strain Collection and Genome Database for Natural Products and Drug Discovery*
11:00 AM – 11:30 AM	I-14 - **Roland Kersten** (University of Michigan) *Biosynthesis of Side-Chain-Macrocyclic Peptides in Plants*
11:30 AM – 12:00 PM	I-15 - **Bo Li** (UNC Chapel Hill) *Biosynthesis of a Copper-Containing Antibiotic*

12:00 PM – 12:15 PM **DEI Workshop Lunch Pick-Up (Ticketed)**

DEI Workshop (Sponsored by P&G) - Ballroom A
Chairs: Lesley-Ann Giddings and Christine Salomon

12:15 PM – 12:30 PM W-01 - **Shanina Sanders Johnson** (Spelman College)
Inclusive Mentorship: Best Practices to Cultivate a Diverse Scientific Workforce

12:30 PM – 12:45 PM W-02 - **Marvella Ford** (Hollings Cancer Center)
My Academic Journey to a Cancer Health Disparities Research Career

12:45 PM – 1:30 PM Q&A

Symposium VI – *Ballroom A*

Innovations in NP Based Controls for Cancer
Chair: Fred Valeriote

1:30 PM – 2:15 PM PL-08 - **Nancy Klauber-DeMore** (Medical University of South Carolina)
The Anti-Proliferative Effects of Oral Boswellia serrata, a Frankincense Extract, in Patients with Breast Cancer

2:15 PM – 2:45 PM I-16 - **David Turner** (Virginia Commonwealth University)
Targeting Nutritional AGE Bioavailability Using Natural Products

2:45 PM – 3:05 PM C-17 - **James McChesney** (University of Mississippi and Cloaked Therapeutics, LLC)
TumorSelectTechnology® Enhancing Safety and Efficacy of Cytotoxic Chemotherapeutics

3:05 PM – 3:25 PM C-18 - **Esther Guzman** (Florida Atlantic University)
Marine Natural Products with Selective Activity Against Triple Negative Breast Cancer 3D Cultures

3:25 PM – 3:45 PM C-19 - **Janae D. Sweeney** (South Carolina State University)
Val16A SOD2 Polymorphism Promotes Epithelial Mesenchymal Transition Antagonized by Muscadine Grape Skin Extract in Prostate Cancer Cells

3:45 PM – 4:05 PM

C-20 - **Sierra McDonald** (University of South Carolina School of Medicine)
Panaxynol Alleviates Murine Colitis Associated Colorectal Cancer via Macrophage Suppression

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4:05 PM – 6:15 PM

Poster Session II – Ballroom B
Poster #'s P-125 – P-242
Chair: Jonathan Chekan

Posters will remain up through Wednesday

All posters need to be picked up by Thursday 9:00 AM
ASP is not responsible for lost or damaged posters

6:30 PM

Buses Depart for An Evening at the South Carolina Aquarium
Buses will Depart and Return to the Front Entrance of the Charleston Area Convention Center

7:00 PM – 11:00 PM

An Evening at the South Carolina Aquarium
(Ticketed Event)

Wednesday July 27, 2022

8:00 AM – 5:45 PM

Registration – ***Ballroom Foyer***

8:00 AM – 5:45 PM

Exhibition – ***Ballroom Foyer***

Symposium VII – *Ballroom A*
Bioengineering and Informatics Technologies
Chair: Karen Nelson

8:30 AM – 9:15 AM

PL-09 - **Wenjun Zhang** (University of California Berkeley)
Natural Product Biosynthesis: Go Beyond Natural Evolution

9:15 AM – 10:00 AM

PL-10 - **Nadine Ziemert** (University Tuebingen)
Bioinformatics Pipelines and Tools to Guide the Discovery of New Natural Products

10:00 AM – 10:30 AM Break – **Ballroom Foyer**

Session W-AM1 – *Ballroom A*

Natural Products Synthesis
Chair: Daniel Romo

10:30 AM – 11:10 AM PL-11 - **Frank Fang** (Eisai)
Transition Metal-Free Assembly of Eribulin: Prins Macrocyclizations in the Halichondrin Series

11:10 AM – 11:30 AM C-21 - **Liela Romero** (Baylor University)
An Organocatalytic Strategy for the Selective Interhalogenation of Alkenes, Alkynes and Dienes

11:30 AM – 11:45 AM C-22 - **Paul Scesa** (Florida Atlantic University)
Role of Macrocyclic Conformational Steering in a Kinetic Route toward Bielschowskysin

11:45 AM – 12:00 PM C-23 - **John MacMillan** (University of California, Santa Cruz)
Harnessing Non-Enzymatic Transformations in Natural Product Biosynthesis

Session W-AM2 – *Ballroom C1/C2*

Genome Mining
Chair: Eric Schmidt

10:30 AM – 11:00 AM I-17 - **Yousong Ding** (University of Florida)
Genome-aided Discovery of New Enzymes

11:00 AM – 11:20 AM C-24 - **Neil L. Kelleher** (Northwestern University)
Correlative Metabologenomics of 111 Fungi Reveals Thousands of Metabolite/Gene Cluster Pairs

11:20 AM – 11:40 AM C-25 - **Jie Li** (University of South Carolina)
Correlational Networking Guides the Discovery of Hidden Lanthipeptide Proteases

11:40 AM – 12:00 PM C-26 - **Wenjia Gu** (Zymergen Inc.)
Targeted Discovery of Natural Products from Massive Metagenomic Diversity

12:00 PM – 1:15 PM Lunch on your own

12:00 PM – 1:15 PM Fellows Meeting – Invitation Only – Meeting Room 4

Session W-PM1 – *Ballroom A*

Natural Products Investigations Around the World: Africa
Chair: Abiodun Falodun

1:15 PM – 1:45 PM I-18 – **Turibio Tabopda Kuiate** (Medical University of South Carolina/ University of Yaounde)
Cytotoxic Steroidal Saponins from Asparagus schweinfurthii Baker (Liliaceae)

1:45 PM – 2:05 PM C-27 - **Nassifatou Koko Tittikpina** (University of Lome)
A LC-MS Method Development led to the Discovery of New Compounds from the Trunk Barks of Pterocarpus erinaceus Poir (Fabaceae)

2:05 PM – 2:25 PM C-28 - **Alexandros Polyzois** (Rhodes University)
Stromatolite Chemical Profiles and Microbial Consortia Vary Throughout Sites Along the Coast of the Eastern Cape, South Africa

2:25 PM – 2:45 PM C-29 - **Elhadj Balde** (Institut de recherche et de développement des plantes médicinales et alimentaires de guinee)
Traditional Guinean Management of Breast Diseases in Low and Middle Guinea

2:45 PM – 3:05 PM C-30 - **Ogechukwu Chukwuemerie** (Nnamdi Azikiwe University Awka Anambra State Nigeria)
Toxicological Analysis and Antimalarial Potentials of Secondary Metabolites of Curvularia lunata, an Endophyte Obtained from the Leaves of Azadirachta indica

Session W-PM2 – *Ballroom C1/C2*

Natural Products Investigations Around the World: Central-South America/Caribbean

Chair: Winklet Galimore

1:15 PM – 1:45 PM	I-19 – **Nandakumara Sarma** (USP) *USP Botanical Dietary Supplements and Herbal Medicines Pan American Expert Panel*
1:45 PM – 2:05 PM	C-31 – **Eduardo Caro-Diaz** (University of Puerto Rico Medical Sciences Campus *Cyanobacterial Pseudo-natural Products: Virtual Synthesis and Evaluation of Drug-likeness*
2:05 PM – 2:25 PM	C-32 - **Paulo Vieira** (University of São Paulo) *Exploring the Chemical Diversity of Phytoparasitic Fungi*
2:25 PM – 2:45 PM	C-33 - **Rita Gonçalves** (Federal University of Espirito Santo) *Avocadene Identified from Persea americana Mill. Seeds as a Potential Anticancer Against Gastric Adenocarcinoma Cells*
2:45 PM – 3:05 PM	C-34 – **Roberto Berlinck** (Universidade De Sao Paulo) *Phomactinine, the First Nitrogen-Bearing Phomactin, Discovered by Extensive Media Optimization and Metabolomics Analyses*

Symposium VIII – *Ballroom A*

Younger Investigators

Chair: Jon Clardy and C. Benjamin Naman

3:20 PM – 3:50 PM	I-20 - **Courtney Thomas** (South Carolina State University) *Determination of Anti-AGE Properties of SC Native Pseudognaphalium obtusifolium*
3:50 PM – 4:10 PM	C-35 - **Kelli McDonald** (Auburn University) *Ashwagandha Botanical-Drug Interactions: Potential CYP Induction*
4:10 PM – 4:30 PM	C-36 - **Ethan Older** (University of South Carolina) *Sulfonolipids: Human Microbial Metabolites with Unique Dual Activity in Mediating Inflammation*

4:30 PM – 4:50 PM	C-37 - **Barbara Adaikpoh** (University of Illinois at Chicago) *Characterization of Endogenous Promoters for the Heterologous Expression of Biosynthetic Gene Clusters in Burkholderia Bacteria*
4:50 PM – 5:10 PM	C-38 **Caitlin McCadden** (University of Florida) *Genome Mining of Bacterial Cytochrome P450 Enzymes for Novel Biocatalysts*
5:10 PM – 5:30 PM	C-39 - **Aswad Khadilkar** (University of California Santa Cruz) *Assigning Mechanism of Action to Natural Products in Multiple Biological Contexts Using Gene Expression and Phenotypic Screening Methods Established by the HIFAN Program*
5:30 PM – 5:45 PM	C-40 - **Zhenjian Lin** (University of Utah) *Ancient Defensive Terpene Biosynthetic Gene Clusters in the Soft Corals*
5:45 PM – 7:00 PM	Dinner on your own

Symposium IX – *Ballroom A*

Financing and Institutional Priorities

Chair: Rick Warner

7:00 PM – 7:30 PM	I-21 - **John Warner** *South Carolina Centers of Economic Excellence*
7:30 PM – 7:50 PM	I-22 – **Patrick Still** (NCCIH) *Funding for Natural Products Research at the National Center for Complementary and Integrative Health*
7:50 PM – 8:10 PM	I-23 – **Michelle Bond** (NIGMS) *Funding for Natural Products Discovery and Analysis at National Institute of General Medical Sciences*
8:10 PM – 8:30 PM	I-24 – **Sean Ash** (Maxim Merchant Capital)
8:30 PM – 8:50 PM	I-25 – **Jin Kun Cha** (National Science Foundation (NSF)) *The National Science Foundation: Funding Opportunities and Priorities*
8:50 PM – 9:20 PM	I-26 – **Rick Warner** (Coastal 8) *Investing in and Building Returns in the Natural Asset Class, At Speed and Scale*

Thursday July 28, 2022

7:30 AM – 1:45 PM	Registration – ***Ballroom Foyer***
7:30 AM – 11:00 AM	Exhibition
11:00 AM – 3:00 PM	Exhibition Dismantling

Session TH-AM1 – *Ballroom A*

Marine

Chair: Amy Wright

8:00 AM – 8:30 AM	I-27 - **Jaclyn Winter** (University of Utah) *Accessing New Terpene Scaffolds from Marine-Derived Fungi*
8:30 AM – 9:00 AM	I-28 - **Emily Mevers** (Virgina Tech) *Chemical Investigations into the Microbiota of Marine Egg Masses*
9:00 AM – 9:20 AM	C-41 - **Nicole Avalon** (University of California, San Diego) *The Structure, Biosynthesis, and Metal-Binding Properties of Leptochelin, a Cytotoxic Metabolite from the Filamentous Marine Cyanobacterium Leptolyngbya sp.*
9:20 AM – 9:40 AM	C-42 – **William Mendoza** (University of Puerto Rico) *Chemoinformatic Synthesis and Analysis of Cyanobacterial Pseudonatural Products*

Session TH-AM2 – *Ballroom C1/C2*

Mass Spectrometry: Tools and Applications

Chair: Lukasz Ciesla

8:00 AM – 8:30 AM	I-29 - **Hosein Mohimani** (Carnegie Mellon University) *Computational Methods for Discovering Bioactive Natural Products by Mining Large Mass Spectral Datasets*
8:30 AM – 8:45 AM	C-43 - **Trevor Clark** (Simon Fraser University) *Evaluation of Ion Mobility Spectrometry for Improving Constitutional Assignment in Natural Products*

8:45 AM – 9:00 AM	C-44 - **Scott Jarmusch** (Technical University of Denmark) *Salting the Earth: Streptomyces-Streptomyces Antibiosis via Lydicamycin Production*
9:00 AM – 9:15 AM	C-45 - **Evelyn Abraham** (Pennsylvania State University) *A Comparison of Genetic and Chemometric Techniques for Authentication of Dried Herbal Products: A Case Study with Ocimum Spp.*
9:15 AM – 9:30 AM	C-46 – **Yi Zhao** (Lehman College, City University of New York & The Graduate Center, City University of New York) *Metabolic Profiling and Alkaloid Analysis of American Aconitum Species by UPLC-qTOF-MSe*

9:30 AM – 10:00 AM	Break

Award Symposium I
Chair: Cindy Angerhofer
Ballroom A

10:00 AM – 10:45 AM	A-01 - **Jason Crawford** (Yale University) Matt Suffness Young Investigator Award 2021 *Metabolism at the Human-Microbe Interface*
10:45 AM – 11:30 AM	A-02 - **Laura Sanchez** (University of California, Santa Cruz) Matt Suffness Young Investigator Award 2022 *Mass spectrometry imaging as a powerful tool for microbial natural product research*
11:30 AM – 12:30 PM	A-03 - **John Cardellina** (ReevesGroup) Varro E. Tyler Prize 2021 *The Long and Winding Road – How a Marine Natural Products Chemist Became a Candidate for the Varro Tyler Prize*

12:30 PM – 1:45 PM	Lunch on your own

Award Symposium II
Chair: Ben Shen
Ballroom A

1:45 PM – 2:45 PM	A-04 - **Bradley Moore** (University of California at San Diego) Norman R. Farnsworth Research Achievement Award 2021 *A Biosynthetic Journey to Discover and Apply Nature's Specialized Chemistry*
2:45 PM – 3:45 PM	A-05 - **Hung-wen (Ben) Liu** (University of Texas at Austin) Norman R. Farnsworth Research Achievement Award 2022 *Exploring the Diversity of Unusual Sugar Biosynthesis*

4:00 PM – 6:15 PM	**ASP Business Meeting -** Ballroom C1/C2 ASP Members Welcome (Associate Members may attend but Voting Privileges are for Full Members Only)
6:30 PM – 7:00 PM	**Closing Reception – *Ballroom Foyer***
7:00 PM – 10:00 PM	**Closing Ceremony and Banquet – *Ballroom A*** (Ticketed Event)

Thank you for your participation in the 2022 ASP Meeting!

See you in Maryland in 2023!

American Society of Pharmacognosy

Award Speakers

A-01 – Jason Crawford

Metabolism at the Human-Microbe Interface

Jason M. Crawford[1,2,3]. [1]*Department of Chemistry, Yale University, New Haven, CT 06520.* [2]*Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT 06536.* [3]*Yale Institute of Biomolecular Design & Discovery, West Haven, CT 06516*

The human microbiome encodes a treasure trove of bioactive small molecules that regulate distinct host-microbe interactions. In this lecture, I will provide an overview on behalf of our group efforts to exploit a human microbiota culture collection for the discovery and characterization of new small molecules that regulate diverse host inflammatory, signal transduction, and DNA damage signaling programs. A collection of natural product examples will be highlighted in the context of a simplified framework for studying host-microbe molecular relationships. Then, I will go into further detail about a recently characterized pathway from the vaginal microbiome member *Lactobacillus iners*, which produces a remarkable family of secreted nucleotide metabolites termed the tyrocitabines that feature an orthoester-phosphate motif, inhibit translational activity, and invoke unexpected biosynthetic machinery. The core tyrocitabine was reconstructed biochemically, illuminating an "Amadori synthase," a polyol-amino acid intermediate, and an "abortive" tRNA synthetase in the process. The broad distribution of related but uncharacterized pathways in microbial genome databases suggests that the tyrocitabines are the founding members of a much broader family of nucleotide antimetabolites.

A-02 – Laura Sanchez

Mass Spectrometry Imaging as A Powerful Tool for Microbial Natural Product Research

Laura Sanchez[1] [1] *Department of Chemistry and Biochemistry, 1156 High St. University of California, Santa Cruz, Santa Cruz, CA 95064*

Mass spectrometry imaging (MSI) has proved to be a powerful tool for both microbiology and tissue pathology. My lab has sought to merge the strengths of applications seen in these fields to specifically explore microbially produced natural products in complex settings. My lab has been focused on better understanding the spatial and temporal production of natural products by microbes in a variety of settings including treatment by exogenous compounds, microbial co-cultures, microbial communities, and host organisms. MSI suffers from a lack of universal protocols despite the fact that it was first described for use with microbes in 2009. We have adapted our MSI platform based on the unique challenges presented by our biological systems by leveraging computational mass spectrometry workflows such as segmentation. Recently, we are exploring additional dimensionality in our experiments with trapped ion mobility spectrometry (tims) which allows for the generation of spatially distinct ion images of isobars and isomers from our biological samples. Short vignettes on our work in cheese microbial communities, *Vibrio fischeri* in the light organ of the Hawaiian Bobtail squid, and treatment of single organism biofilms by bile acids will be covered to highlight the work my lab has accomplished since I started by independent position in 2015.

A-03 – John H. Cardellina II

The Long and Winding Road – How a Marine Natural Products Chemist Became a Candidate for the Varro Tyler Prize

John H. Cardellina II, ReevesGroup, 1137 Treefern Drive, Virginia Beach, Virginia 23451

In this presentation, the metamorphosis of a marine natural products chemist to someone very focused on the chemistry and pharmacology of botanicals will be described and illustrated by examples of the various steps and projects that led him to his current primary focus on the adulteration of botanicals in commerce.

A-04 – Bradley S. Moore

A Biosynthetic Journey to Discover and Apply Nature's Specialized Chemistry

Bradley S. Moore, Scripps Institution of Oceanography & Skaggs School of Pharmacy and Pharmaceutical Sciences UC San Diego

The field of natural product biosynthesis has transformed over the last 35 years since I was an undergraduate student at the University of Hawaii. From tracer experiments with radioisotopes in the late 80s to the multi-omic, big data studies of today, the art of biosynthesis has evolved into an applied science that aims to solve grand challenges in medicine, manufacturing, and the environment. In this Norman R. Farnsworth Research Achievement Award presentation, I will share some of the biosynthetic stories from my career that have allowed us to establish how nature, from microbes to animals, make complex small molecules important to health and disease. Examples will include the glioblastoma drug candidate salinisporamide A from a marine bacterium, the amnesic shellfish toxin domoic acid from planktonic microalgae, and the cosmetic anti-inflammatory agent pseudopterosin from corals. Each example will expand upon the

challenges and opportunities of mixed omics approaches towards producing chemicals unique to the sea.

A-05 – Hung-Wen Liu

Exploring the Diversity of Unusual Sugar Biosynthesis

Hung-wen Liu, Division of Chemical Biology and Medicinal Chemistry, College of Pharmacy, and Department of Chemistry, University of Austin, Austin, TX 78712, USA

Many natural products derive their biological activities from their sugar components. Changing the structures of these sugar moieties can profoundly impact the biological properties of the glycosylated parent compounds. This has led to the modification of natural products with alternative sugar moieties by exploiting the sugar biosynthetic machinery. Realizing the potential of this approach requires both an understanding of the biosynthetic pathway of each target sugar and a detailed mechanistic knowledge of the key enzymes. Scientists have thus begun to unravel the biochemical principles underlying the assembly of glycosylated natural products wherein a core set of enzyme activities mix and match to synthesize structurally diverse carbohydrates. Mechanistic investigation of the responsible biosynthetic enzymes has also revealed several cases involving unique and interesting chemistry to accomplish the specific biosynthetic transformations. Carbohydrate biosynthesis in secondary metabolism has thus been found to include instances of radical mediated chemical transformations, some of which are catalysed by radical SAM enzymes. The biosynthetic roles of selected enzymes in this group, their mechanisms of catalysis, and the insights they can offer for understanding natural product biosynthesis and radical SAM enzymology will be discussed.

PLENARY SPEAKERS

PL-01 – Alexis Rohou

Supporting Drug Discovery and Research with Cryoem in Industry, with an Artisanal Touch

Alexis Rohou, Department of Structural Biology, Genentech, South San Francisco, CA 94080

Cryogenic electron microscopy (cryoEM) can solve the structures of proteins bound by small or large molecules even when crystallization of the protein is impossible. This has led Genentech and other large pharmaceutical discovery groups to invest in cryoEM in order to complement other structural biology techniques and better support drug discovery efforts. I will illustrate how cryoEM enables drug discovery and biological research, using as examples targets of interest bound by small and large molecule drugs or candidates, and I will give an overview of our technology development efforts in the cryoEM space.

PL-02 – Iain Mylchreest

Impact of Advances in Cryo EM for Drug Discovery

Iain Mylchreest[1], Raymond Schrijver[1]. [1]Thermo Fisher Scientific, 168, 3rd Ave, Waltham, MA 02451

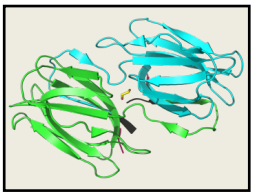
Cryo-electron microscopy (cryo-EM) has come to the forefront as a powerful technique for the structural characterization of proteins relevant for drug discovery. Technological developments around sample preparation, signal processing, faster cameras and image filters, have improved the resolution to near atomic levels, and also allow for higher analytical throughput. The many developments have enabled detailed visualization of previously inaccessible drug targets, that combined with computational modelling, accelerate structured based drug discovery. Recently micro-electron diffraction (micro-ED) emerged as a cryo-EM technique to determine the structure of small crystals. This is relevant for natural products where structural elucidation is hampered by the lack of sufficient quantities of material for traditional analytical methods. New developments in cryo-electron tomography which allows visualization of proteins in the context of the cell are transforming our view of how structures function and leading to the potential development of new drug candidates. An overview of these developments will be discussed.

PL-03 – Barry O'Keefe

Clinical Development of the Antiviral Protein Griffithsin

Lauren R.H. Krumpe[1,2], Shilpa Shenoy[1,2], Curtis J. Henrich[1,2], Jennifer Wilson[2], Joshua L. Fuqua[3], Lisa C. Rohan[4], Kenneth E. Palmer[3] and Barry R. O'Keefe[2,5]. [1]Leidos Biomedical Research, Inc., FNLCR, Frederick, MD, 21702; [2]Molecular Targets Program, CCR, NCI, Frederick, MD, 21702; [3]Center for Predictive Medicine for Biodefense and Emerging Infectious Diseases, University of Louisville, Louisville, KY, 40222; [4]Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA, 15213; [5]Natural Products Branch, DTP, DCTD, NCI, Frederick, MD, 21702

The antiviral protein griffithsin (GRFT) was originally isolated from the reg alga *Griffithsia* sp.. GRFT and its oxidation-resistant



analog Q-GRFT have displayed potent *in vitro* and *in vivo* activity against a number of viruses and have been formulated into potential clinical products that have been approved to progress into Phase I clinical trials. Two clinical trials of formulations of GRFT and QGRFT for use as anti-HIV microbicides have recently been successfully completed. In addition, GRFT and QGRFT have been reported to have broad activity against members of the family *Coronaviridae* including SARS-CoV-1, MERS and SARS-CoV-2. This activity has led to additional clinical trials of an intranasal formulation of QGRFT for potential use in the prevention of coronavirus infections. This talk will detail efforts in the clinical development of GRFT and Q-GRFT for use to prevent infection from HIV and SARS-CoV-2.

Chair Introduction – Tadeusz Molinski

Tadeusz F. Molinski[1,2], [1]Department of Chemistry and Biochemistry, and [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA 92093, USA.

The Earth has warmed since the Industrial Revolution (there is little doubt) due to anthropogenic emissions of CO_2 in amounts comparable to natural sources. Unregulated emissions of CO_2 from industrial activities – power production and transportation, among others – are raising atmospheric, land and ocean sea-surface temperatures by overwhelming the natural capacities of Earth's biome and oceanic sinks to sequester this heat-capturing greenhouse gas. The consequences are potentially catastrophic. This talk will frame the 'current condition' in terms of CO_2 flux and its consequences; what was, what is, and what should be done to bend the Keeling curve towards the goal of saving a planet: ours. In the session that follows, speakers will present 'what can be done': analyses and inventive solutions to 'carbon-sequestration' through capture of CO_2 and repurposing the carbon into commodity chemicals and other materials.

PL-04 – Ming Yang

Design of Single-Site Heterogeneous Catalysts for Energy and Environmental Applications

Ming Yang, Department of Chemical and Biomolecular Engineering, Clemson University, Clemson, SC 29634

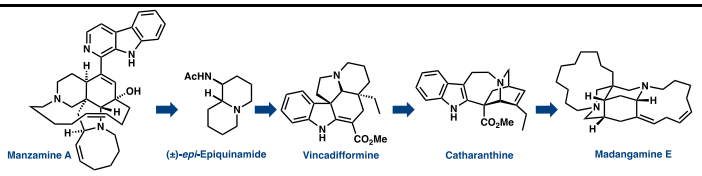
Heterogeneous catalysis is a key enabler in identifying and navigating sustainable energy flow through our fragile ecosystem. The exploration of cost-effective supported metal catalysts to produce sustainable energy and value-added chemicals is at the heart of both fundamental and industrial catalysis research. To allow such a large family of materials to match the elegant and promising chemistry of their corresponding homogeneous catalytic prototypes, perhaps the ultimate design goal of supported metal catalysts is to simultaneously maximize the dispersion of the scarce catalytic metals and to display desired intrinsic chemistry per supported metal atom. Working towards this design goal presents both daunting tasks and new opportunities. The emerging topical research area of single-site catalysis is a subset of these efforts in our community. Made through carefully executed synthesis, these single-site catalytic materials can also serve as appropriate platforms for many fundamental studies, where the detailed electronic structure, coordination condition, interfacial behaviors, and broader scopes of geometry and ligand effects of the supported metal species can now be more explicitly probed and tailored than in many previous heterogeneous catalytic systems. This advanced science has made its way to reaction engineering in fuel gas processing and, more recently, in CO_2 valorization to value-added chemicals. A few vignettes of the author's findings in this field will be discussed in this talk.

PL-05 – Darren Dixon

New Broad Scope Catalytic Strategies for Simplifying Complex Natural Product Synthesis

Darren J. Dixon, Chemistry Research Laboratory, Department of Chemistry, University of Oxford, UK

In this presentation, new "synthesis inspired" user-friendly broad scope catalytic strategies for forging the key carbon-carbon bonds of key late stage synthetic intermediates en route to various complex alkaloid natural products will be described. In one strand, the use of the abundant and venerable tertiary amide as a precursor to reactive iminium and enamine intermediates via reductive activation will be explored as a new approach to manzamine, aspidosperma and vinca alkaloids. Furthermore, the strategic use of multifunctional metal free catalysts to rapidly construct the bicyclic core of madangamine E via enantioselective desymmetrization of readily constructed achiral precursors will be described. The presentation will include details of the newly arising methodologies as well as their provenance and applications in natural product total synthesis.

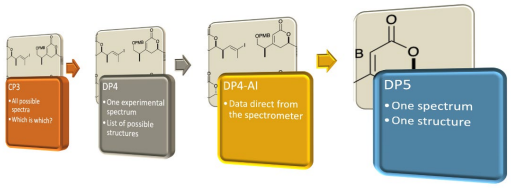


PL-06 – Jonathan Goodman

From Spectrum to Structure: DP4-AI and Data-Driven NMR Analysis

Jonathan Goodman, University of Cambridge

Interpreting NMR spectra is a fundamental part of chemistry and the basis for a large amount of structural determination. How sure can we be that a the spectrum we have corresponds to the molecule we want? As automated synthesis grows in importance, how can we tell our robots how to analyse spectra when data is being generated at a scale beyond the capacity of a human chemist. The DP4 approach to spectral analysis provides answers to these questions. By combining experimental data with ab initio spectral simulation, the algorithm calculates the probability that the analysis is correct. It requires the NMR spectrum of a molecule and a list of candidate structures. This can be reassuring, if the confidence level is high, and useful if it is low, as it signals the need for further analysis. Since its introduction in 2009, the DP4 method has become much easier to use and more appropriate for fully-automatic operation. The latest developments include the direct interpretation of FIDs from spectrometers (DP4-AI) and, most recently, DP5, which calculates an assignment probability without a list of candidate structures.



PL-07 – Ben Shen

Leverage a Large Actinobacterial Strain Collection and Genome Database for Natural Products and Drug Discovery

Dr. Ben Shen-Professor, Departments of Chemistry and Molecular Medicine Director, Natural Products Discovery Center at Scripps Research.

The Natural Products Discovery Center (NPDC) at Scripps Florida houses one of the world's largest actinobacterial strain collections, totaling >125,000 strains. These strains were isolated over the last eight decades and from 69 different countries, spanning at least 88 different genera. A natural products library (NPL) has also been constructed, consisting of ~46,000 crude extracts, ~29,000 partially purified fractions, and ~650 pure NPs, which were made from

~15,000 actinobacterial strains. Current effort has been focused on sequencing the strain collection to establish the Natural Products Genomics Resource Center (NPGRC) for the broad scientific community. Estimated on the assumption of ~30 biosynthetic gene clusters (BGCs) per strain, the ~125,000 strains in the collection could encode >3.75 millions of BGCs, i.e., the potential of producing >3.75 millions of natural products. The potential number of natural products awaiting discovery from the strain collection at Scripps Florida is therefore immense. Selected studies will be presented to inspire the scientific community to leverage the strain collection, the NPL, the NPGRC database, and the associated enabling technologies to promote research and development on natural products and associated applications, and to enable partner organizations to commercialize new products without the need of building and maintaining in-house natural product resources.

PL-08 - Nancy Klauber-DeMore

The Anti-Proliferative Effects of Oral *Boswellia serrata*, a Frankincense Extract, in Patients with Breast Cancer

*Ingrid V. Bonilla[1], Laura Spruill[2], Andrea Abbott[1], Denise Garcia[1], Julie Siegel[1], Rupak Mukherjee[1], Jessica Forcucci [2], Mark Lockett[1], David Cole[1], Eleanor Hilliard[1], George Hanna[4], Mark Hamman[4], Nancy Klauber-DeMore[1 *]*

Frankincense has been used in traditional medicines for over 3,000 years but has yet to yield a defined FDA approved product. *Boswellia serrata.*, the plant genus that produces frankincense resin, has been shown to inhibit tumor growth in pre-clinical models. To evaluate whether *B. serrata* has anti-tumor activity in humans, we performed a "window of opportunity" trial to evaluate the biological effects and safety of a *B. serrata* supplement, BosPure®, in breast cancer patients. An IRB-approved, prospective Phase 1A trial was performed enrolling stage 1-2 endocrine receptor positive invasive breast cancer patients. The control arm consisted of core biopsy and surgical specimens from matched untreated patients. Patients received oral BosPure® 2400mg/day preoperatively until the night before surgery (range 5 to 23 days). Paraffin embedded histology samples were analyzed using antibodies for IHC for proliferation (Ki67) and apoptosis (TUNEL assay). Two board-certified pathologists independently analyzed the samples in a blinded manner. The scores for corresponding samples were examined for inter-rater variability using intraclass correlation tests. The change in Ki67and TUNEL staining from core biopsy to surgical excision specimens was quantified as a percentage and compared between the control and treatment groups using a two-tailed paired t-test. Values are presented as mean± standard error of the mean (SEM). The mean age was 60 (range 46-81). The mean duration of drug intake was 11 days (SEM 6 days; range: 5-23 days). There was one Grade 3 adverse event (intraoperative hypotension – not related to study drug); however, the majority of toxicities were Grade 1. There were 20 patients per group with two excluded in each group at analysis due to technical difficulty with IHC in the core biopsy, leaving a sample size of 18. The Ki67 measurements from the two pathologists had an intraclass correlation of r=0.63, p<0.01 and a significant correlation between the observers (r=0.68, p<0.01). The control group had an increase in proliferation from core biopsy to excision of 54.6±21.4%. In contrast, the BosPure® group had a reduction in proliferation from core biopsy to excision of 13.8±11.7%. The difference in Ki67 staining between core biopsy and surgical excision specimens was statistically significant between the control and BosPure® groups (p=0.008). Changes in cellular apoptosis between the core and surgical specimens were similar in the control and Boswellia groups (p=0.92). BosPure® demonstrated a significant decrease in breast cancer cell proliferation in humans, as compared to matched controls. Combined with the strong safety profile for this oral medication, these findings would suggest a potential therapeutic role for *B. serrata*. Future experiments will identify the specific metabolite combinations from *B. serrata* supplements responsible for the biologic activity.

PL-09 – Wenjun Zhang

Natural Product Biosynthesis: Go Beyond Natural Evolution

Wenjun Zhang, Department of Chemical and Biomolecular Engineering, University of California Berkeley, Berkeley, CA 94720, USA

Natural products are important small molecules for studying, treating, and even causing human diseases, and they typically have unique functional groups and molecular scaffolds that are critical for their biological activities. By exploiting the biosynthetic machinery, it is possible to enhance, vary or diminish the biological activities of parent compounds and apply the biosynthetic machinery to new systems for functional group installation. Zhang lab has revealed and engineered enzymatic machinery for synthesizing many unique pharmacophores and molecular scaffolds of natural products, including but not limited to terminal alkene and alkyne, isonitrile, *N*-hydroxytriazene, epoxyquinone, epoxyketone, cyclohexanecarboxyl-CoA, indolizidine, pyrroloindole and antimycin-type depsipeptides. This talk will highlight a few examples.

PL-10 – Nadine Ziemert

Bioinformatics Pipelines and Tools to Guide the Discovery of New Natural Products

Nadine Ziemert[1,2,3], [1]Interfaculty Institute of Microbiology and Infection Medicine, University of Tübingen, Auf der Morgenstelle 28, 72076 Tübingen, Germany. [2] German Centre for Infection Research (DZIF), Partner Site Tübingen, Germany. [3] Institute for Bioinformatics and Medical Informatics, University of Tübingen, 72076 Tübingen, Germany

Bacterial natural products are one of the main sources for the discovery of novel drugs. However, classical cultivation

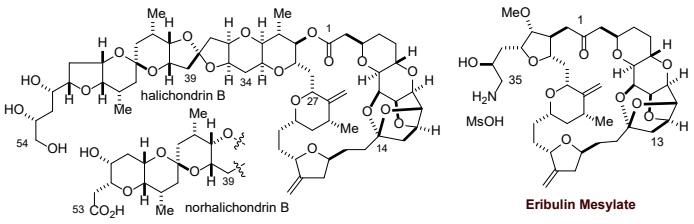
approaches are usually costly and time-consuming and often lead to the rediscovery of known compounds. This is where bioinformatics can help to predict I) where to go sampling in order to find a wealth of undiscovered natural products, II) which strains might have the potential to produce yet unknown compounds, III) which strains are likely to produce antibiotics and IV) under which conditions biosynthetic genes are up- or downregulated. Here we would like to introduce the tools developed at the Ziemert Lab that address the various challenges mentioned above.

PL-11 – Frank Fang

Transition Metal-Free Assembly of Eribulin: Prins Macrocyclizations in the Halichondrin Series

Frank Fang, Hyeong-wook Choi, and Dae-Shik Kim
(Eisai Center for Genetics Guided Dementia Discovery)

The discovery, development, and ultimately commercial manufacture of eribulin is a testament to the power of the NHK (Nozaki-Hiyama-Kishi) reaction to assemble complex natural product-based structures for therapeutic applications. No less than 4 NHK carbon-carbon bond forming steps (C.11-C.12, C.13-C.14, C.19-C.20, and C.26-C.27) were required for the synthesis of eribulin including the crucial macrocyclization event. Insights gained during the process R&D efforts led to the discovery of a stereo- and regio-selective reductive Prins reaction to replace the C.26-C.27 NHK reaction. Inspired by the simplicity of the Prins approach to establish the all-cis pyran ring comprising the C.23, C.25, and C.27 stereogenic centers, a Prins macrocyclization was contemplated for completing the assembly of the macrocyclic ketone characteristic of eribulin. However, the notoriously acid-sensitive polycyclic ketal moiety common to the halichondrins and eribulin would appear to preclude such an approach. It was hypothesized that a ⍟-keto sulphone could serve as an acid-stable progenitor of the polycyclic ketal, thus enabling a Prins macrocyclization reaction. In order to investigate a Prins macrocyclization using a ⍟-keto sulphone as a key feature, new C.1-C.14 and C.15-C.26 fragments would need to be synthesized. This talk will describe: 1) Synthesis of C.1-C.14 *via* an Achmatowicz rearrangement of a C.27-C.35 derived by-product, 2) Synthesis of C.1-C.14 via a trans-ketalization sequence from a C.1-C.13 intermediate, 3) synthesis of C.15-C.26 from D-(-)-quinic acid, and 4) the successful realization of the Prins macrocyclization and the first transition metal-free assembly of eribulin and halichondrins.



INVITED SPEAKERS

I-01 – J Brent Friesen

Can Cannabidiol Help Prevent SARS-CoV-2 Infection?

L Nguyen[1], D Yang[1], V Nicolaescu[2,3], T Best[4], H Gula[2,3], D Saxena[5], J Gabbard[5], SN Chen[6], JB Friesen[6], T Ohtsuki[6], N Drayman[7], A Mohamed[7], C Dann[1], D Silva[8], L. Robinson-Mailman[1], A Valdespino[1], L Stock[1], E Suárez[1], K Jones[9], SA Azizi[9], J Demarco[5], W Severson[5], C Anderson[5], J Millis[10], B Dickinson[9], S Tay[7], S Oakes[8], GF Pauli[6], K Palmer[5], The National COVID Cohort Collaborative Consortium, D Meltzer[4], G Randall[2,3], M Rosner[1, 1]Ben May Dept. for Cancer Research, [2]Dept. of Microbiology, [4]Center for Health and the Social Sciences, [7]Pritzker School of Molecular Engineering, [8]Dept. of Pathology, [9]Dept. of Chemistry, [10]Department of Surgery, U of Chicago, Chicago, IL 60637; [3]Howard Taylor Ricketts Lab, Argonne National Lab, Lemont, IL 60439; [5]Center for Predictive Medicine for Biodefense and Emerging Infectious Diseases, U of Louisville, Louisville, KY 40222; [6]Pharmacognosy Institute and Dept. of Pharmaceutical Sciences, College of Pharmacy, U of IL at Chicago, Chicago, IL 60612

A wide range of interdisciplinary evidence involving human clinical data, animal in vivo experiments, multiple mechanisms of action in vitro experiments, natural product (NP) chemistry, integrity and purity analyses collectively substantiates the prospect of our efforts to advance cannabidiol (CBD) from a drug discovery hit (Sci. Adv. *8*, eabi6110, **2022**) to an anti-SARS-CoV-2 lead. Considering the interplay between chromatographically purified NPs and chemical synthesis, the investigated cannabinoids have pronounced SARs, and the CBD-antagonism of Δ^9-THC underscores the crucial need to distinguish *C. sativa* terms such as "cannabis", "hemp", CBD, and THC. Despite strong data supporting CBD's potential as a preventative agent for early-stage SARS-CoV-2 infection, we caution against premature use of non-medical formulations and are working actively on a clinical trial.

I-02 – Hendrik Luesch

Sec61 Inhibitor Apratoxin S4 Potently Inhibits SARS-CoV-2 and Exhibits Broad-Spectrum Antiviral Activity

Marie O. Pohl[1], Laura Martin-Sancho[2,11], Ranjala Ratnayake[3,4], Kris M. White[5,6], Laura Riva[2,12], Qi-Yin Chen[3,4], Gauthier Lieber[1], Idoia Busnadiego[1], Xin Yin[2,13], Samuel Lin[2,11], Yuan Pu[2,12], Lars Pache[2], Romel Rosales[5,6], Marion Déjosez[7], Yiren Qin[7], Paul D. De Jesus[2,11], Anne Beall[2], Sunnie Yoh[2,11], Benjamin G. Hale[1], Thomas P. Zwaka[7], Naoko Matsunaga[2,12], Adolfo García-Sastre[5,6,8,9,10], Silke Stertz[1], Sumit K. Chanda[2,11], Hendrik Luesch[3,4]. [1]Institute of Medical Virology, University of Zurich, 8057 Zurich, Switzerland, [2]Immunity and Pathogenesis Program, Infectious and Inflammatory Disease Center, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA, 92037, USA, [3]Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA, [4]Center for Natural Products, Drug Discovery and Development (CNPD3), University of Florida, Gainesville, FL, 32610, USA, [5]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, [6]Global Health and Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, [7]Huffington Center for Cell-based Research in Parkinson's Disease, Black Family Stem Cell Institute, Department of Cell, Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, NY 10502, USA, [8]Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, [9]The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, [10]Department of Pathology, Molecular and Cell-Based Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, [11]Current address: Department of Immunology and Microbiology, Scripps Research, La Jolla, CA, 92037, USA, [12]Current address: Calibr, a division of Scripps Research, La Jolla, CA, 92037, USA, [13]Current address: State Key Laboratory of Veterinary Biotechnology, Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin 150069, China

There is a pressing need for host-directed therapeutics that elicit broad-spectrum antiviral activities to potentially address current and future viral pandemics. Apratoxin S4 (Apra S4) is a potent Sec61 inhibitor that prevents cotranslational translocation of secretory proteins into the endoplasmic reticulum (ER), leading to anticancer and antiangiogenic activity both in vitro and in vivo. Since Sec61 has been shown to be an essential host factor for viral proteostasis, we tested Apra S4 in cellular models of viral infection, including SARS-CoV-2, influenza A virus and flaviviruses (Zika, West Nile, and Dengue virus). Apra S4 inhibited viral replication in a concentration-dependent manner and had high potency particularly against SARS-CoV-2 and influenza A virus, with sub-nanomolar activity in human cells. Characterization studies focused on SARS-CoV-2 revealed that Apra S4 impacted a post-entry stage of the viral life-cycle. Transmission electron microscopy revealed that Apra S4 blocked formation of stacked double-membrane vesicles, the sites of viral replication. Apra S4 reduced dsRNA formation and prevented viral protein production and trafficking of secretory proteins, especially the spike protein. Given the potent and broad-spectrum activity of Apra S4, further preclinical evaluation of Apra S4 and other Sec61 inhibitors as antivirals is warranted.

I-03 – Mary Paine

Pharmacokinetic Cannabis-Drug Interactions: Weeding Mechanisms Using Translational Tools

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Cannabis is used worldwide for both recreational and medicinal purposes. Global users aged 15-64 years have increased steadily during the past decade, now estimated at >200 million. This observation likely reflects the increasing accessibility to an array

of products due to relaxing legal restrictions in many countries. These trends raise concern for increased risk of adverse interactions when cannabis is co-consumed with drugs. The most widely studied phytoconstituents in cannabis are the cannabinoids Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Both have been shown *in vitro* to inhibit several cytochrome P450 (CYP) enzymes, which mediate the metabolic clearance of myriad drugs. However, these studies did not account for the low aqueous solubility of THC and CBD nor their non- specific binding to assay components and labware, which likely underestimated inhibition potency and thus, the likelihood of cannabis-drug interactions *in vivo*. Collectively, the potential for THC and CBD to precipitate pharmacokinetic interactions with probe drug substrates for five CYPs (-1A2, -2C9, - 2C19, -2D6, -3A) was mechanistically evaluated using a translational research approach. The aims were to 1) determine the inhibition potency of each cannabinoid against each CYP using human liver microsomes, accounting for low aqueous solubility and non-specific binding; 2) predict the magnitude of a pharmacokinetic interaction between each cannabinoid and CYP probe drug using an *in vitro*-to-*in vivo* extrapolation method; and 3) evaluate the prediction by conducting a three-arm pharmacokinetic study in 18 healthy adult participants administered an oral CYP probe drug cocktail with a placebo brownie or a brownie containing a cannabis extract high in THC or CBD. Results fill a fundamental knowledge gap about the drug interaction potential of oral cannabis products when co-consumed with drugs extensively metabolized by the CYP enzymes, thereby advancing towards the end goal of informing health care providers and consumers about the safe use of these widely available products.

I-04 – Marilyn Huestis

Cannabinoids Offer Unique Mechanisms of Action for New Therapeutics but also Impair Driving & Brain Development

Professor Dr. Dr. (h.c.) Marilyn A. Huestis, Institute for Emerging Health Professions Thomas Jefferson University

As knowledge of the mechanisms of action of cannabinoids grows so does our understanding of the therapeutic opportunities to address unmet clinical needs. The endogenous cannabinoid system plays a critical role in maintaining homeostasis, reproductive, endocrine, and cardiovascular function, motor control, analgesia, memory, and executive function. There are more than 110 phytocannabinoids in the cannabis plant each with their own pharmacological and toxicological profile. Their chemical structure enables them to activate membrane-bound cannabinoid receptors, ion channels, and PPAR nuclear receptors. Understanding cannabinoid mechanisms of action is leading to development of new therapeutics based on novel approaches to a wide spectrum of health issues (e.g. treatment resistant epilepsy, AIDS wasting disease, and potentially cancer, and autoimmune diseases). These new therapies have an enhanced therapeutic index compared to existing medications. However, some of the cannabinoids (e.g. delta-9-tetrahydrocannabinol) have side effects including performance and memory impairment and substantial effects on the developing brain. Natural cannabinoid plant materials & extracts must offer stable, reproducible cannabinoid concentrations and documentation of the efficacy of therapies in double blind, placebo-controlled & randomized clinical studies in relevant patient populations are needed.

I-05 – Erik Sotka

Marine Herbivore Offenses Against Algal Chemical Defenses

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Marine herbivores face profound challenges when feeding on algae. Although algae are generally of higher quality food than terrestrial plants they are among the low quality producers in marine ecosystems, in part because they contain an arsenal of secondary metabolites that deter herbivores. In response to algal defenses, herbivores employ multiple strategies that allow them to tolerate or avoid poorer-quality foods. Offensive traits are determined from the herbivores' point of view and represent their evolutionary solutions to the challenges of feeding on structurally and chemically-defended algae. Here, I outline our current understanding of the evolution of herbivore offenses, with a focus principally on responses to algal chemical defenses. I outline spatial and temporal variation in algal defenses,and highlight our understanding of genetic and phenotypic responses by herbivores.

I-06 – Marcy Balunas

Trachymyrmex septentrionalis Fungus-growing Ants as a Model for Exploring Unique Aspects of Host-microbe Chemical Ecology

Marcy J. Balunas[1]. [1]Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI 48109, USA

Microbial symbioses are increasingly recognized to play an integral role in host structure and function. Small molecule interactions in these host-microbe symbioses are likely to contribute to the complex molecular conversations occurring between bacterial symbionts, eukaryotic hosts, and their pathogens/prey. Many model systems have emerged for interrogating these interactions, including fungus-growing ants, one species of which, *Trachymymex septentrionalis*, resides primarily along the eastern seaboard of the United States. These 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, including the well-studied interactions with *Pseudonocardia* bacterial symbionts that protect both the ants and

their fungus gardens from fungal pathogens. Our recent work has focused on several unique and understudied aspects of this fungus-growing ant symbioses, including exploring variations in *Pseudonocardia* metabolite production within individual ant colonies as well as how ants maintain garden hygiene by sensing pathogens and physically removing pieces of compromised fungus garden. Recent developments from these studies will be presented including experiments combining genomic, metabolomic, and infection analyses to further our understanding of microbial interactions.

I-07 – D. Craig Hopp

The NCCIH Natural Products Clinical Trials Resource: Understanding U.S. Food and Drug Administration Requirements for Natural Products Clinical Trials Research

D. Craig Hopp. National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda, MD 20892

The National Center for Complementary and Integrative Health (NCCIH) has funded many natural product clinical trials in its history. In doing so, NCCIH has encountered a lot of confusion about the regulations surrounding such trials, especially when they involve dietary supplements. To better understand the challenges in this field of research, NCCIH convened a roundtable meeting in August 2020 that included representatives from the supplement industry, the U.S. Food and Drug Administration (FDA), and various components of the National Institutes of Health (NIH). A major recommendation of that meeting was creating a resource that would help clarify the regulations and facilitate communications with the FDA. Consequently, in September 2021, NCCIH launched the Natural Products Clinical Trial Resource, a page on its website designed to assist investigators intending to submit an NIH grant application that includes a natural product clinical trial. The goal is to help those investigators better understand the rules and regulations that govern this type of research. This presentation will highlight features of this web resource and separate fact from fiction regarding some of the commonly held beliefs about clinical trials involving dietary supplements.

I-08 – Amala Soumyanath

Towards Optimized Clinical Trials of Centella Asiatica, a Neurologically Active Botanical

Amala Soumyanath[1,2]. [1]BENFRA Botanical Dietary Supplements Research Center, and [2]Department of Neurology, Oregon Health & Science University, Portland, OR, USA

The BENFRA Botanical Dietary Supplements Research Center at OHSU studies Botanicals Enhancing Neurological and Functional Resilience in Aging. Two botanicals of interest are *Centella asiatica* (gotu kola) and *Withania somnifera* (ashwagandha). The Center has considerable experience with *Centella asiatica*, which is used in Ayurvedic medicine to improve memory. It is a popular dietary supplement for "brain health", and shows potential to be developed as an FDA approved "botanical drug" for the treatment of Alzheimer's Disease. The rational use of botanicals, whether as dietary supplements or botanical drugs, requires their evaluation through optimized clinical trials. Our preclinical studies have confirmed the cognitive effects of *Centella asiatica* and highlighted a role for triterpenes and caffeoylquinic acids as its active compounds. We have developed analytical methods for targeted and untargeted chemical characterization of *Centella asiatica* extracts, as well to measure *Centella asiatica* compounds in biological fluids. In translational clinical studies, we have developed an optimized *Centella asiatica* product and matching placebo, and the examined oral bioavailability of its active compounds in humans. Studies are underway to examine safety, tolerability and biomarkers of target engagement of the product in humans, as a pre-requisite to performing clinical trials evaluating the efficacy of *Centella asiatica* in slowing age- or neurodegenerative disease related cognitive decline.

I-09 – Amala Soumyanath

Microbiota Metabolites Modulate the T helper 17 to Regulatory T cell (Th17/Treg) Imbalance Promoting Resilience to Stress-Induced Anxiety- and Depressive-Like Behaviors

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Chronic stress (CS) disrupts immune homeostasis while gut microbiota-derived metabolites attenuate inflammation, thus promoting resilience to stress-induced immune and behavioral abnormalities. There are both peripheral and brain region-specific maladaptations of the immune response to CS that produce interrelated mechanisms required for the design of novel therapeutics to prevent stress-induced psychological impairment. This study shows that a combination of probiotics and polyphenol-rich prebiotics, a synbiotic, attenuates the CS-induced inflammatory responses in the ileum and the prefrontal cortex promoting resilience to the consequent depressive- and anxiety-like behaviors in male mice. Using a model of chronic unpredictable stress, behavioral abnormalities were associated to strong immune cell activation and recruitment in the ileum while inflammasome pathways were implicated in the prefrontal cortex and hippocampus. Chronic stress also upregulated the ratio of activated proinflammatory T helper 17 (Th17) to regulatory T cells (Treg) in the liver and ileum and ingenuity pathway analysis predicted that the aryl hydrocarbon receptor (AHR) could be driving the synbiotic's effect on the ileum's inflammatory response to stress. Synbiotic treatment indiscriminately attenuated the stress-induced immune and behavioral aberrations in both the ileum and the brain while in a gut-immune co-culture model, the synbiotic-specific metabolites promoted anti-inflammatory activity through the AHR.

I-10 – Jeffrey Johnston

New Chemical Tools and Strategies that Enable Discoveries in Natural Product-Based Therapeutic Development

Jeffrey N. Johnston, Vanderbilt University

Natural products and small molecules are a mainstay of drug development, offering structural and functional topologies to precisely engage receptors. Increasingly complex protein-protein interactions demand greater breadth of structural and stereochemical complexity, as well as size, within a discrete compound collection. Furthermore, the incorporation of fluorine into small molecules can provide directed conformational bias, enhance desirable drug like properties, and improve metabolic stability. All of these features are meaningful only when they are at arm's reach – essentially on-demand – such that attention is focused predominantly on the greater issues of potency and selectivity. Tools that enhance the immediacy of availability and acquisition are in high demand (*JACS* **2016**, *138*, 14160). Chiral proton catalysis using Bis(AMidine) (BAM) ligands has generalized access to numerous types of enantioenriched, functionally complex secondary amines. Now readily available, this feedstock is the platform for new reaction development that provides unfettered access to a broad range of enantiopure products, including α-amino amides and heterocycles. Highlights of our contributions to this area will be described, embedded within our approach to problem selection and study.

I-11 – Tadeusz Molinski

Axinisoside-1. Complete Stereostructure of a Complex Glycolipid

Tadeusz F. Molinski[1,2] and Mariam Salib[1]. [1]Department of Chemistry and Biochemistry, and [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA 92093, USA

Marine invertebrates produce a variety of highly-modified lipids, including bioactive glycolipids. Chromatographic separation of extracts of an Axinellid marine sponge, collected in Western Australia, delivered known sphingolipids (oceanapins) and an unusually complex glycolipid, axinisoside-1. In this talk, the structure elucidation of axinisoside-1 – including stereoassignment all four stereocenters of the tetrahydroxy C_{28} polyketide-like aglycone, terminated by a g-butyrolactone – will be presented. The complete structure was solved by integrated analysis of ECD, NMR and synthesis. The antiinflammatory activity of the oceanapins, and bioactivity of the title compound, will be discussed briefly.

I-12 – Clemens Anklin

Modern Advanced NMR Spectroscopy for non-NMR Experts

Clemens Anklin, Bruker BioSpin Corp., 15 Fortune Drive, Billerica MA 01821, USA

NMR spectroscopy has made great progress over the years but the NMR community has not done the best job in bringing these advances to the wider audience of chemists including natural products scientists. I will try to bridge this gap by presenting a wide array of new methods and their application to natural products. These include experiments for the determination of coupling constants, the use of non-uniform sampling for improvement of the quality of data, acquisition of nuclei other than 1H and 13C, the use of AI/ML in NMR data processing and much more. Some of the recent advances in the technology will also be addressed.

I-13 – Roberto Gil

Reference-Free Quantitative NOE and the Structural Value of Two-Bond Proton-Carbon ($^2J_{CH}$) Coupling Constants for Configurational Analysis Small Molecules

Roberto R. Gil, Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, USA

The Nuclear Overhauser effect (NOE) is a very important tool in Nuclear Magnetic Resonance (NMR) for 3D structural analysis of small organic molecules. In this sense, the quantitative application of NOE is conventionally based on known reference distances that must be separated spectrally and are not always available. In this presentation, a new 3D structure evaluation and selection method will be described that does not require a reference distance, but uses structures optimized by Molecular Mechanics, allowing NOE evaluation even in molecules without suitable reference groups. A new approach to recover the structural information from faster NOESY experiments with shorter recycling delays (semi quantitative conditions) will be presented. In addition, this is complemented by a new method based on the use unsigned long-range proton-carbon coupling constants that allow the determination of the correct relative configuration from the molecular constitution. For this, $^2J_{CH}$ and $^3J_{CH}$ values collected from a single HSQMBC experiment. The study is mainly based on the comparison of $^{2,3}J_{CH}$ values calculated by DFT with the experimental once. The structural value of the $^2J_{CH}$ coupling constants was historically overlooked because of the lack semi-empirical equations such as those existing for 3-bond *J* coupling constants based on the Karplus relationship. The use DFT calculations revealed an impressive degree of structural discrimination when using only $^2J_{CH}$ coupling constants. The robustness of the method will be demonstrated using different small molecules of importance in organic chemistry as proof of concept. The combination of both

methodologies positions them as a viable option for application in different fields of research such as organic, peptide and carbohydrate synthesis, identification and analysis of natural products, as well as in medicinal chemistry.

I-14 – Roland Kersten

Biosynthesis of Side-Chain-Macrocyclic Peptides in Plants

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Plants biosynthesize peptide natural products via the ribosomal pathway. Plant peptides are often cyclized via head-to-tail-macrocyclization, canonical disulfide bonds or crosslinks between aromatic amino acids and other amino acid side chains. The latter side-chain-macrocycles have recently been connected to a copper-dependent plant protein family called the BURP domain (named after founding members BNM2, USPL, RD22 and PG1β). BURP domain peptide cyclases catalyze diverse bond formations in an autocatalytic manner. Here, we give an update on the discovery and biochemistry of BURP domain peptide cyclases involved in side-chain-macrocyclic plant peptides across the plant kingdom.

I-15 – Bo Li

Biosynthesis of a Copper-Containing Antibiotic

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Metal-binding natural products contribute to metal acquisition and bacterial virulence, but their roles in metal stress response are underexplored. We show that a five-enzyme pathway in *Pseudomonas aeruginosa* synthesizes a small-molecule copper complex, fluopsin C, in response to elevated copper concentrations. Fluopsin C is a broad-spectrum antibiotic that contains a copper ion chelated by two minimal thiohydroxamates. Biosynthesis of the thiohydroxamate begins with cysteine and requires two lyases, two iron-dependent enzymes, and a methyltransferase. The iron-dependent enzymes remove the carboxyl group and the α-carbon from cysteine through decarboxylation, N-hydroxylation, and methylene excision. Conservation of the pathway in *P. aeruginosa* and other bacteria suggests a common role for fluopsin C in the copper stress response, which involves fusing copper into an antibiotic against other microbes.

I-16 – David Turner

Targeting Nutritional AGE Bioavailability Using Natural Products

David P. Turner. Massey Cancer Center, Virginia Commonwealth University, Richmond, VA, 23298

A series of published studies from this group defines the increased bioavailability of reactive metabolites called advanced glycation end products (AGEs) as an unexploited opportunity to consider how integrated nutritional behaviors can combine to impact chronic disease. AGEs are significant because their exposure across the life course has significantly increased due to integrated environmental, demographic and social factors that influence nutritional behavior that lead to weight gain, obesity, and increased chronic disease risk. First of kind molecular studies from this lab, have assigned a cause and effect relationship between nutritional AGE exposure and tumor growth and progression in animal models. There is a clear need to molecularly define, and functionally assess the potential of natural compounds that can interfere with the complex chemical reactions and biological pathways that lead to AGE formation. Such information would significantly inform on primary, secondary, and/or tertiary disease prevention strategies aimed at reducing nutritional AGE bioavailability.

I-17 – Yousong Dong

Genome-aided Discovery of New Enzymes

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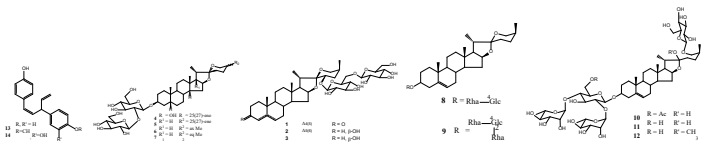
Chemistry is an underlying language of life processes, and small molecules frequently mediate and execute biological functions. Nature has evolved a plethora of functionally diverse enzymes to synthesize compounds with astounding structural diversity. As genome information is exponentially growing, new approaches, particularly those based on sequence similarity, have significantly expanded our capability to access an enormous number of enzyme homologs. However, the lack of deep understanding of enzyme sequence-function-relationship frequently challenges accurate functional assignment of members of the enzyme families, underscoring the critical need for detailed enzymology studies. Here, I will present our recent studies on the functional characterization of members of the ATP-grasp enzyme family, the nitroreductase family, and the Rieske-type enzyme family. Furthermore, I will discuss the application of some enzymes for chemical synthesis.

I-18 – Turibio Tabopda

Cytotoxic Steroidal Saponins from *Asparagus schweinfurthii* Baker (Liliaceae)

Elodie N. Kamdeu[1], Turibio K. Tabopda[1,2,3], Marguerite H. T. Kenmogne[1], Yoshihito Shiono[2], …, Mark T. Hamann[3]. [1]Department of Organic Chemistry, Faculty of Sciences, University of Yaounde 1, Cameroon. [2]Department of Food, Life, and Environmental Science, Faculty of Agriculture, Yamagata University, Japan. [3]Department of Drug Discovery, Biomedical Sciences and Public Health, Medical University of South Carolina, United States of America*

Phytochemical investigation of the root's tubers of *Asparagus schweinfurthii* led to the isolation of fourteen compounds among which six steroidal saponins have been determined for the first time, called Schweinfurthiosides A-F **(1, 5, 10, 4, 2, 3)** as well as eight known compounds. Their structures were determined by spectroscopic methods including 1D and 2D NMR experiments, ESI and HRESIMS. Fractions and some pure isolated compounds were evaluated *in vitro* for their cytotoxic activities against five human solid cancer lines (OVC-5, HepG2, H-125, PANC-1, and U251N (human glioblastoma).



I-19 – Nandu Sarma

USP Botanical Dietary Supplements and Herbal Medicines Pan American Expert Panel

Nandu Sarma and Maria Monagas. United States Pharmacopeia (USP). Dietary Supplements and Herbal Medicines. Twin brook Parkway. Rockville, MD 20852

The 2019 WHO Global Report on Traditional and Complementary Medicine(https://apps.who.int/iris/handle/10665/312342) indicates that in countries from the Pan American region, including Bolivia, Brazil, Cuba, Mexico, and Peru, some herbal ingredients are considered essential medicines because they satisfy the priority health care needs of the population. In addition, according to this WHO report, with increased health care costs, herbal medicines are expected to play a role in the prevention of chronic diseases and on the needs of aging populations, leading to better recognition of the role of herbal medicines in national health systems. Despite this information, pharmacopeial standards for identity, composition, strength, purity, and limits for contaminants, which are required for consistent quality, are not available for many of these plants and the related herbal medicines. Other challenges faced by the region include a lack of research data, expertise from within national health authorities and control agencies, and mechanisms to monitor the safety of practices and products. Considering the role that quality standards play in addressing these matters and its commitment to global public health, USP launched last March 2022 the *Botanical Dietary Supplements and Herbal Medicines Pan American Expert Panel*. The present oral presentation will describe the charge of this Expert Panel in developing USP quality standards (e.g., monographs) and candidate reference standard materials for botanical ingredients and products used in traditional herbal medicines in the Pan-American region.

I-20 – Courtney Thomas

Determination of Anti-AGE Properties of SC Native *Pseudognaphalium obtusifolium*

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Accumulation of Advanced Glycation End products (AGEs) in the body is correlated with several health conditions, including cardiovascular disease, diabetes, and cancer, all of which the Center for Disease Control named as main sources of hospitalizations and deaths in South Carolinians. AGEs form through two main pathways, endogenous nonenzymatic reactions of proteins, lipids or nucleic acids with sugars through the production of reactive dicarbonyl compound Methylglyoxal, and exogenous (dietary) intake of foods which have undergone the Maillard reaction through the production of reactive dicarbonyl compound Glyceraldehyde. The South Carolina natively grown plant, Life Everlasting (*Pseudognaphalium obtusifolium)* has long since been used by natives as a natural healer of common ailments such as sore throat, cold and flu. As a member of the genus *Gnaphalium*, Life Everlasting (LE) is predicted to contain chemical compounds such as flavonoids, sesquiterpenoids, and phytosterols like other members of the same genus. No studies have evaluated the validity of health benefit claims pertaining to Life Everlasting. Our project seeks to do just that. Our overall goal is to evaluate natural products from SC native plant Life Everlasting against AGE accumulation through inhibition of AGE precursors Methylglyoxal (MGO) and Glyceraldehyde (GA). Using an NMR based assay, we show that water solvent extract of Life Everlasting does reduce presence of MGO after both 0- and 24-hour incubation periods. We plan to evaluate the most potent solvent extract against Glyceraldehyde as well. Once determined, we will test AGE precursor inhibition properties of LE extracts, identify active metabolites found in extracts, isolate active metabolite against MGO and GA, test effectiveness (in both test tube and cultured cells) against fully formed AGEs, and determine best growth conditions for producing greatest yield of active metabolite. We hope findings of this study will in the future, provide a natural treatment option against serious diseases.

I-21 – John Warner

South Carolina Centers of Economic Excellence

John Warner[1, 1]*Serial Entrepreneur and Recognized Leader of Innovation and Entrepreneurship in South Carolina*

The South Carolina Research Centers of Economic Excellence Act ("CoEE 1.0"), enacted by the South Carolina General Assembly in 2002, has been a catalyst for economic growth driven by the creation and growth of new technologies, new companies, existing businesses, and high-wage jobs. CoEE 1.0 funded 76 endowed research chairs in 51 centers at the State's three public research institutions—Clemson University, the Medical University of South Carolina, and the University of South Carolina. Approximately $400 million was funded through proceeds from the South Carolina Education Lottery and equal matches from non-state sources. Each research chair was endowed with $4 million to $10 million. A who's who of corporate funders include BMW, Fluor, Michelin, Dominion Energy, and others. Centers are focused in six industry clusters that are critical to the world and South Carolina: Advanced Materials & Nanotechnology, Automotive and Transportation, Biomedical, Energy and Alternative Fuels, Information Science, and Pharmaceutical. The Darla Moore School of Business found that through 2021 CoEE 1.0 had a total economic impact of about $3.9 billion and created about 20,000 jobs generating about $1.2 billion in annual labor income. Mr. Warner is leading a coalition of industry professionals, academic researchers, entrepreneurs, economic developers, and elected officials to promote reauthorizing the Centers of Economic Excellence Act ("CoEE 2.0"). The proposal is for CoEE 2.0 to use the NSF Regional Innovation Engine framework of Use Inspired Innovation, Commercialization, Workforce Development, and Diversity. The General Assembly would fund $300 million in academic research designed to solve a problem an industry partner has identified and is willing to invest in solving. Key to CoEE 2.0 is that $300 million of industry matches can be in industry innovation centers or in entrepreneurial companies which will employ the graduates of the university research programs. When successful, the total of $600 million invested in CoEE 2.0 collaborations will build SC's global reputation to attract resources and talent to develop and commercialize innovations in SC, across the country, and around the world. High-wage jobs in SC will increase by creating, attracting, and growing academic research enterprises, industry innovation centers, and entrepreneurial companies.

I-22 – Patrick Still

Funding for Natural Products Research at the National Center for Complementary and Integrative Health

Patrick C. Still, PhD, National Center for Complementary and Integrative Health (NCCIH)

The National Center for Complementary and Integrative Health (NCCIH) supports research that analyzes fundamental mechanisms, usefulness, and safety of complementary and integrative health interventions and their roles in improving health and health care. NCCIH welcomes applications that fall within its mission to address both mechanistic and clinical questions. Detailed descriptions about the areas NCCIH supports, including biological activities of natural products, such as prebiotics, probiotics, dietary supplements, botanicals, and vitamins, as well as clinical trials involving natural products, can be found on the NCCIH website. The **Fundamental Science Research on Complementary and Integrative Health Approaches, Including Natural Products** NOSI describes NCCIH priorities in innovative basic and mechanistic research or technology/method development research relevant to complementary and integrative health approaches. The webpage for NOT-AT-21-006 includes further information. The **Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR)** at NCCIH is described in more detail on the NCCIH small business research webpage. The **Natural Product Early Phase Clinical Trial R61/R33** are investigator-initiated, early phase, clinical trial awards. This funding opportunity is for milestone-driven testing of pharmacokinetics, bioavailability and assessment of natural products effect on humans. If milestones in the R61 phase are achieved, up to 3 years of additional support through the R33 phase may be awarded to replicate the impact of the natural product. The FOA webpage for PAR-20-218 includes further information. The **Clinical Coordinating Center for NCCIH Multi-Site Investigator-Initiated Clinical Trials of Natural Products UG3 and UH3** encourages cooperative agreement applications for investigator-initiated, multi-site, clinical trials (Phase III and beyond) to study the effects of natural products in NCCIH designated areas of high research priority. The FOA webpage for PAR-20-215 includes further information. The Center places great emphasis on evidence-based complementary therapies "integrated" with and not used as an "alternative" to conventional medicine and seeks to better define and map a path to whole person health by expanding and building on current activities while advancing new research strategies and ideas. Funding opportunity announcements (FOA) details, NCCIH staff points of contact, and relevant webinars are available on NCCIH relevant webpages.

I-23 – Michelle Bond

Funding for Natural Products Discovery and Analysis at National Institute of General Medical Sciences

Michelle R. Bond, Ph.D., National Institute of General Medical Sciences, NIH

The National Institute of General Medical Sciences (NIGMS) supports basic research that increases our understanding of biological processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. NIGMS welcomes

applications that fall within its mission to address fundamental research questions. Detailed descriptions about the areas NIGMS supports, including natural products discovery and analysis, can be found on the NIGMS website. The Institute places great emphasis on supporting investigator-initiated research grants. Funding Opportunity Announcements (FOAs) relevant to the audience will be discussed. FOA details, FAQs, NIGMS staff points of contact, and relevant webinars are available on relevant NIGMS webpages.

I-24 – Sean Ash

Venture capital funding serves as the lifeblood of innovative and novel technologies. It's one of the crucial mediums that enables an idea or concept to go from lab bench to benchmark. For over a decade academics, entrepreneurs and trailblazers have enjoyed relatively easy access to capital from early-stage investors. However, in a post-covid world wrought with inflation, rising interest rates, lingering supply chain issues and new geopolitical risks, investors have dampened their appetite for riskier investments. Venture funding peaked in November 2021 with $70 billion funded for the month. In six short months, that number plummeted over 44% to only $39 billion funded for May of 2022. This presentation will attempt to explore why venture capital funding has contracted, compare this current period with historical contraction cycles and investigate how both venture investors and venture stage companies alike have adapted their approach for this new environment with a specific focus on and petrochemical alternatives in pharmacology.

I-25 – Jin K. Cha

The National Science Foundation: Funding Opportunities and Priorities

Jin K. Cha, Program Director, Chemical Synthesis, Division of Chemistry, National Science Foundation, 2415 Eisenhower Ave, Alexandria, VA 22314, USA

Funding opportunities at the Division of Chemistry of the National Science Foundation will be presented. Emphasis will be placed at research support by the Chemical Synthesis (SYN) Program.
from the SYN program description from the website:
The Chemical Synthesis (SYN) Program supports experimental and computational research on the development of new and efficient synthetic methodologies and on the synthesis of complex and/or challenging chemical structures. Typical synthetic targets include novel structures (including natural products and biomolecules), molecules and structures displaying unique properties, or substances that provide pathways to discover and elucidate new phenomena

I-26 – Rick Warner

Investing in and Building Returns in the Natural Asset Class, At Speed and Scale: A Perspective from the UN Oceans Conference, Lisbon 2023: The Sustainable Blue Economy Investors Forum Focused (Https://Www.Youtube.Com/Watch?V=K-9dcyixqpy&T=5071s) On The Opportunities for Investing Blended Funds into Blended Programs Based on Measurable SDGs And ROIs as the World Rapidly Transitions to Sustainable Blue/Green Economies Within A 2C Warmer World

Frederick Maltby Warner IV, Coastal8.com

Coastal 8 functions as a Resilience Systems Integrator, with coastal communities we develop and build a mix of blended program activations with blended capital; each designed to interact with exiting Island resources and infrastructure. Each "Coastal 8" program set – with the goal of greater resilience and sustainability leads to a more prosperous Blue/Green economy for and by the Island Nation. Blended programs and capital leverage and catalyze each other, by adding programs that jointly foster SDG 14 and SDG 13 we can yield strong, measurable, and rapid gains on SDG8 while driving toward carbon neutrality and biomass prosperity. Rick Warner (Frederick Maltby Warner IV) is the Chair of Coastal8.com and was Co-Vice Chair of the IRAC (Island Reliance Action Challenge) task force. The task force was chartered, by members of the CREF (Caribbean Renewable Energy Forum), with developing a resilience scorecard to speed-up and scale-up island nations efforts to advance their resilience and sustainability needs, in the face of increasing climate change impacts, driven by a 1.5C warming world and resistance to transitions. Coastal 8 and the task force has jointly led the creation of the Blue/Green economy transition (BGet) scorecard (from the IRAC resilience scorecard). The scorecard process solidifies long-term P3 (Public Private Partnership) strategic goals and program needs. It is structured such that ROI and SDG goals are aligned to foster prosperity and resilience for all key stakeholders. Coastal 8's team, brought to the task force it's knowledge and experience as a new type of systems integrator focused on resilience building, blended funds and blended programs deployments. The program deployments in the score card will be designed and built with aligned island nations and with the best of breed capital and strategic supplier stakeholders. Rick and the Coastal 8 team are committed to advancing the use of the BGet Scorecard through the development of a Caribbean based Co-Op, chartered to achieve constructive capital investment into the island nations. We believe through use of the Scorecard, the Co-Op team can evaluate and capitalize an optimized set of programs to make the region and individual islands more robust and less dependent on external support going into the less stable world we all face together.

I-27 – Jaclyn Winter

Accessing New Terpene Scaffolds from Marine-Derived Fungi

Jaclyn M. Winter, Department of Medicinal Chemistry, University of Utah, Salt Lake City, Utah, USA

Terpenes are the largest class of natural products and are produced by all kingdoms of life. The enormous structural diversity observed with this class of molecules often originates from dedicated terpene synthases. In fungi, even though condensation and cyclization reactions occur independently, there are several chimeric bifunctional fungal terpene synthases that catalyze both chain elongation and cyclization reactions from simple C5 universal hemiterpene precursors. Depending on the strategy for initial carbocation formation, terpene synthases are usually categorized as either type I or type II cyclases. In contrast to type II cyclases, type I terpene cyclases are usually associated with more structurally diverse compounds. However, only a limited number of fungal type I cyclases have been functionally characterized to date. Following de novo genome sequencing and assembly of several marine-derived fungal strains, we were able to identify a number of putative terpene biosynthetic gene clusters, many of which contain type I cyclases. These uncharacterized synthases hold considerable promise for the discovery of new structurally complex compounds that can enhance the chemical space of terpene natural products. The identification of type I diterpene and sesterterpene bifunctional fungal terpene synthases, development of alternative platforms for the heterologous production of terpenes, and the biochemical characterization of a new type I diterpene scaffold will be presented.

I-28 – Emily Mevers

Chemical Investigations into the Microbiota of Marine Egg Masses

Paige Banks, Caitlin Winner, Molly Simek, Cole Gannett, Carla Menegatti, Andrew N. Lowell, Emily Mevers, Department of Chemistry, Virginia Tech, Blacksburg, VA, 24061

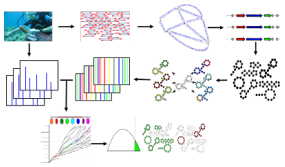
Natural products have played a critical role in drug discovery and innovation for many decades - roughly 65% of all approved small molecule drugs are either natural products, derivatives, or embody a natural product pharmacophore. This is especially true for the treatment of infectious diseases, which have significant and growing unmet needs for new therapeutic agents. The success of natural products in the clinic is due to their evolutionary history, their structures and functions having evolved over millions of years of selective pressures to carry out an essential role for the producing organism. One particularly important role is the production of defensive metabolites by symbiotic microorganisms to protect their eukaryotic host. In an effort to discover new antibiotics, my group uses our understanding of environmental niches to identify systems that are predicted to benefit from specific chemical defenses. One such system are marine egg masses, which have been shown to succumb to fungal pathogens and predation only upon treatment with broad-spectrum antibiotics. We have recently begun to investigate the components of the microbiota and have taken a culturing-based approach coupled to metabolomics to examine the chemical potential of the associated bacterial strains. A family of new metabolites were identified to be produced by a *Streptomyces* sp. that exhibited strong antibiotic activity in binary screens. Isolation, structure elucidation, and synthetic approaches are on-going to explore their pharmaceutical potential.

I-29 – Hosein Mohimani

Computational Methods for Discovering Natural Products by Mining Large Mass Spectral Datasets

Bahar Behsaz, Mustafa Guler, Abhinav Adduri, Yi-Yuna Lee, Liu Cao, Donghui Yan, Benjamin Krummenacher, and Hosein Mohimani[1], [1]Computational Biology Department, Carnegie Mellon University, Pittsburgh, USA.

Natural products are the major source of drug molecules. Currently, 55% of antibacterial drugs, 17% of antifungal drugs, 19% of antiviral drugs, and 57% of anticancer drugs approved by the Food and Drug Administration are natural products or their derivatives. Currently, the dominant technique for discovering novel natural products is bioactivity-guided isolation. However, this technique is limited to the high abundance molecular products of microbial strains. Since most of the widely expressed natural products (NPs) have already been picked, bioactivity-guided techniques now lead to high rediscovery rates of known molecules. An alternative to this approach is mining for the natural product biosynthetic gene clusters (BGCs, clusters of genes responsible for biosynthesis of natural products). While genome mining is sensitive and fast, isolation of the natural products requires expression of BGCs in a heterologous host, a nontrivial and expensive step for many microbial genera. Our laboratory focuses on developing a novel platform for discovering natural product small molecules by integrating genome mining with computational metabolomics. With the advent of high throughput tandem mass spectrometry, metabolomics datasets collected on the supernatant of microbial datasets have become available. However, computational techniques for identifying novel small molecules from these large and complex datasets are in their early stages. Recently, we developed Dereplicator [1], Dereplicator+ [2], and molDiscovery [3] to identify known small molecules by searching their tandem mass spectra against public chemical databases, like PubChem. We further developed MetaMiner [4] and NRPminer [5]-, techniques for predicting the molecular structure of peptide natural products from their BGCs. In this talk, I will present recent progress in our laboratory on discovery of novel non-ribosomal peptides, ribosomally synthesized and post-translationally modified peptides, polyketides and saccharides through integration of genome mining and computational metabolomics.



DEI WORKSHOP PRESENTERS

W-01 – Shanina Sanders Johnson

Inclusive Mentorship: Best Practices to Cultivate a Diverse Scientific Workforce

Shanina Sanders Johnson, Department of Chemistry and Biochemistry, Spelman College, Atlanta, GA 30318, USA

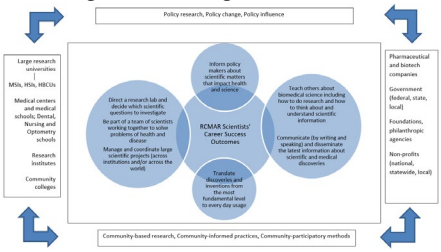
As the United States seeks to ensure a skilled workforce in science, technology, engineering, and math (STEM) fields, scientists and leaders in STEM are reflecting on the practices that can build this workforce. The STEM education pipeline serves as a source of workers and thus, a diverse community of STEM students is a crucial component for future success. In addition, cultivating the potential found in historically underrepresented communities in STEM is equitable from a social justice standpoint to combat the historic exclusion of these individuals. Mentorship is a key component in the recruitment and retention of individuals in STEM. This workshop will discuss the impact of mentorship on student success and explore best practices in inclusive mentoring. The importance of culture in developing authentic mentoring relationships will be presented in an interactive approach to inclusive mentoring practices.

W-02 – Marvella Ford

My Academic Journey to a Cancer Health Disparities Research Career

Marvella Elizabeth Ford, Hollings Cancer Center Medical University of South Carolina

In this presentation, Dr. Marvella Ford will share her academic journey from a small rural town in upstate New York to a nationally renowned cancer health disparities research career. She will discuss the importance of receiving different types of mentoring in achieving academic success. She will present a career development model that was developed by the NIA-funded Resource Centers on Minority Aging Research.



CONTRIBUTED SPEAKERS

C-01 – Fridah Rotich and Joe Mangun

Identifying Antimicrobial Constituents of *Cannabis Sativa* L. (Hemp) Against Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Fridah C. Rotich, Joe Mangun, Joëlle Houriet, Nadja B. Cech. Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27412

Cannabis sativa L. (industrial hemp) is a botanical that has many applications, given its chemical diversity and complexity. More than 480 compounds encompassing several chemical classes have been identified as constituents of this botanical species. Our study investigated the antimicrobial efficacy of this plant against a highly resistant clinically relevant strain of MRSA (USA 300 LAC). An extract of *C. sativa*, and three out of seven fractions resulting from chromatographic separation, completely inhibited the growth of MRSA at a testing concentration of 50 μg/mL. Known antimicrobial compounds, cannabidiol (CBD) and cannabidiolic acid (CBDA) were quantified in the extract and bioactive fractions. The antimicrobial activity of these two compounds were evaluated in terms of minimum inhibitory concentration (MIC) values, and this activity was compared to the antimicrobial activity of the extract and bioactive fractions. The comparison revealed that the extract and two of the bioactive fractions contained adequate concentrations of CBD and CBDA to contribute to their antimicrobial activity. However, one of the active fractions had sub-inhibitory concentrations of CBD and CBDA, suggesting that a different constituent contributed to its antimicrobial activity. Bioinformatic techniques were employed to identify features in bioactive fractions that explain their antimicrobial activity. Results from these analyses will be presented.

C-02 – Prakash Nagarkatti

Role of Epigenome and Microbiome in the Regulation of Inflammation by Cannabinoids

Prakash Nagarkatti and Mitzi Nagarkatti. Department of Pathology, Microbiology, and Immunology University of South Carolina School of Medicine, Columbia, SC 29209, USA

Chronic inflammation is the underlying cause of several clinical disorders from cardiovascular to neurological diseases, and from cancer to obesity. Additionally, there are over 80 different types of uncurable autoimmune diseases against which there are no effective treatments available. The currently available drugs to treat inflammation are either highly immunosuppressive thereby causing increased susceptibility to infections and cancer or fail to effectively treat inflammatory diseases. Thus, clearly, there is dire need to identify new pathways that can lead to development compounds that can suppress chronic inflammation. Studies from our lab in the past two decades have identified Cannabinoids as potential natural compounds that can suppress inflammation without causing over toxicity. Cannabinoids act primarily through the cannabinoid CB1 and CB2 receptors as well as a variety of other receptors expressed widely in the immune system. Research from our lab has shown that cannabinoids act through multiple pathways including apoptosis, polarization from pro-inflammatory Th1 to anti-inflammatory Th2 cell differentiation, and induction of immunosuppressive Regulatory T cells (Tregs) and Myeloid -Derived Suppressor Cells (MDSCs). Our studies have identified that such immunological changes are mediated through regulation of epigenetic pathways including histone modifications, DNA methylation and miRNA induction. Additionally, cannabinoids also alter the microbiome in the gut to induce short-chain fatty acids that attenuate inflammation. In the current presentation, we will highlight such epigenetic and microbiome changes induced by cannabinoids to suppress inflammation (Supported in part by NIH grants: R01ES019313, R01MH094755, R01AI123947, R01AI129788, P01AT003961, P20GM103641, R01AT006888).

C-03 – Robert Driscoll

Utilization of Centrifugal Partitioning Chromatography (CPC) for the Isolation of Cannabinoid Fractions from Cannabis Distillates

Robert P. Driscoll, Roger D. Morin, Process and Application Engineering, Robatel Inc., Pittsfield, Massachusetts

Centrifugal Chromatography instrumentation is used in the natural products, pharmaceutical, cosmetic, and biopharmaceutical industries as a means of isolating individual fractions from complex mixtures of organic components. Fast Centrifugal Partitioning Chromatography [FCPC] offers several advantages versus traditional liquid chromatography methods. In the rapidly expanding cannabis market, FCPC has found a place as an effective means of separating cannabinoid fractions for full spectrum products, and for medical and pharmaceutical consumption. FCPC has been demonstrated as an effective means for Δ9 THC (tetrahydrocannabinol) removal from CBD (cannabidiol) products, to mitigate psychoactive properties, while maintaining the cannabis extracts' medicinal properties. Extensive research has been conducted using FCPC as an effective tool for producing high purity fractions, at reseach and development scale, up to production scale, demonstrating that the FCPC is well adapted to accommodating different solvent systems as a function of the cannabinoid fraction(s) of interest, to acheive THC-free levels of 0.3% or less.

C-04 – Emily Britton

Analytical Approaches for Characterizing Cannabinoids for Quality, Safety, and Research Applications

Emily R. Britton[1], Kim Van Tran[1], Marian Twohig[1], and Christopher Hudalla[2,1] Waters Corporation, 34 Maple St, Milford, MA 01757, [2] ProVerde Labs, 420 Fortune Blvd, Milford, MA 01757

Decriminalization and legalization of cannabis in many regions of the world has led to rapid market growth and research expansion. Cannabinoids remain in the spotlight due to their proven and potential health benefits, indicated by the number of new products, newly popularized cannabinoids, and steadily increasing list of peer reviewed publications. Understanding and annotating cannabinoid content is a foundational need for those who are growing, processing, testing, and researching cannabis, and there are a variety of analytical tools that can accomplish this task. This presentation will highlight fit-for-purpose analytical tools (targeted and non-targeted) to enable scientists to quantify cannabinoids for raw material characterization, formulation and finished product testing, to better understand the complexity of new cannabinoid production methods, and to uncover new insights for research and development.

C-05 – Monica Pupo

Uncovering Functions and Applications of Specialized Metabolites from Microbiomes of Brazilian Stingless Bees

Mônica T. Pupo[1], Gabriela T. de Paula[1], Cristiano Menezes[2], Fabio S. Nascimento[3], Adriano D. Andricopulo[4]. [1]School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo (USP), Ribeirão Preto, SP, 14040-903, Brazil, [2]Brazilian Agricultural Research Corporation (Embrapa), Jaguariúna, SP, 13820-000, Brazil, [3]Faculty of Philosophy, Sciences and Letters at Ribeirão Preto, USP, Ribeirão Preto, SP, 14040-901, Brazil, [4]São Carlos Physics Institute, USP, São Carlos, SP, 13563-120, Brazil

Stingless bees (Tribe Meliponini) are a monophyletic group of eusocial insects belonging to a larger group known as the corbiculate bees (Hymenoptera: Apidae), which includes honeybees, bumble bees, and orchid bees. Stingless bees occur in all tropical and subtropical regions of the world, with approximately 550 species and 61 genera. Brazil harbors around 300 species of native stingless bees, which play important roles in pollination and meliponiculture. The first report of a nutritional symbiosis between the stingless bee *Scaptotrigona depilis* with one fungus was published by Menezes and co-workers in 2015. This finding motivated us to pursue efforts on understanding this symbiotic interaction at molecular level, leading to the identification of the fungal strain as an osmophilic yeast in the genus *Zygosaccharomyces* that supplies ergosterol as a precursor for ecdysteroid biosynthesis. Different species of bees were recently assessed to verify the presence of *Zygosaccharomyces* in brood cells and also the pattern of ergosterol accumulation. The results suggest this nutritional symbiosis is widespread in Brazilian stingless bees. We have also isolated actinobacteria from bees, and they seem to be involved in defensive symbiosis by producing different families of specialized metabolites active against entomopathogens, similar to other social insects, such as attine ants and termites. Our results indicate that stingless bees establish different microbial interactions mediated by small molecules. Therefore, microbial symbionts of stingless bees represent a promising source for chemical ecology research and natural products discovery.

C-06 – Carla Menegatti

Novel Oxidized Alkaloids from The Millipede *Ischnocybe Plicata*

Carla Menegatti,[1] Kenneth Sharp-Knott,[1] Samuel V. G. McNally,[2] Tappey H. Jones,[3] Emily Mevers [1*].[1]Department of Chemistry, Virginia Tech, Blacksburg, VA. [2]Department of Forestry, Oregon. [3]Department of Chemistry, Virginia Military Institute, Lexington, VA*

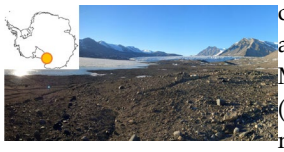
Millipedes are a promising source of novel small molecules. They consist of a diverse class (Diplopoda) of arthropods that are distributed worldwide. Millipedes have evolved repugnatorial glands that contain high concentrations of specialized small molecules that are predicted to have a role in chemical defense. The repugnatorial glands are capable of squirting these fluids over a distance of several inches when a potentially hazard is identified. *Ischnocybe plicata* (Platydesmida; Andrognathidae) is a monotypic millipede species of the Pacific Northwestern United States and feed in aggregations on fungus. When disturbed, *I. plicata* exudes a pine oil or citrus scent, suggestive of terpene production. This ecological observation and the lack of chemical studies on *I. plicata* led us to investigate the specialized metabolites produced by these millipedes. Approximately 300 *I. plicata* adults were collected in down woody debris in coniferous and mixed hardwood forests in Oregon. Extraction and chemical evaluation led to the identification of four new oxidized alkaloids – ischnocybine A-C and ischnocybinone. Full 2D NMR datasets (^{1}H, ^{13}C, COSY, HSQC, H2BC, and HMBC) were acquired on each metabolite to elucidate their planar structures. The molecular formula, respectively, C18H29NO2, C18H27NO3, C20H31NO4 and C22H37NO4 were determined by high-resolution ESI-TOF mass spectrometry. The stereocenters in ischnocybine A-C and ischnocybinone were assigned using NMR and theoretical calculations. Currently these alkaloids are being evaluated in a variety of biological assays, including ecological prey deterrence assays and neurotoxic assays (PDSP).

C-07 – Lesley-Ann Giddings

Molecular Indicators of Environmental Change in an Antarctic Polar Desert

Jacob M. C. Shaffer[1], Lesley-Ann Giddings[2], Becky A. Ball[3], Ross A. Virginia[4], and Jill Mikucki[1]. 1Department of Microbiology, University of Tennessee, Knoxville, TN, USA, 37996, [2]Department of Chemistry, Smith College, Northampton, MA, USA, 01063, [3]School of Mathematical and Natural Sciences, Arizona State University at the West Campus, Glendale, AZ, USA, 85306, [4]Environmental Studies Program, Dartmouth College, Hanover, NH, USA, 03755

Antarctic soils support active, low diversity microbial communities that produce secondary metabolites, which influence community structure and microbial adaptation to changing climates (e.g., solar radiation and salinity). Here, we



characterize the secondary metabolites and their biosynthetic genes within McMurdo Dry Valleys desert soils (inset figure). To determine the microbial secondary metabolite response to varying salinity and limited moisture, soil profiles were collected within and outside a soil 'seep', and total DNA was extracted for 16S rRNA gene amplicon and shotgun metagenome sequencing. Our data suggest that saltier soils are marginally less rich. Metagenome assembled genomes (MAGs) were recovered from the seep, including Actinobacteria (>60% of MAGS). Mostly terpenes, polyketides, and ribosomally synthesized and post-translationally modified peptide biosynthetic gene clusters were identified from these MAGs. Mass spectrometry analyses of these soils indicate the presence of bacterial metabolites, such as tetracycline. Collectively, these data provide insight into microbial responses to changing environmental conditions in extreme desert soils.

C-08 – Skylar Carlson

Understanding the Chemically Mediated Microbiome of *Caulerpa* spp.

Skylar Carlson,[1] Savannah Pierce,[1] Melany Puglisi-Weening[2].[1]Department of Chemistry, University of the Pacific, Stockton, CA 95204 [2]Department of Pharmaceutical Science, Chicago State University, Chicago, IL 60623

Caulerpa spp. is a highly invasive green algae that produces caulerpin and caulpenyne. The surface microbiome of *Caulerpa* spp. from the Mediterranean was found to have a higher abundance of the Gram-negative disease-causing pathogen *Vibrio* spp.. To better understand the relationship between the small molecules produced by the algae and the microbiome we devised a settlement assay. Surface associated bacteria (SAB) were isolated from 6 species of *Caulerpa* spp. from the Florida Keys. Algae were extracted and partitioned to produce a crude extract and three partitions. SAB were then challenged with agar containing the extracts/partitions. Settlement of SAB was observed on extracts containing caulerpin and polar extracts that do not contain caulerpin; suggesting settlement is driven by multiple small molecules not strictly caulerpin. Following this complex settlement activity, we investigated the polar and non-polar algal partitions using MADByTE (Metabolomics And Dereplication By Two-Dimensional Experiments) NMR-metabolomics. Uses HSQC and TOCSY experiments similar structural features are networked in these complex mixtures. Utilizing MADByTE and chasing structural features the metabolites implicated in settlement will be discussed.

C-09 – Emily Brown

Predator Cues Target Signaling Pathways in Toxic Algal Metabolome

Emily R. Brown[1], Sam G. Moore[2], David A. Gaul[2], and Julia Kubanek[2,3]. [1]The Water School, Florida Gulf Coast University, Fort Myers, FL 33965, USA, [2]School of Chemistry and Biochemistry, and [3]School of Biological Sciences, Center for Microbial Dynamics and Infection, Parker H. Petit Institute for Bioengineering and Bioscience, Georgia Institute of Technology, Atlanta, GA 30332, USA

Detection of predators, particularly via chemical cues, trigger defensive behaviors and phenotypic changes in prey organisms. The biochemical mechanisms by which predatory chemical cues are perceived and trigger a response in prey is still poorly understood in planktonic organisms. The phytoplankton *Alexandrium minutum* increases production of paralytic shellfish toxins when exposed to compounds released by copepod predators called copepodamides, but what metabolic pathways are involved in initiating toxin induction remains unknown. In our study LC/MS and NMR-based metabolomics were used to uncover subtle physiological responses of *A. minutum* to copepodamides, including enhancement of butanoate metabolism and arginine biosynthesis. While we were not able to identify a chemoreceptor directly activated by copepod cues, based on the results of inhibition experiments we found that detection of copepodamides appears to disrupt the activity of serine/threonine phosphatases leading to increased jasmonic acid biosynthesis and signaling, which leads to amplified gonyautoxin biosynthesis in *A. minutum*. This study constitutes an important step toward a better understanding of chemosensory ecology of predator-prey interactions in phytoplankton.

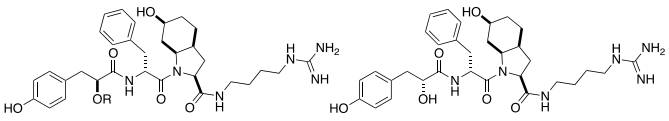
C-10 – Shumel Carmeli

Studies Toward Understanding the Ecological Role of *Microcystis* spp. Modified Peptides

Shira Weisthal-Algor, Rawan Hasan-Amir and Shmuel Carmeli. School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel Aviv University, 69978 Tel Aviv, Israel

During our thirty years study of secondary metabolites of water-bloom-forming cyanobacteria we noticed that these strains produce arrays of structurally similar modified peptides. While studying the chemical content of a massive bloom of a brown *Microcystis* sp. collected during 2012 in Lake Kinneret, Israel, we isolated relatively large amounts of aeruginosins KT608A, KT608B and KT650 and decided to study their influence on the growth of cell lines of cyanobacteria prepared from the bloom

material. The results of this study will be presented.



Aeruginosin KT608A R=H
Aeruginosin KT650 R=Ac

Aeruginosin KT608B

C-11 – Hellen Oketch-Rabah

Ashwagandha Root Chemistry and Potential Liver Toxicity

Hellen A. Oketch-Rabah,[2,3] Scott A. Jordan,[1] Emily F Madden,[2] Amy L Roe,[1,3] Tieraona Low Dog [1,3]. [1]USP Dietary Supplements Admission Evaluation and Labeling Expert Committee (USP DSAEL EC) and [2]United States Pharmacopeia (USP) Staff. [3]Botanical Safety Consortium (BSC)

Withania somnifera root is commonly known as Ashwagandha and is widely used in Indian Ayurvedic medicine (1). Ashwagandha is a well-known adaptogen and is used to treat anxiety, depression, and erectile dysfunction and is a popular dietary supplement in the United States. In 2007 the USP Admission Expert Committee conducted a safety review for Ashwagandha root and based on the long history of apparent safe use in Ayurvedic practices and no reported serious adverse events for products containing Ashwagandha at that time, the EC committee admitted Ashwagandha Root, Root Powder, and Root Dry Extract for *USP-NF* monograph development. Recently, cases of liver toxicity associated with the intake of products containing Ashwagandha were reported including one case from Japan in 2017, 5 reports from the US and Iceland in 2020 and one case in 2021. It has been proposed that DNA damage induced by withanone may be a mechanism for the reported Ashwagandha-mediated liver injury. We present here a review of the chemistry of Ashwagandha root by the Botanical Safety Consortium and examine cases of liver injury associated with intake of products containing Ashwagandha root and propose potential mechanisms and constituents that may be responsible for the reported hepatotoxicity.

C-12 – Wendy Strangman

Assessment of In Vitro ADME of Medicinal Plant Extracts by UPLC-QTOF-MS

Sarah Barr[1], R. Thomas Williamson[1], and Wendy K. Strangman[1]. [1]Department of Chemistry & Biochemistry, University of North Carolina Wilmington

Medicinal plants have been used for millennia as effective treatments for afflictions ranging from headaches to more serious conditions such as cardiac arrythmia and diabetes. Recently, there has been a surge in medicinal plant extract consumption in Western culture, where there is also a high utilization of prescription and non-prescription medications. FDA approved drugs are subjected to a rigorous initial evaluation process to characterize their Absorption, Distribution, Metabolism, and Excretion (ADME) properties. Similar approaches have been applied to individual purified compounds from medicinal plants such as *Gingko biloba* and *Panax quinquefolius*. However, comparatively little has been done towards applying this rigor to more complex herbal extracts. Here we describe our application of this process to extracts of medicinal plants, including incubation of extracts with synthetic gastrointestinal fluids, and subsequent assessment of intestinal passive permeability with parallel artificial membrane permeability assays (PAMPA) and UPLC-QTOF metabolomics data to begin to understand how these complex chemical assemblages translate to observed efficacy in human health.

C-13 – Amy Keller

(–)-Epicatechin Improves Vasoreactivity, Mitochondrial Respiration and Cellular Signaling in a Rat Model of Cardiovascular Disease

Melissa M Henckel[1,2], Ji Hye Chun[3], Leslie A Knaub[1,2], Sara E Hull[1,2], Greg B Pott[1,2], Lori A Walker[4] and Jane E-B Reusch[1,2], Amy C Keller[1,2]. [1]Division of Endocrinology, Metabolism & Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO 80045, [2]Rocky Mountain Regional VA Medical Center, Aurora, CO 80045, [3]Aquillius Corporation, 10918 Technology Pl, San Diego, CA 92127, [4]Division of Cardiology, University of Colorado Anschutz Medical Campus, Aurora, CO 80045

Cardiovascular disease (CVD), characterized by vascular dysfunction, is a major cause of global mortality. Endothelial nitric oxide synthase (eNOS) regulates vasodilation and mitochondrial function, both disrupted in CVD. (–)-Epicatechin, a botanical compound known for its vasodilatory, eNOS and mitochondrial stimulating properties, is a potential therapy for CVD. We hypothesized that (–)-epicatechin would support eNOS activity and mitochondrial respiration, leading to improved vasoreactivity in a thermoneutral-derived rat model of vascular dysfunction. We housed Wistar rats at room temperature (24°C, RT) or thermoneutral (30°C, TN) conditions for a total of 16 weeks and treated them with 1 mg/kg body weight (–)-epicatechin for 15 days. Vasoreactivity, mitochondrial respiration, and eNOS protein expression were measured. TN housing significantly diminished vasodilation ($p<0.05$), reversed in aorta of rats treated with (–)-epicatechin (28.9±4.4% vs. 13.8±5.9% vasodilation capacity, $p<0.05$). Mitochondrial respiration was increased in aorta of animals treated with (–)-epicatechin compared to controls (state 3=18.6 ± 1.7 pmol/s*mg vs. 15.7±1.2 pmol/s*mg, uncoupled=66.4±5.1 pmol/s*mg vs. 51.6±3.6 pmol/s*mg, $p<0.05$ for both). (–)-Epicatechin treated animals housed at TN had diminished eNOS activity compared to TN controls, approaching significance (ratio of peNOS:eNOS, 3.8±1.1 vs. 9.4±1.4, $p=0.06$). These data illustrate (–)-epicatechin's improvement of vasoreactivity and a context-dependent impact on mitochondrial and enzymatic activity; our study advances this natural product as a potential CVD therapeutic.

C-14 – Elizabeth Parkinson

Synthetic Natural Product Inspired Cyclic Peptides for Discovery of Bioactive Natural Products and Biocatalysts

Matthew A. Hostetler,[1] Zachary Budimir,[1] Chloe Smith,[1] Samantha Nelson,[2] Braden Baker,[1] Ramya Modi,[1] Ian Woolsey,[1] Autumn Frerk,[1] Jessica Gantt,[1] Elizabeth Parkinson[1,2]. [1]Department of Chemistry, Purdue University, West Lafayette, IN 47907; [2]Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN 47907

Cyclic peptide natural products are a fantastic source of medicines, including antibiotics and immunosuppressants. Unfortunately, discovering novel cyclic peptides can be an arduous task due to the low expression of many natural product biosynthetic gene clusters and challenging purifications. For this reason, we developed SNaPP (Synthetic Natural Product Inspired Cyclic Peptides). SNaPP expedites bioactive molecule discovery by combining bioinformatics predictions of non-ribosomal peptide synthetases with chemical synthesis of the predicted natural products (pNPs). Head-to-tail cyclic peptides were targeted by using a recently discovered cyclase, the penicillin binding protein-like cyclase, as the initial search input. Analysis of 500 biosynthetic gene clusters allowed for identification of 131 novel pNPs. 51 diverse pNPs were synthesized using solid phase peptide synthesis and solution-phase cyclization. Antibacterial testing revealed 14 pNPs with antibiotic activity, including activity against multidrug-resistant Gram-negative bacteria. Overall, SNaPP demonstrates the power of combining bioinformatics predictions with chemical synthesis to accelerate the discovery of bioactive molecules. Additionally, SNaPP allowed for identification of PBP-like cyclases potentially capable of performing challenging cyclizations, such as for tetrapeptides. We have experimentally confirmed these activities and found one enzyme with a greatly expanded substrate scope that could have great utility as a biocatalyst.

C-15 – Andrew Riley

Discovery of Potent Opioid Ligands Derived from *Picralima nitida* Alkaloids

Simone M. Creed,[1] Madeline R. Hennessy, [1] Anna M. Gutridge, [2] Alexander R. French, [2] Richard vanRijn, [2] Andrew P. Riley[1].

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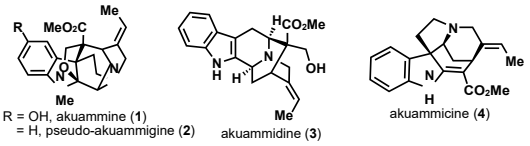
The seeds of *Picralima nitida* contain a family of indole alkaloids known as the akuamma alkaloids, which possess moderate affinity and activity at the opioid receptors. Despite this activity at well- validated analgesic targets and the use of *P. nitida* as a traditional treatment for pain, three alkaloids – akuammine (1), pseudo-akuammigine (2), and akuammidine (3) – produce minimal antinociceptive effects in animal models of pain. Therefore, to identify derivatives of the akuamma alkaloids with improved potency at the opioid receptors, structure-activity relationship (SAR) studies were conductedon 1, 2, and akuammicine (4). Employing a series of highly chemoselective transformations, semisynthetic derivatives of 1, 2, and 4 were prepared to probe the impact of substitutions to the aromatic rings, olefins, and esters. An evaluation of this compound collection at the opioid receptors identified modifications to 2 that produce a selective 35-fold improvement in mu opioid receptor potency and derivatives of 4 with sub-nanomolar affinity for the kappa opioid receptor.



C-16 – Hyun Woo Kim

DeepSAT: Learning Molecular Structures from Nuclear Magnetic Resonance Spectroscopy

Hyun Woo Kim[1,2], Chen Zhang[1,3], Raphael Reher[1,4], Mingxun Wang[5,6], Kelsey L Alexander[1,7], Louis-Félix Nothias[5], Yoo Kyong Han[8], Hyeji Shin[8], Ki Yong Lee[1,8], Pieter C. Dorrestein[5], William H Gerwick[1,5] and Garrison W Cottrell[3], [1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA, USA, [2]College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University, Gyeonggi-do, Republic of Korea, [3]Department of Computer Science and Engineering, University of California, San Diego, La Jolla, CA, USA, [4]Institute of Pharmacy, Martin-Luther-University Halle-Wittenberg, Halle (Saale), Germany, [5]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, CA, USA, [6]Ometa Labs LLC, San Diego, CA, USA, [7]Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA, USA, [8]College of Pharmacy, Korea University, Sejong, Korea

The identification of molecular structure is essential for understanding chemical diversity and for developing drugs leads from small molecules. Nevertheless, the structure elucidation of small molecules by Nuclear Magnetic Resonance (NMR) experiments is often a long and non-trivial process that relies on years of experiential training. To achieve this process efficiently, several spectral databases have been established to retrieve reference NMR spectra. However, the number of reference NMR spectra available is limited and has mostly facilitated annotation of commercially available derivatives. Here, we introduce DeepSAT, a neural network-based structure annotation and scaffold prediction system that directly extracts the chemical properties associated with molecular structures from their NMR spectra. Using only the ^{1}H-^{13}C HSQC spectrum, DeepSAT identifies related known compounds and thus efficiently assists

in the identification of molecular structures. DeepSAT outperforms other available tools and is expected to accelerate the research by improving the identification of molecular structures.

C-17 – James McChesney

TumorSelectTechnology® Enhancing Safety and Efficacy of Cytotoxic Chemotherapeutics

James D. McChesney, PhD. Managing Director, Veiled Therapeutics, LLC; CEO Cloaked Therapeutics, LLC

Veiled Therapeutics has developed an anticancer technology, TumorSelect® Technology, which combines proprietary anticancer prodrugs, nanotechnology, and knowledge of human physiology. Tumors have a voracious appetite for cholesterol which facilitates tumor growth and fuels their proliferation. We have transformed this need into a stealth delivery system to disguise and deliver anticancer drugs with the assistance of both the human body and the tumor cell. Veiled's designer prodrugs are assembled within pseudo-LDL nanoparticulates which carry them to tumor tissues where they are taken up, internalized, and transformed into active drug and kill the cancer cells. This three-prong approach delivers the anticancer drug more selectively to the tumors and thereby avoids or reduces the severe side effect toxicities associated with current chemotherapy. Reduction of side effect toxicity of cancer therapy by our technology will improve patient quality of life, patient retention in treatment regimes, more rapid patient recovery post treatment, and overall patient benefit.

C-18 – Esther A. Guzmán

Marine Natural Products with Selective Activity Against Triple Negative Breast Cancer 3D Cultures

Esther A. Guzmán, Tara. A. Peterson, Amy E. Wright. Marine Biomedical and Biotechnology Research, Harbor Branch Oceanographic Institute at Florida Atlantic University, 5600 US 1 North, Fort Pierce FL 34946, USA

Breast cancer is the most diagnosed cancer and the second leading cause of cancer death among women. Targeted therapies have greatly improved the odds of surviving a breast cancer diagnosis. However, triple negative breast cancers (TNBC)—do not express estrogen receptor (ER), progesterone receptor (PR), and do not overexpress the human epidermal growth factor receptor type 2 (HER 2)—are resistant to targeted therapies. TNBC comprise 10-20% of all breast cancers and tend to be very aggressive, more likely to recur, and metastasize to organs such as the brain and lungs. Compounds from the Harbor Branch Oceanographic Institute (HBOI) natural products library were tested to identify those with the ability to induce apoptosis in triple negative breast cancer cells grown as spheroids (3D cultures). Spheroids formed overnight and were treated for 24h with compounds. Lead compounds were selected based on their ability to induce apoptosis in 3D with no cytotoxicity against the same cells grown in traditional 2D cultures and treated for 72h. Lead compounds show synergy with taxol against TNBC spheroids. Differential proteomic expression in 3D cultures was used to begin to define the mode of action of the compounds. The 3D model used is more clinically relevant, increasing the scientific impact and relevance of this work. Compounds identified to date act in a different manner than traditional chemotherapies, all of which are active in 2D cultures, and may provide new therapeutic options as well as new insights into triple negative breast cancers.

C-19 – Janae Sweeney

Val16A SOD2 Polymorphism Promotes Epithelial Mesenchymal Transition Antagonized by Muscadine Grape Skin Extract in Prostate Cancer Cells

Janae D. Sweeney[1,4], Marija Debeljak[2], Stacy Reil[2], Ana C. Millena[1], James R. Eshleman[2], Channing J. Paller[3] & Valerie Odero-Marah[1,5].[1]Center for Cancer Research & Therapeutic Development, Department of Biological Science, Clark Atlanta University, [2]Departments of Pathology and Oncology, Johns Hopkins School of Medicine, [3]The Sidney Kimmel Comprehensive Cancer Center, [4]Department of Biological & Physical Sciences, SC State University, [5]Department of Biology, Morgan State University

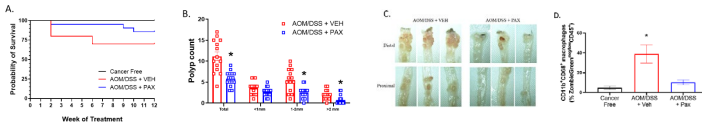
Epithelial Mesenchymal Transition (EMT), allows polarized epithelial cells to assume mesenchymal morphologies, enhancing invasiveness, migration, and induction by ROS. Val16A (Ala) SOD2 polymorphism has been associated with increased prostate cancer (PCa) risk. We hypothesized that SOD2 Ala SNP may promote EMT. Stable overexpression of SOD2 Ala and Val alleles were performed in LNCaP cells, followed by analysis of intracellular ROS and EMT marker protein expression. Treatments were performed with muscadine grape skin extract (MSKE) antioxidant, with or without the addition of H_2O_2 to provide further oxidative stress. Results demonstrated that the Ala-SOD2 allele was associated with marked induction of EMT indicated by higher Snail and vimentin, and increased cell migration, when compared to Val-SOD2 allele or Neo control cells. Ala-SOD2 SNP cells exhibited increased levels of total ROS and superoxide and were more sensitive to co-treatment with H_2O_2 and MSKE, which led to reduced cell growth and increased apoptosis. Additionally, MSKE inhibited Ala-SOD2 SNP-mediated EMT. Our data indicates that treatment with a combination of H_2O_2-generative drugs such as certain chemotherapeutics and antioxidants such as MSKE that target superoxide, hold promising therapeutic potential to halt PCa progression in the future.

C-20 – Sierra McDonald

Panaxynol Alleviates Murine Colitis Associated Colorectal Cancer via Macrophage Suppression

Sierra McDonald[1], Brooke Bullard[1], Brandon VanderVeen[1], Thomas Cardaci[1], Sarah Madero[1], Ioulia Chatzistamou[1], Lorne Hofseth[2], Angela Murphy[1].[1]Department of Pathology, Microbiology and Immunology, University of South Carolina School of Medicine, SC 29209, [2]Drug Discovery and Biomedical Sciences, College of Pharmacy, University of South Carolina, Columbia, SC 29208

Colon cancer is the second leading cause of cancer death in the US for men and women combined. Panaxynol (PAX), a bioactive component in American Ginseng, has been shown to possess anti-cancer properties *in vitro* and was recently shown to suppress DSS-induced colitis in mice. We investigated whether PAX (2.5mg/kg, p.o., 3x/wk for 12 wks) has any promise in alleviating AOM/DSS induced colitis-associated colorectal cancer (CAC) using C57BL/6 female (n=20) and male (n=20) mice. PAX significantly suppressed clinical colitis symptoms and significantly reduced colon polyp number and size, indicative of reduced inflammation and tumorigenesis, compared to vehicle. We demonstrate that PAX reduced total macrophages and increased anti-tumoral M1 macrophages in the lamina propria via flow cytometry. These results were confirmed by RT-PCR in which PAX increased mRNA expression of M1 macrophage cytokines and reduced overall and pro-tumoral M2 macrophage markers. Our results suggest that PAX is effective in reducing colitis and tumor burden in murine CAC possibly through its inhibition of overall and M2 macrophages.

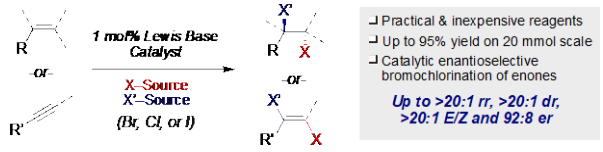


C-21 – Liela Romero

An Organocatalytic Strategy for the Selective Interhalogenation of Alkenes, Alkynes and Dienes

Alexandra Lubaev, Dr. Manjula Rathnayake, Favour Eze, and Prof. Liela Romero. Department of Chemistry and Biochemistry, Baylor University, Waco, TX 76798

Research in the Romero group is focused on the development and mechanistic study of novel catalytic reactions, with applications in natural product synthesis and drug discovery. Inspired by bioactive polyhalogenated natural products, we have developed a unified strategy for the bromochlorination of alkenes, alkynes and 1,3-dienes via Lewis base catalysis. This organocatalytic protocol furnishes vicinal bromochlorides featuring a wide assortment of functionality with excellent regio-, diastereo- and site selectivity. Moreover, this method accommodates the precision installation of Br, Cl and I in various combinations to afford a selection of complementary dihalogenated products. Notably, when 1–3 mol% of a chiral Lewis basic catalyst is employed, a novel enantioselective bromochlorination of alkenes is realized with up to 92:8 er.

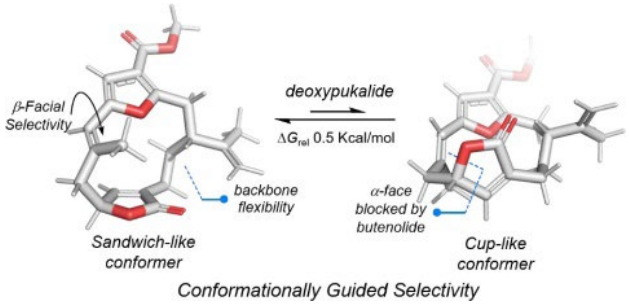


C-22 – Paul Scesa

Role of Macrocyclic Conformational Steering in a Kinetic Route Toward Bielschowskysin

Paul D. Scesa, Lyndon M. West, and Stéphane P. Roche* Department of Chemistry and Biochemistry, Florida Atlantic University, Boca Raton, Florida 33431, United States*

Furanobutenolide cembranoids (FBCs) are the biosynthetic precursors to a wide variety of polycyclic (nor)diterpenes. These metabolites are thought to originate from oxidation of the macrocycle backbone and a series of transannular reactions. Yet the development of a biomimetic route has been hampered by a lack of synthetic methods for the pivotal furan dearomatization in a regio- and stereoselective manner. To address these shortcomings, a strategy of epoxidation followed by a kinetically controlled furan dearomatization is reported. The surprising switch of facial discrimination observed in the epoxidation of macrocyclic derivatives has been rationalized by conformational variation. Conformational analysis by VT-NMR and NOESY experiments at low temperature was supported by DFT calculations to characterize these conformers. We also describe the downstream functionalization of FBCs and how the C-7 epoxide configuration is translated to the C-3 stereogenicity in dearomatized products to secure the requisite 3*S*,7*S*,8*S* configurations for the bielschowskysin synthesis. *J. Am. Chem. Soc.* 2021.

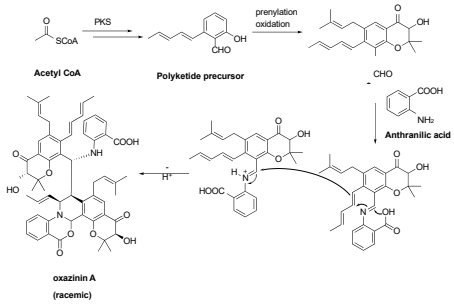


C-23 – John MacMillan

Harnessing Non-Enzymatic Transformations in Natural Product Biosynthesis

John B. MacMillan, Rahul Shingare, Victor Aniebok. of Department Chemistry and Biochemistry, University of California, Santa Cruz

Natural Products that contain one or more non-enzymatic steps in their biosynthesis have expanded the chemical complexity with which to approach historical problems such as drug design. Examples of NPs with non-enzymatic steps in their biosynthesis include the discoipyrroles, ammosamides and homodimericin A. The MacMillan lab has been interested in the identification of molecules that utilize abiotic chemistry in the mechanisms behind the non-enzymatic steps that help produce them. Elucidating the mechanisms behind the formation of these NPs allows us to augment and ultimately utilize their chemistry for biological applications. This presentation will include our approaches to the discoipyrroles, pyronitrins as well as our recent completion of the synthesis and mechanistic study of oxazinin A.



C-24 – Neil Kelleher

Correlative Metabologenomics of 111 Fungi Reveals Thousands of Metabolite/Gene Cluster Pairs

Lindsay K. Caesar[1], Fatma A. Butun[1], Matthew T. Robey[2], Navid J. Ayon[1], David Dainko[1], Raveena Gupta[1], Jin Woo Bok[3], Grant Nickles,[3] Robb J. Stankey[4], Don Johnson[4], David Mead[4], Huzefa A. Raja[5], Kristof B. Cank[5], Cody Earp[5], Nicholas H. Oberlies[5], Nancy P. Keller[3,6], Neil L. Kelleher[1,2,7].[1]Department of Chemistry, Northwestern University (NU) [2]Department of Molecular Biosciences, NU. [3]Department of Medical Microbiology & Immunology, University of Wisconsin-Madison (UW) [4]Varigen Biosciences Corporation, Madison, WI , [5]Department of Chemistry & Biochemistry, University of North Carolina at Greensboro [6] Department of Bacteriology, UW [7]Proteomics Center of Excellence, NU

Natural product (NP) discovery platforms increasingly favor the application of 'Omics' technologies to inform compound discovery, and public initiatives to link complementary –Omics datasets have recently become available. The 'metabologenomics' platform is a viable strategy to investigate NP biosynthesis in bacteria, but it has never been applied in fungi. Metabolomic and genomic investigations into fungal secondary metabolism have illustrated that fungi are both hyper-diverse and underexplored and that their NPs have high promise for bioactivity. Using a correlative dataset of 111 Ascomycetes, we used gene cluster family (GCF) networking and correlation-based scoring metrics to optimize this scalable platform in fungi, grouping 7308 gene clusters into 3007 GCFs. We anchored our findings with a set of 16 known gene clusters from which 25 NPs were detected, observing highly significant correlations for 23/25 case. This -Omics approach to fungi has revealed a few thousands new NP-GCF pairs now awaiting discovery. As a test case, we apply our platform to deorphanize the biosynthesis of the pestalamides, revealing that these NPs are produced by a different pathway than previously reported.

C-25 – Jie Li

Correlational Networking Guides the Discovery of Hidden Lanthipeptide Proteases

Jie Li[1], Dan Xue[1], Ethan A. Older[1], Zheng Zhong[2,3], Zhuo Shang[1], Prakash Nagarkatti[4], Mitzi Nagarkatti[4], Yong-Xin Li[2,3]. [1]Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, USA. [2]Department of Chemistry and The Swire Institute of Marine Science, The University of Hong Kong, Pokfulam Road, Hong Kong, China. [3]Southern Marine Science and Engineering Guangdong Laboratory (Guangzhou), Guangzhou, China. [4]Department of Pathology, Microbiology and Immunology, School of Medicine, University of South Carolina, Columbia, SC, USA

Bacterial natural product biosynthetic genes, canonically clustered, have been increasingly found to rely on hidden enzymes encoded elsewhere in the genome for completion of biosynthesis. The study and application of lanthipeptides are frequently hindered by unclustered protease genes required for final maturation. Here, we establish a global correlation network bridging the gap between lanthipeptide precursors and hidden proteases. Applying our analysis to 161,954 bacterial genomes, we establish 5209 correlations between precursors and hidden proteases, with 91 prioritized. We use network predictions and co-expression analysis to reveal a previously missing protease for the maturation of class I lanthipeptide paenilan. We further discover widely distributed bacterial M16B metallopeptidases of previously unclear biological function as a new family of lanthipeptide proteases. We show the involvement of a pair of bifunctional M16B proteases in the production of previously unreported class III lanthipeptides with high substrate specificity. Together, these results demonstrate the strength of our correlational networking approach to the discovery of hidden lanthipeptide proteases and potentially other missing enzymes for natural products biosynthesis.

C-26 – Wenjia Gu

Targeted Discovery of Natural Products from Massive Metagenomic Diversity

Wenjia Gu, Stephanie Brown, Zach Charlop-Powers, Wenlong Cai, Tom Eyles, Ee-Been Goh, Brandy Hernandez, Bill Hwang, Zachary Kurtz, Andrea Lubbe, Sasha Milshteyn, Parisa Mokthari, Samuel Oteng-Pabi, Andrew Robertson, Delong Tsway, and Oliver Liu Zymergen Inc. Emeryville, CA, USA

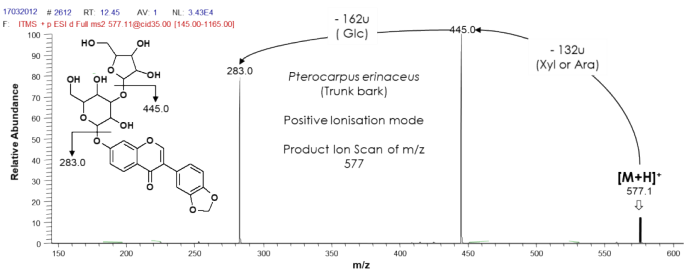
With estimates that >99% of microbial diversity in soils have never been isolated nor studied, the soil metagenome is a tantalizing source of novel natural product diversity. At Zymergen, we have built what we believe to be the largest metagenomic database of natural product biosynthetic gene clusters (BGCs), providing us with access to a vast and untapped universe of chemical diversity. In addition, we have developed multiple high-throughput bioinformatic search tools to identify BGCs that encode novel natural products with applications across drug discovery and agriculture. Here, we show an example of how we can couple a resistance gene-guided search strategy with Zymergen's synthetic biology platform to enable targeted discovery of a previously unknown natural product that can inhibit a validated oncology target.

C-27 - Nassifatou Koko Tittikpina

A LC-MS Method Development led to the Discovery of New Compounds from the TrunkBarks of *Pterocarpus erinaceus* Poir (Fabaceae)

Nassifatou Koko Tittikpina[1,2,3,4,5,6], Gilbert Kirsch[3], Raphaël E. Duval [3,4], Claus Jacob[2], Patrick Chaimbault[1]. [1] Université de Lorraine, LCP-A2MC, Metz F-57000, France. [2] Saarland University, 66123, Saarbrücken, Germany. [3] Université de Lorraine, CNRS, L2CM, F-57000 Metz, France. [4] ABC Platform®, F-54001 Nancy, France. [5] Université de Lomé, FSS, 01 BP 1515, Lome 01, Togo. [6] University of Mississippi, National Center for Natural Products Research, 1019 Thad Cochran Research Center, P O Box 1848 University, MS 38677

The butanol extract of *Pterocarpus erinaceus* exhibited an IC 50 at 1µg/mL against *Staphylococcus aureus* species including a resistant one and consequently, was investigated by developping a LC- MS method. The methodology led to the discovery of new glycosylated flavonoids (with disaccharide moiety connected to the flavonoid through *O*-links as shown below) reportedly never described in nature and in *Pterocarpus sp*. to the best of our knowledge. The LC-MS method and the strategies developed to decipher the new compounds in addition to the compound structures will be presented.



C-28 – Alexandros Polyzois

Stromatolite Chemical Profiles and Microbial Consortia Vary Throughout Sites Along the Coast of the Eastern Cape, South Africa

Alexandros Polyzois[1], Allegra T. Aron[2,3], Asisipho V. Dloboyi[1], Eric W. Isemonger[1], George F. Neuhaus[4], Jarmo C. Kalinski[1], Jason Kwan[5], Kerry L. McPhail[4], Luthando S. Madonsela[1], Pieter C. Dorrestein[2,3], Samantha C. Waterworth[5], Xavier Siwe Noundou[6] and Rosemary A. Dorrington[1]. [1]Department of Biochemistry and Microbiology, Rhodes University, Makhanda 6140, South Africa [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, San Diego, CA, 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 Pharmaceutical Sciences, College of Pharmacy, Oregon State University, Corvallis, OR 97331, USA [5]Division of Pharmaceutical Sciences, University of Wisconsin, Madison, Wisconsin, USA [6]Department of Pharmaceutical Sciences, School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria 0204, South Africa

Microbialites are one of the oldest known extant cellular forms of life on Earth. However, their chemical and microbial diversity remain underexplored. We examined four supratidal microbialite formations on the Eastern Cape coast of South Africa with the goal of investigating their chemical and bacterial communities to reveal relationships within and between sites and relate chemical and microbial diversity profiles. Chemical extracts were characterized by LC-MS/MS while microbial community analyses were generated through 16s rRNA gene metabarcoding. The GNPS, QIIME2 and SIRIUS4 platforms were leveraged to understand the chemical profiles and relationships to microbial community compositions. This differentiated the sites into three distinct clusters, reflecting differing micro-ecosystem conditions and highlighted potential biomarkers. The presented research demonstrates the potential of an integrated genomics and metabolomics approach to understanding the environmental factors that impact the functional diversity of microbialite communities.

C-29 – Elhadj Saidou Balde

Traditional Guinean Management of Breast Diseases in Low and Middle Guinea

E.S. Baldéa,b,, M.S. Traoréa,b, M.A. Baldéa,b, A.O. Baldéa,b, F. Bahb, A.K. Camaraa, S. M. Kéita c, A.M. Baldé a, b aDépartement de Pharmacie Université Gamal Abdel Nasser, Conakry, Guinée bInstitut de Recherche et de Développement des Plantes Médicinales et Alimentaires de Guinée, Dubréka, Guinée, cCentre d'étude et de recherche en environnement, Université Gamal Abdel Nasser, Conakry, Guinée*

Ethnopharmacological relevance: The objective of the present study

was to evaluate traditional Guinean consideration and management of breast diseases. *Materials and methods:* The survey was carried out from January 2011 to December 2012 and targeted traditional medical practitioners in Low and Middle Guinea through questionnaires and oral interviews. *Results and discussion:* A total of 231 people (88 males and 143 females) were interviewed. The age of the participants ranged from 25 to 75 years. Most of the traditional healers (173/231) were mature adults aged between 30 and 60 years and had practiced ethnomedicine for more than 10 years. Based on traditional considerations, the most treated breast diseases were "breast inflammation" (77), "nipple discharge" (74), and "breast hardening" (58). The traditional remedies cited were minerals, animals and mainly plant species. One hundred and three plant species were recorded, of which 82 belonging to 44 families were identified. The most frequently cited plants were Mangifera indica L. (55) and Erythrina senegalensis A.D.C. (35). The most used parts were leaves, accounting for 79.8%. Galenical forms were decoction and paste, administered orally and/or via local application. *Conclusion:* Breast diseases are common in Guinea. The traditional management of these lies mainly on the use of plant species. Of these, M. indica was the most cited and has been previously described with related properties against cancer types. Aiming to rationalize the use of these plants, bioassay-guided fractionations are in progress to determine useful fractions or molecules with antitumor activity for clinical investigations.

C-30 – Ogechukwu Chukwuemerie

Toxicological Analysis and Antimalarial Potentials of Secondary Metabolites of *Curvularia lunata*, an Endophyte Obtained from the Leaves of *Azadirachta indica*

Ogechukwu L. Nwankwo[1],Felix A. Onyegbule[2], Festus B. C. Okoye[2]. [1]Department of Pharmacognosy and Traditional Medicine, Faculty of Pharmacèutical Sciences, Nnamdi Azikiwe University, Anambra State, Nigeria. [2]Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Anambra State, Nigeria

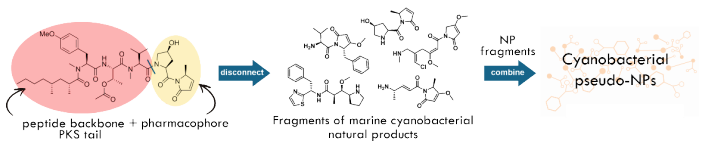
Endophytes are symbiotic microorganisms that reside in the host plant, either intracellular or intercellularly. Phytochemicals of endophytes have generated significant interest in drug discovery programs due to their immense potential towards contributing to the elucidation of new biologically active molecules. *Azadirachta indica* is used traditionally in the management of several ailments. The study was aimed to evaluate the antimalarial potentials and toxicity profile of endophytic extract isolated from the leaves of *A. indica.* Endophytic extract was isolated from *Azadirachta indica* leaves using standard extraction protocols. The extract was screened for its potential antimalarial activities using Peter's curative test method, acute (LD_{50}) and chronic toxicity. The chronic toxicity was assessed by evaluating the effect of administered extracts on the following blood/organ parameters: aspartate aminotransferase (AST), alkaline phosphatase (ALP), alanine aminotransferase (ALT), Blood Urea Nitrogen (BUN), creatinine levels, Packed Cell Volume (PCV), haemoglobin (HB), and Red Blood Cell count (RBC). The endophytic extract was subjected to prophylactic antimalarial assay using Peter's prophylactic test method, and effective dose concentration (ED_{50}) was determined. The endophytic extract screened for antimalarial activity showed very significant activity ($P \leq 0.05$). At 150 mg/kg/day, the extract displayed a dose-dependent parasitemia clearance of *Plasmodium berghei* by 89% and suppressed parasitemia with ED_{50} of 333.33mg/kg. The LD_{50} was >5000 mg/kg and showed no evidence of hepatotoxicity, nephrotoxicity, and haematotoxicity in test animals. *C.lunata* (OM337582) of *A. indica* has potent antimalarial activity associated with a high content of flavonoids and alkaloids with no hepatotoxicity, nephrotoxicity, and haematotoxicity.

C-31 – Eduardo Caro-Diaz

Cyanobacterial Pseudo-Natural Products: Virtual Synthesis and Evaluation of Drug-Likeness

William Mendoza[1], Angel Hernandez[2], 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]Department of Chemistry, University of Puerto Rico - Rio Piedras, San Juan, PR. 00925

To address the decline in structural novelty of cyanobacterial natural products (NPs), we have designed a pseudo-NP library that combines cyanobacterial NP fragments with privileged scaffolds of NPs from a variety of bio-origins. To date, we have computationally produced thousands of pseudo-NP structures, along with their respective computationally predicted physicochemical values and likeness scores (e.g., NP-likeness, sp3 fraction, lead-likeness) by using multiple open-access platforms and drug-design software. Our efforts have identified suitable targets for synthesis and the determination of their *in vitro* bioactivity. Our cyanobacterial pseudo-NP library describes new chemical space for future drug discovery and may represent a new paradigm in small molecule NP-inspired drug design.



C-32 – Paulo Vieira

Exploring the Chemical Diversity of Phytoparasitic Fungi

Vitor de Souza Mazucato[1], and Paulo Cezar Vieira[1]. [1]Department of BioMolecular Sciences, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, 14040-903, Brazil

Two fungi *Fusarium guttiforme* and *Colletotrichum horii* isolated from papaya and pineapple were cultivated in different conditions to explore the chemical diversity produced. A total of 14 compounds were identified. The axenic cultures of fungi in PDB medium led to the production of three compounds, fusaric acid, 9,10-dehydrofusaric acid and tyrosol, while their co-culture has led to the production of four other compounds, fusarinol, fusaric acid complex with magnesium, 9,10-dehydrofusaric acid complex with magnesium and 5-butyl-5-(hydroxymethyl) dihydrofuranone. The change from PDB culture medium to Czapek led to the production of structurally different compounds among them uracil, *p*-hydroxyacetophenone and Cyclo(L-Leu-L-Pro). Biotransformation experiments using the fungus *C. horii* and fusaric acid as substrate yielded three compounds, 7-hydroxyfusarinol, 9,10-dehydrofusarinol and fusarinyl acetate. Epigenetic modulation of *F. guttiforme* with SBHA led to the identification of compounds similar to those obtained from the co-culture in Czapek medium, in addition gibepyrone B and other related compounds. The compounds were tested on papain inhibitory activity, and the results showed that the magnesium complexes presented 56 and 54% respectively of inhibition of papain activity at a concentration of 25.2 and 23.5 μM, respectively.

C-33 – Rita de Cássia Ribeiro Gonçalves

Avocadene Identified from *Persea americana* Mill. Seeds as a Potential Anticancer Against Gastric Adenocarcinoma Cells

Brena R. Athaydes, Giuliano C. Pereira; Cristina Tosta, Ricardo M. Kuster, Rodrigo R. Kitagawa, Rita de Cássia Ribeiro Gonçalves. Graduate Program in Pharmaceutical Sciences, Federal University of Espírito Santo, Vitoria, Brazil. Av Marechal Campos, 1468, CEP 29043-900

This study aimed to evaluate the anticancer potential in adenocarcinoma cells (AGS) of ethyl acetate partition (SEAP) rich in polyhydroxylated fat alcohols (PFAs) extracted from avocado seed. The (-)- ESI FT-ICR MS spectrum of SEAP showed the negative ions of the PFAs avocadene (*m/z* 321.22029 – C17H34ClO3) and avocadyne (*m/z* 319.20464 – C17H32ClO3). SEAP presented CI50 of 45.13 ± 4.25 representing inhibition of 89.54% ± 4.78 of AGS growth at 100 μg/mL. The analysis *in silico* using PASS (Prediction of Activity Spectra for Substances) showed that avocadene is probably active as stimulant of Caspase-3 (0.442) and Caspase-8 (0.476). The potential of interaction of avocadene in the binding site by molecular docking showed donor-donor interaction (2.48Å) with asparagine (ASN213) in caspase 3 and multiple Van der Waals interactions with amino acid residues (ARG258, LEU254, PRO415 and others) in Caspase 8 binding site. These compounds, highlighting the avocadene, demonstrated potential to modulate the apoptosis affecting different pathway of gastric cancer development.

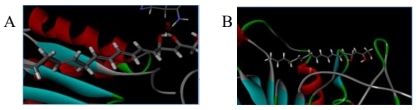


Figure 1 - Molecular docking of avocadene in the active site of caspase 3 (A) and 8 (B), respectively.

C-34 – Roberto Berlinck

Phomactinine, the First Nitrogen-Bearing Phomactin, Discovered by Extensive Media Optimization and Metabolomics Analyses

Leandro da Silva Oliveira,[1] Camila M. Crnkovic,[1,2] Marcelo R. Amorim,[1] Tiago Antunes Paz,[3] Vitor F. Freire,[4] Tiago Venâncio,[5] Antonio G. Ferreira,[5] Roberto G. S. Berlinck[1] [1]Instituto de Química de São Carlos, Universidade de São Paulo, CP 780, CEP 13560-970, São Carlos, SP, Brazil; [2]Faculdade de Ciências Farmacêuticas, Universidade de São Paulo, CEP 05508-000, São Paulo, SP, Brazil; [3]Instituto de Química, Universidade Estadual Paulista, CEP 14800-900, Araraquara, SP, Brazil; [4]Center for Cancer Research, Natural Products Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Frederick, MD, USA; [5]Departamento de Química, Universidade Federal de São Carlos, CEP 13565-905, São Carlos, SP, Brazil*

Phomactins are diterpenes first discovered from growth media of marine-derived fungi of the genus *Phoma* that display significant inhibition of the platelet aggregation factor (PAF), which is implied in a series of biological processes including inflammation, asthma, renal disease, sepsis, pancreatitis and cancer. This investigation combined metabolomics strategies with fungal growth improvement to investigate the production of phomactins by the marine fungus *Biatriospora* sp. CBMAI 1333, leading to the discovery of the nitrogen-bearing phomactinine. Our results guided our decision to produce large-scale cultures for the discovery of novel phomactin variants.

C-35 – Kelli McDonald

Ashwagandha Botanical-Drug Interactions: Potential CYP Induction

Kelli L. McDonald1, Satyanarayana Pondugula2, Jaewoo Choi4,5, Julia Salamat2, Mikah Brandes5,6, Cody Neff5,6, Keila Adams1, Claudia Maier3,4,5, Amala Soumyanath5,6, Robert Arnold1, and Angela I Calderón1. [1]Department of Drug Discovery and Development, Harrison School of Pharmacy, Auburn University, AL 36849, USA, [2]Department of Anatomy, Physiology and Pharmacology, College of Veterinary Medicine, Auburn University, AL 36849, [3]Botanicals Enhancing Neurological and Functional Resilience in Aging (BENFRA) Botanical Dietary Supplements Research Center, Oregon Health and Science University, Portland, OR 97239

Withania somnifera (L.) Dunal, commonly known as ashwagandha, has been used for its health benefits since 6000 BC.

This botanical has been shown to be beneficial to health and contains two bioactive compounds, withanolide A and withaferin A. In the current study, primary human hepatocytes were treated with various standardized ashwagandha extracts, aqueous or ethanol extracts, from roots or leaves. The extract solubility was optimized. Potential medium serum protein-ashwagandha interactions were observed. Via RT-PCR analysis, ashwagandha extracts that initially (in serum medium) indicated possible CYP mRNA downregulation increased to a non-bioactive level, while m-RNA fold increased (in serum-free medium) for all extracts that had initially indicated possible induction. Our initial results show significant induction of CYP3A4 with the ashwagandha ethanol root extract. This study highlights the importance of a rigorous experimental design to assess the potential for BDIs with ashwagandha supplements.

C-36 – Ethan Older

Sulfonolipids: Human Microbial Metabolites with Unique Dual Activity in Mediating Inflammation

Ethan A Older[1], Lukuan Hou[2], Haiyan Tian[3], Li Wang[3], Zachary E Ferris[1], Junfeng Wang[4], Mingwei Cai[2], Dan Xue[1], Prakash Nagarkatti[6], Mitzi Nagarkatti[6], Hexin Chen[5], Daping Fan[4], Xiaoyu Tang[2] and Jie Li[1] [1]Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, USA, [2]Institute of Chemical Biology, Shenzhen Bay Laboratory, Shenzhen 518132, China, [3]College of Pharmacy, Jinan University, Guangzhou 510632, China, [4]Department of Cell Biology and Anatomy, School of Medicine, University of South Carolina, Columbia, South Carolina 29209, USA, [5]Department of Biological Sciences, University of South Carolina, Columbia, South Carolina 29209, United States, [6]Department of Pathology, Microbiology and Immunology, School of Medicine, University of South Carolina, Columbia, South Carolina 29209, USA

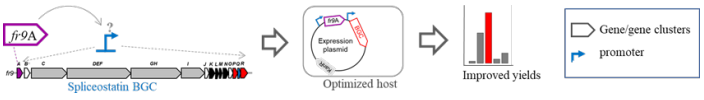
Sulfonolipids (SoLs) are a unique class of sulfonate-containing sphingolipids. However, the biological functions and biosynthesis of SoLs in human microbiota are poorly understood. Here, we report the discovery and isolation of SoLs from a human opportunistic pathogen *Chryseobacterium gleum* DSM16776. We show for the first time the pro-inflammatory activity of SoLs with mice primary macrophages. Furthermore, we used both *in vivo* heterologous expression and *in vitro* biochemical reconstitution to characterize two enzymes, cysteate synthase and cysteate fatty acyltransferase, which are specifically involved in the biosynthesis of SoLs rather than other sphingolipids. Based on these two SoL-specific enzymes, our bioinformatics analysis showed a wide distribution of SoLs biosynthetic genes in microbes that had not been reported as SoLs producers. We selected four of these strains and verified their cysteate synthase and cysteate fatty acyltransferase activities in SoLs biosynthesis. The distribution of SoL-specific biosynthetic enzymes in the context of SoLs' activity in mediating inflammation, a common and fundamental biological process, may suggest a more comprehensive function of SoLs in mediating human health.

C-37 – Barbara Adaikpoh

Characterization of Endogenous Promoters for the Heterologous Expression of Biosynthetic Gene Clusters in *Burkholderia* Bacteria

Barbara I. Adaikpoh, Alessandra S. Eustaquio. Department of Pharmaceutical Sciences, and Center for Biomolecular Sciences, University of Illinois at Chicago, Chicago IL 60607, USA

Under typical laboratory cultivation, most products of biosynthetic gene clusters (BGCs) of *Burkholderia*, a promising source of natural products, are not produced in yields that enable their development. Gram- scale production of autologous spliceostatins (6 g/L) in *Burkholderia* sp. FERM BP-3421 was established, hence our interest to investigate the transcriptional regulation of the spliceostatin BGC for application in heterologous expression. The spliceostatin BGC contains only one pathway-specific regulator gene, *fr9A*, putatively encoding a LuxR-type transcriptional factor. Deletion of *fr9A* followed by genetic complementation supports a role as an activator of spliceostatin gene transcription. We identified four transcript units based on the RNAseq transcriptional profiling of the spliceostatin BGC and in silico analyses for the prediction of bacterial promoters. Promoter activities of these putative promoters were compared to established promoters based on the expression of green fluorescence protein (GFP), and three Fr9A-regulated promoters were identified. We hypothesize that Fr9A-regulated promoters will serve to activate silent BGCs and produce the respective natural products in high yields, which we are currently testing. This project serves to enrich the toolbox for optimizing the heterologous expression of BGCs in *Burkholderia.*



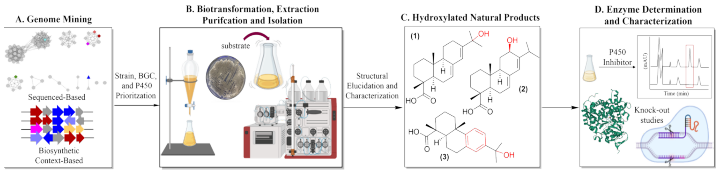
C-38 – Caitlin McCadden

Genome Mining of Bacterial Cytochrome P450 Enzymes for Novel Biocatalysts

Caitlin A. McCadden, Baofu Xu, Jeffrey Rudolf. Department of Chemistry, University of Florida, Gainesville, FL, USA

Biocatalysis employs both *in vitro* enzymes and whole-cell methods to provide enzymatic approaches to synthesizing complex active ingredients, key intermediates, and derivatizing analogs. Using a genome mining approach, we initiated an *in vivo* screen to probe the biocatalytic functionality of predicted cytochrome P450 genes from *Streptomyces*. In doing so, we elucidated the structures of several functionalized products. Most notable is the conversion of abietic acid to 15-hydroxydehydroabietic acid which involves both dehydrogenation and hydroxylation reactions. Hydroxylation is one the most common P450-catalyzed reactions while

dehydrogenation is comparatively less explored, especially in biosynthetic and mechanistic terms.



C-39 – Aswad Khadilkar

Assigning Mechanism of Action to Natural Products in Multiple Biological Contexts Using Gene Expression and Phenotypic Screening Methods Established by the HIFAN Program

Aswad S Khadilkar[1], Akshar Lohith[1], Anam Shaikh[1], Rebecca Pelofsky[1], Nora Gray[4], Amala Soumyanath[4] 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. [4]BENFRA Botanical Dietary Supplements Research Center, Oregon Health and Science University, Portland, OR 97239

Assigning the mechanism of action (MOA) to botanicals, natural products (NPs) and synthetic chemicals continues to be a major challenge. The Center for High-Throughput Functional Annotation of Natural Products (HiFAN) aims to expedite the determination of bioactivity and the MOA of NPs, using phenotypic, transcriptomic, and metabolomic approaches. For this, we carry out innovative, cell-based, targeted-transcriptomic screening in macrophages, non-small cell lung cancer (NSCLC) cell lines and cortical brain tissues of mice, providing agnostic and extensive coverage of critical biological pathways that are believed to be relevant to the health effects of NPs. Functional Signature Ontology (FuSiOn) is one of the technologies used to help elucidate NP bioactivity. The gene signature for each compound is clustered to elucidate MOA using a "guilt by association" metric with known chemical or iCRISPR perturbations, thus, linking bioactive compounds to specific biological processes in cells. Nanostring's nCounter Elements technology measures gene expression signatures of >500 genes from 12 samples per run. Whereas, Nanostring PlexSet enables direct digital, multiplexed and high-throughput detection of up to 96 custom targets in 96 samples per run. We applied FuSiOn and Nanostring technologies to study 1) Lipopolysaccharide stimulated inflammation and observe the effect of NPs to modulate immune response. We profiled **innate immunity** specific 561 genes in nCounter Immunology Panel which includes major classes of cytokines and their receptors, enzymes with specific gene families such as the major chemokine ligands and receptors, interferons and their receptors, the TNF-receptor superfamily, and the KIR family genes. 2) The effect of NPs on overall **NSCLC cell line metabolism**, we acquired gene expression of 768 human metabolic genes to advance efforts towards novel therapeutic targets or biomarkers that take advantage of altered metabolism in cancer. We can profile alterations in 37 distinct pathways that span themes of biosynthesis and anabolic pathways, cell stress, nutrient capture, and catabolic pathways, signaling effecting cellular metabolism and transcriptional regulation. 3) *Centella asiatica* (CA), commonly named gotu kola, is an Ayurvedic herb used to enhance memory and nerve function. Previously, BENFRA Center has shown that water extract of CA (CAW) is neuroprotective, attenuating hippocampal mitochondrial dysfunction and improving memory in mouse models of Alzheimer's disease as well as healthy aging. We acquired expression of 757 **neuro-inflammation** specific genes from cortical tissue samples. Functional annotation of 23 different pathways that span three schemes such as immunity and inflammation; neurobiology and neuropathology; and metabolism and stress were conducted. We show that CAW can increase the expression of synaptic, mitochondrial and antioxidant genes in these mouse models.

C-40 – Zhenjian Lin

Ancient Defensive Terpene Biosynthetic Gene Clusters in the Soft Corals

Paul D. Scesa[1], Eric W Schmidt[1] and Zhenjian Lin[1]. [1]Departments of Medicinal Chemistry and Biochemistry, School of Biological Sciences, University of Utah, Salt Lake City, UT, United States

Marine invertebrates are excellent resource of biomedically important compounds, including FDA-approved drugs. Although some are produced by the symbiotic bacteria in response to host-symbionts interactions, the biosynthesis of most marine invertebrates derived compounds are still unknown. Recently, our discovery showed that animals also have biosynthetic enzymes that function in completely unique ways and make complex, microbe-like natural products. We have created innovative approaches that has proven highly successful solving some of the major problems in animal biosynthesis. Here, we present the identification and characterization of coral-encoded terpene cyclase genes that produce the eunicellane precursor of eleutherobin and cembrene, representative precursors for the >2,500 terpenes found in octocorals. Related genes are found in all sequenced octocorals and form their own clade, indicating a potential ancient origin concomitant with the split between the hard and soft corals. Eleutherobin biosynthetic genes are colocalized in a single chromosomal region. This demonstrates that, like plants and microbes, animals also harbor defensive biosynthetic gene clusters, supporting a recombinational model to explain why specialized or defensive metabolites are adjacently encoded in the genome.

C-41 – Nicole Avalon

The Structure, Biosynthesis, and Metal-Binding Properties of Leptochelin, a Cytotoxic Metabolite from the Filamentous Marine Cyanobacterium *Leptolyngbya* sp.

Nicole E. Avalon,[1] Mariana A. Reis,[2] Allegra T. Aron,[3] R. Thomas Williamson,[4] Matthew J. Bertin,[1] Kelsey L. Alexander,[1] Daniel Petras,[3] F. Alexandra Vulpanovici,[1] Christopher C. Thornburg,[5] Syrena Whitner,[1] Leonor Ferreira,[2] Hyukjae Choi,[1] Pieter C. Dorrestein,[3] Lena Gerwick,[1] Kerry L. McPhail,[5] William H. Gerwick[1,3] [1]Scripps Institution of Oceanography, UCSD, La Jolla, CA, USA; [2]Universidade do Porto Centro Interdisciplinar de Investigação Marinha e Ambiental: Porto, Portugal; [3]Skaggs School of Pharmacy and Pharmaceutical Sciences, UCSD, La Jolla, CA, USA; [4]Department of Chemistry and Biochemistry, University of North Carolina Wilmington, Wilmington, NC, USA, [5]College of Pharmacy, Oregon State University, Corvallis, OR, USA

Leptochelin, a mixed NRPS-PKS product isolated from the Indonesian marine cyanobacterium *Leptolyngbya* sp., has a unique structure with thiazoline and oxazoline rings, bromobenzyl and bromophenol features, and an epoxide. With nine chiral centers, abundance of heteroatoms, and multiple non-protonated carbon atoms, structure elucidation has proven challenging. Nevertheless, the compound remains of high interest due to its metal-binding properties and potent cytotoxicity against several cancer cell lines. Leptochelin promiscuously binds metals including iron, copper, cobalt, and zinc. The 8.4 Mbp genome of the leptochelin producer was sequenced, and the putative biosynthetic gene cluster (BGC) was identified using a retrobiosynthetic analysis. Current efforts are focused on the heterologous expression of the leptochelin BGC to definitively link it to the product molecule. Further structural studies are also underway to determine the configuration at each of the chiral centers.

C-42 – William Mendoza

Chemoinformatic Synthesis and Analysis of Cyanobacterial Pseudonatural Products

William Mendoza[1], Angel Hernandez[2], 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. Department of Chemistry, University of Puerto Rico - Rio Piedras[2]

Cyanobacteria produce secondary metabolites that have been well-documented to possess potent and selective bioactivity of a broad spectrum of diseases like viruses, bacteria, fungus, and cancer. Even though this highlights the critical role of natural products (NPs) for drug discovery, the novelty of structural scaffolds, especially of cyanobacterial origin, has largely remained steady for decades. To address this, we have virtually produce thousands of pseudo-NP structures library that combines cyanobacterial natural product pharmacophores, thought to be responsible for their biological activity (e.g. α,β-unsaturated system of Gallinamide A, epoxy ketone of Carmaphycin B) with privileged scaffolds from a variety of non-cyanobacterial NPs, that will modulate target selectivity and improve drug-likeness. Also, we have computationally predicted physicochemical values, likeness scores (e.g. NP-likeness, sp3 fraction, lead-likeness); using multiple open-access platforms and drug-design software and have identified suitable targets for synthesis and *in vitro* bioevaluations. Our cyanobacterial pseudo-NP library describes new chemical space for future drug discovery and development and may represent a new paradigm in drug design.

C-43 – Trevor Clark

Evaluation of Ion Mobility Spectrometry for Improving Constitutional Assignment in Natural Products Mixtures

Fausto Carnevale Neto[1,2,3,Δ], Trevor N. Clark[1,Δ], Norberto P. Lopes[2], Roger G. Linington[1]. [1]Department of Chemistry, Simon Fraser University, Burnaby, BC, Canada. [2]Núcleo de Pesquisa em Produtos Naturais e Sintéticos (NPPNS), Department of Biomolecular Sciences, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil. [3]Northwest Metabolomics Research Center (NW-MRC), Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA. [Δ]Authors contributed equally

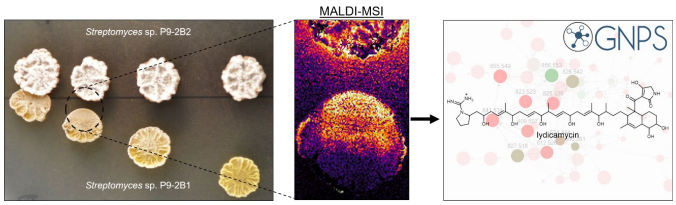
Untargeted metabolomics is one of the most prevalent methods for chemical characterization in the field of natural products. Conventional workflows use liquid chromatography coupled to high resolution tandem mass spectrometry (LC-MS^2) for small molecule detection and assignment. While processing and annotation methods continue to improve for LC-MS^2 data, many aspects of data acquisition can be optimized to improve detection and annotation using these processing tools. This study examined one of these factors, ion mobility spectrometry (IMS), to assess the effect of including IMS on MS^2 data quality. A test mixture of 20 commercial standards containing multiple overlapping compounds and configurational isomers was analyzed under four different acquisition modes; data dependent acquisition (DDA), data independent acquisition (DIA), IMS-DDA, and IMS-DIA and four different mixture complexities, high or low concentration spiked into a natural product extract or methanol. Each data file was processed using both the commercial UNIFI software platform and the public Global Natural Products Social molecular network (GNPS) platform for annotation of the standard compounds. IMS drastically increased annotation performance, ranging from 2 to 12 additional annotations dependent on mixture complexity and MS^2 acquisition mode.

C-44 – Scott Jarmusch

Salting the Earth: Streptomyces-Streptomyces Antibiosis via Lydicamycin Production

Scott A. Jarmusch[1], Jingling Wang[1], Zhijie Yang[1,2], Aaron Anderson[1], Tilmann Weber[2], Ling Ding[1]. [1]Department of Biotechnology and Biomedicine, Technical University of Denmark, Søltofts Plads 221, DK-2800 Kongens Lyngby, Denmark. [2]The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark, Kemitorvet, building 220, 2800 Kgs. Lyngby, Denmark

Streptomyces-Streptomyces interactions are some of the least explored when investigating these prolific producers of antibiotics. Serendipitously, *Streptomyces* sp. P9-2B2 induced sporulation of all strains tested when co-cultivated with ecologically relevant Streptomyces spp. from Jægersborg Deer Park, Denmark. Distance-based assays indicated sporulation was induced via diffusible metabolites. Using the combination of MALDI-MSI to visualize metabolite distribution, as well as GNPS molecular networking and genome mining, the responsible secondary metabolites were identified as a suite of lydicamycins. Sporulation-inducing secondary metabolites are uncommon in literature, making this discovery important for further understanding the lifecycle of these microbes in the presence of secondary metabolites.

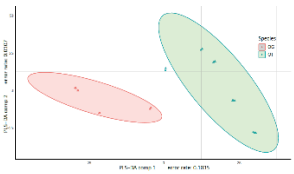


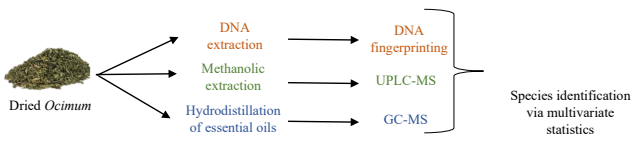
C-45 – Evelyn Abraham

A Comparison of Genetic and Chemometric Techniques for Authentication of Dried Herbal Products: A Case Study with *Ocimum* Spp.

Evelyn J. Abraham[1,2], *E. Diane Weatherspoon*[3], *Joshua J. Kellogg*[1,2]. [1]*Intercollege Graduate Degree Program in Plant Biology,* [2]*Department of Veterinary and Biomedical Sciences, Pennsylvania State University, University Park, PA 16802, USA,* [3]*Mass Spectrometry Lab, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA*

The increasing popularity of herbal medicines raises the potential for product adulteration. Advances in metabolomic instrumentation and data analysis, as well as genetic fingerprinting, have improved species-level identification of botanicals. However, there is no consensus on the optimal approach for robust authentication of consumer botanical products. This study compares the ability of three approaches, liquid and gas chromatography – mass spectrometry and DNA fingerprinting, to successfully differentiate between three *Ocimum* species using multivariate statistical techniques. Results indicate that chromatography datasets provide greater distinction between species using both supervised (PLS-DA) and unsupervised (PCA) multivariate models.





C-46 – Yi Zhao

Metabolic Profiling and Alkaloid Analysis of American *Aconitum* Species by UPLC-qTOF-MS^e

Yi Zhao[1,2], *Dake Zhao*[3], *Edward J. Kennelly*[1,2]. [1]*Department of Biological Sciences, Lehman College, City University of New York, Bronx, NY,* [2]*Biology PhD Program, The Graduate Center, City University of New York, New York, NY,* [3]*School of Life Science, Yunnan University, Kunming, P.R. China*

Aconitum species have been used for centuries as traditional Chinese and Ayurveda medicines to treat inflammations and other conditions. However, there are limited reports on how American *Aconitum* species are used medicinally. In this study, different parts (flowers, roots, stems, and leaves) of two American *Aconitum* species, *A. columbianum* and *A. uncinatum*, were collected from cultivated and wild specimens. Along with three other species native to Asia and Europe, a total of 175 samples were analyzed using UPLC-qTOF-MS^e. These results were aligned and normalized with an internal standard using Progenesis QI. An in-house database consisted of 839 *Aconitum* alkaloids and 147 flavonoids was established and uploaded to Progenesis QI for compound identification. PCA results show that two American species are clustered closely, and separated further from the European species and Asian species, suggesting that American species may have a distinct chemical profile due to evolutionary and/or morphological differences. Nineteen marker features of the two American species are found by OPLS-DA and tentatively identified. Among these marker compounds, acoapetaludine D and carmichaenine D could only be observed in *A. uncinatum*, whereas tadzhaconine could only be found in *A. columbianum*. A molecular network of the alkaloids has been established based on the fragment database and compound measurements information. This network may help to explain the diterpenoid alkaloid biosynthesis pathway in *Aconitum*, and uncover bioactive compounds with anti-inflammatory activity without the cardiotoxicity often associated with *Aconitum* diester alkaloids.

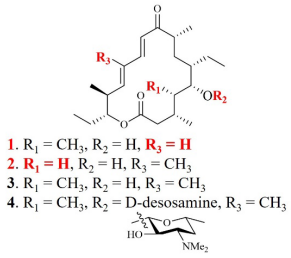
Poster Presentations – Session I

P-001 – Changyeol Lee

Desmethyl Tylactone-Based Macrolides Suggest Incorporation of Either Methylmalonyl CoA or Malonyl CoA

Changyeol Lee[1], Imraan Alas[1], Nathaniel J. Brittin[1], Doug R. Braun[1], Scott R. Rajski[1], and Tim S. Bugni[1]. [1]Pharmaceutical Sciences Division, University of Wisconsin–Madison, Madison, WI 53705, USA

A marine *Micromonospora* sp. was investigated due to antibacterial activity. Preliminary investigation indicated diverse macrolides related to tylactone. After more detailed analysis of the structures using NMR, two new desmethyl tylactone-based macrolides, tylactone A (**1**) and B (**2**). The structures were determined using 1D- and 2D-NMR and HRMS experiments. Previously, desmethyl analogs of erythromycin have been made through pathway engineering, but to the best of our knowledge these represent the first desmethyl analogs isolated. Importantly, we observed production of the macrolides with and without the methyl groups. This suggests that the bacterium can use either methylmalonyl CoA or malonyl CoA for the biosynthesis of the macrolide core. The genome was sequenced and a biosynthetic gene cluster (BGC) with 61% similarity to tylactone was found. While preliminary analysis of the BGC suggested preference for methylmalonyl CoA, the structures indicate potential for promiscuity. The structures supporting that hypothesis will be presented.



1. $R_1 = CH_3$, $R_2 = H$, **$R_3 = H$**
2. **$R_1 = H$**, $R_2 = H$, $R_3 = CH_3$
3. $R_1 = CH_3$, $R_2 = H$, $R_3 = CH_3$
4. $R_1 = CH_3$, R_2 = D-desosamine, $R_3 = CH_3$

P-002 – Mei Wang

Chemical Authentication and Speciation of *Salvia* Botanicals

Mei Wang[1], Joseph Lee[2], Jianping Zhao[2], Bharathi Avula[2], Amar G. Chittiboyina[2], Ikhlas A. Khan[2,3]. [1]Natural Products Utilization Research Unit, Agricultural Research Service, USDA, University, MS 38677, [2]National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University, MS 38677, [3]Division of Pharmacognosy, Department of BioMolecular Sciences, School of Pharmacy, University of Mississippi, University, MS 38677

Members of the genus *Salvia* have been used as a culinary herb and also prized for their purported medicinal attributes. Since physiological effects can vary widely between species of *Salvia*, it is of great importance to accurately identify botanical material to ensure safety for consumers. In the present study, an in-depth chemical investigation was performed utilizing GC/Q-ToF combined with chemometrics. Twenty-four authentic plant samples representing five commonly used *Salvia* species, *viz. S. apiana, S. divinorum, S. mellifera, S. miltiorrhiza,* and *S. officinalis,* were analyzed with the GC/Q-ToF technique. The high-resolution spectral data were employed to construct a sample class prediction (SCP) model based on stepwise reduction of data dimensionality followed by principal component analysis (PCA) and partial least square discriminant analysis (PLS-DA). This model demonstrated > 99.9 % accuracy for prediction ability. In addition, marker compounds present in each species were identified. A personal compound database and library (PCDL) containing characteristic compounds with the high-resolution mass spectra data from each species was constructed to reduce the time required and increase the confidence level for compound identification and classification of different *Salvia* species. By combining GC/Q-ToF and chemometrics, unambiguous identification of *Salvia* botanicals was achieved accurately and efficiently. This high throughput method can be utilized for species specificity and to probe the overall quality of various *Salvia*-based finished products.

P-003 – Richard Fitch

Endogenous Lipids as Normalization Standards for Natural Product Quantitation in Plants and Animals

Richard W. Fitch,[1] Callie E. Gernand,[1] Brianna E. Nirtaut,[1] Ralph A. Saporito,[2] Rebecca D. Tarvin,[3] David C. Cannatella,[3] Santiago Ron,[4] and Karina Klonoski.[5] [1]Department of Chemistry and Physics, Indiana State University, Terre Haute, IN 47809. [2]Department of Biology, John Carroll University, University Heights, Ohio 44118. [3]Department of Integrative Biology, The University of Texas at Austin, Austin, TX 78712. [4]Divison de Amfibios, Museo de Zoologica, Pontificia Universidad Católica del Ecuador, Quito, EC170135, Ecuador. [5]Department of Environmental Science, Policy, & Management, University of California at Berkeley, Berkeley, CA 94720

Obtaining reliable quantitative data in mass spectrometry analysis is challenging as compounds vary in their ionization efficiency and fragmentation. Moreover, matrix effects affect extraction efficiency and can cause highly irregular responses for different compound types based on polarity, solubility, ionizability and other factors. For most natural products there are no commercial analytically pure isotopic standards that can be used to calibrate sample responses. Our laboratory is focused on the analysis of alkaloids from amphibian and plant sources. We typically perform liquid or solid-phase extraction for isolation but also dilute-and-shoot crude analyses (akin to QUECHERS analysis, primarily by GC-MS) to have a gauge of alkaloid relative abundances prior to workup. We have found that endogenous plant and animal lipids can be useful for normalizing data when internal standards are unavailable or impractical to use. Herein we present comparative lipid and alkaloid data for several species of poison frogs from Hawai'i, Madagascar and South America as well as from the Kentucky Coffeetree and compare to results based on mass and measurements of original specimens.

P-004 – WITHDRAWN

P-005 – Nicole Avalon

The GNPS Suspect Library Expands Mass Spectrometry-Based Annotation of the Apratoxin Family of Natural Products

Nicole E. Avalon,[1,2] Wout Bittremieux,[2] Sebastian P. Rohrer,[1] Lena Gerwick,[1] Pieter C. Dorrestein,[2] William H. Gerwick[1, 2] [1]Scripps Institution of Oceanography, UCSD, La Jolla, CA, USA; [2]Skaggs School of Pharmaceutical Sciences, UCSD, La Jolla, CA, USA

The family of apratoxins are cytotoxic cyclodepsipeptides isolated from marine filamentous cyanobacteria. Using untargeted tandem mass spectral data, molecular networks were created on the Global Natural Products Social (GNPS) molecular networking platform and confirm the presence of several known apratoxins in the crude extracts of *Moorena bouillonii* from the Gerwick Lab culture collection. The GNPS suspect library, an open-access spectral library for untargeted metabolomics that contains MS^2 spectra for 87,916 chemical analogs, was used to expand the annotation of the apratoxin cluster beyond four apratoxins matching tandem mass spectral data from the reference library (apratoxins A, C, D, and F) to include six novel apratoxin suspects. Structural hypotheses could be made for four of the apratoxin suspects based on the associated MS^2 fragmentation patterns. Attempts to isolate these minor metabolites are underway, to perform orthogonal structural confirmation through NMR experiments. Additionally, the proposed structural differences correlate with differences that are plausible based on the enzymatic domains present in the apratoxin biosynthetic gene cluster. This case study points to the utility of the GNPS suspect library for discovery and targeting of potential analogues of natural products.

P-006 – T'ea Cameron

An Improved In-House Prioritization Protocol for Identifying Fungal Metabolites via LC-MS Data

T'ea P. Cameron,[1] Kristof B. Cank,[1] Tyler N. Graf,[1] Cedric J. Pearce,[2] Nicholas H. Oberlies[1]. [1]Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, Greensboro, NC, 27407, USA; [2] Mycosynthetix Inc, Hillsborough, NC, 27278, USA

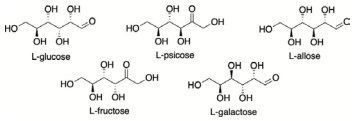
A major challenge common to natural products is the re-isolation of unwanted metabolites. To address this reoccurring problem, dereplication strategies were developed to screen the extracts and fractions of fungal cultures for compounds of non-interest. In addition, this method can be used to seek out fungi that biosynthesize compounds of high value. In this project we present here a test case of our in-house updated dereplication protocol that works through an ultra-performance liquid chromatography-photodiode array-high-resolution tandem mass spectrometric (UPLC-PDA-HRMS-MS/MS) method utilizing accurate mass, retention time, UV, and fragmentation of the compounds. Our method was automated through MZmine and Python to significantly cut back on the time of the analysis and to allow high throughput screening. We have improved the efficiency of the method by adding mass defect filtering as an option to screen the extracts for compounds of interest. This method is shared with the public through scripts of the publicly available programs. We have also shared a small library of mycotoxins that can be used to test the effectiveness of the method.

P-007 – Claudia Boot

The Shadow Metabolism of Rare Sugars and Their Potential for Carbon Sequestration

Claudia M. Boot1,2, Bethany Avera3, Stephanie Cardinalli1,2, Peter Baas4, James Henriksen2, Rich Conant2. 1Department of Chemistry, Colorado State University, Fort Collins, CO 80523, USA, 2Department of Ecosystem Science and Sustainability, Fort Collins, CO 80523, USA, 3Department of Soil and Crop Sciences, Colorado State University, Fort Collins, CO 80523, USA, 4Corteva Agriscience

The non-dominant enantiomer of common D-sugars are thought to be extremely rare or nonexistent in nature, however, we have observed a widespread shadow metabolism for L-sugars in soils from across the US. Diverting just a fraction of the carbon (C) that flows through terrestrial ecosystems into a pathway that forms L-sugars may provide an innovative and scalable method for C sequestration. We conducted 10-day soil incubations using five ^{13}C-1 labeled L-sugars to track their fate as respired carbon, persistence as a sugar, or biotic transformation by the soil microbiome into something other than CO_2. NMR spectroscopy was used to integrate the ^{13}C-1 signal over time to trace the persistence and transformation of the ^{13}C-1 labeled L-sugars. We found that respiration accounted for just 5% of the added ^{13}C on average and instead the majority of the ^{13}C remained in the chloroform- extractable fraction. Within the chloroform extracts we observed small but significant reductions in the ^{13}C-1 signal for allose ($p<0.0001$), fructose ($p<0.0001$), and galactose ($p=0.0034$), but no significant change for glucose or psicose. Our ongoing work is focusing on longer term resistance to decomposition and expanding understanding of L-sugar-specific C sequestration potential and synthesis pathways.



P-008 – Jack Silver

A New Method to Calculate Preparative Gradients for Natural Products

Jack Silver Teledyne ISCO

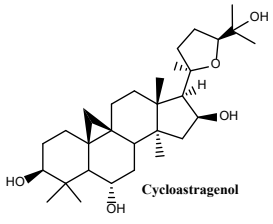
Chemists often need to purify compounds as part of the discovery and synthesis workflow for new compounds. The recently developed time-on-target (ToT) algorithm allows calculation of a focused gradient and enables fast, efficient purification from a single scouting run using preparative high-performance liquid chromatography, preparative supercritical fluid chromatography, or flash chromatography. Because method development is extremely simple using the ToT algorithm, scouting runs can be performed in combination with assay-directed fractionation to create efficient purification methods for unknown compounds. The scouting gradient can be run with either analytical or preparative columns. When preparative columns are used for the scouting gradient, enough sample is available for assay directed fractionation.

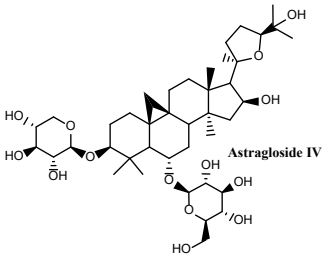
P-009 – Fadime Aydoğan

Analytical and Phytochemical Studies on Six *Astragalus* Taxa from Anatolia

Fadime Aydoğan[1,2], Shabana I. Khan[2], Zulfiqar· Ali [2], Ikhlas A. Khan [2]
[1]Department of Pharmaceutical Botany, Faculty of Pharmacy, Dicle University, 21280, Sur, Turkey,[2] National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University, 38677, Oxford, MS, USA

Astragalus L., is represented by approximately 3000 taxa in the world and is also the largest genus in Turkey (Anatolia) where it is represented by 479 taxa. Astragalus polysaccharides (APS) and triterpene saponin derivatives are two main components of *Astragalus* L. In this study, we aimed analytical studies of six *Astragalus t*axa (Anatolia) and the isolation, structural identification of over 30 triterpene saponins from *Astragalus strictispinus*. The isolates with their biological activities will be presented.





P-010 – Warren Vidar

The Compound Interaction Term for Identifying Synergists in Complex Mixtures

Warren S. Vidar[1], Tim U. H. Baumeister[2], Daniel A. Todd[1], Roger G. Linington[2], Olav M. Kvalheim[3], Nadja B. Cech[1]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC 27402, USA, [2]Department of Chemistry, Simon Fraser University, Burnaby, BC, V5A 156, Canada, [3]Department of Chemistry, University of Bergen, Bergen 5020, Norway

It is often argued that complex natural product mixtures contain constituents that work in concert (synergistically, additively, or antagonistically) to achieve their biological effects. However, it remains a challenge to predict synergy in complex mixtures using existing models. With this research, we developed a novel approach to find synergists by introducing the compound interaction term (CIT). The CIT is obtained by multiplying together the individual peak areas (obtained by LC-MS analysis) of any two mixture components to create a new value that represents the combined abundance of both components. This value is then added to the metabolomics data matrix and analyzed using partial least squares and selectivity ratio (SR) analyses, where high SR values correspond to variables (LC-MS features or CIT) with high correlation to biological activity. To test the utility of the CIT for identifying synergists, we designed mixtures to simulate botanical fractions and spiked each with berberine (a known antimicrobial) and piperine (a known synergist). We tested the mixtures for antimicrobial activity against *S. aureus* and collected metabolomics data for the mixtures using LC-MS. Results showed that the CIT for berberine and piperine produced high SR values even compared to the SR values for either berberine or piperine separately. This suggests that neither berberine nor piperine alone in low concentrations can completely inhibit *S. aureus* but must be in combination to exhibit their biological effect. This new approach may be applied to other complex mixtures to identify compounds that exert synergistic biological effects.

P-011 – Kabre Heck

Quantitative Analysis of Anthocyanins from Various Extracts of *Euterpe Oleracea* Mart. (Açaí) Fruits, Raw Materials, and Dietary Supplement Capsules by LC-MS-QTOF

Kabre L. Heck, Lauren M. Walters, Madeline L. Kunze, Angela I. Calderón. Department of Drug Discovery and Development, Harrison College of Pharmacy, Auburn University, Auburn, AL 36849

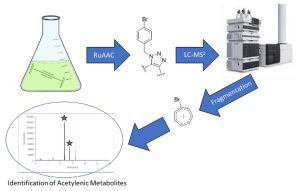
Euterpe oleracea Mart., commonly known as açaí, is a fruit that grows on a palm tree native to the Amazon region. Açaí is among the top 40 botanicals used in the U.S., and cancer patients increasingly use açaí containing dietary supplements to complement their conventional chemotherapeutic agents. *E. oleracea* presents many health benefits, the most prominent being antioxidant and anti-inflammatory activities. Standardization based on chemical quantitation is an analytical technique used to determine the exact chemical makeup of a plant species. Quantitation of the *E. oleracea* constituents in fruits, raw materials, and dietary supplement capsules is a crucial preliminary step to complete before utilizing extracts for biological assays. Açaí has four main anthocyanin analytes: cyanidin 3-glucoside, cyanidin 3-sambubioside, cyanidin 3-rutinoside, and peonidin 3-rutinoside. In this study, we report how we were able to scale up production of our extraction methods and a LC-MS quantitative analysis of anthocyanins in various açaí materials that is fast while very reproducible and accurate. The study was also assessed for intraday (0 day) and interday (5 day) accuracy in addition to assessing the 30-day stability of anthocyanins in acidic methanol solution. The method produced percent relative standard deviations (%RSD) below 5% for all extracts. The developed method is useful to assure quality for açaí materials used in food and dietary supplements industries.

P-012 – Daniel Back

Untargeted Identification of Alkyne-Containing Natural Products Using Ruthenium-Catalyzed Azide Alkyne Cycloaddition Reactions Coupled to LC-MS/MS

Daniel Back, Brenda Shaffer, Joyce Loper, Benjamin Philmus, Department of Pharmaceutical Science, Oregon State University, Corvallis, OR. Agricultural Research Service, US Department of Agriculture, Corvallis, OR

Copper mediated azide-alkyne cycloadditions (CuAAC) have played a vital role in the discovery and structure elucidation of acetylenic natural products, however CuAAC 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 known and new natural products containing both terminal and internal alkyne functionalities

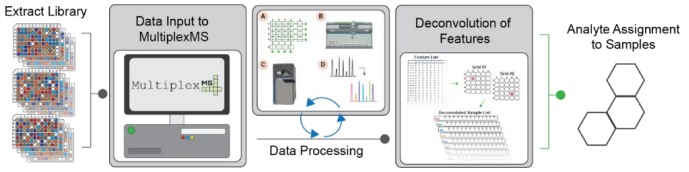


P-013 – Michael Recchia

MultiplexMS – An Ultra-High-Throughput MS-Based Multiplexing Platform for Increased Sample Throughput

Michael J.J. Recchia, Tim U.H. Baumeister, Dennis Y. Liu, Roger G. Linington. Department of Chemistry, Simon Fraser University, Burnaby, British Columbia V5A 1S6, Canada

Advances in high-throughput multi-omics have revolutionized the field of natural products (NP) discovery, becoming an integral tool for prioritizing and directing the isolation of new chemical entities from living organisms. Indeed, metabolomics, an "omics" branch focused on the comprehensive chemical characterization of complex extracts, has benefitted from these improvements and remains at the forefront of NP discovery. Despite these advancements, a bottleneck remains in the speed of chromatographic separation of complex NP samples. To address this bottleneck, a two-dimensional, ultra-high-throughput analytical sampling strategy was developed to increase MS screening up to 20-fold compared to traditional methods. The platform, named MultiplexMS, is an open-access MS-based tool for the analysis and reconstruction of pooled samples to increase the screening throughput of large NP extract libraries. We describe the development of the MultiplexMS platform, implementation of 'proof-of-concept' experiments, limitation trials to assess pooling constraints, and a final validating experiment to identify bioactive molecules when used in tandem with NP Analyst.



P-014 – Deepa Acharya

Microbial Biotransformation and LCMS Based Metabolomics for Advancing Natural Products for Crop Protection Uses

Deepa D. Acharya[1], Matt Chase[1], Elizabeth Ibwe[1], Negar Garizi[1].
[1]Corteva Agriscience, 9330 Zionsville Rd, Indianapolis, IN 46268

Natural product discovery is in a period of renaissance, owing to advances in sequencing and mass spectral technology. However, developing an initial natural product hit with biological activity into a product for crop protection is a challenging process, requiring several stages of characterization. A key aspect in this process is generating a diverse array of analogs for thorough structure-activity relationship studies. Owing to the complexity of the structures of these natural products, they are often intractable to synthetic modifications. Thus, microbial biotransformation is an excellent way to create novel analogs of the active natural product. Microbial enzymes can produce structural modifications in exogenous compounds and can be rapidly screened to generate a rich diversity of structural analogs. They can perform stereoselective reactions such as hydroxylation, oxidation, and glycosylation. At Corteva, a large collection of microbes is used to generate analogs of active natural products. The large datasets generated are analyzed using high resolution tandem mass spectrometry coupled with molecular networking, which is used to tease apart these complex mixtures to identify the analogs of interest. Molecular networking exploits the structural relatedness of these analogs to identify different biotransformations and potential candidates for SAR. This presentation will include examples where natural products were screened through the biotransformation panel in a high throughput fashion and analyzed using LC-MS/MS systems, along with informatics approaches deployed to automate the downstream analysis and build predictive databases.

P-015 – Andrés Mauricio Caraballo-Rodríguez

Hundreds of Strains, Thousands of Compounds: Validating the True Biosynthetic Potential of Actinobacteria

Andrés Mauricio Caraballo-Rodríguez[1], Bahar Behsaz[2], Hosein Mohimani[2], Pieter C. Dorrestein[1]. [1]Collaborative Mass Spectrometry Innovation Center, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA; [2] Computational Biology Department, School of Computer Science, Carnegie Mellon University, Pittsburgh, PA, USA

There is a gap between the potential and the actual production of small molecules encoded in microbial genomes. Among them, non-ribosomal peptides (NRPs) are molecules of interest due to their wide range of biological activities and clinical use. Several computational tools associated with mass spectrometry (MS) data have been developed in the last decade to accelerate the investigation of the genomic potential of bacteria as a source of undiscovered metabolites. In this work we provide reference mass spectrometry (MS) datasets from hundreds of actinobacteria strains, resulting in thousands of detected small molecules. We identified the detected molecules by combining experimental and in silico libraries of mass spectrometry data. Furthermore, we validated the discovery of a new family of NRPs from *Streptomyces* sp. by isolation and structural elucidation using NMR and MS techniques. We envision the use of the acquired reference MS-based datasets to be used for discovery of microbial molecules beyond NRPs, such as siderophores, polyketides and other chemical classes.

P-016 – Andrew McAvoy

MAS-SILAC Reveals Homogentisic Acid as an Intermediate in Natural Product Biosynthesis

Andrew McAvoy, Paxton Threatt, and Neha Garg, School of Chemistry and Biochemistry, Georgia Institute of Technology, 901 Atlantic Drive, Atlanta, GA 30332, USA

Burkholderia cepacia complex (Bcc) bacteria are responsible for opportunistic infections in cystic fibrosis (CF) patients. A subset of *B. cenocepacia* strains exhibit a pigmented phenotype due to production of pyomelanin. Previous metabolomic studies demonstrate that pigmented *B. cenocepacia* strains are associated with novel biotransformation of trimethoprim. However, these trimethoprim biotransformation products were not structurally characterized and pyomelanin-associated metabolism remains poorly understood. To explore metabolomic changes associated with an active pyomelanin pathway, we conducted liquid-chromatography-tandem mass spectrometry (LC-MS/MS) analysis on extracts from pigmented and non-pigmented *B. cenocepacia* strains cultured with and without trimethoprim, using mutant strains with reversed pyomelanin production phenotypes to control for strain-specific metabolomic differences. To provide insight into the biosynthetic origins of pigment-specific metabolites and guide structural annotations, we developed an annotation strategy called MAS-SILAC (**M**etabolite **A**nnotation assisted by **S**ubstructure discovery and **S**table **I**sotope **L**abeling by **A**mino acids in **C**ell culture). Our results demonstrate that pyomelanin production is associated with production of sulfur-containing metabolites. Specifically, we identify homogentisic acid as a key intermediate in production of pigment- specific metabolites and characterize the endogenous compound which biotransforms trimethoprim, linking pigment production to a novel mechanism of xenobiotic biotransformation.

P-017 – Armando Moreno-Velasco

Resin Glycosides from the Brazilian Jalap Root (*Operculina hamiltonii*), a Purgative Remedy

Armando Moreno-Velasco,[1] Rogelio Pereda-Miranda,[,1], Pedro Flores-Tafoya,[1] Mabel Fragoso-Serrano,[1] Suzana Guimarães Leitão[2].*
[1]Departamento de Farmacia, Facultad de Química and Programa de Maestría y Doctorado en Ciencias Químicas, Universidad Nacional Autónoma de México, Ciudad Universitaria, Mexico City 04510, Mexico, [2]Faculdade de Farmacia, Universidade Federal do Rio de Janeiro, CCS, Bloco A, Ilha do Fundão, 21941-590, Rio de Janeiro, Brazil

Brazilian Jalap root, a traditional medicinal plant complex still considered to be a useful treatment for enteric disorders due to its purgative activity, can be found as a crude root drug and powders sold by herbalists in traditional markets as well as an ingredient in some over-the-counter phytopharmaceuticals as pills, syrups, and hydro-alcoholic extracts retailed by drug stores in Brazil. Chemical analysis of methanol-soluble resin glycosides from "batata-de purga" or "batatão", *O. hamiltonii* (G. Don) D.F. Austin & Staples, the jalap root with yellow flowers, was performed through semipreparative recycling C-18 HPLC. One novel tetrasaccharide and four pentasaccharides, all having a 11*S*-hydroxy hexadecanoic acid as aglycone. Their structures were elucidated by high-field NMR spectroscopy and electrospray ionization mass spectrometry.

P-018 – Robert Shepherd

Solving a Molecular Puzzle: Structure Elucidation of Chlorinated Cyclopentene Derivatives from a *Perciomia* sp. (Strain G1144)

Robert A. Shepherd[1], Kristof B. Cank[1], Sonja L. Knowles[1], Manuel Rangel-Grimaldo[1], Huzefa A. Raja[1], Zoie L. Bunch[1], Nadja B. Cech[1], Christopher A. Rice[2], Dennis E. Kyle[3], Joseph O. Falkinham III[4], Joanna E. Burdette[5], Nicholas H. Oberlies[1]. [1] Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, Greensboro, NC 27412, [2] Department of Pharmaceutical and Biomedical Sciences, University of Georgia, Athens, GA 30602, [3]Center for Tropical & Emerging Global Diseases, University of Georgia, Athens, GA 30602, [4] Department of Biological Sciences, Virginia Tech Center for Drug Discovery, Blacksburg, VA 24061, [5] Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL 60612

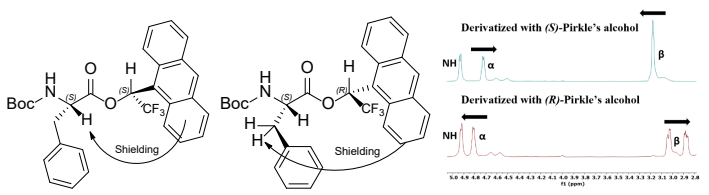
A marine-derived fungus, *Perciona* sp., was isolated from decaying *Spartina* (cord grass) stems collected from Holden Beach, NC. Extraction of the fungus yielded three new chlorinated cyclopentene derivatives along with a known compound, rhytidhyester D. While halogenated metabolites have been isolated in abundance from marine-derived organisms, two of the compounds represent trichlorinated cyclopentene polyketides, which have been observed only rarely from nature. The elucidation of their planar structures was performed using mass spectrometry (MS) and multi-dimensional nuclear magnetic resonance spectroscopy (NMR). The relative and absolute configurations were determined using high- resolution MS, NMR spectroscopy, Mosher's ester analysis, and various computational NMR calculations. All compounds were tested against *Naegleria fowleri*, quorum sensing inhibition, and antibacterial assays, but all were inactive. Thus, their specific bioactivity remains an area for further consideration.

P-019 – Jared Wood

Anisotropic NMR Validation of Atypical Chiral Auxiliary Models: Application to α-Amino Acids

Xiao Wang,[a] Jared S. Wood,[b] Ryan Cohen,[a] William H. Gordon,[b] Wendy K. Strangman,[b]. Ana C. Barrios Sosa,[b] R. Thomas Williamson[b*] [a]Analytical Research & Development, Merck & Co. Inc., Rahway, NJ, USA. [b]Department of Chemistry and Biochemistry, University of North Carolina Wilmington, Wilmington, NC 28409*

In modern drug discovery, determining the absolute configuration of amino acids has become of paramount importance due to the increasing development of novel peptides for the engagement and modulation of therapeutic targets. The synthesis of small molecules with high functionality has been facilitated by the incorporation of both natural and unnatural (or "unusual") amino acids. To date, there is still an unmet need for an efficient and universal approach for determining the chirality of alpha (α), beta (β), (α)-hydroxy, and tertiary amino acids. Recent studies have shown that selective chiral agents can induce significant chemical/structural differences in compounds, thus supporting the development of a unique methodology that addresses this issue. Our laboratory has discovered the first evidence that the reaction of a protected amino acid with a chiral aryltrifluoromethyl alcohol (Pirkle's alcohol) can provide products with distinct NMR spectroscopy signatures that can be used for the confident assignment of absolute configuration. Upon validation of the method with simple α-amino acids, the overarching goal presented in this thesis is to refine and extend this methodology to more complex amino acids.

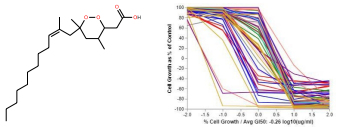


P-020 – Rohitesh Kumar

Structure Elucidation, Absolute Configuration and Biological Evaluation of Cyclic Peroxide from *Plakinastrella sp*

Rohitesh Kumar[1], Rhone K. Akee[1], Lucero Martinez[2], Christopher C. Thornburg[1], Tanja Grkovic[2, 3], and Barry R. O'Keefe[2, 3] [1]Natural Products Support Group, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, Frederick, Maryland 21702-1201, United States; [2]Natural Products Branch, Developmental Therapeutic Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Frederick, Maryland 21702-1201, United States [3]Molecular Targets Program, Center for Cancer Research, National Cancer Institute, Frederick, Maryland, 21702-1201, United States

Marine sponges of the genus *Plakinastrella* are a rich source of cyclic peroxides that exhibit a wide range of biological activities. During the search for anti-cancer natural products, a new cytotoxic cyclic peroxide was isolated from the organic extract of *Plakinastrella* sp. Structural elucidation and absolute configuration assignment was determined by extensive NMR studies and application of Mosher's ester derivatization. This compound exhibited potent activity against SR (leukemia), LOX IMVI (melanoma), and UO-31(renal) cell lines in the NCI-60 cancer cell line cytotoxicity assay.

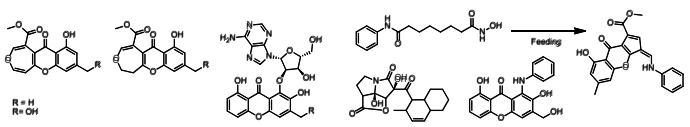


P-021 – Oh-Seok Kwon

New Natural and 'Unnatural' Compounds from Endophytic Fungus *Chalara* Sp. with Potent *In Vitro* And *In Vivo* Activity

Oh-Seok Kwon[1], Mahsa Khoshbakht[2], Jason Srey[2], Donovon A. Adpressa[2], James A. Strother[1], Sandra Loesgen[1,2]. [1]University of Florida, FL 32080. [2]Oregon State University, OR 97330*

The strategy of one strain many compounds (OSMAC) has been shown as powerful tool to activate silent biogenetic gene clusters in microorganisms. Fungal endophyte *Chalara* sp. produces a variety of unique of polyketides. Among them the isofusidienol class of antibiotics, adenine coupled xanthones, as well as anilino-containing chalaniline A & B after feeding the histone deacetylase (HDAC) inhibitor vorinostat. Here, OSMAC and media optimization supported by mass spectrometry-based metabolomics led to the isolation of bioactive xanthones and new pyrrolizidines. All compounds were tested *in vitro* for antimicrobial activity and screened in a recently developed *in vivo* zebrafish behavior assay for anti-nociceptive activity.

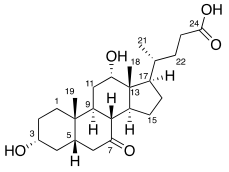


P-022 – Yern-Hyerk Shin

Discovery of a Bile Acid Eliciting Response of Chemotactile Receptor of Octopus

Yern-Hyerk Shin[1], Patric Vaelli[2], Nicholas Bellono[2], Jon Clardy[1]. [1]Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School and Blavatnik Institute, Boston, MA 02115, USA, [2]Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA 02138, USA

A bile acid, 3α,12α-dihydroxy-7-oxo-5β-cholanic acid (**1**), was discovered during cultivation of a *Vibrio* sp. The strain was isolated from fiddler crab (*Uca pugnax*), the main prey of two-spot octopuses *Octopus bimaculoides*. A large-scale culture of the strains was extracted with ethyl acetate, and compound **1** was purified from the extract as a pure state through various chromatographic methods. The planar structure of **1** was elucidated based on 1D & 2D NMR spectroscopy and mass spectrometry data. The absolute configurations of **1** were identified as 3*R*, 5*S*, 8*R*, 9*S*, 10*S*, 12*S*, 13*R*, 14*S*, 17*R*, and 21*R* configurations through relative configuration analysis using NOESY NMR spectral data and optical rotation values. Compound **1** showed robust activity eliciting specific response at chemoreceptor (CR) 518 of the octopus.



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P-023 – Matthew Pin

NP-MRD: The Natural Products Magnetic Resonance Database

Matthew T Pin[1], Tamara Jordan[1], Jonghyeok Kim[1], Ben J Ledingham[1], Dana Allen[2], Mark Berjanskii[2], Zachary Budinski[2], Xuan Cao[2], Raynard Dizon[2], Vasuk Gautam[2], Rajarshi Ghosh[3], Niranjan Govind[4], AnChi Guo[2], Amy M Jystad[4], Eleanor Knutson[4], Jay Koller[3], Brian L Lee[2], Robert Mah[2], Andrew Maras[1], Eponine Oler[2], Harrison Peters[2], Ella F Poynton[1], Ryan Renslow[4],Manoj Rout[2], Saurav Sarma[3], Zinat Sayeeda[2], Victoria Sullivan[4], Pegah Tavangar[1], Jeffrey A van Santen[1], Vera Yang[1], Lloyd W Sumner[3], David S Wishart[2], John R Cort[4], Roger G Linington[1]. [1]Department of Chemistry, Simon Fraser University, Burnaby, BC, Canada, [2]Department of Biological Sciences, University of Alberta, Edmonton, Canada, [3]Department of Biochemistry, University of Missouri, Columbia, USA, [4]Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA 99352, USA

The Natural Products Magnetic Resonance Database (NP-MRD, np-mrd.org) is a comprehensive, open access, searchable, and connected NMR Data repository for natural products, metabolites, and other biologically derived chemicals. The database houses derived (e.g. chemical shift assignments), raw (FID), and simulated NMR data presented through a frontend

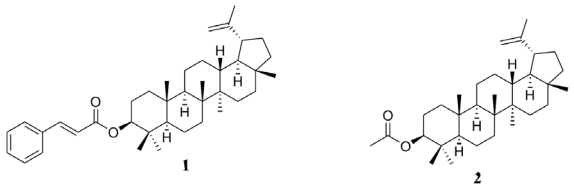
website and links to external resources. Application of the NP-MRD suite can facilitate dereplication, enable structure validation or revision, and support correction of erroneous or missing chemical shift assignments. Community deposition of NMR spectra is supported via a simple to use drag and drop interface. Additionally, the database can (among other presently unforeseen applications) provide utility in the development of new AI-based approaches to structure determination and chemical shift or spectral prediction. The presentation will consist of an overview of the NP-MRD's current functionality and future development objectives.

P-024 – Alec Brundle

Lupeol Esters from American Groundnut (*Apios americana*)

Nanea K. Perkins, Mackenzie J. Perpetua, Natalie C. Stagnitti, Alec P. Brundle, Emily J. Schafer, and Stephen T. Deyrup. Department of Chemistry and Biochemistry, Siena College, Loudonville, NY 12211

Apios americana is a plant that was traditionally used as a food-source by indigenous North Americans. Its use as a food crop later expanded to Japan and it is now being grown in the UK and South Korea as well. Previous research has identified several secondary metabolites along with the nutrient content of this crop plant, but further research is warranted due to its outstanding health benefits, medicinal properties, and its potential for use in cosmetics. Chemical investigation, including 1D and 2D NMR spectra, of the non-polar extract of *A. americana* tubers found the first evidence of lupeol esters in this plant. Lupeol esters are known to have several beneficial effects including anti-inflammatory, anticancer, and skin-cell regrowth activities. Further data provided evidence that of the lupeol esters present, lupeol cinnamate (**1**) and lupeol acetate (**2**) are the most abundant, and that lupeol esters are present in quantities greater than 7 mg per gram of dry *A. americana*.

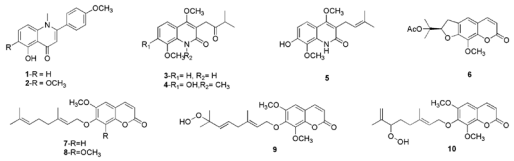


P-025 – Young-Won Chin

Alkaloids and Coumarins from the Leaves of *Orixa japonica*

Piseth Nhoek[1], Pisey Pel[1], Young-Mi Kim[1], Young Hee Choi[2], Young-Won Chin[1].[1]College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 08826, Republic of Korea, [2]College of Pharmacy, Dongguk University-Seoul, Gyeonggi-do 10326, Republic of Korea

Phytochemical study of the leaves of *Orixa japonica* led to the isolation of five new alkaloids (**1**–**5**) and five new coumarins (**6**–**10**), together with 28 known compounds. The structures of all isolated compounds were elucidated by their (1D and 2D) NMR spectroscopic data and MS data. The ECD was theoretically computed to aid the proposal of absolute configuration of compound **6**.



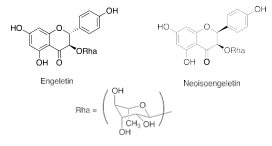
Isolated new compounds from the leaves of *Orixa japonica*

P-026 – Emily Schafer

Large Anisotropic Effect Observed in Natural Products from *Smilax auriculata*

Mackenzie J. Perpetua, Natalie C. Stagnitti, Sarah M. Dauphin, Gabrielle L. DeAngelis, Alec P. Brundle, Emily J. Schafer, and Stephen T. Deyrup. Department of Chemistry and Biochemistry, Siena College, Loudonville, NY 12211

Traditional Chinese Medicine has a long history of using different organisms as materia medica. One of these organisms is the plant *Smilax glabra* which has been used to treat dysentery and joint pain. We studied the native North American vine *Smilax auriculata* since it is closely related to *S. glabra* and little is known about its chemistry. Chemical investigation using 1D and 2D NMR spectroscopy of *S. auriculata* tubers determined that the major secondary metabolites were flavonoid glycosides. Specifically, engeletin (**1**) and neoisoengeltin (**2**) were partially purified and identified. Intriguingly, a large anisotropic effect ($\Delta\delta$ ~1.8 ppm) was observed in these natural diastereomers based on the relative configuration of the rhamnose and aromatic ring moieties. Computational studies supported the idea that H-5′ is positioned closer to the face of the aromatic ring in **2** than in **1**.



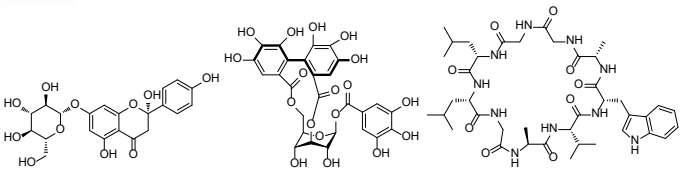
P-027 – Yoon Seo Jang

Phenolic Compounds and Cyclic Peptides from *Jatropha podagrica* Leaves and their Anti-SARS-CoV-2 Activity

Yoon Seo Jang[1], Bum Soo Lee[1], Se Yun Jeong[1], Da Eun Lee[1], Eon Chung Park[1], Kyung Ah Kim[1], Bora Kim[1], Yoon Suk Lee[1], Seung Hye Cho[1], Yeo Rang Cho[1], Gang Min Noh[1] and Ki Hyun Kim[1]. [1]School of

Pharmacy, Sungkyunkwan University (SKKU), Suwon 16419, Republic of Korea

Jatropha podagrica leaves have been used as a traditional medicine for analgesic, tonic, and purgative. As a part of ongoing studies to discover bioactive natural products, six phenolic compounds (**1-6**) including one new flavonoid glycoside (**1**) and two cyclic peptides (**7-8**) were isolated from leaves of *J. podagrica*. Their chemical structures were determined by detailed analysis of 1D and 2D NMR (^{1}H-^{1}H COSY, HSQC, HMBC, and NOESY), LC/MS analysis as well as ECD data. The isolated compounds were evaluated for the inhibitory activity on spike protein of pseudotyped-SARS-CoV-2.



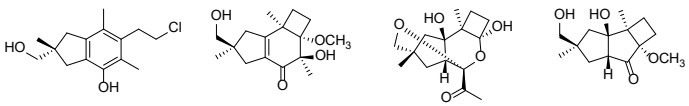
1 2 3

P-028 – Se Yun Jeong

Novel Sesquiterpenoids including Nor-Repraesentane -Type Sesquiterpenes from Poisonous Mushroom *Russula japonica*

Se Yun Jeong[1], Bum Soo Lee[1], Da Eun Lee[1], Yoon Seo Jang[1], Eon Chung Park[1], Kyung Ah Kim[1], Bora Kim[1], Yoon Suk Lee[1], Seung Hye Cho[1], Yeo Rang Cho[1], Kang Min Noh[1] and Ki Hyun Kim[1]. [1]School of Pharmacy, Sungkyunkwan University, Suwon 16419, Republic of Korea

Russula japonica Hongo (Russulaceae) is a poisonous mushroom distributed in Asian countries, such as Korea, China, and Japan. As part of our systematic study on Korean wild mushrooms, a chemical investigation of *R. japonica* fruiting bodies resulted in the isolation and structural characterization of 23 sesquiterpenoids, which are consisted of ten illudalane-type (**1-7** and **20-22**) and nine protoilludane-type sesquiterpenes (**8-15** and **23**), as well as four nor-repraesentane-type sesquiterpenes (**16-19**), which feature unprecedented C_{13} backbone with 4/5/5-fused tricyclic skeleton. The chemical structures of novel compounds (**1-19**) were established by detailed analysis of 1D and 2D (^{1}H-^{1}H COSY, NOESY, HSQC, and HMBC) NMR, HR-ESIMS, DP4+, optical rotation, ECD calculations, and X-ray crystallography.



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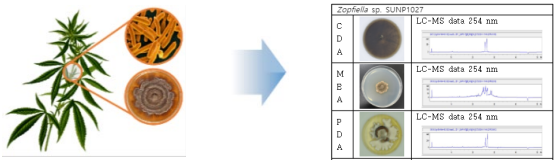
P-029 – Da Eun Lee

Isolation of Endophytes from *Cannabis sativa* and Novel Compounds from Cannabis-associated Endophytic Fungus *Zopfiella* sp.

Da Eun Lee[1], Bum Soo Lee[1], Se Yun Jeong[1], Yoon Seo Jang[1], Eon Chung Park[1], Kyung Ah Kim[1], Bora Kim[1], Yoon Suk Lee[1], Seung Hye Cho[1], Yeo Rang Cho[1], Kang Min Noh[1] and Ki Hyun Kim[1]. [1]School of Pharmacy, Sungkyunkwan University (SKKU), Suwon 16419, Republic of Korea

Cannabis sativa is known for its bioactive substances, but it has been regulated as a drug because of addiction. We investigated endophytes of *C. sativa*, which is expected to produce bioactive substances. We isolated a total of 27 fungal strains from *C. sativa*, and they were identified using ITS rDNA sequences. In particularly, the LC/MS-based analysis including GNPS networking revealed that *Zopfiella* sp. grown in the CDA medium showed the presence of interesting molecules. The LC/MS-guided isolation of the MeOH extracts of *Zopfiella* sp. led to the isolation of two new sesquiterpenes, and their chemical structures were elucidated by analysis of 1D and 2D (^{1}H-^{1}H COSY, HSQC, HMBC and NOESY) NMR and HR-ESIMS as well as ECD calculation.

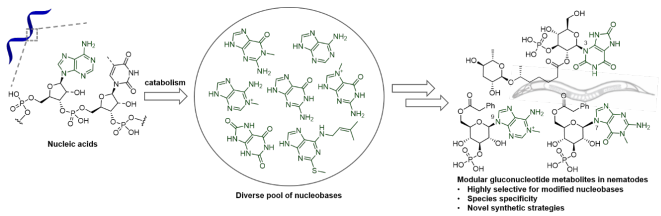


P-030 – Brian Curtis

Beyond Ribose: Gluconucleosides in Nematodes

Brian J. Curtis, Russell N. Burkhardt, Arnaud Tauffenberger, Bennett W. Fox, Jude Andrzejewski, Chester J. J. Wrobel, Jingfang Yu, and Frank C. Schroeder. Boyce Thompson Institute and Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

Few nucleic acid-derived natural products have been identified from animals, despite the ubiquity of nucleosides in living organisms. From metabolomic analyses of *C. elegans* and related nematodes, we identified a family of novel gluconucleosides incorporating modified nucleobases derived from RNA and/or DNA degradation. The biosynthesis of these modular metabolites was found to be regulated by conserved signaling pathways, e.g. insulin signaling, and compound profiles differ depending on nematode species, age, and sex. We developed novel synthetic strategies to access gluconucleosides and corresponding phosphates for unambiguous structure elucidation and biological exploration of this novel metabolite family which may serve as chemical signals.



P-031 – Jianping Zhao

NMR Approach for Quality Assessment of Copaiba Oil

Jianping Zhao [1], Mei Wang [2], Joseph Lee [1], Zulfiqar Ali [1], Ikhlas A. Khan [1]. [1]National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University, MS 38677; [2]Natural Products Utilization Research Unit, ARS. Department of Agriculture, University, Mississippi 38677

Copaiba oil has been traditionally used for the treatment of various disorders, and widely used as a fixative in the cosmetic industry. Copaiba oil is obtained from *Copaifera* trees. *C. langsdorffii, C. officinalis, and C. reticulata* are the most important commercial sources, and the most prized copaiba oils are rich in *β*-caryophyllene. More than 230 constituents have been reported from *Copaifera* species. Chemical composition of copaiba oils obtained from different *Copaifera* species varies significantly. Adulteration of Copaiba oil by the addition of cooking oils or other cheap oils were reported. So far, there is no official standards for Copaiba essential oil existed, leading to difficulties in the quality control and the safety assurance of the products. The aims of this study include: i) to evaluate the variation and distribution of chemical composition in copaiba oil samples; and ii) to detect the outlier samples and explore possible adulteration based on the NMR profile information. As the results, significant variation of the chemical composition was observed for some of the investigated samples by comparing their NMR spectral fingerprints, and the samples were classified into four groups (A – D) by the chemometric analysis. 20 out of the 36 (~55.6%) commercial samples obtained from the market were found to be adulterated.

P-032 – Melissa Henckel

Thermoneutral Induced Glucose Intolerance in Rats is Reversed with (–)-Epicatechin Treatment

Melissa M Henckel[1,2], Ji Hye Chun[3], Leslie A Knaub[1,2], Sara E Hull[1,2], Greg B Pott[1,2], David G Ramirez[1,2], and Jane E-B Reusch[1,2], Amy C Keller[1,2]. [1]Division of Endocrinology, Metabolism & Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO 80045, [2]Rocky Mountain Regional VA Medical Center, Aurora, CO 80045, [3]Aquillius Corporation, 10918 Technology Pl, San Diego, CA 92127

Diabetes is a life-threatening and debilitating disease, typified by glucose intolerance and insulin resistance. (–)-Epicatechin is a plant compound of interest for the treatment of diabetes, showing improved carbohydrate metabolism in previous studies. We hypothesized that (–)-epicatechin would alleviate thermoneutral housing-induced glucose intolerance. Male Wistar rats were housed at either thermoneutrality (TN, 30°C) or room temperature (RT, 24°C) for 16 weeks, and intraperitoneal glucose (GTT) and insulin tolerance tests (ITT) were conducted at the beginning and end of the study. The last 15 days of the study, each animal was gavaged with either 1 mg/kg body weight of (–)-epicatechin or vehicle. Rats housed at TN had significantly elevated plasma glucose area under the curve (AUC) during the GTT compared to those at RT (10,916.3±1,183.4 vs. 7,860.0±2,362.6, $p<0.05$) but similar simultaneous insulin secretion (TN=175.7±32.2 vs. RT=159.7±26.2). When treated with (–)-epicatechin, rats at TN had improved glucose tolerance as compared with TN controls (AUC=8,380.3±630.1 vs. 10,916.3±1,183.4, $p<0.05$) and increased simultaneous insulin secretion (AUC=253.5±61.5 vs. 175.5±32.2, $p<0.05$). There were no differences in insulin sensitivity between any of the groups. (–)-Epicatechin treatment in RT animals resulted in a higher percentage of insulin positive cells (12.0±1.0 vs. 8.3±2.4 in RT controls); all (–)-epicatechin-treated animals had significantly less insulin per tissue area as compared with non-treated animals ($p<0.05$). These data support that (–)-epicatechin improved glucose tolerance via increased insulin production and secretion. This study underlines the potential use of (–)-epicatechin as a treatment for managing glucose metabolism in those suffering from diabetes.

P-033 – Mallika Kumarihamy

Evaluation of Berbamine, a *Bis*-benzyltetrahydroisoquinoline Alkaloid, in Combination with Choloroquine in *Plasmodium berghei* Mouse Malaria Model

Mallika Kumarihamy[1], Surendra Jain[2], Narayan D. Chaurasiya[3], Shabana I Khan[1], Babu L. Tekwani[3] and Ilias Muhammad[1]. [1]National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University MS 38677, [2]HD Biosciences, San Diego, CA 92121; [3]Department of Infectious Diseases, Southern Research, Scientific Platforms, Southern Research Birmingham AL 35205

Berbamine (BRM), a *bis*-benzyltetrahydroisoquinoline alkaloid, was identified as a prominent antimalarial constituent of *Berbeis thunbergii*, commonly known as Japanese barberry. Barbamine was further evaluated *in vivo* in combination with choloroquine in *P. berghei* mouse malaria model. Treatment with BRM alone produced only partial suppression of parasitemia. Treatment of *P. berghei* infected mice with BRM (ip; 3.7-33.3 mg/Kg) in combination with CQ (oral; 33.3 mg/Kg) once daily for three days showed complete suppression of parasitemia and cured 60 % of mice. Treatments with CQ alone did not produce any cure at this dose. The combination of CQ and BRM significantly potentiated the antimalarial activity without any apparent toxicity or adverse effects to mice, as indicated by increase in mean survival time of mice and also overcame the recrudescence that was observed with the CQ monotherapy. This study is in line with the previous reports on tetrandrine and cepharanthine, the analogs structurally related to BRM, which also showed an enhanced effect on CQ-resistant malaria in primate and mice malaria models, respectively. These study support further evaluation of BRM and BRM rich extracts in combination with other antimalarial drugs, which are under clinical use in different part of the world to combat the problem of drug resistance.

P-034 – Johanne Gerstel

Echinacea Purpurea: Inhibition or Enhancement of Rhinovirus Replication by Different Extraction Methods

Gerstel, J.A.[1,2] and Langland, J.O.[1,2] [1]Ric Scalzo Institute for Botanical Research, Southwest College of Naturopathic Medicine, Tempe, Arizona, USA 85282. [2]Biodesign Institute Center for Immunotherapy, Vaccines, & Virotherapy, Arizona State University, Tempe, Arizona, USA 85281

Rhinovirus infections are associated with the common cold. Symptomology and complications of rhinovirus infections are often linked to the immune response and the expression of the cytokine, IL-8. Rhinovirus complications may include chronic bronchitis, sinusitis, otitis media and asthma. *Echinacea purpurea* has historically been used as a therapy for rhinovirus infections, but results from clinical studies have been controversial. Many studies conclude that *Echinacea* is an effective therapeutic against the rhinovirus infections, whereas an equal number of reports claim the opposite. The purpose of our study was to investigate the biological activities of *Echinacea* root extracted in both water and ethanol. Results demonstrated a dramatic difference in the antiviral activity between the different root extractions. Ethanol extracts of the root inhibited viral replication by inhibiting viral cellular attachment. In contrast, a water extract of the root led to an enhancement of rhinovirus replication. This enhancement led to an approximate 100-fold increase in virus replication levels and does not appear to be associated with the host antiviral interferon response. Our data suggests that different extraction methods will likely produce significantly different physiological responses to *Echinacea* and could lead to very different outcomes in clinical trials.

P-035 – Ping Jiao

Maizinol™, a *Zea mays* Leaf Extract for Improving Sleep Quality

Ping Jiao, Mesfin Yimam, Teresa Horm, Mei Hong, Lidia Brownell, Qi Jia, Unigen Inc., 2121 South State Street, Suite 400, Tacoma, WA 98405, US

According to CDC, 70 million Americans suffer from chronic sleep problems. Sleep insufficiency and sleep disorders can affect the overall health and quality of life. Maizinol is a natural sleep aid, stress, and mood health ingredient developed from *Zea mays* (corn) leaf extract. Melatonin is a hormone where its potential sleep aid effects arising from the activation of MT1 and MT2 receptors. Human melatonin receptor binding assays showed Maizinol binds to both melatonin receptors, with a greater affinity for MT2 receptor with an IC_{50} value of 56.6 μg/mL and an inhibition constant (K_i) of 28.3 μg/mL, while an IC_{50} of 229 μg/mL and a K_i of 119 μg/mL was observed for MT1. Maizinol could produce endogenous physiological melatonin-like effects for better sleep quality. Maizinol also increases endogenous biosynthesis of serotonin and melatonin via regulating key rate limiting enzymes in the melatonin and serotonin synthesis pathways, such as serotonin N-acetyltransferase and tryptophan-5-hydroxylase. Maizinol inhibits activity of the liver enzyme tryptophan dioxygenase, which could free up more starting materials for serotonin/melatonin conversion. Maizinol was evaluated for its effect on sleep quality and overall well-being in a double blind, placebo-controlled clinical trial, administered orally at 250 and 500 mg/day. Participants who received Maizinol showed a statistically significant and dose-correlated reduction in salivary cortisol (up to 36%); increase in deep sleep time (up to 30 minutes); increased total sleep time (up to 10%); improvement in sleep quality (up to 49%) and enhanced profile of mood state (36 – 58%). Maizinol is a safe nutritional supplement clinically proven for a 24-hour support with a better quality and efficiency of sleep at night and improved mood state and overall well-being during the day. Details of human clinical trial and MOA studies of Maizinol will be presented and discussed.

P-036 – Colby Borges

Identification of Cytochrome P450 Enzyme Inhibitors in Cinnamon (*Cinnamomum verum*) Using a Biochemometric Approach

Colby H. Borges[1], Preston K. Manwill[1], Rakshit S. Tanna[2], Tyler N. Graf, Daniel A. Todd[1], Nicholas H. Oberlies[1], Mary F. Paine[2] and Nadja B. Cech[1]. [1]Department of Chemistry and Biochemistry, University of North Carolina Greensboro, Greensboro, NC 27402. [2]Department of Pharmaceutical Sciences, College of Pharmacy and Pharmaceutical Sciences, Washington State University, Spokane, WA 99202

Cinnamon (*Cinnamomum* spp.) is used worldwide for both culinary and medicinal purposes. Regarding the latter, increasing cinnamon consumption particularly among prediabetic and diabetic patients has, in part, been spurred by growing putative evidence that chronic consumption of large quantities of cinnamon (3-6 g daily) has beneficial effects on blood glucose homeostasis and insulin sensitivity. This usage pattern raises concern for potential adverse cinnamon-drug interactions in this patient population, who typically take multiple medications. Current pre-clinical data on potential cinnamon-drug interactions is limited to a few reports of cinnamon powder or the major constituents *trans*-cinnamaldehyde and 2-methoxycinnamaldehyde inhibiting the activity of certain drug metabolizing enzymes, specifically the cytochrome P450s (CYPs). This study aimed to identify specific constituents from *Cinnamomum verum* that inhibit the activity of select CYPs. A *C. verum* extract was prepared and fractionated using normal phase chromatography. The extract and fractions were analyzed by untargeted UPLC-MS-based metabolomics and evaluated for their *in vitro* inhibitory activity against CYP2C9, -2D6, and -3A. Interpretation of the data using biochemometrics, a multivariate statistical approach that combines biological and chemical data to identify chemical constituents associated with biological activity, will be presented.

P-037 – Preston Manwill

UPLC-MS-Based Metabolomics Reveals Variability in Commercial Cinnamon Products

Preston K. Manwill, Tyler N. Graf, Daniel A. Todd, Nicholas H. Oberlies, and Nadja B. Cech. Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27402, USA

Botanical products remain a vast reservoir of pharmacological and chemical diversity utilized worldwide for myriad medicinal applications both as complex mixtures and as the source of new chemical entities. The supply of diverse botanical products has grown exponentially with products now readily available to consumers via online retailers. The quality, botanical authenticity, and chemical profile of these products constitute a major health concern for consumers. Cinnamon (*Cinnamomum* spp.) represents a prime example of this. Cinnamon is often touted for its beneficial anti-diabetic properties, such as lowering blood glucose, cholesterol, and triglyceride levels. Unfortunately, cinnamon also contains coumarin, a small molecule with hepatotoxic effects. The levels of coumarin vary among *Cinnamomum* species, with higher levels observed in *C. cassia*, C. *loureiroi*, and *C. burmannii*, while trace amounts are observed in *C. verum*. In the present study, we analyzed the chemical profiles of 59 commercially available cinnamon products and 8 authenticated cinnamon samples using ultra-high-performance liquid chromatography–high-resolution mass spectrometry (UPLC–HRMS). The chemical profiles were evaluated using untargeted metabolomics tools and targeted quantitative methods. The chemical diversity and similarity between commercially available cinnamon products will be presented.

P-038 – Richard van Breemen

Chemical Standardization of Milk Thistle (*Silybum marianum* L.) Using UHPLC-MS/MS with the Method of Standard Addition

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Milk thistle (*Silybum marianum* L. Gaertn.) is native to the Mediterranean and is cultivated widely as a medicinal plant. Extracts of milk thistle seeds have been used for over 2000 years primarily for liver problems and hepatoprotection. Milk thistle extract consists of >60% silymarin, which is a mixture of flavonolignans and flavonoids with antioxidant and anti-inflammatory properties including silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, silydianin, and taxifolin. A quantitative assay of 7 milk thistle flavonolignans plus taxifolin in milk thistle extract was developed based on UHPLC-MS/MS. Deuterated genistein and daidzein were used as internal standards. Separation of each analyte was achieved <10 minutes using a C18 UHPLC column, and quantitative analysis was carried out using negative ion electrospray with selected reaction monitoring tandem mass spectrometry on a triple quadrupole mass spectrometer. The method of standard addition was used to eliminate possible matrix effects caused by the complex botanical extract. For comparison, external calibration was used for quantitative analysis using analytical standards of each analyte dissolved in the UHPLC mobile phase. Although both analytical methods produced identical values for most analytes, significant ion suppression or enhancement was observed for three milk thistle compounds indicating the superior accuracy of the method of standard addition.

P-039 – Ying Gao

Optimization of Ultrasound Assisted Extraction of Ginsenosides from Roots of *Panax quinquefolius*

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American ginseng (*Panax quinquefolius* L.) is one of the most commonly used medicinal herbs worldwide. Ginsenosides (saponins) are known to be the main active ingredients in American ginseng. Common ginsenosides extraction methods require extensive processing time and a long period of heating which lead to the degradation of heat-sensitive ginsenosides (saponins). The goal of this study is to develop a more efficient extraction method with less processing time and increased recovery of ginsenosides. Traditional and novel methods such as Codex Standard Method, Japanese Pharmacopeia (17th Edition), United States Pharmacopoeia (40th Edition), European Pharmacopoeia (9.0 Edition), Chinese Pharmacopoeia (2015 Edition), and Ultrasound Assisted Extraction were tested and compared using dried American ginseng roots. After extractions, High Performance Liquid Chromatography (HPLC) was used to analyze 11 different ginsenosides (Rg1, Re, F11, Rg2, Rb1, Rb2, Rb3, Rc, Rd, Rg3, and Rh2) in the extracts. The processing time and extraction efficiency were compared and the extraction conditions for Ultrasound Assisted Extraction method were optimized.

P-040 – Colby Laws

Antibacterial Activity in *Hypericum calycinum* Against Methicillin-Resistant *Staphylococcus aureus*

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Extracts from root and aerial portions of *Hypericum calycinum* (creeping St. John's Wort) have shown antimicrobial activity when

screened against the clinically relevant Gram-positive bacterium Methicillin-Resistant *Staphylococcus aureus* (strain AH1263). Sample analysis performed with liquid chromatography coupled to a Q Exactive mass spectrometer allowed for creation of scores and loadings plots through principal component analysis. One feature was found to match the accurate mass of chinesin I, a molecule found in other *Hypericum* species, which has previously reported antibacterial activity against *Staphylococcus aureus*. Further experiments are underway to confirm the presence of chinesin I, as well as compare potentancy of *H. calycinum* to known antibiotics.

P-041 – Karon Rowe

Centella Asiatica Extract and Compounds Provide Resilience Against Age Related Behavior Changes in Drosophila Melanogaster

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Centella asiatica (CA) is a medicinal herb presumed by Eastern medicine to improve memory. A CA water extract (CAW) has been shown to improve cognition in aged mice and it has been proposed that the active compounds include triterpenes (TT) and caffeoylquinic acids (CQA). We therefore tested the role of these compounds in ameliorating age-related behavioral deficits in *Drosophila melanogaster*. We compared the effects of CAW, equivalent concentrations of TT, CQA, CQA + TT, and appropriate controls on the performance of *Drosophila melanogaster* in fast phototaxis assays. The extracts were added to the food during their fourth to sixth weeks of life. The flies were then tested in the fast phototaxis assay because at six weeks of age their performance is significantly reduced compared to young flies. CAW treatment significantly improved the flies' behavior when compared to controls. A similar effect was shown for treatment with TT, CQA, and CQA + TT compared to the control. The effects were seen in both female and male flies. The improvement between the treated flies and the controls shows that CAW can improve age-related deficits when given during mid-age. The similar effects of CAW and TT, CQA, and CQA + TT suggest that both, TT and CQA, are mediating the beneficial effects of CAW although their effects are not additive.

P-042 – Nathan Ezzone

Detection of Bioactive Constituents from *Aralia vietnamensis*

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The *Aralia* genus, native to Asia, North and South America, and Mexico, consists of more than 70 species many of which have traditionally been used medicinally to treat diabetes, hepatitis, stomach ulcer, rheumatism, and other diseases. Several biologically active constituents have been isolated from this genus including dammarane-type terpenoids, triterpenes, triterpene saponins and sterols. *Aralia vietnamensis* is a species of this genus that is found in Vietnam and the presented research will display the efforts for the isolation and structure elucidation of potential novel anticancer natural products and unidentified inactive constituents. Hyphenated techniques in phytochemical analysis have enabled dereplication of known bioactive constituents from phytochemical extracts. Global Natural Product Social Molecular Networking (GNPS) will be used to identify potential bioactive compounds of LC-MS fingerprints generated using the Thermo Q-Exactive Orbitrap with Vanquish-H UHPLC from the *A. vietnamensis* chloroform extract. Structures of unknown molecules will be determined by 1D- and 2D-nuclear magnetic resonance techniques.

P-043 – Ibrahim Almarabi

Anti-Diabetic Activity of Diterpenes from *Juniperus communis* Through a Dual α, γ PPAR Mechanism

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Juniperus communis (*J. communis*) has been traditionally used for diabetes mellitus, hypertension, arthritis and different other medicinal uses around the world. It also has shown a promising result as anti-diabetic agent in several studies. However, the mechanism of its anti-diabetic effect and the active chemical component are unknown. In a parallel line, agents possess Peroxisome Proliferator-Activated Receptors (PPARs) dual α/γ properties are remarkable biological targets as anti-diabetic hits with minimum side effects over PPAR α or PPAR γ alone. In a recent published work by our research group, a collection of traditionally anti-diabetic plants has been screened for their PPARs α/γ properties, and surprisingly Juniperus genus plants have shown encouraging findings which made a further phytochemical study such a logical path for further work to figure out their main active chemical components. The aim of this study is to identify the active chemical compounds that work through PPARs α/γ properties from *J. communis*. Our initial results indicate that diterpene specialized metabolites compounds are the main generator of *Juniperus communis* anti-diabetic activity.

P-044 – Ella Vardeman

Ethnopharmacology of *Argemone mexicana* L. for Caribbean Women's Health

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Medicinal plants are frequently used in Caribbean ethnomedicine as low-cost, culturally relevant treatments for women's health concerns. *Argemone mexicana* L., a top-reported medicinal plant for gynecological infections in the NYC Dominican community, is processed and sold as different preparations. It is hypothesized that these processing differences impact the bioactivity and chemistry of *A. mexicana.* Analysis using ultra-high-performance liquid chromatography-quadrupole time-of-flight mass spectrometry showed chemical variance between unprocessed (dry or fresh whole plants) and processed (dried, chopped, and packaged) samples. These differences are also reflected in antimicrobial screenings against pathogenic *Gardnerella vaginalis* and beneficial *Lactobacillus* species, where unprocessed specimens show more potent antibacterial activity than processed specimens. Additionally, unprocessed specimens were antimicrobial against pathogenic bacteria at lower concentrations than beneficial bacteria. Varying levels of known antimicrobial benzoquinone alkaloids may be responsible for at least part of the observed microbiological activity and have been assessed by quantitative HPLC analysis.

P-045 – Savannah Anez

Medicine in our Backyard: Exploring the Bioactivity of Appalachian Plants

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The Appalachian region, which extends more than 1,000 miles from southern New York to northeastern Mississippi, contains the highest total amount of endemic flora and fauna species in North America. The region has also been inhabited by humans for millennia, and a rich history of nutritional and medicinal usage has emerged. The current project explores for novel bioactive species and chemistry in potentially overlooked, but traditionally important, native Appalachian plants. Species that had documented usage, both by Native American communities as well as European settlers in the region, were selected for collection and study, including *Pilea pumila*, *Usnea barbata*, *Asarum canadense*, *Arisaema triphyllum*, *Equisetum* sp., and *Collinsonia canadensis*. Each plant was extracted with 80% aqueous methanol, and subsequently partitioned into water, butanol, ethyl acetate and hexane fractions. The antibacterial activity of each fraction was evaluated using a broth microdilution assay, testing against an antimicrobial-resistant *Staphylococcus aureus* (CDC strain 681). *Pilea pumila* showed a minimum inhibitory concentration of 156 µg/mL. *Usnea barbata* showed a minimum inhibitory concentration of <20 µg/mL, and *Equisetum sp.* showed a minimum inhibitory concentration of 39 µg/mL. The active plants have been targeted for metabolomic follow-up to understand the underlying chemical principals that are potentially driving the observed bioactivity.

P-046 – Sarah Barr

Evaluation of Digestive Transformation and Passive Permeability of *Withania somnifera* (Ashwagandha) Plant Extracts via UPLC-MS

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Medicinal plants contain complex mixtures of secondary metabolites that not only improve the plant's overall fitness but have been co-opted by humans for millennia to treat diseases, infections, and afflictions with remarkable success. In the last few decades, plant extracts have begun to filter through the FDA drug approval process with the goal of being patented and sold as prescribed pharmaceuticals. Due to the complex nature of these extracts, only two botanical drugs have been approved by the FDA as of February 2022. Failure of approval is generally attributed to high variability of plant products, issues with identification of the active pharmaceutical ingredient(s) (API), or acquiring enough biological assay information to prove adequate quality control can be maintained. This research will examine the effects of simulated gastrointestinal microenvironments on the metabolite profile of *Withania somnifera* L. (Dunal) extract and whether these transformations improve or diminish passive permeability using parallel artificial membrane permeability assays (PAMPA) coupled with mass spectrometry-based analyses. *W. somnifera*, commonly known as Ashwagandha, is a medicinal plant used to combat insomnia, inflammation, and neurodegenerative disorders. While permeability profiles have previously been determined for specific bioactive compounds in *W. somnifera*, including withanone and withanolide A, little research has been published investigating transformation, permeability, and stability of the whole plant extract. This hybrid methodology, once tested and verified, can act as a new platform technology for botanical drug candidates with poorly characterized APIs.

P-047 – Gil Belofsky

Antimicrobial Isoflavans and Other Metabolites of *Dalea jamesii* (Fabaceae)

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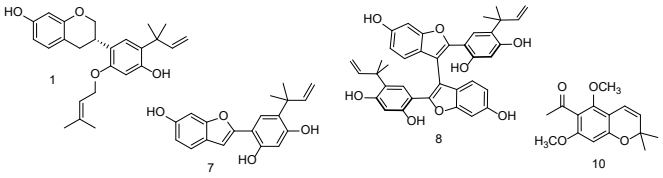
The phytochemical investigation of extracts of *Dalea jamesii* root and aerial portions led to the isolation of ten phenolic compounds. Six previously undescribed prenylated isoflavans, ormegans A-F (**1**-**6**), were characterized, along with two new arylbenzofurans (**7**, **8**) a known flavone (**9**), and a known chroman (**10**). The structures of the new compounds were deduced by NMR spectroscopy, supported by HRESI mass spectrometry. The absolute configurations of **1**-**6** were determined by circular dichroism spectroscopy. Compounds **1**-**9** exhibited in vitro antimicrobial activities, causing 98% or greater growth inhibition at concentrations as low as 4-5 ◎M against methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus faecalis* (VRE), and *Cryptococcus neoformans*. Interestingly, the most active compound was the dimeric arylbenzofuran **8** (>90% growth inhibition at 2.5 ◎M) against both MRSA and VRE, ten-fold more active than its corresponding monomer (**7**).



P-048 – Jennifer Obike

Alkaloids from Kratom (*Mitragyna speciosa*) and Generation of Semisynthetic Analogues

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Mitragyna speciosa (Korth.) Havil. (Rubiaceae) is a medicinal plant native to countries in South-East Asia that are commonly known as kratom. The leaves of the plant have been used to treat common illnesses and are popular for their energizing and pain-alleviating effects. This plant is also known to possess psychostimulant- and opiate-like properties, which have been attributed primarily to the major component of the plant, mitragynine, an indole alkaloid that is a partial agonist of the human μ-opioid receptors (MOR). We worked on the isolation of several alkaloids present in the plant, particularly mitragynine. These materials were used to generate semisynthetic analogues, particularly 7-hydroxymitragynine and mitragynine pseudoindoxyl.

P-049 – Miriam Velazquez

Bioactive Compounds Isolated from The Bark of *Aesculus Glabra*

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The genus *Aesculus* (Hippocastanaceae or Sapindaceae) is distributed worldwide with a diverse chemical profile. *Aesculus hippocastanum* and *A. chinensis* var have been used for a range of ailments like chronic venous insufficiency and heart disease. The seeds of *A. glabra* from the state of Ohio, commonly known as Ohio buckeye or American buckeye, have been traditionally used by the Cherokee to make poultices for soothing pains and aches. The chemical constituents of some *Aesculus* species include triterpenoids, saponins, flavonoids, coumarins, carotenoids, long fatty chain compound and some other classes of compounds. Preliminary Structure-Activity Relationship (SAR) studies has shown a diverse chemical library and possible anticancer properties from saponin and triterpenoid isolated compounds. The objective of this study is to isolate bioactive compounds from the bark of the tree and screen cytotoxic activity in different cancer cell lines. Bioactive compounds will also be tested for effect angiogenesis, which affects development of new blood vessel vasculature involved in endothelial cell proliferation and cell migration. This process plays a critical role in cancer metastasis and bioactive compounds could be considered as a potential source of new drug leads the treatment of cancer. Thus, it is noteworthy to study *A. glabra* for its potential in the treatment of cancer.

P-050 – Teal Jordan

Wild Health Tonic: Understanding the Phytochemistry of Ramps (*Allium tricoccum* Ait.) in Pennsylvania

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Ramps/wild leeks (*Allium tricoccum* Ait.) are a wild perennial species native to the deciduous forests of eastern North America. Known for their unique onion and garlic flavor, ramps have long been foraged and considered a wild spring tonic and functional food. In recent years, the demand for ramps has greatly expanded, while information on their nutritional and medicinal properties has remained extremely limited. This study examined the influence of phenological stage, harvest location, and morphological traits on ramp phytochemistry and identified major anthocyanins in ramps for the first time. Allicin was quantified using HPLC-UV, the total phenolic content was quantified using the Folin-Ciocalteu assay, and major anthocyanins were identified using LC-MS/MS. Our research creates a foundation for understanding the influences on key bioactive compounds in ramps and supports the development of scientifically based, sustainable ramp harvesting for maximum health benefits.

P-051 – Yuka Koike

Antithrombin Activity of Jidabokuippo and Identification of Active Compounds

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Kampo is a traditional form of medicine used in Japan. We have been investigating the mechanism of action of stasis-resolving formula (SRF), Kampo medicines used for improvement of static blood (Oketsu). SRFs have been reported to show anticoagulation activity and improvement of blood viscosity, however, the mechanism of action of SRFs is still unclear. We hypothesized that SRFs might inhibit thrombin because it plays an important role in blood coagulation. Our screening of SRFs possessing antithrombin activity provided Jidabokuippo (JDI) which used to cure sprain and bruise. Bioassay-guided fractionation of JDI led to the isolation of two compounds. Both compounds exhibited significant antithrombin activity, indicating these may be a part of active compounds contributed to improvement of static blood. The evaluation of the antithrombin activity of SRFs, isolation and identification of active compounds, and antithrombin activity of isolates will be presented.

P-052 – Ermias Mekuria Addo

Secondary Metabolites from the Branches of Vietnamese *Beilschmiedia yunnanensis*

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The species *Beilschmiedia yunnanensis* Hu (Lauraceae) is a tree endemic to southern China and Vietnam. In our continuing efforts to isolate and characterize cytotoxic secondary metabolites from tropical (medicinal) plants, the methanol extract of the branches of *B. yunnanensis* collected in Vietnam were found to exhibit a moderate cytotoxic potency (IC_{50} value of 8.4 μg/mL) against the human HT- 29 colorectal cancer line. This bioactive extract was subjected to bioassay-guided fractionation and isolation using liquid-liquid partition and silica gel open column chromatography, resulting in a number of active subfractions. Some of the active fractions were then purified by normal- and reversed- phase HPLC to afford two new, and several known compounds (e.g., wikstresinol and 9′-*O*-(*E*)-feruloyl-5,5′-dimethoxylariciresinol). The structures of the isolated compounds were characterized by NMR spectroscopy and high-resolution electrospray ionization mass spectrometry. The biological evaluation of these isolates and further isolation work on the remaining active fractions is currently undergoing.

P-053 – Sogol Momeni

Chemically Induced Cryptobiosis in Tardigrades

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Limno-terrestrial tardigrades are known to tolerate and survive various extreme conditions. They have evolved different survival strategies such as entering the dormant states, for example cryptobiosis. Cryptobiotic tardigrades shrink their bodies and form tun-state in response to environmental stress. Many studies have been performed on cryptobiotic tardigrades, especially during desiccation. However, the mechanism that leads to cryptobiosis is still not fully understood. Recent studies have shown that tardigrades' intrinsically disordered proteins (TDPs) may play important role in cryptobiosis. According to our observations, certain specialized plant metabolites present in tardigrades' bryophyte habitats (mosses and lichens) can induce tardigrade cryptobiosis. We will present experimental data to support our hypothesis that certain specialized metabolites found in bryophytes are involved in cryptobiosis induction through their interactions with TDPs.

P-054 – Joseph Gerdt

Microbial Natural Products Influence Bacteriophage Efficacy

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Bacteriophages (viruses that infect bacteria) sculpt microbial communities and have promise as antimicrobial agents. We hypothesize that the metabolic environment influences the ability of bacteria to defend themselves from bacteriophages. Here we discuss our discovery of a microbial natural product that helps defend *Vibrio cholerae* from bacteriophages. *V. cholerae* is the causative agent of the severe diarrheal disease cholera. Bacteriophages that prey on *V. cholerae* may be employed as phage therapy against cholera. However, the influence of the chemical environment on the infectivity of vibriophages has been unexplored. We discovered that a common metabolite produced by gut microbes—linear enterobactin (LinEnt), represses vibriophage proliferation. We found that the anti-phage effect by LinEnt is due to iron sequestration and that multiple forms of iron sequestration can protect *V. cholerae* from phage predation. This discovery emphasizes the significance that the chemical environment can have on natural phage infectivity and phage-based interventions.

P-055 – Savannah Pierce

The Anti-Microbial Properties of Traditional Chinese Medicine Mushroom *Ganoderma Lucidum Against Porphyromonas Gingivalis*

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Traditional Chinese Medicine (TCM) is a holistic medical practice that has been used for thousands of years and these herbal remedies remain the only treatment source for rural areas globally today. Mushrooms used in TCM are believed to increase longevity. These mushrooms are commercially available as supplements in the form of powders, teas, and many other forms. *Ganoderma lucidum* is commonly known as Ling Zhi in China or Reishi in Japan. Although these mushrooms have been used extensively for centuries, there is a deficit in the identification of the individual bioactive constituents. Dr. David Ojcius, Biomedical Sciences Department Chair at Dugoni School of Dentistry, has begun to study these mushrooms for their antimicrobial properties against *Porphyromonas gingivalis,* a pathogen that is strongly associated with periodontal disease. Preliminary anti-microbial assay data demonstrated crude methanol and ethanol extracts of the mushroom powder inhibited oral pathogens while not suppressing commensal populations. The Carlson lab has extracted *G. Lucidum* powder in 100% EtOH, 50:50 EtOH: MeOH, and 100% MeOH following this preliminary data and the traditional preparation of a tincture for the oral cavity. Efforts to isolate and identify antimicrobial and antioxidative constituents is underway. Those antimicrobial agents that are selective for pathogenic bacteria over commensal organisms will be fully characterized. The characterization of these bioactive small molecules will aid in designing effective treatments to prevent periodontal disease while preserving commensal bacteria.

P-056 – Zachary Lane

Metals, Metabolites, and Microbes Associated with the Marine Tunicate, *Botryllus schlosseri*

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Metals play an important role in cellular functions, repair and regeneration, and chemical defenses. Environmental change and ocean acidification have resulted in increases in invasive species as well as in vital nutrients, such as metals. Tunicates, also known as ascidians or sea squirts, and their associated microbes may serve as a model to explore how these changes affect marine ecosystems. In this study, we performed metabolomics, metallomics, and genomics of *Botryllus schlosseri*, an invasive colonial Ascidian species whose metabolite profiles, metal concentrations, and microbial community compositions are not fully understood. Preliminary metabolomics results indicated variations in metabolite profiles based on seasonality and temperature. Genomic analyses revealed that the *B. schlosseri* microbiome is dominated by alpha-, beta-, and gamma-proteobacteria, and metals analyses displayed consistent levels of cobalt, copper, nickel, and zinc. Ongoing studies will continue to explore how changes in the marine environment affect metal uptake mechanisms, metabolite production, and microbial community profiles of *B. schlosseri*.

P-057 – Melany Puglisi

Is there a Selective Advantage from Chemical Mediation of the *Caulerpa* spp. Microbiome?

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Vibrio, including known pathogens to benthic marine organisms, have been reported to be occur in high densities of microbial populations on the surface of the *Caulerpa cylindracea*. Our previous studies explored the role of metabolites from *Caulerpa* spp. in the formation of the algal microbiome. Laboratory settlement assays demonstrated that solvent partitions from eight species induced the settlement of 38 isolated strains, including *Vibrio* spp., isolated from the surface of the algae. Chemical investigation of the structural features in complex mixtures that caused settlement of SAB using MADByTE (Metabolomics And Dereplication By Two-Dimensional Experiments) NMR-metabolomics are ongoing. As we continue to explore the chemical ecology of the microbiome of *Caulpera* spp. from the Florida Keys, our aims in this study are to 1) determine if extracts and metabolites will induce the settlement of *Vibrio* spp. in field experiments; and 2) understand the potential for environmental microbial transfer of *Vibrio* spp. from *Caulerpa* spp. to neighboring algae and seagrasses. In the first set of experiments, active partitions from *Caulerpa* spp. incorporated in A1 media in petri dishes were attached to the reef 25 cm from *Caulerpa* spp. for 2 weeks. In the second set of experiments, solvent partition enriched agar on sterile screens were placed 2 cm from healthy *Caulerpa* fronds for 72 hours. Both sets of experiments were caged. Upon collection, the media were swabbed and plated on TCBS media to detect the presence of *Vibrio* spp. and preserved for DNA analysis. The results from these experiments will be reported.

P-058 – Carlismari Grundmann

Combining Modern Mass Spectrometry Methods for Analysis of Interspecies Interactions of Microorganisms Associated with Trachymyrmex Ants

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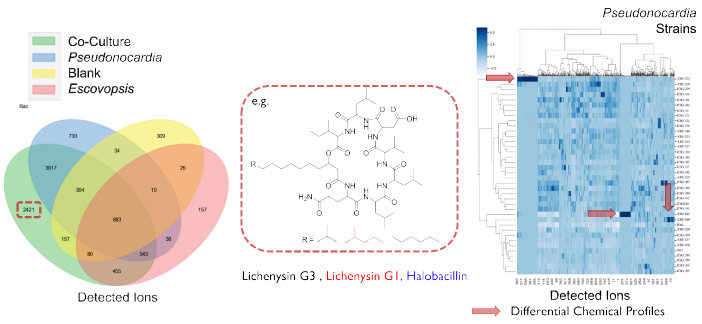
This project proposes a systematic study of the metabolic profiles from the interaction between symbiotic *Pseudonocardia* (36 strains) and parasite *Escovopsis* (2 strains), isolated from Amazonian *Trachymyrmex* ant colonies. Analysis (LC-MS/MS and Molecular Networking) of the co-cultures revealed the elicitation of the bacterial metabolism in the presence of the fungus. Results also suggest that these *Pseudonocardia* are a promising array of new compounds, according to the differential chemical profiles of some strains and bioassays against *S. aureus*.



P-059 – Eunah Jeong

A Wood-decaying Fungus *Polyporus brumalis* Detoxifies an Antifungal Phytochemical Baicalein via *O*-xylosylation

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Microorganisms have evolved their own strategies to survive under toxic environments. The wood-decaying fungi are the dominant decomposers of organic plant matters in ecosystem, and have been well studied for their capability to degrade cellulose and lignin. As plants produce chemically diverse antifungal substances, we hypothesized that wood-decaying fungi possess metabolic capability for attenuating those phytochemicals. Baicalin is a major flavonoid of *Scutellaria baicalensis*, which is a 7-*O*-glucuronidated derivative of its antifungal aglycone, baicalein. The fermentation broths of 14 wood-decaying fungi species cultured with baicalin were analyzed by LC-MS/MS. Among the tested species, *Polyporus brumalis* showed the most diverse biotransformation. The MS/MS fragmentation patterns suggested that deglucuronidation followed by pentosylation of the aglycone occurred. Targeted isolation and NMR analysis confirmed the presence of 7 previously unknown baicalein xylosides in the fermentation broth. The antifungal activity evaluation of the isolates against *Aspergillus flavus* revealed that the xylosides are much less toxic than baicalein, which implies *O*-xylosylation is a detoxification strategy of *P. brumalis*.

P-060 – Huong Pham

Anti-inflammatory Sesquiterpenes Induced by the Non-competitive Coculture of Two Basidiomycetous Fungi *Phellinus orientoasiaticus* and *Xylodon flaviporus*

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Cocultivation has become a popular approach to enhance the microbial secondary metabolism under standard laboratory conditions, where these metabolites are restricted to monoculture. Here, instead of selecting solid plates containing inhibition zones to conduct chemical analysis by LC-MS, we explored the specialized metabolome induced by the non-competitive coculture of *Phellinus orientoasiaticus* (Hymenochaetaceae) and *Xylodon flaviporus* (Schizoporaceae). Three new cyclohumulanoid sesquiterpenes, named 6-nor-4-hydroxy-1,3(4)-distepuren-14-oic acid (**1**), 6-hydroxysterpuric acid (**2**), 13-hydroxy-7-deoxypaneolilludinic acid (**3**), along with five known analogues (**4**–**8**) were isolated, which were identified based on MS, NMR, and ECD analysis. By comparing the chemical profiles of the EtOAc extracts of co- and axenic cultures, it was found that compounds **1**, **2**, and **5** were exclusively detected in the coculture. The LC–MS analysis indicated *P. orientoasiaticus* was the producer of **1**-**7**. Besides, the biological assessment showed the isolates **1**–**7** inhibited nitric oxide production of LPS-treated RAW276.4 cells in a range of 15.9 to 38.0 % at 100 μM. These results elucidate not only the fungus-fungus interaction metabolism in non-competitive coculture but also demonstrate their potential contribution to the drug discovery field in the future.

P-061 – Cole Stevens

Interkingdom and Intraspecies Signaling Influences Presence, Metabolism, and Predatory Specialization of Myxobacteria

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Often investigated as models for cooperative behaviors or as sources for therapeutic lead compounds, myxobacteria are also key contributors to nutrient cycling within soils as generalist predators. However, while a recent correlation between myxobacterial taxonomic distance and specialized metabolism has been revealed, the predatory capacity of myxobacteria does not correlate with phylogeny, and there are no readily identifiable genetic indicators of prey range. Results from investigation of myxobacterial perception of inter- and intra-kingdom chemical signals have informed our ability to identify quorum signals that influence prey range, determine phytohormones that encourage antibacterial production, and isolate novel myxobacteria for future natural product discovery efforts.

P-062 – Stephen Deyrup

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

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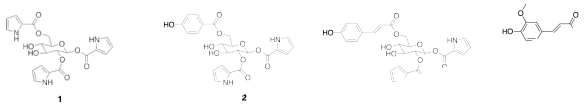
The Emerald Ash Borer (*Agrilus planipennis*) is an invasive exotic of great ecological importance as it has been decimating ash trees in North America. Although larval stages have been shown to be eaten and parasitized, the adults are not regularly consumed by predators. This indicates the possible presence of chemical defenses in the adult stage of *A. planipennis*. A sample of the beetles was collected, ground, and extracted to separate the chemicals into different extracts for analysis. The chemical extracts underwent 2D-NMR analysis to obtain structural information. Various signals in the dqfCOSY spectra provided evidence of the presence of acyl moieties and an acyl-substituted glucose. These structural characteristics match those found in buprestins, a series of defense molecules described from other beetles in the same family as *A. planipennis*. Analysis of the 2D-NMR spectra, along with LC-MS studies demonstrated that there are at least six different buprestins present in adult Emerald Ash Borers (**1–6**). The presence of buprestins in *A. planipennis* helps to explain why these brightly colored pests are not readily preyed upon by native insectivores.



P-063 – Kojo Acquah

Ecological Role and Antifungal Activity of the Honey Bee-Associated Bacterium *Bombella apis*

Kojo S. Acquah[1,2], Delaney L. Miller[3], Irene L. G. Newton[3], and Marcy J. Balunas[1,2]. [1]Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, USA, [2]Division of Medicinal Chemistry, Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT 06269, USA, [3]Department of Biology, Indiana University, Bloomington, IN, 47408, USA*

Honey bees have immense impact on our economy and in our complex interconnected ecosystems. They play an important role serving as pollinators of plants which is critical for plant growth and survival. Animals and other organisms directly rely on plants and plant products such as fruits, seeds and nuts for food and shelter. Honey bees have undergone a dramatic population decline in recent years, likely due to a combination of several environmental stressors including parasitic and pathogenic infections as well as habitat changes. Our previous research showed that *Bombella apis*, a honey bee bacterial symbiont, protects the bee against fungal pathogens. Genome mining revealed that *B. apis* possesses biosynthetic gene clusters (BGCs) of interest, including a type I polyketide synthase (PKS). Results from our ongoing isolation and identification of antifungal metabolites from *B. apis* will be presented. To ascertain where in the bee colony these symbionts are localized, we compared the metabolomes of four strains of *B. apis* with those from critical colony environments such as nurse heads, nectar, dissected worker guts from nurse bees, instar larvae and their diet. Further studies will investigate the antifungal mechanisms of *B. apis* metabolites and quantify their abundance in bee and colony environments.

P-064 – Deeya

Looking for Defensive Small Molecules in a Freshwater Sponge and its Symbiotic Algae

Deeya, Emily Mevers. Department of Chemistry, Virginia Tech, Blacksburg, VA, 24061, USA

Marine sponges and their microbial symbionts have been proven to be a conspicuous source of bioactive metabolites with some of these metabolites being approved by the FDA, including Cytarabine (Cytosar- U®), Vidarabine (Vira-A®), and Eribulin mesylate (Halaven®). This success has inspired our current research effort into the defensive small molecules produced by freshwater sponges and their symbionts (i.e., algae and bacteria). Freshwater sponges are an underexplored ecological system but have the potential of being a source of bioactive compounds, like marine sponges. *Spongilla lacustris* is a freshwater sponge that has been shown to harbor endosymbiotic algae, *Zoochlorella* in addition to complex bacterial community. We hypothesize that the algae may produce defensive secondary metabolites similar to the endosymbionts of marine sponges. Preliminary chemical investigations into freshwater sponges from Richmond, Virginia, and their symbiotic algae has led to refined chemical fractions possessing antimicrobial activity. Further purification of the metabolites in the extract of the algae has led to a metabolite that exhibited modest activity against both gram-positive and gram-negative bacteria and fungal pathogens.

P-065 – Grayce Dyer

Assessment of Marine Filamentous Cyanobacteria Biodiversity in Puerto Rico Using Sequencing of Seven Hypervariable Regions of the 16s rRNA Gene

Grayce Dyer[1], Ingrid Montes[2], Eduardo Caro[1], [1]School of Pharmacy, University of Puerto Rico Medical Sciences Campus, San Juan, PR 00901, [2]Omics Lab, Comprehensive Cancer Center, San Juan, PR 00901

This study, to the best of our knowledge, is the first comprehensive survey of the biodiversity of marine filamentous cyanobacteria in Puerto Rico using a genomic approach. As molecular techniques have become more accessible and reliable, 16S rRNA sequencing has emerged as the gold standard for bacterial taxonomic studies. We have collected a total of 34 unique cyanobacteria samples from 31 sites around the coast of Puerto Rico and sequenced these samples at seven hypervariable regions (V2-V4, V6-V8, V9) of the 16S rRNA gene. Sequencing several hypervariable regions of the gene will allow a more in-depth comparison of samples and should provide clearer insight into microbial community diversity and taxonomy which historically has relied on microscopy to phylogenetically classify marine cyanobacteria. This approach will allow us to select and explore genetically unique cyanobacterial samples to direct our search for novel natural product scaffolds.

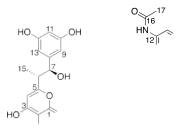
P-066 – Kalindi Morgan

Rifamycin Shunt Natural Products from *Salinipora arenicola* RJA3005

Kalindi D. Morgan,[1,3] Doralyn S. Dalisay,[4] Teatulohi Matainaho,[5] Katherine S. Ryan,[1] and Raymond J. Andersen[1,2]. [1]Departments of Chemistry and [2]Earth, Ocean and Atmospheric Sciences, University of British Columbia, 2036 Main Mall, Vancouver, B.C., Canada V6T 1Z1, [3]Department of Chemistry and Biochemistry, University of Northern British Columbia, 3333 University Way, Prince George, B.C., Canada V2N 4B6, [4]Center for Chemical Biology and Biotechnology (C2B2), Department of Biology, College of Liberal Arts, Sciences and Education, University of San Agustin, Iloilo City, Philippines, [5]University of Papua New Guinea

Cultures of the tropical marine strain *Salinipora arenicola* RJA3005, harvested from a Papua New Guinea marine sediment, produced salinorcinol (**1**) and salinacetamide (**2**), which had previously been reported as products of engineered and mutated strains of the rifamycin pathway in *Amycolatopsis mediterranei*, but had not been reported before as natural products. This work reports the NMR data for the structure elucidation of **2** for the first time.

Intriguingly, data from an initial feeding study of 1,2- $^{13}C_2$-acetate and U-$^{13}C_6$-glucose, demonstrate that the most likely precursor for the 3,5- dihydroxybenzene moiety found in salinorcinol is derived from the shikimate pathway.



1 **2**

P-067 – Kara Talbott

California Algae and their Surface Associated Bacteria: Natural Products and Chemical Ecology

Kara Talbott,[1] Skylar Carlson[1], Department of Chemistry, University of the Pacific, Stockton, CA, 95211, USA

Marine algae and their associated bacteria have played a crucial role in the discovery of new natural products with a wide range of applications. In the decade 1997 to 2008, there were 600 new natural products reported from marine bacteria. Coupled with the fact that as few as 1% of marine microbes have been characterized this suggests there is great potential for algal surface associated bacteria (SAB) to produce novel natural products. The Carlson Lab is building a library of algal SAB with antibacterial and anticancer activity. Moreover, we are looking into the role small molecules play in establishing the algal microbiome. Algae are surface sterilized and spread on agar containing the antifungal cycloheximide to create a lawn of bacteria from which individual bacteria are then isolated. The bacterial strains are grown up in A1 liquid media and extracted with ethyl acetate. These extracts will be tested for pharmaceutically relevant activity. In parallel, the seaweed is identified, frozen, lyophilized, then extracted and partitioned. The algal extracts will be screened for their ability to settle various microbes isolated from the surface and from other environmental samples in order to examine the small molecule influence in establishing the microbiome. Our two-fold – pharmaceutical and chemical ecology approaches – will allow us to build a library of microbes and compounds from California algae and their SAB.

P-068 – Fatma Al-Awadhi

Biological Profiling and Molecular Networking Guided Exploration of a Library of Marine Sponges and Tunicates Collected Off Umm Al Maradim Island in Kuwait

Fatma H. Al-Awadhi[1], Mariam Al-Shammali,[1] Khaled Orabi[1]. [1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait

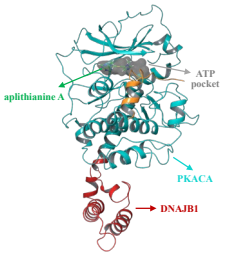
Oceans represent the largest biosphere, which constitute more than 70% of the Earth's surface and considered as infinitive resource of macro and microorganisms that possess unique chemical structures and biological activities. Despite the extensive Kuwait marine biodiversity, studies on the Kuwaiti marine invertebrates for the identification and isolation of unique bioactive natural products is almost non-existent. Kuwaiti marine organisms, mainly from sponges and tunicates, were collected from the coral reefs around Umm Al-Maradim island. A library, composed of nearly 70 fractions, was generated from these samples. These fractions were screened against MDA-MB-231 breast cancer cells and two strains of G+ve and G-ve bacteria (*S. aureus* and *E.coli*). The overall biological profiling revealed the potential of marine invertebrates for the discovery and development of cytotoxic agents; however, no positive antibacterial effects were observed. The active fractions were prioritized, and their LC–MS/MS spectra were obtained and analysed by GNPS platform, identifying several molecular networks that likely contain potentially unique molecules distributed in different marine species. Further HPLC purification of these prioritized fractions is underway to guide the discovery of new therapeutically active marine-derived lead compounds.

P-069 – Lin Du

Discovery of a New Class of Protein Kinase Inhibitors from an Extract of *Aplidium* sp.

Lin Du[1], Brice A. P. Wilson[1], Ning Li[2], Masoumeh Dalilian[1,3], Dongdong Wang[1], Emily A. Smith[1,3], Antony Wamiru[1,3], Ekaterina I. Goncharova[1,3], Ping Zhang[2] and Barry R. O'Keefe[1,4]. [1]Molecular Targets Program, CCR, NCI, Frederick, MD; [2]Center for Structural Biology, CCR, NCI, Frederick, MD; [3]Leidos Biomedical Res., FNLCR, Frederick, MD; [4]Natural Products Branch, DTP, DCTD, NCI, Frederick, MD.

The DNAJB1-PRKACA (PKADJ) oncogenic gene fusion has been identified as an antitumor target against the rare fibrolamellar hepatocellular carcinoma. A high-throughput sandwich ELISA assay was developed to identify selective modulators of the PKADJ catalytic activity by screening the prefractionated natural product library recently created by the NCI Program for Natural Product Discovery (NPNPD). Bioassay-guided fractionation of the extract of a marine tunicate, *Aplidium* sp., led to the discovery of five new adenine analogues, including two unprecedented alkaloids, aplithianines A (**1**) and B (**2**). Aplithianine A showed potent inhibition against the activity of PKADJ and PKA with an IC_{50} value of 1.1 μM. Co-crystallization and X-ray diffraction experiments revealed that **1** inhibited the activation of the PKA catalytic subunit by competitively binding to the ATP binding site. Human kinome profiling of the brominated analogue of **1** (**1a**) against a panel of 370 kinases revealed potent inhibition against only 8 kinases with IC_{50}s < 50 nM. A convenient, four-step total synthesis of **1** has been completed which enables further evaluation of aplithianines as antitumor leads in cell-based assays and xenograft models.



P-070 – Erin Marshall

Exploration of Arctic Ocean Bacteria – New Drug Leads to Modulate Pain

Erin M. Marshall[1], Chenxi Zhu[1], Haoyi Yao[2], Giuliana Panieri[2], Monica Deadmond[1], Amelia Bunnell[1], James A. Strother[1], Sandra Loesgen[1]. [1]The Whitney Laboratory for Marine Bioscience, University of Florida, Gainesville, FL, USA, [2]Department of Geosciences, CAGE - Centre for Arctic Gas Hydrate, UiT The Arctic University of Norway, 9037, Tromsø, Norway

Microbial secondary metabolites fulfill a multitude of ecological functions. For example, they aid in the sequestering of nutrients, inter- and intra-species communication, and defense. Arctic marine bacteria have adapted to live in an extreme environment with fluctuating light, pressure, temperature, and nutrient availability. Here we outline a study of the unique metabolites produced by a subset of 85 marine bacterial strains, isolated from the arctic waters and sediments near the archipelago of Svalbard. The seafloor here contains unique gas hydrate pingo formations and methane seeps, which affect local microbiomes and potentially metabolite evolution and production. All extracted strains were screened chemically and for bioactivity in anti-bacterial, anti-fungal, and cytotoxicity assays. Using an OSMAC approach, activity-guided fractionation, and MS-based metabolomics, several metabolites were identified and characterized. Compounds were also tested in a novel *in vivo* zebrafish-based behavioral assay that evaluates pain relief. Compounds with anti-nociceptive activity are followed up with *in vivo* zebrafish whole-brain calcium imaging to determine their site and mode of action, and *in vitro* receptor binding/functional studies at NIMH's Psychoactive Drug Screening Program (PDSP).

P-071 – Andrew Kim

Biosynthesis and Synthesis of Natural Product Peptides from Cyanobacteria

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Hundreds of secondary metabolites from marine cyanobacteria have been reported in the literature. Out of those hundreds of metabolites, a significant number of these molecules have been isolated from the genus *Lyngbya.* Many of the characterized secondary metabolites from *Lyngbya* are peptides or peptide-containing substructures, several of which are cytotoxic or possess protease inhibition activity. The putative gene cluster of a potential protease inhibitor, tychonamide A, isolated from a

Lyngbya-like clade gives insight into the biosynthesis of the peptide especially the construction of the 3-amino 2,5,7-trihydroxy-8-phenyloctanoic acid (Atpoa) portion of the molecule for which the absolute configuration has yet to be assigned. In addition to the biosynthetic gene cluster analysis, a second cyanobacterial peptide, unnarmicin D, isolated from *Trichodesmium thiebautii* showed the ability to bind to both the mu opioid and delta opioid receptors while reducing proinflammatory cytokines in BV-2 microglial cells. The dual functionality of unnarmicin D will have the potential to reduce dependence and treat neuropathic pain. We are currently synthesizing a panel of analogues based on molecular modeling studies to optimize a peptide lead compound. Peptides from cyanobacteria have shown promise as leads in drug discovery, which will be further investigated in these studies.

P-072 – Bailey Bell

Ecteinamines: Highly Functionalized Nonribosomal Peptides from a marine *Micromonospora* Species

Bailey Bell†, Qihao Wu†, Marc Chevrette‡, Michael Thomas§, Scott Rajski†, Tim Bugni†. †Pharmaceutical Sciences Division, University of Wisconsin–Madison, 777 Highland Ave, Madison, WI, 53705, United States, ‡Wisconsin Institute for Discovery and Department of Plant Pathology, University of Wisconsin–Madison, 425 G Henry Mall, Madison, WI, 53706, United States, §Department of Bacteriology, University of Wisconsin–Madison, Madison, Wisconsin 53706, United States

By applying the strain prioritization tool Hierarchical Clustering Analysis and Principal Component Analysis (*hcapca*) to a library of 109 marine *Micromonospora sp*. we identified strain WMMB482 as a candidate for further investigation. Metabolomic analysis of the WMMB482 extract revealed a novel nonribosomal peptide, deemed ecteinamine. We also identified 17 additional ecteinamine analogs using molecular networking through the Global Natural Products Social Molecular Networking (GNPS) website and confirmed their structures via LCMS/MS and NMR. The ecteinamines possess a highly unique chemical scaffold with several uncommon functional groups, including a menaquinone-pathway- derived 2-naphthoate ring and the first example of a naturally occurring ◎◎◎[CH2NH] "reduced amide". Extensive analysis of ecteinamine biosynthesis revealed that an unclustered set of biosynthetic genes and novel enzymology drive ecteinamine assembly, emphasizing the unique nature of these compounds. Additionally, the ecteinamines were found to have affinities for nickel, zinc, cobalt, and copper, suggesting that these compounds function as broad-spectrum metallophores in the metal-limited marine environment.

P-073 – Matthew Bertin

Time-Series Studies to Detect Toxins and New Drug Leads from Harmful Algal Blooms (HABs)

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Resolving *in situ* temporal and spatial patterns of specialized metabolite and toxin production is challenging due to variability in biotic and abiotic production triggers. We have investigated two HAB groups: *Pseudo-nitzschia*, the domoic acid-producing diatom in Narragansett Bay (NB), RI, and *Trichodesmium*, the open-ocean blooming cyanobacterial genus in the Gulf of Mexico, which is well known for its ecological role in nitrogen fixation. Our time-course results from NB detailed distinct seasonal multi-species assemblages of *Pseudo-nitzschia*; some with the capacity to produce high concentrations of domoic acid. After seven years of sampling *Trichodesmium* blooms, we discovered that *Trichodesmium* species showed distinct chemotypes, and *T. thiebautii* is a prolific producer of specialized metabolites, many with promising biological activities. Investigating algal and cyanobacterial species through time-course studies has provided insight into the seasonal production of toxins and established new knowledge with respect to the specialized metabolite composition of *Trichodesmium* species.

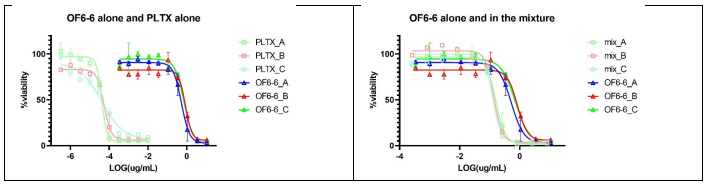
P-074 – Evgenia Glukhov

On the Hunt for New Toxin Families Produced by a Mediterranean Strain of the Benthic Dinoflagellate *Ostreopsis cf. ovata*

Eva Ternon[1,2], Evgenia Glukhov[1], Emily Trytten[1], Rodolphe Lemée[2] and William H. Gerwick[1,3] [1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA 92093, USA, [2]Laboratoire d'Océanographie de Villefranche (UMR 7093), Sorbonne Université, CNRS, 06230 Villefranche-sur-Mer, France, [3]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, CA 92093, USA

The microalga *Ostreopsis* cf. *ovata* is a benthic dinoflagellate identified from multiple tropical, subtropical, and temperate locations, and is known to produce an extremely potent polyol toxin named palytoxin (2680 Da). The present work focuses on two new families of toxins that were obtained from cultures of a Mediterranean strain of *Ostreopsis* cf. *ovata*. The new toxins were

named the liguriatoxins (MW ~2000 Da) and rivieratoxins (MW ~1400-1500), and were obtained via cytotoxicity guided isolation from cultured dinoflagellate. The small amounts of isolated compounds only allowed for acquisition of high-resolution mass spectrometry MS^1 and MS^2 data followed by molecular networking using the GNPS tool. We also evaluated the new toxins for cytotoxicity towards the human lung cancer NCI-H460 cell line. None of the six new compounds appear to be structurally similar to palytoxin based on the limited structure data; however, they share long polyhydroxylated chains of high molecular weight. The cell cytotoxicity concentrations (CC_{50}) of the new purified toxins when tested individually ranged between 0.68 and 3.12 µg/mL with the liguriatoxins showing higher potency than rivieratoxins. Interestingly, the potency of the mixture of toxins was significantly more cytotoxic, suggesting synergistic interactions of these *Ostreopsis* toxins.



P-075 – Zacharie Maw

Molecular Networking Driven Discovery of New Natural Products From Complex Metabolite Mixtures From a Surfactant Chemical Elicitor Study in Marine *Streptomyces*

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The bacteria of the genus of *Streptomyces* are known for making many unique and complex bioactive natural products. Biosynthetic gene cluster analysis of these bacterial genomes reveals that there are likely many more natural products to be discovered from this chemically rich genus. As a community, we need to explore new and innovative ways to induce or upregulate the "silent" natural products to help bridge the gaps between biosynthetic gene clusters and known natural products. Chemical-bacterial interactions between *Streptomyces* and environmentally produced surfactants remain largely unexplored. While it is known that this class of chemical can interfere with sporulation in *Streptomyces coelicolor*, effects on natural product production remain unknown. We look to explore the use of surfactants, also known as surface-active molecules, as chemical elicitors for the upregulation or induction of silent natural products. For this study, we used a genetically diverse group of marine *Streptomyces* and surfactants from both natural and synthetic origins. Due to a large number of biotransformations in the extracts, our standard metabolomic analysis could not differentiate between compounds related to the added surfactants and potential new natural products. Using molecular networking we can create structural groups of all molecules found in each extract to help identify interesting chemistry. This research will give insight into the effectiveness of using surfactant molecules as a tool to find new silent natural products.

P-076 – Margaret Redick

Metabolomics of Deep-Sea Methane Seeps

Margaret Redick[1], George Neuhaus[1], Susie Cummings[2], Lila Ardor Bellucci[3], Andrew Thurber[2,3], Kerry McPhail[1]. [1]Department of Pharmaceutical Sciences, College of Pharmacy, [2]Department of Microbiology, College of Science, [3]College of Earth, Ocean, and Atmospheric Sciences, Oregon State University, Corvallis, Oregon 97331, USA

Deep sea methane seeps are home to a high diversity of microbial life. The unique metabolism of these microbes, which consume methane, makes them of interest due to potential applications for human and environmental health and well-being. In this study, microbial mats and sediment cores were each collected from an old and a new methane seep, both at approximately 1000m depth. Cores were sectioned by depth and divided for chemical and biological analyses. For chemical profiling, sediment was extracted overnight in methanol, filtered, dried, and reconstituted at 10 mg/mL in methanol for analysis by high resolution LC-MS/MS. The Global Natural Product Social Molecular Networking (GNPS) platform was used to create a molecular network based on the MS^2 data. Compound classifications were predicted based on the fragmentation spectra using SIRIUS and CANOPUS. Primer7 was used to compare the chemical profiles and identify which compounds are the primary drivers of differences between the different sites and depths with the goal of connecting the diversity of chemical compounds with that of the microbial communities at the two contrasting sites.

P-077 – Lois Kyei

Isolation of Bioactive Metabolites from Microbes associated with Moon Snail Egg Masses

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The marine environment is home to complex ecosystems that are underexplored for natural products. In particularly, the egg masses of marine invertebrates are thought to be chemically defended because they lay egg masses in the open environment without physical protection, yet they do not appear to be preyed upon. The hypothesis is that these egg masses are chemically defended by microbial symbionts. Using a function-first approach, my research objective is to chemically investigate bacteria associated with the moon snail egg masses in order to discover novel bioactive small molecules and to explore the biomedical potential of the isolated metabolites. Thus far, I have isolated nine

compounds from non-polar extracts from Actinobacteria *Tsukamurella* sp. that was isolated from egg masses collected in Florida. Six of these metabolites exhibit antimicrobial activity against gram-positive bacteria, *Staphylococcus aureus* and *Bacillus subtilis*. Structure elucidation of these metabolites is an on-going effort.

P-078 – George Neuhaus

Metabolomics Spatial Survey of Living Stromatolites

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Evidence of life on earth dates back more than 3.4 billion years in the form of lithified layers of complex microbial mats known as stromatolites. Modern, extant stromatolites are comparatively rare but have been documented globally. To increase understanding of extant stromatolite microbial community structure and chemical ecology, a multi-faceted investigation of phylogenetic composition and small molecule production of the microbial communities was performed across a stromatolite formation in the Eastern Cape of South Africa. Species diversity is correlated with molecular diversity between sampling stations and key specialized metabolites are highlighted, including a family of new hexadepsipeptides. Due to low isolation yields (≤50 μg), structure elucidation was driven by analysis of tandem MS spectra, utilization of community-based tools (e.g. GNPS, Sirius, CANOPUS), and partial NMR data. This investigation will facilitate understanding of the metabolic functional guilds present, as well as identification of the microbial producers of exceptional specialized metabolites.

P-079 – Margaret Hill

Investigation of *Phaeobacter inhibens* S4 as a Putative Probiotic for Shrimp Aquaculture

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Acute Hepatic Necrosis Disease (AHPND) is a limiting factor for the production of *Penaeus* shrimp in aquaculture systems. AHPND is caused by pathogenic strains of *Vibrio parahaemolyticus* that inject binary toxins PirA and PirB into prey cells using a Type 6 Secretion System, which causes the deterioration of epithelial cells in the shrimp's hepatopancreas. *Phaeobacter inhibens* S4 is a marine Gram-negative bacterium that produces the broad-spectrum antibiotic tropodithietic acid (TDA) and shows promise as a probiotic tool to mitigate infections in oyster larvae by the pathogen *Vibrio coralliilyticus*. In this study, we show that S4 increases the survival rate of brine shrimp when challenged with the AHPND-causing strain *V. parahaemolyticus* PSU5579. *Artemia* nauplii pre-treated for 24 hours with *P. inhibens* and then challenged with *V. parahaemolyticus* showed a 1.84-fold increase (to 70%) in survival 48 hours post challenge as compared with a challenged control (no probiont: 38% survival). S4 was further found to significantly improve the survival rate of the white leg shrimp, *Litopenaeus vannamei* post-larvae (PL) when challenged with PSU5579. Using available genetic mutants of S4, it was found that an intact AHL quorum sensing system and biofilm production are important to PL protection, but not TDA production. This is despite modest sensitivity of PSU5579 to TDA (MIC = 15.625 μg/mL). These results suggest that S4 should be further evaluated as a tool to mitigate the risks of AHPND in shrimp aquaculture systems, and that antibiotic production does not appear to be a vital mechanism for host protection.

P-080 – Priscilla Winder

High-Throughput Screening of a Marine Compound Library Identifies Anti-*Cryptosporidium* Activity for Leiodolide A

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Cryptosporidium sp. are apicomplexan parasites that cause diarrhea in immune compromised humans and young livestock leading to malnutrition and death. It is highly contagious and currently, there are no effective drugs on the market to treat immune compromised people. A high throughput assay was designed to screen the Harbor Branch Oceanographic Institute at FAU enriched fraction library derived from marine organisms for potent anti-*Cryptosporidium* compounds. 3,764 fractions were screened in the assay resulting in 23 fractions that potently inhibited the growth of *Cryptosporidium parvum*. Bioassay guided fractionation of the active fractions from a deep-sea sponge, *Leiodermatium* sp., resulted in the purification of leiodolide A with an EC_{50} of 103.5 nM. Differences with the originally published material based on solubility, stereochemistry, and upon final

purification, a broadening of the side chain resonances by NMR will be discussed.

P-081 – Margaret Paige Banks

Moon Snail Egg Mass Leads to Novel Staccopin Compounds

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Marine ecosystems are an untapped area for biomedical research as they are highly unexplored yet contain extensive biodiversity. The Mevers' lab is interested in studying marine egg masses as many lack obvious defense mechanisms yet remain unharmed in the natural environment. Bacteria from moon snail eggs have been isolated from SW Florida, Massachusetts, and Puerto Rico. Of particular interest to our lab is a *Streptomyces* stain isolated from moon snail eggs in Florida. *Streptomyces* are prolific producers of medicinal natural products, and the strain isolated from our lab is shown to produce staccopins, which are a family of linear peptides with known activity as cysteine protease inhibitors. Only two staccopin compounds have been published in the literature, but the masses isolated in our lab show six new potential analogues of these known compounds. The antimicrobial activity of this family of compounds has yet to be determined. To begin assessing biological activity, a large-scale growth (32L) in yeast malt extract was performed, which resulted in a low production of staccopin compounds. To improve production of these novel compounds, a media study was performed to determine if specific media would upregulate the desired compounds. The media study consisted of A media, Marine Broth, Potato Dextrose, R2A, and RAM, and these medias were selected as they have various carbon and nitrogen sources. A media and R2A were determined to upregulate staccopin compounds. Large scale growth of the optimized media conditions was performed. The projected structures will be presented along with activity of the *streptomyces* bacteria.

P-082 – William Perera

Analysis of Synthetic Dyes in Cosmetic and Food Products by High-Performance Thin-Layer Chromatography

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Dyes are substances used in Food, Beverages, Drug and Cosmetic Industries to improve appearance of final products or users. The U.S. Food and Drug Administration under the Color Additive Status List provides current information about the status and limitations of the most common dyes used in foods, drugs, devices, or cosmetics. The development of suitable methods to detect non-authorized dyes and quantify allowed ones is crucial in a quality control environment. High-Performance Thin-Layer Chromatography (HPTLC) is a technique that is widely used in the Dietary Supplement Industry. The technique is simple, robust, flexible, cost-effective and has a faster turnaround when compared to other analytical techniques. These advantages make HPTLC a useful tool for multiple applications across many industries. Herein is described the HPTLC analysis of multiple dyes using a normal phase chromatography. A two-step development method on silica gel was used to separate hydrophobic from hydrophilic compounds. Densitometric analysis in absorption mode was performed directly on the HPTLC plate to quantify selected dyes in food, beverage, and cosmetic samples from the market.

P-083 – Fumiaki Nakamura

A New Approach to Maximize Utilization of Unclassified Small Pieces of Marine Organisms

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Marine organisms have evolved their metabolism in environments different from terrestrial ones, and their secondary metabolites comprise a unique library of compounds with different structures and biological activities. In particular, secondary metabolites from marine invertebrates living at depths of more than 100 m, which are difficult for researchers to collect by hand using SCUBA, have not been fully explored. Dredging is often used to collect organisms that inhabit these environments, but since most samples are collected as fine fragments after being crushed and shredded, it is difficult to sort the samples and, as the result, most of the unclassified samples are discarded, making it difficult to maximize the biological resources. In this study, from the viewpoint of SDGs, we aim to maximize the large amount of mixed small pieces of marine organisms generated during dredge collection. Contrary to the conventional way, the process starts with (1) purification of active compounds from the whole extract of the unclassified small pieces, then proceeds to (2) identification of the sample that contains the active compounds by analysis based on the metabolome database prepared from the classified and identified samples collected simultaneously in the dredging. The proposed inverted procedure for the search of natural products was verified using the sample mixture (24.6 kg wet weight) collected by dredging at Yaku-Sinsone (166-167 m), Kagoshima Prefecture, Japan.

P-084 – Koshi Machida

Changes Over Time of Metabolite Profile in the Decay Process of Marine Sponge

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Many secondary metabolites with unique structures and biological activities have been reported from marine sponges. Recently, it has become revealed that many symbiotic microorganisms in the sponges are producers of these secondary metabolites. Biosynthesis of secondary metabolites by microorganisms in sponges is one aspect of the relationship between sponges and symbiotic microorganisms, but the degradation of secondary metabolite profile after the end of this symbiotic relationship has not been studied. In this study, to gain knowledge on the degradation of secondary metabolites in the sponge after the end of the symbiotic relationship, we used LC-MS to analyze changes over time of secondary metabolites in the sponge *Theonella* sp. from Kochi Prefecture during the decomposition process. As a result, we found three compounds which were thought to be degradation products of theonellamides

P-085 – C. Benjamin Naman

Natural Products Isolated from South and East China Sea Cyanobacteria and Synthesized Analogues Lead to the Discovery of a New Pharmacophore for Ion Channel Modulation

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Marine filamentous cyanobacteria have been shown to produce a variety of structurally diverse natural products that exhibit ion channel modulating pharmacology, most probably to affect their chemical ecology and deter predation. After the discovery of some structurally related lipopeptides from the South and East China Seas, it was recognized that analogues in the series have been isolated from very distant geography and are reportedly produced by organisms of disparate taxonomy. Many of these related molecules have been obtained in the present study by natural product isolation, library accession, or chemical synthesis, and all were shown to modulate ion channels in vitro. While the biogenesis and ecological roles of these molecules are being investigated further, it is here proposed that a core structural subunit of the compounds represents a previously unknown pharmacophore for ion channel modulation.

P-086 – Stephanie Heard

Adenylation Domain Substrate Selectivity in Fungal Nonribosomal Peptide Biosynthesis

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Marine fungi have historically been a prolific source of bioactive natural products, including those of the well-studied nonribosomal peptide class. The advent of whole genome sequencing has allowed for the discovery and investigation of new cellular machinery that was previously inaccessible. Using the power of bioinformatics, researchers can predict new chemical structures in a more high-throughput manner. Though fungal natural product biosynthesis shares some similarities with bacterial systems, eukaryotic systems have tended to be less well characterized. We have contributed to these characterization efforts using bioinformatic-guided natural product isolation to interrogate nonribosomal peptides from marine fungi. Fungal nonribosomal peptide synthetases are notorious for incorporating a wide range of unique, nonproteinogenic building blocks that increase product diversity and functionalization. Both the adenylation and condensation domains of each synthetase module appear to play gatekeeping roles in the incorporation of new building blocks. Through my work with the marine-derived strain *Aspergillus flavipes* CNL-338, I have combined bioinformatics and biochemistry to elucidate the substrate selectivity of several fungal adenylation domains. By focusing on conserved active site residues, the function of uncharacterized adenylation domains can now be more accurately predicted, particularly for novel substrates. These fungal pathways have proven to be more divergent from bacteria than originally thought, but continuing to decipher higher order systems is critical.

P-087 – Ying Cong

Substrate Selectivity of AgeMTPT N-Terminal Prenyltransferase

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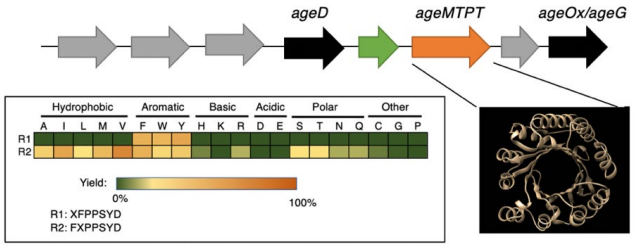
AgeMTPT protects the N-terminus of short peptides with isoprene and the C-terminus as a methyl ester, but its substrate scope is unknown, limiting its application. Here, we investigate the substrate selectivity of the prenyltransferase domain, revealing a requirement for N-terminal aromatic amino acids, but with tolerance for diverse uncharged amino acids in the remaining positions. To demonstrate the potential of the method, substrate selectivity data were used in the enzymatic modification of leu-enkephalin at the critical N-terminal residue. AgeMTPT active-site

mutagenesis led to an enzyme that reverse-geranylates the N-termini of peptides. These data reveal the potential applications of enzymatic peptide protection in synthetic biology.



P-088 – Feng Li

Sea Urchin Polyketide Synthase SpPks1 Produces the Naphthalene Precursor to Echinoderm Pigments

Feng Li, [1] Zhenjian Lin,[1] Eric Hill,[2] Craig A. Townsend,[2] and Eric W. Schmidt[1] [1] Department of Medicinal Chemistry, University of Utah, Salt Lake City, Utah 84112 USA [2] Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218 USA*

Echinoderms such as sea urchins are deeply pigmented by oxidatively polymerized, aromatic compounds, the echinochromes and relatives. Previous genetic experiments implicate an animal genome-encoded polyketide synthase (PKS), SpPks1 in the biosynthesis of aromatic polyketides, the echinochromes and relatives from sea urchins and other echinoderms. Here, we express and purify SpPks1 performing biochemical experiments to demonstrate the sea urchin protein is responsible for the synthesis of 1,3,6,8-tetrahydroxynaphalene (ATHN). Since ATHN is a plausible precursor of echinochromes, this result defines the biosynthetic pathway to the ubiquitous echinochrome pigments. Truncation experiments showed that, unlike other type I iterative PKSs so far characterized, SpPks1 produces the naphthalene core using solely ketoacylsynthase, acyltransferase, and acyl carrier protein domains, delineating a new class of aromatic PKSs. Phylogenetic analyses indicate that SpPks1 and its homologs are widespread in echinoderms and their closest relatives, the acorn worms, reinforcing their fundamental importance to echinoderm biology.

P-089 – Taifo Mahmud

Biosynthesis and Ecological Roles of the Antidiabetic Drug Acarbose

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Acarbose is a bacterial-derived α-glucosidase inhibitor clinically used to treat patients with type 2 diabetes. As type 2 diabetes is on the rise worldwide, the market demand for acarbose has also increased. Despite its significant therapeutic importance, how this pseudooligosaccharide is made in nature is not completely understood. Inspections of genome sequence databases also revealed the wide distribution of acarbose and related pseudooligosaccharide biosynthetic gene clusters in bacteria, raising a question as to why pseudooligosaccharides are produced by many bacteria. Here, we report the complete biosynthetic pathway to acarbose, involving GDP-valienol and 4-aminoDGG. GDP-valienol is derived from valienol 7-phosphate, catalyzed by three cyclitol modifying enzymes, whereas 4-aminoDGG is produced from dTDP-4-amino-4,6-dideoxy-D-glucose and maltose by the glycosyltransferase AcbI. The final assembly process is catalyzed by a novel pseudoglycosyltransferase enzyme, AcbS, which catalyzes non-glycosidic C-N bond formation. Further studies also suggest that acarbose may provide multiple competitive advantages to the producing bacteria in their native environment.

P-090 – Tyler Alsup

The Missing Piece to the Puzzle: Insights into Biosynthesis of the Phenalinolactone Diterpene Core

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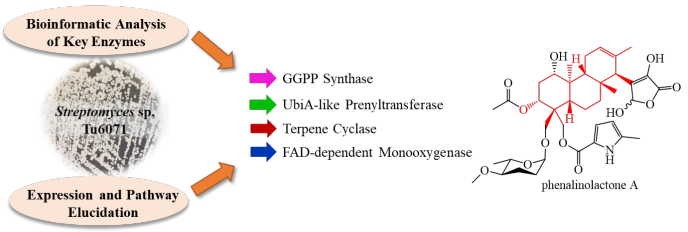
Terpenes are the largest family of natural products with over 80,000 known members wielding a vast array of biological activities. Their activities against bacteria, fungi, viruses, and cancer cell lines have driven an interest in the field of natural products research to seek out novel terpenoids with desired bioactivities. While the products of many terpenoid biosynthetic gene clusters have been determined, gaps in knowledge of their biosynthesis persist. As an important example, the phenalinolactone diterpenoids were characterized nearly two decades ago in *Streptomyces* sp. Tü6071, however, the intricacies of the construction of their diterpene core are elusive. Biosynthetic insights into assembly of the phenalinolactone diterpene core will be presented.



P-091 – Melanie Higgins

Natural Product Sugar Biosynthesis

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Natural products are a rich source of structural and chemical diversity making them prime candidates for various applications,

most notably in medicine. Since carbohydrates are particularly abundant in nature and have a wide range of biological functions, it is not surprising that many natural products contain carbohydrate moieties. There are currently at least 344 distinct carbohydrate structures identified among known natural products produced by bacteria alone.[1] They have important functions related to the bioactivities of the molecules and have been linked with several pharmacological properties, such as solubility, transport, and bioavailability. Consequently, modifying the structures of these sugars can significantly influence the bioactivity and bioavailability of natural products. One approach to impart these modifications is to use sugar biosynthetic machinery. However, a fundamental understanding of the biosynthetic enzymes is key. My research group is focused on investigating enzymes involved in natural product sugar biosynthesis to expand glycodiversification of small molecules for drug development.

P-092 – Sanath Kandy

Bioinformatic Discovery of a Prenyltransferase Cyclase Containing RiPP Gene Cluster

Sanath Kavuthian Kandy[1] and Jonathan R. Chekan[1], [1]University of North Carolina at Greensboro

Natural products have always formed the basis of therapeutic drugs and medicines throughout human history. Ribosomally synthesized and post-translationally modified peptides (RiPPs) are a recent addition to the other well-known classes of natural products. The discovery of RiPPS has been accelerated by the recent advancements in bioinformatics and genome mining. In this study, we used a class-agnostic genome mining approach to discover a new RiPP modification catalyzed by a prenyltransferase+cyclase fusion enzyme. To confirm our bioinformatic result, we overexpressed the biosynthetic enzymes in a heterologous system and assayed their activity using LC-MS. We successfully identified the prenylated peptide product from the MS and MS/MS data from LC-MS. Successful characterization of the prenylated product may lead to the identification of a new type of RiPP modification found in diverse RiPP classes.

P-093 –Jeffrey Rudolf

Two Novel Bacterial Diterpene Synthases Construct 6,10-Bicyclic Eunicellane Diastereomers

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Terpenoids are the largest and most structurally diverse family of natural products. There are over 80,000 known terpenoids; however, less than 2% of these (≅1500) are of bacterial origin. The eunicellane diterpenoids are a unique family of natural products seen in marine organisms, plants, and bacteria. In collaboration with Prof. Loesgen at the UF Whitney Lab, we recently discovered benditerpenoic acid (BND), a eunicellane diterpenoid, from *Streptomyces* sp. (CL12-4), its biosynthetic gene cluster, and the terpene synthase (Bnd4) responsible for constructing benditerpe-2,6,15-triene, the 6,10-bicyclic hydrocarbon core of BND. Concurrently, we also discovered another bacterial terpene synthase, TS118, that forms a diastereomer of benditerpe-2,6,15-triene. Bnd4 and TS118 only share 24% protein sequence identity. Here, we used a series of biochemical, bioinformatics, and theoretical experiments to investigate the mechanisms of these eunicellane-forming diterpene synthases. TS118 is encoded within an unknown BGC with several other uncharacterized biosynthetic genes and additional studies to identify the genuine NP encoded by this BGC are now underway.

P-094 – Dan Xue

Discovery of New N,N-dimethylated Lanthipeptides Via Pathway Refactoring Features a Unique Methyltransferase

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Lanthipeptides represent one of the most well-studied family of ribosomally-synthesized and post translationally-modified peptides (RiPPs) and possess a variety of biological activities. Class III lanthipeptides have only been reported recently. Here, we report the refactoring and heterologous expression of a Firmicutes-derived biosynthetic gene cluster (BGC) in *Bacillus subtilis*, leading to discovery of a new family of class III lanthipeptides. This new family features a N,N-dimethylation of the lanthipeptides, which had not been reported in class III lanthipeptide. In addition, the N,N-dimethylation significantly enhanced the antibiotic activity of this family, motivating us to study the corresponding methyltransferase. We characterized the substrate specificity of the methyltransferase and identified the precursor peptide recognition motif via site-directed mutagenesis and *in vitro* enzymatic reconstitution. Utilizing the unique feature of this methyltransferase, we produced N,N-dimethylated unnatural lanthipeptides with a variety of peptide lengths and improved their antibiotic activity.

P-095 –Jingfang Yu

Serotonin Biosynthesis and Metabolism in *C. elegans*

Jingfang Yu[1], Merly C. Vogt[2], Bennett W. Fox[1], Diana Fajardo Palomino[1], Chester J. J. Wrobel[1], Brian J. Curtis[1], Henry H. Le[1], Oliver Hobert[2], and Frank C. Schroeder[1] [1] Boyce Thompson Institute and Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14853, USA.[2] Department of Biological Sciences, Columbia University, Howard Hughes Medical Institute,*

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The neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) plays a central role in animal behavior and physiology[1-5], and many of its functions are regulated via evolutionarily conserved biosynthesis and degradation pathways[6-8]. Using a mutant-based comparative metabolomics approach in combination of stable-isotope labeling, chemical synthesis, MS and NMR spectroscopy, we delineate a new model for serotonin metabolism in the model system *C. elegans*. We first show that, unexpectedly serotonin is abundantly produced in non-neuronal tissues via phenylalanine hydroxylase (PAH-1), in addition to canonical biosynthesis via tryptophan hydroxylase (TPH-1) in neurons. Next, we demonstrate that most serotonin in *C. elegans* is used to produce a novel class of serotonin derived modular glucosides (MOGLs), which we named sngl#1-4 (serotonin *gl*ucoside). The MOGLs sngl#3-4 integrate an additional anthranilic acid moiety, which we hypothesized is attached by a carboxylesterase (CEST) homolog, which we recently showed play a central role in the assembly of MOGLs and modular ascarosides.[9-11]. By screening the metabolomes of a library of 14 available *cest* knockout mutant strains, we showed that biosynthesis of sngl#3 and sngl#4 requires *cest-4*, which catalyzes attachment of anthranilic acid to the 6-position of serotonin- and indole glucosides. Expression patterns of CEST-4 indicate that serotonin-derivatives are transported between different tissues. Lastly, we show that bacterial indole production interacts with serotonin metabolism via CEST-4. Our results reveal a previously unrecognized complexity of neurotransmitter metabolism and further suggest that serotonin, or its newly identified derivatives, may serve signaling functions between different tissues.

P-096 – Peng Zhang

Genome Mining for Bifunctional Terpene Synthases in a Marine-Derived Fungus Unveils a Type I Diterpene Synthase Involved in the Formation of an Unprecedented 5-8-6 Tricyclic Ring System

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Since the discovery of the type I chimeric (or bifunctional) diterpene synthase PaFS in 2007, a limited number of this class of enzymes have been discovered over the last ten years. In this study, a new type I chimeric diterpene synthase TndC was characterized from the marine fungus *Aspergillus flavipes* CNL-338 by genome mining approach, and heterologous expression of TndC in ZXM144 yeast strain led to the discovery of a type I diterpene backbone **(1)**, which bear an unique 5-8-6 tricyclic skeleton. The cyclization mechanism of **1** was elucidated by the isotope labeling study. The function of the P450 TndB was preliminarily characterized by genetic disruption. Additionally, oxidative transformation of **1** into Talaronoid C **(2)** was characterized by bioconversion through feeding [1-^{13}C] labeled **1** into *A. flavipes*. Thus, our discovery not only implies the possibility for discovery of other new type I chimeric diterpene synthases in the future, but also indicates TndC may be the intermediate enzyme responsible for converting a 5-8-5 ring system to 5-8-6-X ring system.

P-097 – Stella Thomaz de Lima

Cyclopeptide Biosynthetic Gene Clusters are Widely Distributed in Plants

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While plants are well known for their terpene and alkaloid metabolites, they are also prolific producers of peptidic natural products. As plants do not employ NRPS machinery, many of these molecules are ribosomally synthesized and post translationally modified peptides (RiPPs). We recently demonstrated using RNA-seq that the diverse cyclopeptide alkaloids (CPAs) from *Ceanothus americanus* specimen (New Jersey Tea) are indeed biosynthesized using a RiPP pathway. By mining the entire NCBI plant protein database, we identified over 1000 putative precursor peptides, most of which are found clustered together with a predicted biosynthetic enzyme. Moreover, these genetic cassettes were found in the genome of every sequence eudicot plant including well known model and commercial plants such as *Coffee arabica*, *Vitis vinifera*, *Theobroma cacao*, *Mangifera indica*, *Cannabis sativa*, *Arabidopsis thaliana*, *Brassica carinata*, and others. Plants cyclopeptides can be classified according to their chemical skeleton into up to eight types. Among the explored plant database, we could match multiple different classes of cyclopeptides including type I from *Ziziphus* and *Ceanothus americanus* to type IV found in *Hibiscus* roots to a specific precursor peptide gene. To confirm our predictions, *C. arabica* plants were extracted (roots, stems, and leaves) and analyzed by LC-MS/MS, and molecular networking revealed multiple new cyclopeptides that directly correlated with the bioinformatically identified gene sequences. Our research will facilitate a deeper understanding of the metabolic profile of common plants leading to the discovery of potential new drugs in medicine and/or agriculture.

P-098 – Ethan Underwood

Discovery of Conserved Peptide Sequences to Gain Insight into Cyclopeptide Alkaloid Formation in *Ceanothus americanus*

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Ceanothus americanus is a flowering plant native to North America which has been used for generations in folk medicine. Decades of isolation work have revealed that the roots of *C. americanus* are rich in cyclopeptide alkaloid natural products. Some of the cyclopeptide alkaloids isolated from *C. americanus* and cyclopeptide alkaloids as a group have been shown to display a variety of biological activities, including but not limited to analgesic, antibacterial, and antifungal. Each of these could prove to be promising potential drug leads. Despite their long history, little is known about their biosynthesis. In this study we used RNA-sequencing to reveal that these abundant natural products are ribosomally synthesized and post-translationally modified peptide (RiPP) natural products. In addition to linking known molecules to their biosynthetic precursors, our results allowed us to predict and identify new cyclopeptide alkaloid analogs present in *C. americanus*.

P-099 – Margaret Hill & Melany Puglisi

The URI College of Pharmacy's Pharmacognosy Club – a model for ASP Student Chapters?

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The University of Rhode Island has a wealthy history of pharmacognosy research, dating back to the College of Pharmacy's founding dean, Dr. Hebert W. Youngken Jr. who established a medicinal plant garden that would be used by faculty members and students for many years to come. The Pharmacognosy Club was established by founding members, Dominic DeFilipi and Julia V. Law, to provide students with an opportunity to explore their interests in traditional medicine systems, herbal medicine, and pharmacognosy. In more recent years, the main initiative of the Pharmacognosy Club has shifted to introducing students to natural products research. The current executive board has implemented teaching lab environments that have 1) educated individuals on research opportunities and provided them with laboratory techniques that are necessary in pharmacognosy related research, 2) connected students with principal investigators at the university, and 3) have helped bridge the gap between those who have had access to opportunities such as these, and those who haven't. If the American Society of Pharmacognosy were to create student chapters and induct our club as the first, we would be able to expand our network of student-run organizations and create more opportunities for the next generation of pharmacognosists.

P-100 – Harald Gross

Discovery of Novel RiPPs from *Nocardia* spp. with Unprecedented Skeletons Using a Metabologenomic Approach

Harald Gross[1], Hamada Saad[1]. [1]Department of Pharmaceutical Biology, Pharmaceutical Institute, University of Tübingen, 72076 Tübingen, Germany

Bacteria from the genus *Nocardia* are foremost known in a medical context since they cause severe infections to humans and animals via nocardiosis. However, they have emerged over the last two decades also as talented producer strains of structurally diverse and highly bioactive natural products. Beside nonribosomal peptides and polyketides, *Nocardia* spp. are also privileged producers of ribosomally synthesized and post-translationally modified peptides (RiPPs). Employing genome mining, we identified two RiPP gene clusters: One was coding for a lanthipeptide with an unprecedented peptide sequence and an unusual high number of predicted modifications, while the other was a lasso peptide. In order to track down the resultant RiPPs, a three-layered metabolomic workflow was designed and applied, which involved OSMAC-mass spectrometry, stable isotope labeling and 2D-NMR. Application of the latter led to the isolation of lanthipeptides nocathioamide A-C and the lassopeptide nocapeptin. The nocathioamide family represents the first-in-nature combinatorial tribrid RiPPs hovering over three different classdefining biosynthetic machineries of lanthipeptides, LAPs and thioamitides, decorated with an additional unique PTM, while nocapeptin bears an unique new ring closure among lassopeptides.

P-101 – Jake Wilson

Discovery of Antibacterial Phosphonopeptides from *Bacillus velezensis*

Jake Wilson[1,2], Toshiki Nakao[1], Happy Kwok[1], Jerry Cui[1], Yeying Zhang[1], Chase M. Kayrouz[1], Tiffany M. Pham[1], Hannah Roodhouse[1], and Kou-San Ju[,1,2,3,4]. [1]Department of Microbiology, The Ohio State University, Columbus, OH 43210. [2]Division of Medicinal Chemistry and Pharmacognosy, The Ohio State University, Columbus, OH 43210. [3]Center for Applied Plant Sciences, The Ohio State University, Columbus, OH 43210. [4]Infectious Diseases Institute, The Ohio State University, Columbus, OH 43210*

Phosphonic acids are a class of microbial natural products that have potent inhibitory activities. A carbon-phosphorous bond allows phosphonates to mimic primary metabolites which contain phosphate esters and carboxylic acids, leading to the inhibition of essential metabolic pathways. Consequently, numerous members of this class have been commercialized as antimicrobials and herbicides. Of microbes with the potential to produce phosphonates, actinobacteria have been the focus of recent discovery efforts due to the diversity of their biosynthetic gene clusters (BGCs) and their storied ability to produce

pharmaceutically relevant compounds. Despite the widespread taxonomic distribution of phosphonate BGCs, their metabolism in other bacteria has been largely underexplored. Here we describe the isolation, chemical characterization, and bioactivity of phosphonopeptides produced by *Bacillus velezensis*. Bioinformatic analyses identified a phosphonoalamide-like BGC in a *Mycobacteroides abscessus* subsp. *massilience* genome shown to be heavily contaminated with DNA from *Bacillus velezensis*. Purification and structure elucidation of phosphonate metabolites from *Bacillus velezensis* revealed two new phosphonopeptides, which we name phosphonoalamide E and F. Both compounds exhibited antimicrobial activity against plant and human pathogens, highlighting their potential for development as pesticides or antibiotics.

P-102 – Susan Egbert

Identifying the Squamatic Acid Biosynthetic Gene Cluster in Lichen *Cladonia uncialis*

Susan Egbert[1], Jordan Hoffman[2], James Lendemer[2], John L. Sorensen[1] Duleeka Gunawardana[3], Michele Piercey-Normore[3] [1]Department of Chemistry, University of Manitoba, Canada, [2]Institute of Systematic Botany, New York Botanical Garden, City University of New York, USA. [3] School of Science and the Environment, Memorial University of Newfoundland, Canada

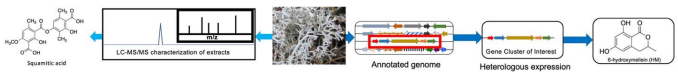
Lichens are chemically understudied super-organisms composed of mycobionts, photobionts, and other microbial symbionts. Research interest in lichens today extends beyond their biological importance into the therapeutic potential of their diverse secondary metabolites. However, due to the naturally slow growth of lichens, it has been difficult to culture the mycobiont in laboratory conditions and to find host organisms for the heterologous expression of biosynthetic genes. Only within the last two years have mycobiont genes been successfully expressed in another organism. Here we identify the BCG for squamatic acid produced in the thorn lichen, *Cladonia uncialis*. We examined the genomic data of *C. uncialis* and used annotation tools, such as antiSMASH, to identify potential squamatic acid BGCs. A putative BGC for squamatic acid was selected based hypothetically necessary genes for squamatic acid production: polyketide synthase (PKS), O-methyltransferase (OMT), and cytochrome P450(CYP450). This study proposes the final steps of squamatic acid biosynthesis including the OMT and thioesterase (TE) domain. We provide evidence to support the hypothesis that OMT catalyzes the methylation of the hydroxyl group on C4 and the thioesterase catalyzes the reaction to form 4-O-demethylbarbatic acid. Subsequent LC-MS/MS analysis was performed to detect and quantify squamatic acid in specimens of *C. uncialis*. This study demonstrates the proposed mechanisms for the final steps of squamatic acid biosynthesis and further elaborates on lichen secondary metabolite production and selection of heterologous hosts.

P-103 – John Sorensen

Linking Genes to Molecules in Lichen Fungi through Metabolite Profiling and Heterologous Expression of Biosynthetic Genes

Susan Egbert, Harman Gill, and John L. Sorensen. Department of Chemistry, University of Manitoba, Winnipeg, Manitoba, Canada R3T 2N2

Lichen fungi, symbiotic associations between fungal (*mycobiont*) and algal partners (*photobiont*), are characterized by their ubiquity, occupying diverse ecological and geological niches. Lichen fungi have demonstrated an ability to produce a variety of novel bioactive natural products such as usnic acid. However, slow growth rates and challenges with laboratory culturing have limited the pace of discovery. Research carried out both in our laboratory, and numerous others around the world, has revealed that lichen fungi harbour a number of silent or 'cryptic' biosynthetic gene clusters. This suggest that the full biosynthetic potential of lichen fungi has yet to be revealed.



We have two complementary approaches to the discovery of new natural products in lichen fungi. One major focus in on examining the metabolite profile with LC-MS/MS techniques and using resources such as GNPS to identify metabolites and link this information to biosynthetic gene clusters in the genome. This presentation will describe our recent results on linking squamatic acid to a gene cluster. Complementary to this approach is the heterologous expression of cryptic gene clusters in a heterologous host to assign conclusive function. Recent work with 6-hydroxymelinin gene cluster will be described.

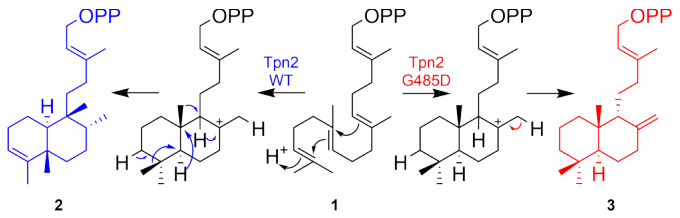
P-104 – Emma Stowell

A Single Residue Exhibits Mechanistic Control over Tpn2, a Bacterial Diterpene Synthase from *Kitasatospora* sp. CB02891

Emma A. Stowell[1], Michelle A. Ehrenberger[1], Chin-Yuan Chang[2], Jeffrey D. Rudolf[1]. [1]Department of Chemistry, University of Florida, Gainesville, FL, USA; [2]Department of Biological Science and Technology, National Yang Ming Chiao Tung University, Hsinchu, Taiwan, ROC

In this study, we use a structure-guided approach to probe the function of the bacterial diterpene synthase Tpn2 from *Kitasatospora* sp. CB02891. Tpn2 is responsible for the cyclization of geranylgeranyldiphosphate **1** to the clerodane terpentedienyl diphosphate **2**. However, the Tpn2 active site can be manipulated by the mutation of a single key active site residue to favor an altered deprotonation pattern, resulting in the formation of the labdane diterpene syn-CPP **3**. This is the first example of a syn-CPP synthase of bacterial origin, paving the way for future

identification of unknown TSs through uncovering the roles of various active site residues.



P-105 – Daniel Icenhour

Unlocking the Biosynthetic Potential of *Streptomyces* Through Transcriptional Regulators Using Synthetic Biology

Daniel G. Icenhour[1], Jeffrey D. Rudolf[1]. [1]Department of Chemistry, University of Florida, Gainesville, FL, USA

Secondary metabolism in *Streptomyces* is controlled by complex transcriptional regulatory networks that results in the repression of over 90% of predicted biosynthetic gene clusters (BGCs) in most species. While the TetR family of regulators (TFRs) is the largest family of transcriptional regulators within this genus, there remains an extremely limited number of characterized TFRs whose cognate ligand and functional role have been elucidated. Therefore, we propose that a more comprehensive understanding of this family of regulatory proteins, will aid in activating normally silent BGCs and help unlock this large biosynthetic potential many *Streptomyces* possess. To achieve this goal, we have developed a reporter system to screen compounds against uncharacterized TFRs from *Streptomyces* in the gram-positive model organism *Bacillus subtilis*, to help minimize physiological differences. This system employs a hybrid TFR that has been built by fusing the ligand binding domain (LBD) of an uncharacterized TFR to the DNA-binding domain (DBD) of the widely used TetR protein. Taking advantage of the fact that TFRs are comprised of two independently functioning domains, this chimera is able to bind the respective ligand of a targeted TFR, as well as the well-known promoter of TetR used to regulate the expression of mGFP. We will use bioinformatic analysis to identify TFRs to screen based on sequence similarity to known TFRs and use computational docking to predict which compounds to screen as potential ligands. Through the identification of the different ligands TFRs bind, we will then be able to better understand the roles of these regulatory proteins and to what extent they are involved in secondary metabolism.

P-106 – Imraan Alas

Micromonospora's Biosynthetic Gene Cluster Diversity Warrants Broad Spectrum Investigation

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Investigations of the bacterial genus *Micromonospora* (family *Micromonosporaceae*) have enabled the development of secondary metabolites critical to human health, such as gentamicin and over 740 additional bioactive compounds from 1974 to 2005. Efforts historically focused on primarily terrestrial families (*Streptomycetaceae*) have led to an undervaluing of marine ecosystem families like *Micromonosporaceae*, despite the fact that investigation of marine *Micromonospora* bacteria continue to yield chemically diverse and bioactive compounds as impactful lead compounds. This significant disparity between terrestrial and marine-based microbes (as secondary metabolite producers) is highlighted in the National Center for Biotechnology Information's (NCBI) genomic databases, where 4,965 *Streptomyces'* genomes are stored compared to 474 *Micromonospora* genomes. In order to highlight the biosynthetic potential of *Micromonospora*, we sequenced and assembled 25 genomes using antiSMASH v6.0.1, queried identified biosynthetic gene clusters (BGCs) against a preprocessed dataset of ~1.2 million BGCs, and sorted into 29,955 gene cluster families (GCFs) using the program Biosynthetic Gene Clusters – Super Linear Clustering Engine (BiG-SLiCE). This pre-processed dataset generated from complete and draft genomes from NCBI Ref-Seq, fungi and archaea genomes from NCBI GenBank, metagenome-assembled genomes (MAGs), and BGCs from Minimum Information about a Biosynthetic Gene cluster (MiBiG), forms a near-comprehensive dataset of publicly available BGCs. Of the 581 total *Micromonospora* BGCs identified by antiSMASH and defining unique BGCs as not clustering into the 29,955 gene cluster families in BiG-SLiCE using a distance threshold of 900, we observed 318 unique *Micromonospora* BGCs. These results highlight the strength of marine *Micromonospora* bacteria as an underexplored biosynthetically diverse source of new natural products.

P-107 – Sylvia Kunakom

Genome Mining for rSAMs involved in Actinobacterial Ribosomally Synthesized and Post-translationally Modified Peptide (RiPP) Biosynthesis

Sylvia Kunakom[1], Hiroshi Otani[1], and Nigel J. Mouncey[1]. [1]DOE Joint Genome Institute, Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, CA, 94720

Ribosomally synthesized and post-translationally modified peptide (RiPPs) are one of the structurally and functionally diverse classes of secondary metabolites. Discovery of new RiPPs requires multiple robust genome mining strategies by searching for posttranslational modification enzymes and precursor peptides. A common posttranslational modifying enzyme involved in RiPP biosynthesis is radical S-adenosyl-L-methionine (rSAM) that catalyzes a versatile range of chemical transformations on the peptide. In order to discover rSAMs catalyzing novel reactions, we have performed bioinformatic analyses to identify RiPP biosynthetic gene clusters (BGCs) encoding rSAM from an Actinobacterial genomic database and clustered them using a

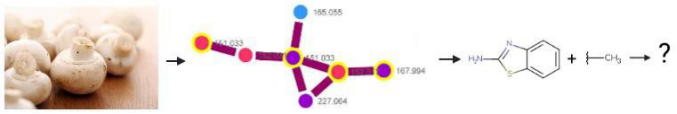
sequence similarity network. RiPP BGCs predicted to encode a novel rSAM reaction were further manually curated. A total of 20 RiPP BGCs were selected for functional characterization. These RiPP gene clusters will be synthesized, heterologously expressed in selected host strains, and the cognate metabolite will be detected via LC-MS.

P-108 – Xiaoling Chen

Predicting Novel Aryl Hydrocarbon Receptor (AHR) Ligands by Global Molecular Networking

Xiaoling Chen[1], Joshua J. Kellogg[1]. [1]Department of Veterinary and Biomedical Sciences, The Pennsylvania State University, University Park, PA, 16802, USA

The aryl hydrocarbon receptor (AHR) has been shown to have a key role in gut homeostasis and immunity. Both agonist and antagonist activity of dietary AHR ligands are of interest to better understand the influence of diet on gut health. White button mushrooms have been shown to contain several benzothiazole derivatives that act as AHR agonists. Using a molecular networking method, combing a library of known ligands and fungal metabolomics data, we predicted the presence of a previously unknown AHR ligand in white button mushrooms. A methylated 2-amino-benzothiazole was projected to be present as an AHR agonist. The benzothiazole derivative was isolated, structurally confirmed with ^{1}H NMR, and its activity validated in an *in vitro* AHR model.

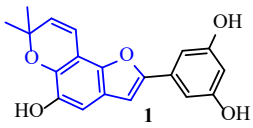


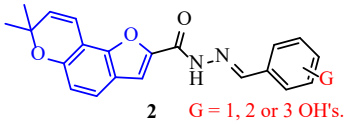
P-109 – Geneive Henry

Antioxidant and Pro-oxidant Effects of Synthetic Moracin K-inspired Phenolic Derivatives

Geneive E. Henry, Jessica Saylor, and Olivia Basile. Department of Chemistry, Susquehanna University, Selinsgrove, PA 17870

Moracin K is one of over two dozen benzofurans isolated from the *Morus* plant genus. While antioxidant and anticancer activities have been reported for many of the moracins, there is little pharmacological data for moracin K. In this study, a series of moracin K-inspired synthetic phenolic furanochromenes containing one, two or three hydroxy groups and a hydrazone linker between the furanochromene and phenolic moieties were evaluated for their antioxidant and prooxidant effects. Antioxidant activity of the phenolic furanochromene derivatives was determined using the cupric ion, Cu(II), reducing antioxidant capacity (CUPRAC) assay to determine the influence of the number and location of hydroxy groups on the Cu(II) ion reducing ability. In the presence of Cu(II), phenolic compounds have the ability to produce reactive species (ROS), leading to a prooxidant effect. To explore the potential of these derivatives to also act as pro-oxidants, their ability to cleave DNA in the presence of Cu(II) ions was examined. For both the copper (II) ion reduction and the DNA cleavage assays, derivatives containing the *ortho*-dihydroxy arrangement had the greatest effects, confirming a link between the Cu(II) ion reducing capacity and DNA cleavage ability.



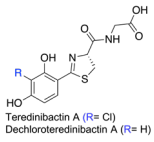


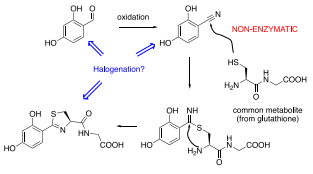
P-110 – Youjung Sung

Biosynthesis and Total Synthesis of Teredinibactins

Youjung Sung, Bailey W. Miller, Margo G. Haygood, and Eric W. Schmidt. Department of Medicinal Chemistry, College of Pharmacy, University of Utah, 30 South 2000 East, Salt Lake City, UT 84112

Teredinibactin A and dechloroteredinibactin A are newly reported secondary metabolites isolated from *T. turnerae* T7901. Teredinibactins bind to a variety of metals, implying that they may be involved in regulating metal ion concentrations. These compounds consist of a 2,4-dihydroxylated phenol connected to thiazoline and glycine. Aromatic thiazoline or thiazole compounds are often components of siderophores or other nonribosomal or ribosomal peptide products. However, no putative biosynthetic gene clusters for such compounds could be found in the *T. turnerae* T7901 genome. This led us to hypothesize that the key linkage may be formed non-enzymatically. Here, we describe chemical, genetic, and enzymological approaches to understand the biosynthesis of this new class of azoline ionophores.





P-111 – Empress Williams

Biochemometric Studies of the Antimicrobial Properties of *Turnera diffusa*

Empress Williams[1], Chantal Pelzer[2], and Nadja B. Cech[3]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, 1400 Spring Garden St, Greensboro, NC 27412

New antimicrobial leads are in high demand due to the rise in multidrug-resistant bacterial infections. Plant natural products are an essential component in medicinal drug discovery. Traditionally, botanicals were widely used as a remedy for bacterial infections. *Turnera diffusa*, also known as damiana, is a flowering plant native to Mexico, South and Central America, and

the southern United States. *Turnera diffusa* was historically used by Native Americans as a hallucinogen, expectorant, and general wellness tonic. Currently, it is used most prominently for its stimulant properties. Preliminary research supports the antimicrobial properties of *Turnera diffusa. Turnera diffusa* leaf extract and fractions were dissolved in dimethyl sulfoxide at concentrations of 10 μg/mL and 100 μg/mL and tested against Methicillin-Resistant *Staphylococcus aureus* (MRSA) to observe bacterial inhibition. The extracts were characterized by ultra-performance liquid chromatography coupled with high-resolution mass spectrometry (UPLC-HRMS). The results suggest the presence of the known constituents ellagic acid, quercetin 3-O-β-d-gentiobioside, velutin, and pinocembrin. Experiments employing biochemometric methodologies to link the chemical composition of the extract with their antimicrobial activity are ongoing.

P-112 – Charmaine Lindsay

Penicillium aurantiacobrunneum is a Promising Source of Cytotoxic Compounds

Charmaine A. Lindsay[1], Choon Y. Tan[1], Gerardo D. Anaya-Eugenio[1], Chad A. Rappleye[2], Richard J. Spjut[3], Esperanza Carcache de Blanco[1], A. Douglas Kinghorn[1], Harinantenaina L. Rakotondraibe[1]. [1]Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, [2]Department of Microbiology, The Ohio State University, Columbus, Ohio 43210, United States, [3]World Botanical Associates, Bakersfield, CA 93380, United States*

Despite advances in anticancer research, cancer is the second leading cause of death in the U.S.A. and thus remains an area of high research need. Natural product drug discovery is an important means of probing for novel anticancer compounds. Fungi represent a promising source for exploration for such compounds, and lichen-associated mycobionts are no exception. Already, mycobionts have shown an ability to produce cytotoxic compounds, and lichen-associated mycobionts possess the added value of being able to produce compounds that are unique to their symbiosis. Encouraged by these findings, *Penicillium aurantiacobrunneum* (Trichocomaceae), an associated mycobiont from the U.S. endemic lichen *Niebla homalea* (Ramalinaceae), was investigated for the unique and cytotoxic compounds present. This study resulted in the isolation of a novel tetramic acid derivative and known cytotoxic compound citreoviridin (6.0 ± 1.6 μM, MCF-7; 8.2 ± 2.7 μM, A2780) as well as the alkaloid PF1140. Structure elucidation and the possibility to produce derivatives through future mycobiont feeding experiments will be discussed herein.

P-113 – Yulin Ren

Analysis of Chemical Components of the Different Parts of Aronia Berry Grown in Ohio

Tyler Frank[1], Gunnar Meyer[1], Ryan Slaughter[2,3], Gong Wu[4], Arpad Somogyi[4], Gary Gao[2,3], A. Douglas Kinghorn[1], and Yulin Ren[1]. [1]*Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy,* [2]*OSU South Centers,* [3]*Department of Horticulture and Crop Science, College of Food, Agricultural, and Environmental Sciences, and* [4]*Mass Spectrometry and Proteomics, Campus Chemical Instrumentation Center, The Ohio State University, Columbus, OH 43210, United States*

Aronia berry, *Aronia melanocarpa* (Michx.) Elliott (Rosaceae), is a shrub native to North America, of which the fruits (Aronia berries) are gaining popularity in the food industry. Our previous investigations demonstrated that a chloroform-soluble extract of Aronia berries collected near Piketon in Ohio exhibited cytotoxicity against a small panel of human cancer cells, and that one of these active components is ursolic acid. This triterpene was found to show a growth inhibition toward MDA-MB-231 human breast cancer cells and inhibitory effects on NF-κB p65 and mitochondrial transmembrane potential. Thus, herein, a dried powder of each of the stems, twigs, leaves, and flowers and the frozen fresh fruits of Aronia berry were extracted with ethanol followed by dichloromethane (DCM). The DCM-soluble extracts have been analyzed by LC-MS/MS techniques. The results showed that the phytochemical component profiles varied in the different plant parts, and the compound numbers detected decreased in the sequence leaves, twigs, stems, flowers, and fruits. The peak at the retention time of 22.79–22.80 min was determined as ursolic acid [m/z: 457.3663 (calc.; m/z: 457.3682)] by comparison of its fragment pattern with those of the standard sample. Ursolic acid appeared in all of the samples tested, with the relative abundance increased in the sequence fruits, stems, leaves, flowers, and twigs. These indicate that all parts of Aronia berry investigated contain ursolic acid, and its content in twigs or flowers is greater than that in fruits.

P-114 – Yulin Ren

Cytotoxic Components of the Stems of *Cryptolepis dubia* Collected in Laos

Yulin Ren[1], Avery McMaster[1], Elizabeth Kaweesa[2], Kongmany Sydara[3], Mouachanh Xayvue[3], Djaja D. Soejarto[2,4], Joanna E. Burdette[2], and A. Douglas Kinghorn[1]. [1]*Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210, United States,* [2]*Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, United States,* [3]*Institute of Traditional Medicine, Ministry of Health, Vientiane, Lao People's Democratic Republic,* [4]*Science and Education, Field Museum of Natural History, Chicago, IL 60605, United States*

While the isolation of cardenolides and pyridine alkaloids from *Cryptolepis dubia* (Burm.f.) M.R. Almeida [sym.: *C. buchananii* Roem. & Schult.] (Apocynaceae) has been reported previously, no indole alkaloids have been isolated from this plant so far. Herein, several indole alkaloids, including the new chlorine-containing analogue, chlorocrypine, and other types of natural products isolated from the stems of *C. dubia* collected in Laos, are presented. The structures of the new compounds were determined by analysis of their spectroscopic data and confirmed by the MS^1 and MS^2 spectra. The major MS fragment ions of chlorocrypine were

found to be formed from removal of its chlorine. All of the isolates were evaluated for their cytotoxicity against a small panel of human cancer cell lines, and several compounds were found to be active. A major active compound showed potent cytotoxicity against all the human cancer cell lines tested, with the IC_{50} value found to be less than 1.0 μM, while chlorocrypine exhibited selective cytotoxicity toward OVCAR3 human ovarian cancer cells (IC_{50} 5.9 μM). These results indicate that *C. dubia* shows antitumor potential, and hence further investigation for this species seems justifiable for the potential discovery of new anticancer agents.

P-115 – Yulin Ren

The Configuration at C-17 and the Resultant ECD and NMR Spectra of Selected Cardenolides

Yulin Ren, James R. Wilson, Xiaolin Cheng, A. Douglas Kinghorn. Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210, United Staters

Cardenolides are an important group of steroidal natural products, with several members being used for the treatment of congestive heart failure and found more recently to show potent antineoplastic and anti-infective activities. The structures of cardenolides have been determined traditionally by analysis of their NMR spectroscopic data, and the absolute configurations of several of these compounds have been defined by investigation of their electronic circular dichroism (ECD) and NMR spectra and single-crystal X-ray diffraction data. However, the ECD spectra of these compounds seem to vary depending on the nature of the substituents at the steroid core and the C-17 lactone unit, while the ^{13}C NMR resonance observed at the C-12 position changes greatly based on the C-17 configuration. To rationalize these observations, both the experimental and calculated ECD and NMR spectra of digoxigenin and (+)-stebloside and selected derivatives in the context of their 3D conformations have been investigated. The results showed that ECD signals of these compounds changed due to the substituents on their aglycones and the configuration at C-17. However, the lactone unit of these cardenolides orients away from the steroid ring system in the 17β-cardenolides, but it folds toward the C-12 position in their C-17α isomers. As a result, the ^{13}C NMR resonance of C-12 in the 17α-cardenolides shifts upfield up to 9.0 ppm when compared with those in their 17β-epimers, owing to an anisotropic effect. Thus, the ^{13}C NMR resonance of C-12 seems to be indicative of the C-17 configuration of cardenolides.

P-116 – Zarna Raichura

Development of Cytochrome P450 Cocktail Inhibition Assay to Predict Botanical-Drug Interaction using LC-MS-QTOF

Zarna Raichura[1], Kabre Heck[1], Kelli McDonald[1], Jaewoo Choi[3,4], Mikah Brandes[4,5], Cody Neff[4,5], Claudia Maier[2,3,4], Amala Soumyanath[4,5], Robert Arnold[1], and Angela I Calderón[1]. [1]Department of Drug Discovery and Development, Harrison College of Pharmacy, Auburn University, AL 36849, USA, [2]Department of Chemistry and [3]Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, [4]Botanicals Enhancing Neurological and Functional Resilience in Aging (BENFRA) Botanical Dietary Supplements Research Center and [5]Department of Neurology, Oregon Health and Science University, Portland, OR 97239

Many older adults worldwide with multiple diseases come across polypharmacy, resulting in drug interactions when taken concomitantly with botanicals. It is essential to contemplate the inhibition of major metabolizing enzymes CYP450 as one of the primary mechanisms of the pharmacokinetic drug interactions to assure the safe use of combination therapies. We have developed an *in-vitro* inhibition metabolizing enzyme cocktail assay using human liver microsomes; which involves the use of 10 different probe substrates simultaneously with 10 FDA approved CYP450 isoforms with an incubation time of 15 minutes. This assay was then evaluated with LC-MS, enabling faster analysis with better reproducibility. The column used for optimum separation of compounds is a Poroshell 120 CS-C18, which provides enhanced loadability and peak shape. So far, we have optimized each metabolite's chromatography, sample preparation, and ionization potential. The following steps involve determining CYP inhibitor concentration with full IC_{50} curves and as a proof of concept, the screening CYP inhibition of *Withania somnifera* (L.) Dunal (Ashwagandha) extracts. Ashwagandha is one of the most widely used botanical dietary supplements in the U.S. for cognitive impairment.

P-117 – Rosa Jenifer Muñoz-Gómez

Antidiabetic Sterols from *Peniocereus greggii* Roots

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The decoction from the roots of *Peniocereus greggii* (PGD) possesses a hypoglycemic and antihyperglycemic action *in vivo*. The active compounds were identified as peniocerol (**2**), desoxyviperidone (**3**), viperidone (**4**), viperidinone (**5**) and a new chemical entity 3,6-dihydroxycholesta- 5,8(9),14-trien-7-one (**6**). The sterols **2** and **6** promoted insulin secretion *in vitro*. Compound **3** decreased blood glucose levels during an oral glucose tolerance test and an intraperitoneal insulin tolerance test in hyperglycemic mice, showing its activity as insulin sensitizer agent. Also a mitochondrial bioenergetic experiment confirmed that compound **3** behaves as an insulin sensitizer agent by a mechanism that may involve mitochondrial proton leak. Finally, an UPLC method for quantifying the compound **3** and **4**, in the crude drug was developed and validated.

P-118 – Daniela Rebollar-Ramos

α-Glucosidase and PTP-1B Inhibitors from *Malbranchea dendritica*

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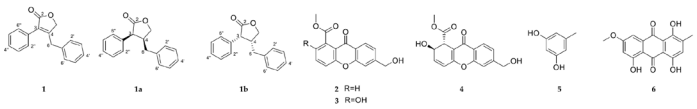
Fractionation of different extracts of *Malbranchea dendritica* led to the isolation of gymnoascolide A (**1**), sydowinin A (**2**), sydowinin B (**3**), AGI-B4 (**4**), orcinol (**5**), erythroglaucin (**6**), deoxyadenosine (**7**), adenosine (**8**), thymidine (**9**), and uridine (**10**). Compound **1** inhibited ◎-glucosidase *in vitro* (IC_{50} = 0.556 ± 0.009 mM, mixed-type inhibition) and *in vivo* during an oral sucrose tolerance test. Compound **1** was reduced with Pd/C to yield the mixture of enantiomers **1a** and **1b**; with similar activity against ◎-glucosidase (IC_{50} = 0.396 ± 0.003 mM). Docking analysis predicted that **1**, **1a**, and **1b** bind to an allosteric site of the ◎-glucosidase enzymes. Xanthone **3** non-competitively inhibited PTP-1B (IC_{50} of 0.081 ±0.004 mM). Docking analysis revealed that **3** might bind to an allosteric site of the enzyme in agreement with its kinetic behavior.



P-119 – Reema Al-Qiam

Homoisoflavonoids with Cytotoxic Activity from the Bulbs of *Bellevalia Longipes*

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Seven new homoisoflavonoids were identified from the bulbs of *Bellevalia longipes* Post (Asparagaceae) as well as thirteen known and one new natural homoisoflavonoid. The structure elucidation of these were determined via 1D and 2D NMR data analyses along with HRMS data, while absolute configurations were assigned using ECD spectroscopy. In addition to classical structural elucidation, a system to rapidly classify homoisoflavonoids into one of three structural classes was developed. 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-120 – Logan Breiner

Structure-Activity Relationship of Pleuromutilin Triazolyl Derivatives

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Antibiotic resistant pathogens are a rising global threat, directly responsible for 1.3 million deaths per year, a figure that is projected to increase to 10 million by 2050. One way to combat this looming specter is the use of hybrid conjugates or bidentate drugs, antibiotics with related targets connected via a covalent linker. Pleuromutilin is one such candidate for these conjugates as it has two easily and selectively functionalizable moieties—a glycolic alcohol, and a vinyl group. Pleuromutilin was first isolated from the mushroom *Clitopilus scyphoides*, and two derivatizes are FDA approved antibiotics. These agents target the peptidyl transferase center (PTC) in the ribosome, adjacent to the sites of other classes of antibiotics. Twenty-two derivatives of pleuromutilin were synthesized using a sequence of azidation and cycloaddition reactions. Modifications of the glycolic alcohol were found to retain activity against MRSA when terminated with alcohols, amines, alkyl chains, or aromatic groups (4-16 μg/mL). However, all attempts to derivatize the vinyl abolished activity. Computational modeling of the active derivatives in the bacterial ribosome revealed that glycolic alcohol analogs engage favorably with rRNA while the vinyl derivatizations adopted unfavorable binding conformations, thus supporting the experimental data. These results establish sites where linker connection will be tolerated with future work focusing on using this knowledge to generate bidentate hybrid antibiotics at the glycolic alcohol position and exploring potential solutions to realize activity with vinyl functionalized derivatives.

P-121 – Zachary Kohanov

Towards the Total Synthesis of Thermorubin: Optimization of Hauser-Kraus Annulations

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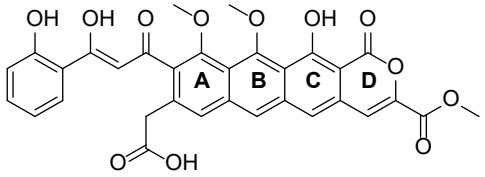
Thermorubin is a promising and unique secondary metabolite with a novel, bacteriostatic mechanism of action. This antibiotic binds between the large and small ribosomal unit and inhibits initiation of protein synthesis. Isolation of thermorubin is difficult, requiring specific growth conditions, and creation of derivatives would enable improvement of its pharmacokinetic properties. The molecule also has poor water solubility and is readily degraded upon exposure to air in organic solvents. Therefore, implementing a total synthesis of thermorubin is imperative for creating a stable and more potent antibiotic. In order to ascertain this material, the creation of the tetracyclic core is the first main portion of synthesis. Rings A, C, and D will be created through two similar annulations to an aromatic intermediate using Hauser-Kraus conditions. A model system has been extensively tested and optimized conditions will be applied to the total synthesis intermediate once fully optimized.



P-122 – Riya Bhanushali

Discovery of Non-Opioid Pain Relievers from Marine Organisms

Riya Bhanushali,[1] Madison Greene,[1] Yifan Liang,[2] Bhuwan Khatri Chhetri,[2] Jaehoon Shim[3], Lee Barrett[3], Clifford Woolf,[3] Julia Kubanek.[1,2] [1]School of Biological Sciences, [2]School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA 30332, [3]Boston Children's Hospital, Boston, MA 02115

Due to their highly addictive nature and widespread availability, the number of deaths related to opioid overdose has been steeply increasing with 68,630 deaths reported nationwide in 2020.[1] Hence, it is crucial to find novel compounds that target non-opioid mechanisms of pain relief. Our study focuses on marine natural products-based discovery of non-opioid analgesics using a $Na_v1.7$ voltage-gated sodium channel ion flux assay and a $Na_v1.5$ assay to assess cardiac toxicity.[2] By selectively blocking $Na_v1.7$ without inhibiting other isoforms, a $Na_v1.7$ antagonist can work as a promising pain treatment.[3] Of 1593 extracts screened using the $Na_v1.7$ assay, tropical algae, *Halymenia* sp. and *Gibsmithia hawaiiensis*, were prioritized. Two glycolipids were isolated from the bioactive fraction of *Halymenia* sp. and represent hits for $Na_v1.7$. As only sub-milligram quantities of the bioactive extract fraction were available from *G. hawaiiensis*, we anticipate natural product identification to be done using microcrystal electron diffraction (MicroED) in the nanogram scale range.[4] The lead compound(s) are expected to reveal the bioactive pharmacophore, hence leading way for structure activity-based drug design.

P-123 – Bernard Somers

Crila Herbal Supplement Reduces Lower Urinary Tract Symptoms in Latino Men

Bernard Somers[1], Betsy Singh, MD[2], Laura J. Camacho Choza, MD[3], Pablo F. Gonzalez Limon, MD[3], Francisco Gomez Regalado, MD[3], Nadina Jose, MD[4]. [1]Department of Medicinal Chemistry, Rutgers University New Brunswick, NJ, [2]BRCG Medical Research Group, Midlothian, VA, [3]PanAmerican Clinical Research Group, Mexico, [4]Department of Health Informatics, Rutgers University Newark, NJ

Lower urinary tract symptoms (LUTS) are commonly experienced by men as they age, affecting 56% of men ages 50-79 and 70% of men ages 80-89. A study of 3,301 participants published in *Urology* indicates black and Hispanic men have the greatest incidence of LUTS[1]. Previously, a single group open label trial at three hospitals in Vietnam was performed over 2 months to assess Crila® herbal supplement in 189 men. 89.2% showed a beneficial response on the International Prostate Symptom Score ($p<.001$). A Prospective Open-Label Dietary Supplement clinical study was approved by two Ethics Committees in Mexico to study oral Crila® herbal supplements (*Crinum latifolium* L var. crilae Tram & Khanh) in 49 men with LUTS. Crila® was taken orally for 90 days in Guadalajara and Querétaro, Mexico. Every 30 days symptom severity was quantified using an AUASI Questionnaire to determine the benefits of Crila®. 88% of the men showed improvement in their LUTS after study completion while significant improvement was observed from Day 0 to each subsequent visit, and from Day 30 to Day 90 ($p=0.006$). When comparing Visit 1 to all 3 following visits, we observe a significant decrease ($p<0.001$) in total prostate score on the AUA survey.

AUA/Prostate Cohort		n	Paired Differences: Mean	Paired Differences: Std. Deviation	Paired Differences: Std. Error Mean	Significance: One-Sided p	Significance: Two-Sided p
Pair 1	Total (Baseline)	49	16.33	5.153	0.736	<.001	<.001
	Total (First)	49	11.92	5.578	0.797		
Pair 2	Total (Baseline)	49	16.33	5.153	0.736	<.001	<.001
	Total (Second)	49	10.71	5.443	0.778		
Pair 3	Total (Baseline)	49	16.33	5.153	0.736	<.001	<.001
	Total (Final)	49	8.29	5.642	0.806		

P-124 – Lesley-Ann Giddings, Brian Murphy and Christine Salomon (ASP DEI Committee)

Equity in Action: The ASP Summer Research Fellowship Program

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One critical challenge facing STEM fields in the US, which is reflected within the ASP, is a lack of racial and ethnic representation among our membership, leadership, award recipients, and meeting speakers. To correct for the underrepresentation of Black, Indigenous and Latinx (BIL) students in our field, the ASP DEI and Executive Committees, ASP Foundation, and ASP Fellows collaborated to develop the Summer Research Fellowship (SRF) program. The program offers 1) a 2.5 month stipend for students to engage in research under a mentor in the natural product sciences; 2) 12 weekly online professional development workshops focused on science communication as well as exposure to graduate programs and careers in natural products; and 3) a special online ASP webinar for students to present their research to an international audience. The first cohort (2021) was highly successful, with at least one student accepted to a natural products graduate program and several others receiving prestigious research fellowships and awards (remainder of the cohort are still engaged in undergraduate studies). Importantly, most students in the first cohort are continuing to pursue research in the field of natural products chemistry. Students in the second cohort (2022) have begun their research, participating in the weekly workshops and preparing for their presentations. Several students in both cohorts are attending the 2022 ASP meeting, so please be sure to visit their posters and welcome them. The DEI committee is is seeking additional support through grants and donations to continue the successful SRF program.

Poster Presentations Session II

P-125 – Rosemary Dorrington

Screening Southern African Marine Invertebrate Extract Libraries for Novel Antimicrobials

Jarmo-Charles J. Kalinski[1], Rosemary A. Dorrington[1,2], Dele Abdissa, Michelle Isaacs[1], Idris Njanje[1], Shirley Parker-Nance[2,3], Alexandros Polyzois[1], Tarryn Potts[1], Sinobomi Marwarwa[1], Rui W. Krause[1]. [1]Department of Biochemistry and Microbiology, Rhodes University, Makhanda, South Africa [2] South African Institute for Aquatic Biodiversity, Makhanda, South Africa [3] South African Environmental Observation Network Elwandle Node, Gqeberha, South Africa

Antimicrobial resistance is one of the major global health challenges of the 21st century and there is a great need for novel antimicrobial compounds to combat drug resistant pathogenic bacteria. Natural products have played a major role in antibiotic drug discovery and the largely unexplored marine environment holds immense potential for the discovery of new chemical entities. We have developed a pipeline to isolate antimicrobial compounds from natural product extract libraries derived from marine invertebrates and their associated microbiota. More than 500 extracts representing species endemic to Southern Africa were initially screened for activity against *Escherichia coli* and *Staphylococcus aureus*. Active extracts were analyzed using LCMS/MS-based molecular networking through Global Natural Products Social (GNPS), as well as SIRIUS4. to dereplicate known marine natural products and identify extracts containing novel chemistry that were prioritized for bioassay-guided isolation of active compounds. We will report on our screening results as well as the structures and biological activities of selected isolates.

P-126 – Elijah Bring Horvath

Clinical Antibiotic Resistance and Overcoming Multidrug-Resistant Bacterial Pathogens

Elijah R. Bring Horvath[1,2], Matthew A. Mulvey[2], and Jaclyn M. Winter[1] [1]Department of Medicinal Chemistry and [2]Department of Pathology, University of Utah, Salt Lake City, Utah, USA

Antibiotic resistance (AR) is currently recognized by the World Health Organization as a leading global health issue. As of 2019, the CDC expects 2.8 million AR infections, resulting in 35,000 deaths to occur each year in the US. This number represents a 152% increase in expected mortality rate due to AR infections in just over six years. Among resistant microbes, multi-drug resistant (MDR) pathogens represent the greatest threat. MDR bacterial strains are often resistant to multiple classes of antibiotics, leaving clinicians with few alternative treatment options. Recently, we isolated a MDR strain of *Escherichia coli* from a patient at the University of Utah and found that it harbored more than a dozen genes associated with AR, and was also determined to be resistant to multiple classes of antibiotics. This inspired us to explore mechanisms of AR in bloodstream pathogens isolated from patients in Salt Lake City, UT. Using several comprehensive bioinformatics tools, we discovered many more MDR strains. In an effort to combat these MDR strains, we have integrated genomic and chemical-based approaches for accessing new antimicrobial agents produced by microbes isolated from the hypersaline environment of Great Salt Lake using our MDR strains as screening tools. Several natural products with potent activity against MDR strains of *E. coli* and *Staphylococcus aureus* have been identified, as well as their respective biosynthetic gene clusters. The diverse antibiotic potential of Great Salt Lake Actinobacteria and antibiotic resistance mechanisms identified in our clinical isolates will be discussed.

P-127 – Shukria Akbar

Antimicrobial Potential and Chemical Profiling of Maggot Associated Bacteria

Shukria Akbar[1], Daniel S.May[2], Adam Book[2], Laura Muller[2], Caitlin Carlson[2], Tim S. Bugni[1], Cameron R. Currie[2] [1]Pharmaceutical Sciences Division, University of Wisconsin-Madison, Madison, WI, United States, [2]Department of Bacteriology, University of Wisconsin-Madison, Madison, WI, United States

The increasingly dire threat to public health from antibiotic-resistant pathogens demands the discovery of structurally novel antimicrobials; ideally, such compounds would be both structurally and mechanistically novel. Accordingly, underexploited yet stable environmental niches rank among the most important possible sources of such compounds. The goal of this study was to investigate the antimicrobial potential of understudied bacterial strains associated with maggots, the fly larvae that feed on dead organisms. In this study, bioactive antimicrobial extracts were analyzed using untargeted metabolomics. Hierarchical clustering analyses & principal component analysis (HCAPCA) were performed to identify isolates with the largest number of unique metabolites. The selected strains were scrutinized for structural dereplication using Global Natural Product Social (GNPS) molecular networking and Nuclear Magnetic Resonance spectroscopy (NMR) was used to elucidate the structures of active unknown metabolites. We found that select bacterial isolates displayed diverse antibacterial and antifungal activities. Several bacterial strains prioritized based on HCAPCA appeared to generate unknown chemical entities. The metabolomic output for one of these strains (SID10270) that has exhibited Gram-negative antibacterial activity is now undergoing structure elucidation efforts. Overall, this study demonstrates that maggot-associated bacteria represent a useful source of unique antimicrobials; while working on the active component from SID10270, there are several other strains in the pipeline that could contribute to drug discovery efforts.

P-128 – Daniel May

Macrolide Glycosyltransferases Render Antibiotics Harmless to *Streptomyces* but Lethal for *E.coli*

Daniel S. May[1], Shukria Akbar[1,2], Tim S. Bugni[2], Cameron R. Currie[1].[1]Department of Bacteriology, University of Wisconsin-Madison, Madison, WI, USA, [2]School of Pharmacy, University of Wisconsin-Madison, Madison, WI, USA

Diverse *Streptomyces* strains were grown on sub-inhibitory concentrations of antibiotics to induce the production of new natural products. Out of 100 *Streptomyces* strains grown in the presence of the macrolide antibiotic erythromycin, 10 strains demonstrated new Gram-negative inhibition against *Escherichia coli*. Comparative metabolomics and molecular networking of the strains revealed new compounds related to erythromycin when the strains were grown with erythromycin. This suggested that erythromycin was modified by the *Streptomyces* strains. The difference in mass between the new compound and erythromycin was equivalent to an additional glucose, indicating that erythromycin had been glycosylated. The *Streptomyces oleD* gene encodes a macrolide glycosyltransferase that modifies diverse macrolides, rendering them inactive. The 10 *Streptomyces* strains were sequenced, and each strain contained an *oleD* homolog. Additionally, three previously sequenced *Streptomyces* strains were predicted to contain *oleD* homologs and were selected for further studies. The 13 *oleD*-encoding *Streptomyces* strains were tested for their ability to glycosylate four macrolide antibiotics: erythromycin, spiramycin, tylosin, and josamycin. The strains varied in their ability to glycosylate each of the four macrolides, and this variability was consistent with the phylogeny of the *oleD* homologs. The glycosylated erythromycin inhibited growth of *E. coli*, but not other Gram-negative pathogens, suggesting a role for these inactivated macrolides as targeted antibiotics.

P-129 – Frank Surup

Structural Complexity Of Azaphilones From The Family Hypoxylaceae

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The family Hypoxylaceae is well-known for the production of a large diversity of azaphilones in their stromata (fruiting bodies). The presence or absence and the structural architecture of the metabolites serve as a valuable chemotaxonomic tool for genus and species delimitation. We even identified them in fungal fossils obtained by an archeological survey, demonstrating that the pigments remained stable for more than a millennium. Many azaphilones possess various important bioactivities. For instance, the highly complex heterodimeric hybridorubrins, composed of mitorubrin and fragirubrin moieties, strongly inhibited *Staphylococcus aureus* biofilm formation in contrast to their monomeric counterparts. Analysis of the genome of *Hypoxylon fragiforme* revealed the presence of two separate candidate biosynthetic gene clusters (BGCs) *hfaza1* and *hfaza2* being likely responsible for azaphilone formation. We are using metabolomics as a tool to explore the chemical diversity of azaphilones in the Hypoxylaceae and to deduce their biosynthetic logic.

P-130 – Cole Gannett

Structure Activity Relationship of Esters of Blasticidin S

Cole Gannett[1], Paige Banks[1], Emily Mevers[1], Andrew N. Lowell[1] [1]Department of Chemistry, Virginia Tech, Blacksburg, VA (US)*

Antimicrobial resistance (AMR) is one of the largest and most dire threats to human health across the globe. With the lack of new antibiotic classes being introduced, a growing area of research involves repurposing underexplored antibiotics. Blasticidin S is a peptidylnucleoside antibiotic with reported broad-spectrum antibacterial and antifungal activity that was used as an agricultural fungicide in Japan; however, it has never been sufficiently explored for clinical use as an antibiotic. Despite its activity against both Gram-negative and Gram-positive bacteria, very few semi-synthetic derivatives of blasticidin S have been created, though these analogs have shown an increase of potency over the parent metabolite. Inspired by these promising results, we created a library of ester derivatives at the carboxylic acid functionality with the goal of increasing the potency and specificity for bacteria over fungi. Twelve ester derivatives were synthesized and six were selected and screened against thirteen human bacterial and fungal pathogens. Interestingly, smaller esters retained the important Gram-negative activity while also improving activity against various strains of *Staphylococcus aureus*. With respect to fungal activity, only blasticidin S inhibited the growth of *Candida albicans* at the concentrations tested. This study confirms that reassessing previously discovered natural products as potential antibiotics holds promise as a new approach for creating next-generation of antibiotics.

P-131 – Jin Yi Tan

Partnering with Community Centers to Perform *"Environment to Bioassay"* Antibiotic Discovery

Jin Yi Tan[1], Ahmad Qdafi[2], Nuala McSweeney[2], Jonathan Rodriguez[2], Brian T. Murphy[1]. [1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL. [2]Boys & Girls Club of Chicago, Chicago, IL

Microorganisms are a major source of antibacterial drugs needed to combat the growing threat of antibiotic resistance, but a typical pipeline employed for microbial drug discovery is highly time

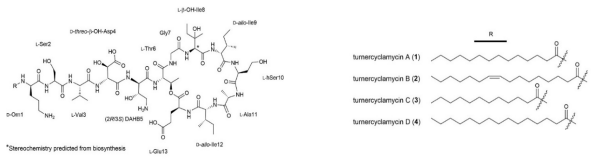
consuming, labor intensive, and often results in re-isolation of known antibiotics. We are developing an "environment to bioassay" antibiotic discovery approach that combines high-throughput cultivation experiments and robotics with a custom, 3D-printed dual sided agar plate assay (DAPA) to rapidly screen and select for antibiotic-producing bacteria. This framework allows us to accomplish many stages of the microbial drug discovery pipeline directly from single bacterial colonies in a semi-automated fashion, and offers an advantage in terms of scale and capacity. Importantly, our approach facilitates more comprehensive access to diverse portions of the culturable microbiome from environmental samples. This project is integrated with educational outreach efforts in partnership with community centers from underserved areas of Chicago, such as the James Jordan Boys & Girls Club. There are three central components to the outreach program – field work, applied science experiments, and environmental literacy – with the goal of inspiring marginalized students to become the next cohort of university STEM majors, who will then employ their knowledge to support sustainable practices within the community. Overall, we aim to demonstrate 1) the feasibility and efficiency of an environment to bioassay antibiotic discovery approach, and 2) that high- impact research can be successfully integrated with community partnerships.

P-132 – Albebson Lim

Turnercyclamycins, Gram-Negative Specific Bacterial-Acting Lipopeptides Isolated from *Teredinibacter turnerae*

Albebson L. Lim[1], Bailey W. Miller[1], Zhenjian Lin[1], Jeannie Bailey[2], Kari L. Aoyagi[3], Mark A. Fisher[3], Louis R. Barrows[4], Colin Manoil[2], Margo G. Haygood[1], and Eric W. Schmidt[1]. [1]Department of Medicinal Chemistry, University of Utah, [2]Department of Genome Sciences, University of Washington, [3]Department of Pathology and ARUP Laboratories, University of Utah, [4]Department of Pharmacology and Toxicology, University of Utah

Turnercyclamycins are lipopeptides isolated from an intracellular symbiont of shipworms, *Teredinibacter turnerae*. Their predicted biosynthetic gene cluster is encoded in the genomes of all sequenced *T. turnerae strains*. They specifically kill Gram-negative bacteria without toxicity to normal human kidney cells, and without evident hemolytic activity. They are also active against multi-drug resistant *Acinetobacter* complexans, as well as colistin-resistant *A. baumannii*, and *mcr-1* expressing *E. coli* suggestive of a different molecular mechanism than colistin. They retained activity *in vivo* and have similar PK to clinically used lipopeptides. Recent investigation using passaged strains and genetic deletions reveal key features differentiating the mechanisms of turnercyclamycins from those of colistin, the current last-line agent used in treating *Acinetobacter* infections.



P-133 – Suzzudul Shuvo

A Dual-sword Approach to Rejuvenate Tetracycline

Suzzudul Islam Shuvo, Zachary A. Kohanov, Andrew N. Lowell. Department of Chemistry, Virginia Polytechnic and State University, Blacksburg, VA 24061, USA*

The antibiotic tetracycline was FDA approved in 1953 but resistance arose in 1959, which prompted the need for developing active derivatives to regain potency (e.g. Minocycline, 2nd generation or Tigecycline, 3rd generation). While continuing this approach by making more semisynthetic derivatives of tetracycline, we are also adopting a new approach for extended defense against resistance, which is to bind tetracycline to another antibiotic that targets a nearby site, using a covalent linker. As t;,.etracycline is fairly polar, the first step is to protect the hydroxyls of the C3, C10, and C12 positions to reduce its polarity and make it more amenable to chemical reactions. The next step is to derivatize its C7 and C9 position (via-Electrophilic aromatic substitution) or the C2-amide position (using Mannich-like conditions). The third step is to deprotect the hydroxyl positions and check the derivatives for antimicrobial activities. Beyond giving us advanced derivatives with enhanced potency, this will also give us insight into where a long chain can be attached without losing activity. These linkers will allow us to covalently bind tetracycline derivatives to another antibiotic that targets nearby sites, thus extending defense against resistance.

P-134 – Keelie Butler

Genome Mining Reveals New RiPP Natural Product in Pathogenic *Streptococcus*

Keelie S. Butler[1], Jonathan R. Chekan[1]. [1]University of North Carolina at Greensboro

Ribosomally synthesized and post translationally modified peptides (RiPPs) are a growing class of natural products. Through bioinformatic advancements, genome mining for these RiPP natural products is leading the way for the discovery of new analogs and modifications. In this study, we focus on using this genome mining strategy to search for putative new RiPP classes. Using this strategy, a well conserved RiPP gene cluster was found within several human commensal and pathogenic bacteria, including members of the *Streptococcus* genus, such as the important human pathogen *Streptococcus pneumoniae*. We aimed to express these gene clusters, identify the suspected product, and assess the enzymology as well as bioactivity. Successful expression and enzymatic activity assays revealed the formation of a product confirmed by LC-MS and a putative new enzymatic reaction,

supported by preliminary NMR data. Understanding the biosynthesis of this new natural product may lead to important insight into the pathogenesis of clinically relevant Streptococci.

P-135 – Daniel Zagal

Metagenomic Analysis of Dietary Supplement Plant Microbiomes

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Microbial communities within plant microbiomes are dynamic and shaped by a myriad of factors. Changes in the microbiome of dietary supplement (DS) plants (DSPs) can be key factors explaining frequently described metabolomic variability of cultivars and subsequent heterogeneous composition of DS products marketed under the same label. Metagenomic analysis of DSPs can provide insight into the factors affecting the composition of their microbiomes. Field collections in Alaska, Colorado, and Pennsylvania produced 280 environmental DNA (eDNA) samples from popular DSPs, *Rhodiola rosea* and *Actaea racemosa*, and their congeners, *R. integrifolia* and *A. rubra*, respectively. Endophytes were collected from leaf stem and root, and epiphytes from aerial parts and rhizosphere. Statistical analysis of alpha and beta diversity shows significant differences in microbial diversity between congeners, as well as between plant parts. Root endophyte and rhizosphere epiphyte samples have the highest diversity, followed by aerial parts epiphytes. Additionally, endophytic and epiphytic microbiomes of individual DSPs differ significantly in diversity, with the former being less diverse. Together, the four million sequences of over 40,000 distinct sequences processed illustrate that individual DSP can have unique microbiomes that vary not only by species but also by plant part, among other factors. Current advances in gene sequencing make metagenomic analyses more approachable, allow for new forms of authentication of DSs, and enable studies of the relationship between microbiomes and metabolite production.

P-136 – Joseph Egan

Mass Spectrometry Pattern Queries in Ometa Flow for Class Specific Lead Generation

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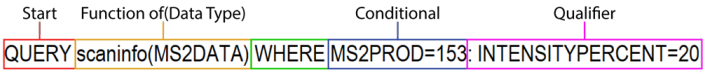
Mass Query Language (MassQL) is a programming language specifically designed to rapidly access and parse information from mass spectrometry experiments. Using a simple query structure, hundreds of files can be quickly parsed using a chemistry-first intuition leveraging diagnostic MS^2 fragments, MS^1 isotopic relationships, or class specific fragmentation patterns and/or neutral losses. Using MassQL from the Ometa Flow platform, we demonstrate the ability to parse historic data collections for compound classes using diagnostic fragmentation in MS^2 to discover flavonoids, leverage MS^1 isotopic information to highlight halogenated compounds, and construct class-specific MS^1 search patterns through extrapolation of in-source fragmentation. MassQL in the Ometa Flow environment provides a flexible and easily applied language for MS data query allowing for streamlined discovery workflows built for large scale applications.



P-137 – Mohammad Khasawneh

Salvadora Persica Fruits Attenuates DMBA-Induced Mammary Cancer in Female Albino Rats

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Naturally occurring phytochemicals especially polyphenolic compounds have received increasing attention as chemopreventive agents. The chemopreventive potential of the ethanolic extract of *Salvadora Persica L.* fruits SP, (the arak tree or miswak) on 7,12-dimethylbenz (a) anthracene (DMBA)-induced mammary carcinogenesis in female albino rats was investigated in this work. Ethanolic extract of SP fruits was supplemented to the experimental groups at a concentration of 500 mg/kg body weight for 22 weeks. Administration of SP extract suppressed DMBA-induced mammary carcinogenesis as revealed by incidence of tumors in histological investigation. There was a significant reduction in cell proliferation and an increase in apoptosis with downregulation of estrogen receptor expression in the mammary tissue of SP-treated animals. Additionally, SP extract prevented the oxidative damage induced in breast tissues of DMBA-treated rats. SP treatment also decreased the viability of MCF-7 breast cancer cells and induced early and late apoptosis and induced S cell cycle arrest. The chemo-preventive properties and anticancer effects of SP could be attributed to its anti-oxidative and a high percentage of phenolic compounds and esters which were detected here in the SP fruit extract.

P-138 – Sang Kook Lee

Antitumor Activity of Pulvomycin, a Macrolide from *Streptomyces* sp., Via Targeting STAT3 Signaling in Docetaxel-Resistant Triple-Negative Breast Cancer Cells

Woong Sub Byun, Eun Seo Bae, Jinsheng Cui, Hyen Joo Park, Dong-Chan Oh and Sang Kook Lee. College of Pharmacy, Natural Products Research Institute, Seoul National University, Seoul 08826, Republic of Korea

Pulvomycin, a macrolide, was isolated from the marine-derived actinomycete *Streptomyces* sp. HRS33. In the present study, a docetaxel-resistant TNBC cell line (MDA-MB-231-DTR) was established, and mechanisms for the antitumor activity of pulvomycin were investigated. Levels of activated STAT3 (p-STAT3 [Y705]) increased in docetaxel-resistant cells, and knockdown of STAT3 recovered the sensitivity to docetaxel in MDA-MB-231-DTR cells. Pulvomycin effectively inhibited the proliferation, suppressed the activation of STAT3 and subsequently induced G_0/G_1 cell cycle arrest and apoptosis. Pulvomycin also significantly inhibited the invasion and migration of MDA-MB-231-DTR cells through the modulation of epithelial-mesenchymal transition markers. In an MDA-MB-231-DTR-bearing xenograft mouse model, the combination of pulvomycin and docetaxel effectively inhibited tumor growth through STAT3 regulation. These findings suggest that the combination of docetaxel and pulvomycin is a potentially effective strategy for overcoming docetaxel resistance in TNBC by targeting STAT3 signaling. (Acknowledgement: This research was funded by the National Research Foundation of Korea (NRF) grants funded by the Ministry of Science and ICT (MSICT) (grant number: 2021R1A4A2001251).

P-139 – Zachary Ferris

Grincamycins P–T: Rearranged Angucyclines from Marine *Streptomyces* Inhibit Cell Lines of the Rare Cancer Pseudomyxoma Peritonei

Zachary E Ferris[1], Zhuo Shang[1], Douglas Sweeney[2], Alexander B Chase[2], Ethan A Older[1], Dan Xue[1], Prakash Nagarkatti[3], Mitzi Nagarkatti[3], Traci L Testerman[3], Paul R Jensen[2], Jie Li[1]. [1]Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208, [2]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, California 92093, [3]Department of Pathology, Microbiology and Immunology, School of Medicine, University of South Carolina, Columbia, South Carolina 29209

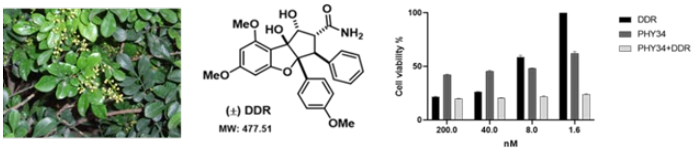
While marine natural products have been investigated for anticancer drug discovery, they are barely screened against rare cancers. Thus, in our effort to discover potential drug leads against the rare cancer pseudomyxoma peritonei (PMP), which currently lacks effective drug treatments, we screened extracts of marine actinomycete bacteria against the PMP cell line ABX023-1. This effort led to the isolation of nine rearranged angucyclines from *Streptomyces* sp. CNZ-748, including five new analogues, namely, grincamycins P–T. The chemical structures of these compounds were unambiguously established based on spectroscopic and chemical analyses. Particularly, grincamycin R possesses an S-containing α-l-methylthio-aculose residue, which was discovered in nature for the first time. All of the isolated compounds were evaluated against four PMP cell lines and some exhibited low micromolar inhibitory activities. To identify a candidate biosynthetic gene cluster (BGC) encoding the grincamycins, we sequenced the genome of the producing strain and compared the BGCs detected with those linked to the production of angucyclines with different aglycon structures.

P-140 – Elizabeth Kaweesa

Cytotoxic Activity of Didesmethylrocaglamide in High Grade Serous Ovarian Cancer

Elizabeth N. Kaweesa[1], Tyler A. Wilson[2], Djeneba H. Diakite[1], Jacqueline M. Bazioli[1], Yulin Ren[2], A. Douglas Kinghorn[2], James R. Fuchs[2] and Joanna E. Burdette[1]. [1]Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL 60607, [2]Division of Medicinal Chemistry and Pharmacognosy, The Ohio State University, Columbus, OH 43210, USA

Didesmethylrocaglamide (DDR) is a naturally occurring derivative of rocaglamide with potent antitumor activity isolated from *Aglaia* plant species (Fig.1). DDR displays nanomolar cytotoxic activity in high grade serous ovarian cancer (HGSOC) cell lines including OVCAR3. HGSOC is the fifth leading cause of death in women and requires new treatments to help tackle resistance. We found that DDR induced cytotoxicity in ovarian cancer cell lines and activated caspase-3 indicating pro-apoptotic activity. In addition, DDR was cytotoxic in PEO4 cells resistant to platinum and PARP inhibitors. Further studies indicate that blocking autophagy or DNA repair in combination with DDR increased cell death in the sensitive and resistant models. Effective cytotoxicity in drug-resistant cell models suggests DDR has potential as a new therapeutic strategy against HGSOC.



P-141 – Manead Khin

Aulosirazole, Foxo3a Nuclear Translocator, as a Drug Lead For High-Grade Serous Ovarian Cancer

Manead Khin[1], Lydia J. Davis[1], Jimmy Orjala[1], Joanna E. Burdette[1]. [1]Department of Pharmaceutical Sciences, University of Illinois at Chicago, College of Pharmacy, Chicago, IL 60612

Ovarian cancer, the fifth leading cause of cancer-related death in women, is the most aggressive gynecological malignancy in the world. Among the various subtypes of ovarian cancer, high-grade serous ovarian cancer (HGSOC) is the most common and lethal due to lack of early detection and frequent chemoresistance. Aulosirazole, an isothiazolonaphthoquinone alkaloid isolated from the terrestrial cyanobacterium, *Nostoc* sp. UIC 10771, demonstrated bioactivity against OVCAR3 (IC_{50} = 301 ± 80 nM), and was found to induce FOXO3a nuclear translocation. Phosphorylation and subsequent translocation of the FOXO3a transcription factor from the cytoplasm to the nucleus has tumor suppressive effects. FOXO3a phosphorylation by JNK leads to nuclear localization, while FOXO3a phosphorylation by AKT tends to result in cytoplasmic localization. Aulosirazole led to phosphorylation of both JNK and AKT in western blot analyses, but the JNK phosphorylation was still able to stimulate FOXO3a nuclear localization according to immunocytochemistry. Aulosirazole induced cleavage of PARP in western blot analysis and increased apoptotic cell population in AnnexinV/PI assay. It also regulated known downstream FOXO3a targets such as BCL2 and p21. In hollow fiber assay, aulosirazole reduced OVCAR5 cell viability *in vivo.* Currently, there are no FDA-approved drugs targeting FOXO3a nuclear localization, suggesting that aulosirazole may have an innovative mechanism of action. Future studies will focus on FOXO3a knockdown studies and *in vivo* models.

P-142 – Herma Pierre

Verticillin A-Polymer Loaded Surgical Buttresses for Effective Targeted Therapy Against Pancreatic Cancer

Zeinab Y. Al-Subeh[1,2], Herma C. Pierre[2], Priscilla S. Redd[1], Cedric J. Pearce[3], Aaron H. Colby[4,5], Nicholas H. Oberlies[2,], Kebin Liu[1,6,7,*]. [1]Department of Biochemistry and Molecular Biology, Medical College of Georgia, Georgia Regents University, Augusta, GA, 30912, [2]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, 27412, [3]Mycosynthetix, Inc. Hillsborough, NC, 27278, [4]Department of Biomedical Engineering, Boston University, Boston, MA, 02215, [5]Ionic Pharmaceuticals, LLC, Brookline, MA, 02445, [6]Georgia Cancer Center, Medical College of Georgia, Augusta, GA, 30912, [7]Charlie Norwood VA Medical Center, Augusta, GA, 30904*

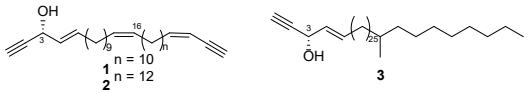
Pancreatic cancer is one of the most malignant diseases worldwide. While the lifetime risk of developing pancreatic cancer is low (1.7%), the estimated 5-year survival rate in the US alone is 11%. The main treatment modality is surgical resection with adjuvant chemotherapy (the latter of which has improved the prognosis of patients); however, due to the short and rapid progression of the disease, nearly quiescent early symptoms while the cancer is localized, and frequent lymphatic metastasis, most patients (~80%) are unable to undergo surgery at the time of diagnosis. Thus, effective chemotherapeutics are vitally important. Herein, we report a verticillin A-polymer coated buttress as an extended-release drug formulation against *in vivo* solid pancreatic cancer tumors. This formulation had a high tolerable dose (800 μg or 32 mg/kg body weight), reduced the systemic toxicity of verticillin A, and prevented gemcitabine-resistant pancreatic tumor recurrence in 80% of the murine models.

P-143 – Lucero Fructuoso

Cytotoxic Asymmetrical Polyacetylene Alcohols from Marine Sponge *Cribochalina vasculum*

Lucero Martinez[1], Susan M. Ensel[2], Rhone K. Akee[2], Brian D. Peyser[1], John R. Britt[2], Jason R. Evans[1], Barry R. O'Keefe[1,3] and Tanja Grkovic,[1,3]. [1]Natural Products Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute; [2]Natural Products Support Group, Leidos Biomedical Research Inc., Frederick National Laboratory for Cancer Research; [3]Molecular Targets Program, Center for Cancer Research, National Cancer Institute, Frederick, MD 21702

As part of a continuing search for new metabolites with anti-cancer activity, bioassay-guided fractionation of the organic extract of sponge *Cribrochalina vasculum* yielded three new asymmetrical polyacetylenes, namely durynes G-I (**1-3**). Their planar structures were elucidated by combined spectroscopic and spectrometric techniques and the absolute configuration of the chiral centers at the C-3 position was determined via modified Mosher's ester method and chiroptical methods. In the NCI-60 cancer cell cytotoxicity panel, the new natural products showed potent cytotoxic activity and selectivity for melanoma cell lines, in particular the LOX IMVI cell line with GI_{50} values in sub-micromolar range.



P-144 – Gabriel Castro-Falcón

Structure and Candidate Biosynthetic Gene Cluster of a Manumycin-Type Metabolite from *Salinispora pacifica*

Gabriel Castro-Falcón[1], Kaitlin E. Creamer[1], Alexander B. Chase[1], Min Cheol Kim[1], Douglas Sweeney[1], Evgenia Glukhov[1], William Fenical[1], and Paul R. Jensen[1]. [1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California, San Diego, La Jolla, California, 92093, United States

A new manumycin-type natural product named pacificamide and its candidate biosynthetic gene cluster (*pac*) were discovered from the marine actinobacterium *Salinispora pacifica* CNT-855. The structure of the compound was determined using NMR, electronic circular dichroism, and bioinformatic predictions. The *pac* gene cluster is unique to *S. pacifica* and found in only two of the 119 *Salinispora* genomes analyzed across nine species. Comparative analyses of biosynthetic gene

clusters encoding the production of related manumycin-type compounds revealed genetic differences in accordance with the unique pacificamide structure. Further queries of manumycin-type gene clusters from public databases revealed their limited distribution across the phylum Actinobacteria and orphan diversity that suggests additional products remain to be discovered in this compound class. Production of the known metabolite triacsin D is also reported for the first time from the genus *Salinispora*. This study adds two classes of compounds to the natural product collective isolated from the genus *Salinispora*, which has proven to be a useful model for natural product research.

P-145 – Nolan Barrett

Probing the Antibiotic Mechanism of Action of Marine Natural Products Using a Combined ^{1}H-NMR And LC/IM-MS Metabolomics Approach

Nolan H. Barrett[1], Anne Marie Sweeney-Jones[2], Carter K. Asef[2], Facundo M. Fernández[2], and Julia Kubanek[1,2]. [1]School of Biological Sciences, Georgia Institute of Technology, Atlanta, GA, USA; [2]School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, USA

The study of the metabolome provides snapshots into the ongoing chemical workings of living systems. Metabolomics approaches can be applied to a variety of problems. One challenge for the development of first-in-class antibiotics is elucidating the mechanism of action (MOA) of a new drug candidate. Here, we demonstrate the value of metabolomics in discovering potential MOAs of a family of marine natural product antibiotics. The cladophorols, isolated from *Cladophora socialis*, are oligomeric polyphenols with selective activity against methicillin-resistant *Staphylococcus aureus* (MRSA), via an unknown MOA. This study's goal was to use metabolomics to determine potential MOAs for cladophorols by comparing the metabolomic profile of MRSA cells exposed to cladophorol D vs. antibiotics of known MOA. These chemical fingerprints were obtained with both proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) and liquid-chromatography ion-mobility mass spectrometry (LC/IM-MS). Based on metabolomic profiles, cladophorol D significantly perturbs MRSA metabolism via a different MOA than other antibiotics. Integration of ^{1}H-NMR and LC/IM-MS-based metabolomics data is leading to the identification of metabolites associated with antibiotic exposure, including polar molecules with electronegative heteroatoms and aromatic-based functional groups. This approach enables detection of altered biochemical pathways within MRSA cells when treated with various antibiotics, providing a systems-level analysis of potential molecular targets and MOAs for natural product drugs.

P-146 – Lukasz Ciesla

Cellular Membrane Affinity Chromatography Columns for Drug Discovery

Caroline Goodman, Urmila Maitra, Lukasz Ciesla. Department of Biological Sciences, University of Alabama, 2320 Science and Engineering Complex, Tuscaloosa, Alabama 35487-0344

Natural products are a rich source of pharmacologically active compounds. However, due to technical constrains the currently used high-throughput screening techniques are not compatible with complex natural samples. One of the greatest challenges in the identification of new drug leads from natural products is the complexity of the extracts, that requires enormous amount of time and effort to discover biologically active secondary metabolites. Cellular membrane affinity chromatography (CMAC) is an approach that allows for the identification of compounds, present in complex matrices and specifically interacting with the immobilized transmembrane protein. CMAC columns have proven to be useful in screening plant extracts and smoke condensates for new ligands targeting different classes of transmembrane proteins, e.g.: ligand-gated ion channels, GPCRs, and protein transporters. The use of CMAC columns is ideally suited to build libraries of pharmacologically active natural compounds that further might be tested using modern screening platforms. It is estimated that approximately 50% of all drug discovery programs focus on transmembrane proteins. The CMAC columns can easily be applied in drug discovery laboratories to identify novel drug templates that can be further used to treat certain forms of cancer, neurodegenerative diseases, chronic pain, diabetes, and many other illnesses.

P-147 – Xinhui Yu

New Cyclic Octadepsipeptides from South African Stromatolites

Xinhui Yu,[1] George F. Neuhaus,[1] Julius C. Habiyaremye,[1] Allegra T. Aron,[2] Alexandros Polyzois,[3] Daniel Petras,[2] Emily C. Gentry,[2] Eric W. Isemonger,[3] Xavier Siwe Noundou,[3] Samantha C. Waterworth,[4] Jason C. Kwan,[4] Rosemary A. Dorrington,[3] Pieter C. Dorrestein,[2] and Kerry L. McPhail[1]. [1]Department of Pharmaceutical Sciences, College of Pharmacy, Oregon State University, Corvallis, OR 97331, USA, [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, San Diego, CA, 92093 USA, [3]Department of Biochemistry and Microbiology, Rhodes University, Makhanda 6139, South Africa, [4]Division of Pharmaceutical Sciences, University of Wisconsin, Madison, WI 53705, USA

Stromatolites are lithified layers of complex microbial mats that existed more than 3.4 billion years ago and are still found in modern forms. A barrage pool formed by living stromatolites near Schoenmakerskop in the Eastern Cape, South Africa was chosen as a study site for investigating the composition and small molecule production of the microbial community. As part of this larger study, two new, biologically active octadepsipeptides have been isolated from organic extracts of stromatolite collections made in 2018 and 2021. Following their purification in sub-milligram amounts, the structure elucidation of these macrocycles, which possess nominal masses of 957 and 985 Da, was accomplished

using NMR spectroscopy and tandem mass spectrometry. A modified, enhanced sensitivity Marfey's method confirmed the amino acid composition both natural products and supported a variation in one of the two alpha hydroxy acid residues present in the structures. Ongoing collaborative work includes identification of the presumed cyanobacterial producer and non-ribosomal peptide biosynthetic genes.

P-148 – Antonio Hernandez

Identification of Pyreudione Analogs from a Freshwater Sponge-Derived *Pseudomonas* sp.

Antonio Hernandez, Radhika Dhakal, Tatyana Ndekwe, Kevin Kim, Chase M. Clark, Nyssa Krull, Brian T. Murphy, Department of Pharmaceutical Sciences, Center for Biomolecular Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60607, USA

Since 1981 through present day, natural products or their derivatives have accounted for >50% of FDA approved antibacterials on the market. Further, marine sponges along with their associated microbes have been a plentiful source of bioactive natural products including several drugs used in the clinic, such as eribulin (breast cancer), vidarabine (antiviral), cytarabine (leukemia), among others. However, their freshwater counterparts continue to be an understudied source despite their ubiquitous distribution across global freshwater environments. In this study we investigate *Pseudomonas* sp. isolate SP509 from a freshwater sponge that was collected in the Apostle Islands in 2018. We performed bioassays and found that the extract of this isolate was inhibiting the growth of *Staphylococcus aureus* ATCC 29123. Following separation and dereplication it was determined this isolate was producing pyreudiones A-D, all previously characterized molecules and some with antibacterial properties. In this study we show chromatographic, mass spectra, and proton NMR data suggesting that SP509 is producing pyreudiones that are uncharacterized since these molecules were first identified in 2016.

P-149 – Shengnan Jin

High-resolution ESI-QTOF-MS/MS and Semi-Preparative HPLC to Characterize Minor Antimycobacterial Metabolites from an Engineered *Streptomyces atratus*

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

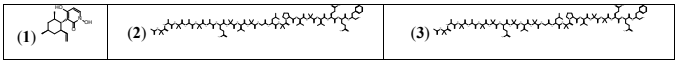
The genus *Streptomyces* has been one of the most prolific sources for potential antimicrobial agents. A high-throughput screening approach has been established to characterize minor metabolites from an engineered *S. atratus* with activity against *Mycobacterium tuberculosis* (M.tb) and ESKAPE pathogens. The new methodology advances the recognition and purification of minor bioactive components via (i) generation of 108 non-selectively enriched micro fractions in a 96-well format via semi-preparative HPLC after injecting 3 mg of crude microbial extract. (ii) evaluation of all microfractions for antimycobacterial activity against M.tb H37Rv. (iii) acquisition of high-resolution ESI-QTOF-MS/MS spectra for all 108 microfractions subsequent structural characterization and chemical class annotation via the following in silico methods: CSI: FingerID and CANOPUS on SIRIUS-4.9, assigning confidence scores for annotated molecule using the COSMIC workflow. (iv) Targeted isolation of minor bioactive constituents that are likely new compounds via semi-prep HPLC with multiple injections of 15 mg of crude extract. The workflow will be demonstrated for a low-abundance bioactive compound that has been isolated and its structure characterized as being N-acyl amino acids (NAAAs) and derivatives.

P-150 – Heather Winter

Unique Structural Motifs of Antimicrobial Fungal Compounds Pyridoxatin, Trilongin BII and Trilongin BIII Against Highly Drug-Resistant *Acinetobacter Baumannii* (AB5075)

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

1-3 were found in our studies as potent antimicrobials against the highly-drug resistant Gram-negative organism, *Acinetobacter baumannii* (strain AB5075). These compounds were isolated from fungal extracts as part of an antimicrobial screening of 2,500 fungal extracts derived from the library of 55,000 fungal extracts at Mycosynthetix. **1** had been previously isolated as rotamers that are not separable. **2** and **3** were previously reported in literature as peptaibols. Further structural elucidation of **2** and **3** was pursued. Evaluation of *in vivo* efficacy and cytotoxicity in a previously described *Galleria mellonella* model showed no toxicity and moderate antimicrobial efficacy of **1**, while **2** and **3** demonstrated toxicity. **1** is being pursued in collaborative mouse models and analog syntheses.



P-151 – Lydia Davis

Metabolomic Investigation of Cytotoxin Production In The Freshwater Sponge-Associated Cyanobacterium, *Nostoc* sp. UIC 10607

Lydia J. Davis[1], Aleksej Krunic[1], Elizabeth N. Kaweesa[1], Manead Khin[1], Joanna E. Burdette[1], Jimmy Orjala[1]. [1]Department of Medicinal

Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, USA

Analogs of the cytotoxic depsipeptide, hapalosin, were identified in extracts from the freshwater sponge-associated cyanobacterium, *Nostoc* sp. UIC 10607. A comparative metabolomic workflow was used to determine culture conditions that enhanced secondary metabolite production. Replicate extracts of miniaturized cultures grown under differential culture conditions were analyzed by HR-ESI-LC-MS/MS. Tandem datasets were processed using mzMine2. The Metaboanalyst platform was used for untargeted statistical analysis of MS1 features. Feature-based molecular networking via the Global Natural Products Molecular Networking workbench and Cytoscape was used to identify families of metabolites and to query MS2 spectral databases. Sirius software was used to investigate the identity of upregulated features. Using this workflow, nitrogen availability and heat shock experiments were found to greatly influence metabolite expression of the hapalosin group. Interestingly, two additional hapalosin analogs were identified for the first time under diazotrophic conditions. Optimized culture conditions are being utilized to isolate these metabolites.

P-152 – Takeshi Tsunoda

Glucosyltransferase/Phosphatase Bifunctional Enzyme from the Acarbose Biosynthetic Pathway in Streptomyces Glaucescens Gla.O

Takeshi Tsunoda, Shumpei Asamizu, and Taifo Mahmud. Department of Pharmaceutical Sciences, Oregon State University, Corvallis, Oregon 97331

Acarbose, an α-glucosidase inhibitor used clinically to control type II diabetes, is produced by many actinobacteria, including *Actinoplanes* and *Streptomyces*. Bioinformatic analysis of the acarbose gene clusters in *Actinoplanes* sp. SE50/110 (the *acb* cluster) and *S. glaucescens* GLA.O (the *gac* cluster) revealed notable differences between the two clusters, leading to the notion that the Acb pathway is different from the Gac pathway. However, to date, only the Acb pathway has been studied in significant depth, whereas the Gac pathway remains elusive. To this end, we investigated both the *acb* and the *gac* clusters and found that GacI, a large protein unique to the Gac pathway, is similar to two Acb proteins, AcbI (a glycosyltransferase) and AcbJ (a phosphatase). Biochemical characterization of GacI confirmed its dual catalytic functions, whereas structural modeling showed the presence of two domains corresponding to those functions. Truncations of GacI showed that both domains are functionally independent. Interestingly, genome mining studies suggest that homologues of the bifunctional enzyme GacI are distributed more widely in nature than those of discrete AcbI and AcbJ.

P-153 – Kristie Francis

Discovery and Investigation of Survivin-Targeting Marine Natural Products from the Deep-water Gorgonian *Ellisella paraplexauroides*

Kirstie T. Francis, Esther A. Guzmán, Tara A. Peterson, Priscilla L. Winder, Peter J. McCarthy, John K. Reed, and Amy E. Wright, Harbor Branch Oceanographic Institute, Florida Atlantic University, 5600 US 1 North, Fort Pierce, FL 34946 USA

Survivin is a protein which is highly expressed in cancer cells but not in differentiated tissues, making it a tumor-selective target for new therapies. Survivin plays a multitude of roles in the growth and survival of cancer cells including the promotion of mitosis and inhibition of apoptosis. High expression of survivin in cancer cells is correlated with drug resistance and poor patient prognosis. A growing body of data suggests that survivin is a good target for cancer therapy. A high content imaging assay was used to identify fractions in the Harbor Branch Marine Natural Products Enriched Fraction Library that reduced the levels of survivin protein in the A549 lung carcinoma or DLD-1 colorectal adenocarcinoma cell lines. A fraction from the gorgonian *Ellisella paraplexauroides* was active against both cell lines. It was further separated following bioassay guided fractionation using sequential liquid chromatographic steps to yield a series of pure compounds. The structures of these compounds were elucidated through interpretation of spectroscopic data including 1D and 2D NMR and mass spectrometry revealing a series of polyhydroxylated cholestenones with novel placement of oxygenated functional groups. Compounds within the series show varying levels of survivin inhibition, suggesting essential components of the pharmacophore, and secondary biological testing gave insight into how these compounds may be acting in the cancer cells.

P-154 – Sang Hoon Jung

Anti-Allergic Property Of N, N - Dicoumaroylspermidimne Isolated from *Lithospermum Erythrorhizon* on Mast Cells and Ovalbumin-Induced Allergic Rhinitis

Tam Thi Le[a,b,#], Tae Kyeom Kang[a,#], Wook-Bin Lee[a], Sang Hoon Jung[a,b*] [a]Natural Product Research Center, Korea Institute of Science & Technology (KIST), Gangneung 25451, Republic of Korea. [b]Division of Bio-Medical Science & Technology, KIST School, Korea University of Science and Technology (KIST), Gangneung 25451, Republic of Korea.[#]*

Lithospermum erythrorhizon (LE) roots are used in traditional herbal medication that has been used in Korea and China for centuries to cure smallpox, measles, macular eruptions, eczema, burns, and carbucles. The purpose of the current study was to isolate and characterize anti-allergic active components in an ethanolic extract of LE roots. By chromatographic separation, two novel anthraquinones, one newly discovered chemical and nineteen other recognized compounds were extracted from LE ethanolic extract. Their chemical structures were elucidated by

the analysis of nuclear magnetic resonance (NMR) spectroscopic data in one dimension (1D) and two dimensions (2D), as well as high-resolution mass spectrometry (HR-MS). Among these identified compounds, N1",N3"-dicoumaroylspermidine strongly reduced the release of β-hexosaminidase and the production of IL-3, IL-4, and IL-13 from IgE-sensitized and BSA-stimulated RBL-2H3 cells. Then, using the OVA-induced allergic rhinitis mice model, the therapeutic benefits of N1",N3"-dicoumaroylspermidine against allergic rhinitis were determined by allergic nasal symptoms and the quantity of inflammatory cells in nasal lavage fluid (NALF). N1",N3"-dicoumaroylspermidine exhibited apparent anti-allergic characteristics, and its therapy improved nasal symptoms while lowering Th2-related cytokines. Thus, N1"',N3"'-dicoumaroylspermidine may be advantageous in the treatment of allergic rhinitis as an effective and a safe disease therapeutic agent.

P-155 – Victoria Anderson

Analyte-Driven Analysis of Untargeted Mass Spectrometry Metabolomics for Natural Products Discovery

Victoria M. Anderson[1], Warren S. Vidar[1], Andre Cote[2], Roger G. Linington[2], Nadja B. Cech[1]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27412 Department of Chemistry, Simon Fraser University, 8888 University Drive, Burnaby, BC, Canada, V5A 1S6

In mass spectrometry metabolomics datasets, a single chemical entity can be represented by many features (detected ions). This complexity can cloud meaningful data interpretation. An analyte-driven analysis produces a more concise dataset that simplifies the interpretation of data. The utility of a new open-source data processing package (MS2Analyte) was tested using data from the botanicals *Camellia sinensis* and *Rosmarinus officinalis*. Quantification was similarly accurate using either features or analytes. Principal component analysis revealed marked overlap between the feature-based and analyte-centric analyses despite a 40% reduction of analyzed variables in the analyte-based dataset. A biochemometric analysis identified a more than 50% reduction in the complexity of the selectivity ratio plot for the *Rosmarinus officinalis* making the identification of active chemical constituents more straightforward. These experiments demonstrate the benefits of analyte-centric analysis approaches for natural products discovery.

P-156 – Francisco Chacon

Inhibition of Angiotensin-Converting Enzyme (ACE) Activity by Isolated Cannabinoids from *Cannabis sativa* L.

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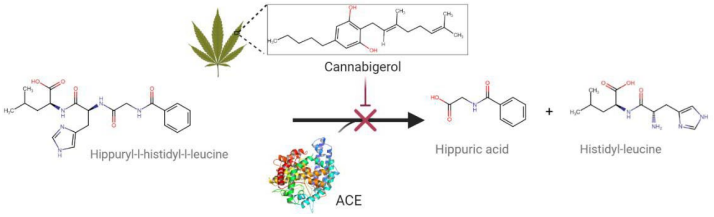
The pharmacological activity of *Cannabis sativa* L. is largely attributed to the plant's secondary metabolites, particularly C21 terpeno-phenolic compounds (the "cannabinoids"); however, the mechanistic effects/interactions of cannabinoids on blood pressure regulation have yet to be described. A molecular docking study demonstrated binding of several cannabinoids at the active site of the angiotensin-1 converting enzyme (ACE), an essential component in the renin-angiotensin system. And subsequent evaluation using an *in vitro* enzymatic reaction assay suggested potential interactions between cannabinoids from C. *sativa* and ACE.

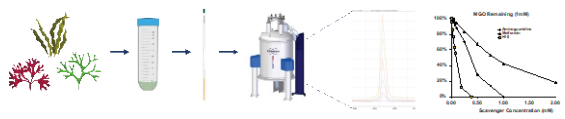


P-157 – George Hanna

Screening of Edible Seaweed with a Novel Direct qNMR Methylglyoxal Scavenging Assay

George S. Hanna[1], Mark T. Hamann[1, 1]Department of Drug Discovery and Biomedical Sciences, Medical University of South Carolina, Charleston, SC 20425, USA

Impaired glucose metabolism and diabetes afflicts an estimated 50% of Americans. Hyperglycemia leads to in an increase in reactive α-carbonyl and unsaturated aldehyde containing molecules, which have broad detrimental effects on human health. It is now widely believed that reducing exposure and controlling their concentrations in the body can slow the progression of aging-related degenerative diseases. This has become a promising route for the development of targeted interventions that range from nutrition, pharmaceuticals, lifestyle guidance and food processing methods. Among the diverse set of reactive aldehydes that can arise from the oxidation and peroxidation of sugars and lipids; methylglyoxal has emerged as a prominent contributor to the development and progression of diabetes, cardiovascular disease, and neurodegeneration. Presented here for the first time is a rapid qNMR technique for evaluating the methylglyoxal scavenging ability of extracts and pure molecules through direct measurement of methylglyoxal. The methylglyoxal scavenging activity of a diverse set of edible marine macroalgae and their chemical constituents is reported and show promise for the development of novel botanical drugs to control the negative effects of hyperglycemia. The goal is to develop effective and sustainable supplements and therapeutics to address the dramatic increase in the cost of healthcare and a drastic reduction of lifespan that appears to result from aldehyde driven metabolic disorder.

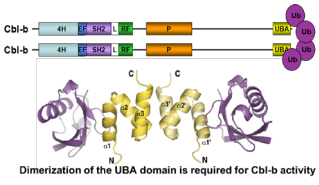


P-158 – Quan Khong

Photochemical Dimerization of Plakinidine B Results in Potent Inhibition of the Cbl-b Ligase

Lin Du[1], Quan T. Khong[1], Brice A. P. Wilson[1], Masoumeh Dalilian[1,2], Emily A. Smith[1,2], Antony Wamiru[1,2] , Ekaterina I. Goncharova[1,2], Tanja Grkvoic[1,3], Barry R. O'Keefe[1,3]. [1]Molecular Targets Program, CCR, NCI, Frederick, MD; [2]Leidos Biomedical Res., FNLCR, Frederick, MD; [3]Natural Products Branch, DTP, DCTD, NCI, Frederick, MD

Dimeric natural products can deliver an increased potency and selectivity against target proteins with active dimeric forms. The E3 ubiquitin-protein ligase Cbl-b represents an attractive target for immunotherapeutic intervention in cancer. A high-throughput sandwich ELISA assay was developed to identify small molecule inhibitors of Cbl-b by screening the MTP prefractionated library of >175k natural product fractions. Bioassay-guided fractionation of the active fractions of a marine sponge *Plakortis* sp. afforded an unprecedented dimeric alkaloid plakoramine A (**1**). Chiral separation of the racemic-**1** led to the purified enantiomers (+)-**1** and (-)-**1** which inhibited the Cbl-b activities with IC_{50} values at 7.5 and 9.7 μM, respectively. In contrast, the monomeric alkaloid precursor of **1**, plakinidine B (**2**), showed only weak inhibition against Cbl-b (IC_{50} 167 μM) but significant higher antiproliferative activities (Avg. GI_{50} 0.18 μM) than (+)-**1** and (-)-**1** (Avg. GI_{50}s > 30 μM) in the NCI-60 cancer cell cytotoxicity screen. Plakoramine A (**1**) represents the first reported dimer of the plakinidine alkaloids. Scrutinization of the purification conditions revealed a previously undescribed, non-enzymatic route to form **1** via photochemical conversion of **2** in the presence of O_2 and H_2O.



P-159 – Dayani Sarath Parakumge

Tolypocladamides A-G: Peptaibols from the Fungus *Tolypocladium inflatum* That Inhibit Ras/Raf Interaction

Sarath P. D. Senadeera,[†] Dongdong Wang,[†] Chang-Kwon Kim,[†] Emily A. Smith,[†,‡] Curtis J. Henrich,[†,‡] David E. Durrant,[§] Deborah K. Morrison,[§] Karen L. Wendt,[ǂ] Robert H. Cichewicz,[ǂ] John A. Beutler[†]. [†]Molecular Targets Program, Center for Cancer Research, National Cancer Institute, Frederick, Maryland 21702-1201, United States. [‡]Basic Science Program, Leidos Biomedical Research, Inc., Frederick National Laboratory of Cancer Research, Frederick, Maryland 21702-1201, United States. [§]Laboratory of Cell and Developmental Signaling, Center for Cancer Research, National Cancer Institute, Frederick, Maryland 21702-1201, United States. [ǂ] Department of Chemistry and Biochemistry, University of Oklahoma, Norman, Oklahoma 73019, United States

Seven new peptaibols named tolypocladamides A-G have been isolated from an extract of the fungus *Tolypocladium inflatum* which inhibited the Ras/Raf signaling pathway in a cell-based high-throughput screening assay. Each peptaibol contains 11 amino acid residues, an octanoyl or decanoyl fatty acid chain at the N-terminus, and a leucinol moiety at the C-terminus. Their peptaibol sequences were elucidated based on extensive 2D NMR and HR-ESI-MS^2 fragmentation analyses. Amino acid configurations were determined by advanced Marfey's analyses. Tolypocladamides A-G showed significant Ras/Raf interaction inhibition with IC_{50} values ranging from 0.5 to 5.0 μM in a NanoBRET assay, however, no interaction was observed in a surface plasmon resonance assay for binding of the compounds to wild type of G12D mutant Ras constructs or to the Ras binding domain of Raf.

P-160 – Remington Poulin

Ecologically Inspired Drug Discovery from Marine Phytoplankton: Cures from Competition

Caleb Demers[1], Kristy Syhapanha[2], Eric Nerger[3], Jana Held[4], Georg Pohnert[2], and Remington X. Poulin[1] [1]Department of Chemistry & Biochemistry, Center for Marine Science, University of North Carolina Wilmington, USA. [2]Department of Chemistry and Earth Sciences, Friedrich Schiller University Jena, Germany. [3]Department of Chemistry and Applied Biosciences, ETH Zürich, Switzerland. [4]German Center for Infectious Research, University Clinic Tübingen, Germany*

Phytoplankton, microscopic unicellular photoautotrophs, are known to compete using waterborne cues in a process called allelopathy. While allelopathy has been well documented in many species, few causative allelochemicals have been described. This provides a unique opportunity for planktonic allelochemicals to serve as a source of potentially novel chemistry for drug discovery. This is particularly true for the discovery of antimalarial compounds as many phytoplankton, including the dinoflagellate *Karenia brevis*, share evolutionary histories with the malarial causing parasite, *Plasmodium falciparum*. Exudates from eight species of phytoplankton with known allelopathic activity against *K. brevis* were antimalarial against the asexual blood stage of *P. falciparum*. Intracellular extracts were also antimalarial. MS-based dereplication yielded no known antimalarial compounds suggesting novel chemistry. Further research aims to identify the causative antimalarial compounds as well as to expand the drug discovery platform by increasing the number of phytoplankton species and pathogens tested.

P-161 – Richard Tehan

Structure and In Situ Molecular Cartography of Tortuosins, Putative Inhibitors of Elongation Factor-1 alpha From the Fungus *Paraisaria tortuosa* nom. prov.

Richard M. Tehan[1], Connor B. Dooley[1], Daphne R. Mattos[1], Joseph W. Spatafora[2], Jane E. Ishmael[1], Kerry L. McPhail[1]. [1]Department of Pharmaceutical Sciences, Oregon State University, Corvallis, 97331 OR, USA. [2]Department of Botany and Plant Pathology, Oregon State University, Corvallis, Oregon 97331

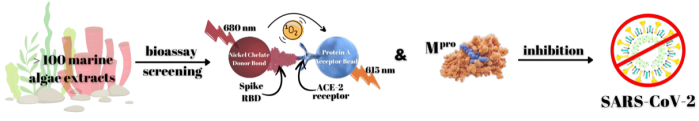
From a new fungal pathogen of beetle larvae, *Paraisaria tortuosa* Tehan & Spatafora nom. prov., we report the molecular structures structure and biological activity of the tortuosins. This extensive new family of N-methylated cycloheptapeptides contains putative inhibitors of eukaryotic translation elongation factor 1A (eEF1A). We performed an in situ molecular cartography analysis of the host-pathogen system, to visualize the distribution and relative concentration of specialized metabolites in their native system. To further investigate the chemical ecology of tortuosins, as well as other metabolites of *P. tortuosa*, we profiled the production of *P. tortuosa* we profiled the production of tortuosins by ranging North American *Paraisaria* species and propose that tortuosins are mycotoxins in potentially fatal *Paraisaria*-associated food-borne poisonings.

P-162 – Marie Matos-Hernandez

Compound Activity Mapping for SARS-Cov-2 Antiviral Marine Cyanobacterial Extracts

Marie L. Matos-Hernandez[1], Grayce Dyer[1], Chris A. Morales-Colón[2], Joel Cassel[3], 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]Department of Chemistry, College of Natural Sciences, University of Puerto Rico, Rio Piedras Campus, San Juan, PR 00925.[3]The Wistar Institute, University of Pennsylvania 3601 Spruce St, Philadelphia, PA. 19104

Several recent reports have provided structural insights to key regulatory proteins of SARS-CoV-2 and their susceptibility to be inhibited by compounds like those produced by marine algae. We therefore embarked on a hypothesis-based expansion of a pre-existing marine natural product library and high- throughput screening of this library for activity against multiple SARS-CoV-2 molecular targets. Through compound activity mapping, we present here a metabolomic analysis that shows the ability of multiple extracts and subfractions to inhibit the main protease (M^{pro}) of SARS-CoV-2 and/or to disrupt the ACE-2/Spike protein interaction *in vitro* with selectivity over non-viral host factors; M^{pro} selectivity index of >13.3 and 7.5 for Thrombin and Cathepsin L respectively; ACE-2/Spike selectivity index of >35.1 for PD-1/L1. This screen also identified one pure compound to date that selectively inhibits both viral targets (M^{pro} IC_{50} = 7.5 μg/mL and S/ACE-2 IC_{50} = 2.9 μg/mL).



P-163 – Sarah Dietrick

Isolation and Identification of Fungal Natural Products Against Multi-Drug Resistant Pathogenic *Candida albicans* and Newly Emerging *Candida auris* Strains

Sarah G. Dietrick and Bill J. Baker. Department of Chemistry, University of South Florida, Tampa, FL 33620, USA

Design and optimization of a growth-inhibition assay was achieved to conduct high throughput phenotypic screening of an extract library containing 10,000 fungal extracts. Fungal samples were collected from mangroves across Florida and Mexico and subject to the optimized growth-inhibition assay to identify promising fungal species against both *Candida auris* and *Candida albicans*. Further analysis of extracts and fractions was performed via NMR spectroscopy, Liquid Chromatography Mass-Spectrometry (LC-MS), and the Global Natural Products Social Molecular Network (GNPS) which facilitated rapid dereplication and targeted isolation of novel bioactive secondary small molecules. Fungal specimen were identified based on their ITS gene sequcence.

P-164 – Manuel Rangel Grimaldo

Metabolomic Profile of the Human Pathogen *Aspergillus Flavus* and its Non-Pathogenic Close Relatives

Manuel Rangel Grimaldo[1], E. Anne Hatmaker[2,3], Huzefa Raja[1], Hadi Pourhadi[1], Sonja Knowles[1], Rafael W. Bastos[4], Gustavo H. Goldman[4], Antonis Rokas[2,3], Nicholas Oberlies[1]. [1]Department of Chemistry, University of North Carolina at Greensboro, Greensboro, NC, USA. [2] Department of Biological Sciences, Vanderbilt University, Nashville, TN, USA. [3] Evolutionary Studies Initiative, Vanderbilt University, Nashville, TN, USA. [4] Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil

The mold *Aspergillus flavus* is a causative agent of aspergillosis and fungal keratitis infections in humans. Although *A. flavus* is commonly isolated from patients, species closely related to *A. flavus* are rarely isolated from patients and are not considered clinically relevant. To gain insights into why this is the case, we compared the metabolomic profile between seven *Aspergillus* strains (*A. flavus* NRRL 501 and NRRL 1957, *A. parasiticus* NRRL 502 and NRRL 2999, *A. nomiae* NRRL 6108, and *A. arachidicola* IC26645 and IC26646). The growing conditions for all the strains were carried out under two clinically relevant conditions. To accomplish this, each strain was grown in two different temperatures, at 23˚C (room temperature) and 37 ˚C (body temperature) and, with or without 6 mg/ml salinity to simulate the physiological conditions of tears. Additionally, the virulence for all strains was evaluated using an invertebrate model of fungal disease (*Galleria mellonella* larvae). This study revealed that temperature changes impacted metabolite production in all

species. In contrast, the saline environment has no impact on secondary metabolite production.

P-165 – Sean Romanowski

Development of a *Burkholderia* Host via Exploitation of Restriction-Modification Systems

Sean Romanowski[1], Sylvia Kunakom[1], Bruno S. Paulo[1], Alessandra Eustáquio[1]. [1]Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL, 60612, USA

Burkholderia are a β-Proteobacteria which have been shown to be prolific producers of natural products (NPs). There is a critical need in the field of drug discovery for the development of host bacteria beyond the commonly used *E. coli* for the purpose of heterologous expression of NPs. The *Burkholderia* strain FERM BP-3421 is a prolific producer of NPs, up to g/L quantities, making it ideal for host development apart from the issue of low transformation efficiency. We have sequenced the methylome and identified putative restriction-modification (RM) systems present in FERM BP-3421. These genes consist of a single type IV restriction endonuclease (REase), two solo type II methyltransferases (MTase), and two RM pairs of type II and type III. We seek to exploit the RM systems of FERM BP-3421 to hasten the process of transformation of genetic constructs in two ways. One, by designing plasmids encoding for the MTases endogenous to our host to be expressed in *E. coli*. By passaging genetic constructs through such an *E. coli* strain prior to transformation into FERM BP-3421 we will bypass the REases of our host. And two, by deleting the REases which are present in FERM BP-3421 thereby circumventing the ability of FERM BP-3421 to degrade incoming DNA. The development of a high yield, high transformation efficiency Burkholderiales host will contribute to natural product discovery.

P-166 – Victoria Casimir

Bioassay-guided-fractionation and isolation of SARS-CoV-2 ACE-2/Spike inhibitors from the brown algae Lobophora Variegata

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

Even though multiple vaccines have been developed for SARS-CoV-2, 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, providing potential antiviral leads for COVID-19 drug discovery and development. After screening >100 marine-derived extracts, we performed bioassay-guided-fractionation and isolation of SARS-CoV-2 ACE-2/Spike inhibitors from the brown algae *lobophora variegate*, which showed potent and selective antiviral activity.

P-167 – Kevin Tidgewell

Exploration of a Marine Cyanobacterial Extract Library for Identification of Sigma 2 ligands for Pain and Cancer Therapeutic Lead Discovery

Andrea L. Hough[1], Katelyn Grenell[1], Asef Faruk[1], Jane E. Cavanaugh[1], Eduardo Caro-Diaz[2], Benedict Kolber[3], Kevin Tidgewell[1]. [1]Graduate School of Pharmaceutical Sciences, Duquesne University, [2]Graduate Department of Pharmaceutical Sciences, University of Puerto Rico—Medical Sciences Campus [3]Department of Neuroscience and Center for Advanced Pain Studies, University of Texas at Dallas

Marine cyanobacteria are a prolific source of biologically active metabolites with diversity of chemical structure and pharmacological activity. These cyanobacterial natural products can serve as a promising source of inspiration for the development of therapeutic agents used in the treatment of many diseases of interest, such as CNS disorders, pain, and cancer. We have generated a library of 409 fractions from 37 field collected cyanobacterial samples and screened these fractions against a panel of CNS receptors using radiolabeled ligand competitive-binding assays. Upon analysis of the binding activity, we found that a significant amount of hits from our cyanobacterial samples were at the sigma 2 receptor. Sigma 2 has been known to be involved in CNS disorders and pain, as well as being upregulated in certain types of breast cancer, specifically, Triple Negative Breast Cancer (TNBC). For these reasons, cyanobacterial fractions with sigma 2 binding affinity were prioritized and studied further using High-Performance Liquid Chromatography, Mass Spectrometry, and Nuclear Magnetic Resonance. We found that fractions with a high affinity for sigma 2 fell into distinct groups based on cytotoxic potential or lack of cytotoxic activity. We are currently examining these fractions to identify chemotypes which may provide cytotoxic sigma 2 ligands for utility as cancer chemotherapeutics and non-toxic sigma 2 ligands which would be interesting for pain and neurodegenerative disorders.

P-168 – Márcio Barczyszyn Weiss

Chemoprospection of Brazilian Cyanobacteria Using Metabolomics and Biological Assays

Márcio B. Weiss[1], Maria G. S. Bueno[1], Jaewon Yoon[1], Leonardo F. Figueiredo[1], João P. Brandão[1], Fernanda R. Jacinavicius[1], João Costa Filho[2], Vítor F. Freire[3], Frederico J. G. Filho[2], Roberto G. S. Berlinck[3], Camila M. Crnkovic[1]. [1]School of Pharmaceutical Sciences, University of São Paulo, São Paulo, SP 05508-000, Brazil; [2]Institute of Chemistry of São Paulo, University of São Paulo, São Paulo, SP 05508-900, Brazil; [3]Institute of Chemistry of São Carlos, University of São Paulo, São Carlos, SP 13566-590, Brazil

Natural product screening programs have uncovered new molecules with various biological activities and unique scaffolds. A common obstacle in screening efforts is the rediscovery of known compounds. Expanding source diversity and applying innovative prospection approaches are critical to prioritize samples that contain new and bioactive compounds. Cyanobacterial strains from the Culture Collection of the Institute of Botany (CCIBt) in Brazil were cultured, the cultures extracted, and pre- fractionated. Fractions were tested for cytotoxic and antibiotic activities and analyzed by mass spectrometry. Molecular Networking (MN) analysis allowed sample prioritization and preliminary dereplication. Three out of 10 cyanobacterial strains were prioritized based on biological activity results and/or the chemical profile of bioassay tested samples. MN results obtained for a *Brasilonema* sp. culture extract indicated a large diversity of unique features, including novel analogs of previously reported peptides. Fractions obtained from *Anagnostidinema* sp. and *Desertifilum* sp. culture extracts were bioactive and presented unique MN features. Results support the efficiency of our chemoprospection strategy and the metabolic potential of Brazilian cyanobacteria.

P-169 – Jacqueline Moraes Bazioli

Cytotoxic Effect of *Epicoccum* sp.-Derived Pyridone Against High Grade Serous Ovarian Cancer

Jaqueline Moraes Bazioli[1,2], Daniel Yuri Akiyama[2], Robson Amaral[3], Kamilla Swiech[3], Taícia Pacheco Fill[2] and João Ernesto de Carvalho[1]. [1]Faculty of Pharmaceutical Sciences and [2]Institute of Chemistry - University of Campinas, Campinas, São Paulo, Brazil 13083-859. [3]Faculty of Pharmaceutical Sciences of Ribeirao Preto - University of São Paulo, Ribeirão Preto, São Paulo, Brazil 14040-900

Epicoccum sp. is a ubiquitous ascomycete in the Didymellaceae family known to produce a wide variety of biologically and chemically useful natural products. Large-scale cultivation of *Epicoccum* sp. was performed in Potato Dextrose Agar (PDA) for 12 days in darkness at 27 °C. Using separation techniques, five fractions were obtained from the crude extract. Fractions 2 and 3 from *Epicoccum* sp. have shown remarkable cytotoxicity at 4.89 and 4.25 µg/mL against the high grade serous ovarian cancer cell line, OVCAR3. Through bio-guided fractionation, epipyridone compound was isolated from the active Fraction 2, exhibiting IC_{50}-value of 61.66 µg/mL against the OVCAR3 cell line, after 48 h treatment. Among future perspectives, we intend to isolate more compounds and investigate the mechanism of action regarding cytotoxicity observed.

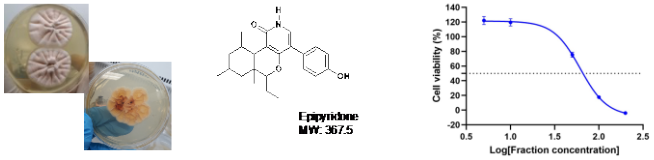


Fig. 1: *Epicoccum* sp.; epipyridone compound; Dose-dependent effect of epipyridone in OVCAR3 cells.

P-170 – Nathan Brittin

Hit Prioritization of Antifungals

Nathan Brittin[1], Dave Aceti[1], Tim Bugni[1], [1]School of Pharmacy, University of Wisconsin - Madison, 777 Highland Ave Madison WI, 53705

Antifungal resistance is an increasingly severe problem with the emergence of multi-drug resistant (MDR) fungal pathogens such as Candida auris. High levels of resistance and mortality associated with MDR fungal pathogens dictate the need to discover and exploit new classes of antifungals that work by new mechanisms of action. Natural products represent a well spring of chemical diversity to support antifungal discovery. Therefore, one approach to discovering antifungals is high-throughput screening (HTS) of natural product libraries. Importantly, we need to effectively prioritize hits with a focus on new chemical classes with new mechanisms of action. A combination of yeast chemical genomics and computational metabolomics provides a way to prioritize hits that can illuminate new classes and new mechanisms. Chemical genomics enables the identification of key mechanism of action features, especially those that make a hit mechanistically novel. At the same time, computational metabolomics tools such as SIRIUS, NP Classifier, and GNPS help to extract chemical and structural information from liquid chromatography tandem mass spectrometry (LC-MS/MS) datasets and provide structural information to complement chemical genomics. Our results indicate that the combined application of CG and computational metabolomics provides a promising strategy for evaluating and prioritizing natural products with antifungal activities.

P-171 – Charles Veltri

Soluble Antidermatophyte Compounds Produced by *Chromobacterium vaccinii*

Alisha Harrison[1], Maria Lozoya[2], Luer Wang[3], Remy Kargodorian[1], Scott Soby[1], Charles A. Veltri[2]. [1]Biomedical Sciences Program, College of Graduate Studies, Midwestern University, Glendale, AZ 85308. [2]Department of Pharmaceutical Sciences, College of Pharmacy, Midwestern University, Glendale, AZ 85308. [3]College of Dental Medicine, Midwestern University, Glendale, AZ 85308

Fungal infections are an increasingly prevalent and serious global health care concern. Superficial infections caused by dermatophytes are the most common type of human fungal infections world-wide, with tinea pedis and onychomycosis as the most frequent clinical cases. Although new antifungal treatments have become available, the renal and hepatic toxicity of systemic antifungals and the emergence of resistance continue to be issues with the drug class. *Chromobacterium vaccinii*, a gram-negative betaproteobacterium isolate from cranberry bogs, produces fungistatic and mycodysplasic compounds that are correlated with quorum sensing (QS). *C. vaccinii* spontaneously produces QS receptor protein mutants (CviR$^-$) at low frequencies. Fungal growth inhibition is significantly reduced in *C. vaccinii cviR-*

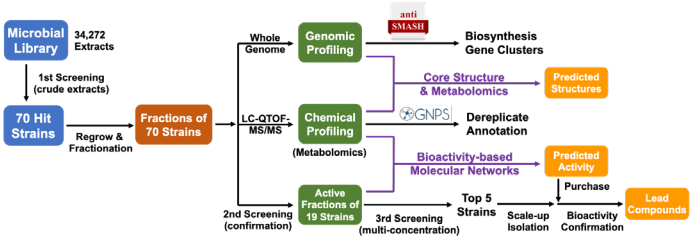
mutants, compared to wild type strains We will present data *C. vaccinii* and its QS mutant strain (cviR-) to produce differential soluble autoinducers and metabolomes to confirm the connection between a specific set of compounds and their effects on dermatophytic fungi.

P-172 – Fei Yang

"E-PurE" Platform of Drug Discovery from Microbial Library—Integrating Metabolomics, Genomics and High-throughput Screening for the Anticancer Drug Discovery Targeting KRAS Mutation

Fei Yang[1,2], Osama G. Mohamed[1,2], Pamela Schultz[1,2], Ashootosh Tripathi[1,2]. [1]Natural Products Discovery Core, Life Sciences Institute, University of Michigan, Ann Arbor, MI, USA, [2]Department of Medicinal Chemistry, College of Pharmacy, University of Michigan, Ann Arbor, MI 48109, USA

Repeated isolation and low efficiency have been the bottlenecks of the traditional activity-guided discovery from natural products. Based on our unique collection of microbial library, we have established a 3-dimensional E-PurE (**E**xtracts to **Pur**e **E**ntity) platform integrating the cutting-edge metabolomics, genomics, and high-throughput screening to dereplicate and speed up the identification and discovery of drug lead compounds. In particularly, this platform has been applied in the anticancer drug discovery targeting KRAS mutation, which consists of untargeted metabolomic analysis based on LC-QTOF-MS/MS, whole genomic profiling with pathway and structure prediction, and high-throughput screening with stepwise confirmation of bioactivity. In addition, standardized library generation, automated fractionation, and bioactivity/feature-based molecular network analysis are built-in to enhance the platform.

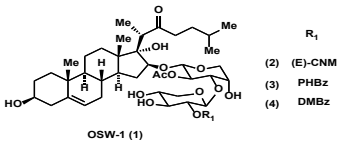


P-173 – Jorge Berrios-Rivera

Discovery of New Oxysterol-Binding Protein (OSBP)-Targeting Antiviral and Anticancer Compounds from Nature

Jorge L. Berrios-Rivera[1], Inès Forrest[2], Susan L. Nimmo[1], and Anthony W. Burgett[1]. [1]Department of Pharmaceutical Sciences, University of Oklahoma Health Sciences Center, 1110 Stonewall Ave., Oklahoma City, OK 73117. [2]Department of Chemistry, The Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA 92037

The natural product OSW-1 (**1**), isolated from the plant *Ornithogalum saundersiae*, has broad-spectrum antiviral and precision anticancer activity through targeting oxysterol-binding protein (OSBP) and OSBP-related protein 4 (ORP4). Multiple natural product compounds closely related to OSW-1 (**2-4**) have also been reported in the literature. However, these compounds have not been evaluated for OSBP or ORP4 binding, nor for antiviral or anticancer activity. We have isolated OSW-1 and related compounds from the plant material through improving the literature isolation protocol. Testing the biological activity of compounds **2-4** in OSBP and ORP4 binding assays, cellular assays, as well for antiviral and anticancer activity, will be reported. Determining the binding affinity to OSBP and ORP4 and the biological activity of these related OSW-1 compounds will provide further understanding of OSW-1 SAR and progressively guide the development of new OSBP- and ORP4-targeting compounds for pre-clinical drug development as novel antiviral and anticancer drugs.

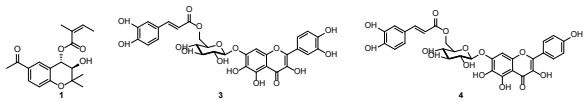


P-174 – José Alberto Gutiérrez-González

α-Glucosidase Inhibitors from *Ageratina grandifolia*

José Alberto Gutiérrez-González[1], Araceli Pérez-Vásquez[1], Rafael Torres-Colín[2], Manuel Rangel-Grimaldo[1], Daniela Rebollar-Ramos[1], Rachel Mata[1]. [1]Faculty of Chemistry, Universidad Nacional Autónoma de México, CDMX, 04510, [2]Biology Institute, Faculty of Chemistry, Universidad Nacional Autónoma de México, CDMX, 04510

The investigation of the aerial parts of *Ageratina grandifolia* led to the isolation of a new chromane, named 2,2-dimethyl-3*R*-hydroxy-4*S*-(1angeloyloxy)chromane (**1**), along with eight known compounds, including three flavonoids (**2–4**) and five chromenes (**5–9**). Compounds **1**-**9** were tested against α-glucosidase with IC_{50} values ranging from 0.79 to 460 μM (acarbose, IC_{50} = 300.0 μM). The most active compounds were **3**, and **4**. Kinetic analysis of **3** revealed its mixed-type inhibitor nature.

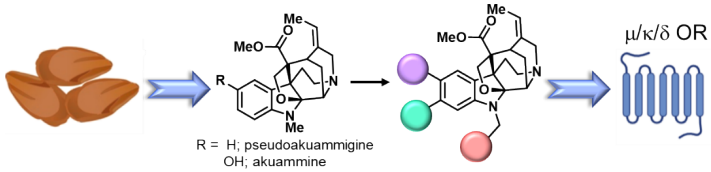


P-175 – Madeline Hennessy

Akuamma Alkaloids: From Seeds to Drug Leads

Madeline Hennessy [1], Anna Gutridge [2], Alexander French [2], Richard van Rijn [2-5], and Andrew Riley[1] [1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago [2]Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue [3]Purdue Institute for Drug Discovery, Purdue [4]Purdue Institute for Integrative Neuroscience, Purdue [5]Purdue Interdisciplinary Life Sciences Graduate Program, Purdue

For centuries, morphine and its semi-synthetic derivatives have been the cornerstone of pain management. While these clinically relevant drugs are excellent analgesics, their prolonged use can elicit severe, life- threatening side effects by the activation of the mu opioid receptor (μOR). To discover novel classes of opioid analgesics that might lack these side effects, we isolated six monoterpene indole alkaloids from the seeds of the akuamma plant (*Picralima nitida*). An unbiased screen of >45 central nervous system receptors revealed the akuamma alkaloids possess moderate opioid receptor affinity. Herein, we report the first structure-activity relationship studies of akuammine and pseudoakuammigine that probe how these alkaloids interact with the opioid receptors. Using chemoselective transformations a series of derivatives were prepared and evaluated at the opioid receptors. This new ligand class will be leveraged as chemical probes to study opioid receptor signaling and, ultimately, into new analgesic drug leads.

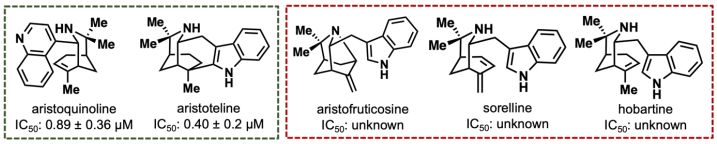


P-176 – Lisa Rusali

Accessing the *Aristotelia* Alkaloids for Addiction and Abuse

Lisa E. Rusali[1], Andrew P. Riley[1]. [1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612

Several alkaloids isolated from *Aristotelia chilensis*, including aristoquinoline and aristoteline, have recently been identified as antagonists of the α3β4 nicotinic acetylcholine receptor (nAChR), a promising target for the treatment of substance use disorders. Previous studies have identified more than 30 additional *Aristotelia* alkaloids, but their activity remains largely uninvestigated. Herein, we report biomimetic studies to synthesize these alkaloids, along with their analogues. We also present a preliminary evaluation of their functional activity at the α3β4 nAChR. This work will expand our understanding of the structure- activity relationships between the nAChRs and the azabicyclic core of the *Aristotelia* alkaloids. These results, in turn, will aid in developing highly potent and selective pharmacological probes to study the role of the α3β4 nAChR in substance use disorders.

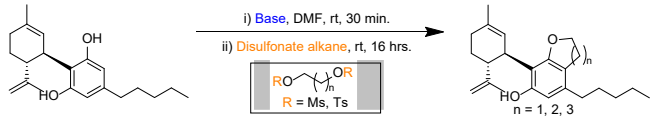


P-177 – Zach Stryker

Access to Previously Undescribed Cannabidiol Derivatives

Zach Stryker, Francisco Leon. Department of Drug Discovery and Biomedical Sciences, University of South Carolina, Columbia, SC, 29201, USA

Cannabidiol (CBD) derived from *C. sativa* has recently garnered much attention for its therapeutic non-psychoactive pharmacological effects. However, the efficacy of CBD remains limited due to poor specificity, potency, and oral bioavailability. Nevertheless, CBD derivatives may overcome many of the limitations associated with natural CBD and may be developed for the treatment of a variety of physiological conditions. Here we report a novel synthetic scheme generating CBD-derived dihydroxybenzofuranols and chromanols. Under basic conditions, the resorcinol ring generates a resonance structure capable of initiating nucleophilic substitution of ditosylated alkanes. This methodology may be extended to synthesize a wide array of heterocycles from resorcinol rings.



P-178 – Shuvendu Das

Functional Expression of human Cytochrome P450 (hCYP) in a Novel C1 Fungal Protein Expression System

Shuvendu Das[1, 2], Reid Hogan[1], Ronen Tchelet[3], Mark Emalfarb[3] and Mark Arnold[1, 2]. [1]Center for Biocatalysis and Bioprocessing, The University of Iowa, 2501 Crosspark Road, MTF-Suite C100, Coralville, IA 52241, USA, [2]Department of Chemistry, University of Iowa, Iowa City, IA 52242, [3]Dyadic International, Inc. 140 Intracoastal Pointe Drive, Suite # 404, Jupiter, Florida 33477

High protein yield (> 25 g/L) is a major challenge in the pharmaceutical industry, specifically to enhance the production of biologics, or of enzymes required for the chiral synthesis of small molecule drugs. A novel protein expression platform capable of such high production yields is under investigation. This expression system uses a proprietary strain of *Myceliopthora thermophila* fungal cells (C1) developed by Dyadic International for production of enzymes used by the biofuels industry. Recombinant protein is secreted by this C1 cellular factory, thereby producing a relatively clean supernatant product with demonstrated yields as high as 80 g/L for a single enzyme within a matrix of 100 g/L of total protein. We are interested in translating this C1 expression platform for pharmaceutical applications, including for the manufacturing of biologics, enzyme reagents and vaccines. We chose hCYP2D6 as a pharmaceutically important enzyme for this study. This presentation will focus on a

recombinant C1 strain engineered to produce the hCYP2D6 enzyme and to demonstrate its ability to mimic "human liver" drug metabolism. We have used a FDA approved drug, dextromethorphan, to confirm this activity. Our findings demonstrate how these C1 cells can mimic as a "microbial human liver" by metabolizing dextromethorphan to dextrorphan in 2 to 3 hours. As far our knowledge goes, this is the first report for the expression of hCYPs in a non-yeast fungal expression system.

P-179 – Giorgis Isaac

Integration of the Natural Product Atlas in Mass Spectrometry-Based de novo Discovery and Screening Applications

Giorgis Isaac,[1] Hans Vissers,[2] Jeff Goshawk,[2] Jeffrey A. van Santen,[3] and Roger Linington[3, 1] Waters Corporation, Milford, MA 01757, [2] Waters Corporation, Wilmslow, UK, [3] Department of Chemistry, Simon Fraser University, Burnaby, British Columbia V5A 1S6, Canada

The Natural Products Atlas (NP Atlas) is a database of microbial natural product structures. It was created by a consortium of data curators and is available as an open access resource to the natural product research community (www.npatlas.org) . NP Atlas contains information on microbially-derived natural products published in the peer-reviewed primary scientific literature. Here we have developed two different desktop versions of NP Atlas libraries that allow direct searching of high resolution UPLC-Tof and ion mobility mass spectrometry data against the NP Atlas database. The Progenesis QI version of NP Atlas library supports the de novo discovery workflow, and the UNIFI version of the library is designed for screening workflows. In a de novo discovery workflow, the NP Atlas library was utilized within Progenesis QI software to interrogate UPLC-Tof MS/MS data. This allowed de novo identification of compounds in microbial extract using exact mass, fragment ions, and isotopic distribution. The screening workflow was utilized within the UNIFI software, as it provides the opportunity to perform focused searches to generate quick identification. These focused searches can be performed against NP Atlas ID, or a search within genus, species, or organism type. Both versions of the libraries are batch search enabled, with initial compound identification based on precursor exact mass, theoretical fragments, and isotopic distribution scores. Following initial identification, a custom database containing exact mass, fragment ion, RT, isotopic distribution, and CCS (collisional cross section value derived from ion mobility experiment) can be created for future use or to construct a focused custom library that is specific to a given research project. If an ion mobility-enabled instrument is used to generate the data one can also generate experimental CCS values for all known and unknown precursor and fragment ions to increase the confidence of compound identification. Lastly, both versions of the library have direct links to compound NP Atlas and gives the opportunity to fully utilize the additional features available in the Web version of NP Atlas. These queries include cluster analysis, node analysis, and connections to the Biosynthetic Gene Cluster (MIBiG) repository, and the Global Natural Products Social Molecular Networking (GNPS) platform.

P-180 – Brian Murphy

Toward Antibiotic Discovery from a Bacterial Colony

Chase Clark, Sofia M. Costa*, Maryam Elfeki*, Jeongho Lee*, Antonio Hernandez, Rui Ma5, Linh Nguyen, Shrikant Mantri2, Nyssa Krull, Jin Yi Tan, Erin Conley, Emma Li, Karen John, Mario Augustinovic, Tatyana Ndweke, Sesselja Omarsdottir4, Stefan Green, Sanghyun Cho5, Ahmad Qudafi3, Scott G. Franzblau5, Nadine Ziemert2, Laura M. Sanchez6 and Brian T. Murphy Dept. Pharmaceutical Sciences, College of Pharmacy; University of Illinois at Chicago2 University of Tubingen3 Boys & Girls Club of Chicago4 University of Iceland5 Institute for Tuberculosis Research, UIC6 University of California Santa Cruz*

For nearly a century, the field of microbial natural products (NP) drug discovery has relied on cultivatable bacteria to supply the therapeutic lead pipeline. Thus, building libraries of cultivatable bacteria and their associated NPs has been this field's cornerstone since the 1930s. However, a major obstacle toward discovering new chemical space is the lack of strain diversity/high degree of strain duplication, which leads to NP redundancy in these microbial libraries. Further, many resources are invested in the process of fermenting, extracting, fractionating, analyzing, and screening NPs from a highly redundant library. This limitation has crippled discovery efforts in our field. To address this, we sought to design a discovery pipeline that reduced this redundancy and maximized the amount of information obtained from a single bacterial colony. Herein we present a summary of these efforts, which include design and implementation of the MALDI-TOF MS data acquisition and bioinformatics pipeline IDBac to streamline strain library creation, and implementation of a high-throughput robotics platform to screen environmental isolates on a custom 3D-printed dual-sided agar plate assay.

P-182 – Alex Swystun

Metallophore Production from Deep Arctic Marine Sediment Derived Bacteria Using Single Cell Culturing and High-Throughput Bioassay Methods

Alex Swystun[1], Margaret Walter[2], R. Thomas Williamson[1], Kevin Kiser[2], Blake Ushijima[2], Wendy K. Strangman[1] Department of Chemistry and Biochemistry[1], Department of Biology and Marine Biology[2], University of North Carolina Wilmington, Wilmington, NC 28409

Metal ions play many important roles in environmental chemical ecology and in human health. Acquisition of these often-scarce metals is critical for microbial survival and fitness. As a strategy for metal acquisition, many species of bacteria rapidly produce low molecular weight, metal-chelating natural products called

metallophores. The most widely studied group of these are iron-chelating siderophores. When metallophores bind to metals, their structures often change dramatically; this molecular structure change can be critical for bioactivity and future pharmaceutical applications. Using a series of deep arctic sediment cores and traditional culturing techniques, a preliminary library of 30 isolates was generated and screened for metallophore production. To increase bacterial diversity and improve culturing and assay efficiency, a microfluidic single-cell bacterial sorter was incorporated to isolate and culture individual bacterium from these samples. These micro-cultures were then assayed for production of metallophores using an automated liquid handling system with the goal of discovering new metallophores specific to a variety of metals including iron, zinc, and copper. Metal-specific chelators will be characterized and screened in a panel of bioassays to assess potential bioactivity to determine pharmaceutical potentials.

P-183 – Mohamed Ibrahim

Advancements Towards the Identificatory of an Orally Bioavailable, Brain-Penetrant Compounds with Selectivity for the Cannabinoid Type 2 Receptor

Ospanov M[1,2], Sulochana SP[3], Paris JJ[3], Rimoldi JM [3], Ashpole N[3], Walker L[1], Ross SA [1,3], Shilabin AG[4] & Ibrahim MA[1] [1]National Center for Natural Products Research, School of Pharmacy, The University of Mississippi, MS 38677, US. [2] Department of Chemistry and Technology of Organic Substances, Natural Compounds and Polymers, Al-Farabi Kazakh National University, al-Farabi ave. 71, Almaty, Kazakhstan [3] Department of BioMolecular Sciences, School of Pharmacy, University of Mississippi, MS, 38677, USA. [4]Department of Chemistry, East Tennessee State University, Johnson City, TN 37614, USA

Modulation of the endocannabinoid system (ECS) is of great interest for its therapeutic relevance in several pathophysiological processes. The CB2 subtype is largely localized to immune effectors, including microglia within the central nervous system, where it promotes anti-inflammation. Recently, a rational drug design toward precise modulation of the CB2 active site revealed the novelty of Pyrrolo[2,1-c][1,4]benzodiazepines tricyclic chemotype with a high conformational similarity in comparison to the existing leads. These compounds are structurally unique, confirming their chemotype novelty. In our continuing search for new chemotypes as selective CB2 regulatory molecules, following SAR approaches, a total of 24 selected (S,E)-11-[2-(arylmethylene)hydrazono]-PBD analogs were synthesized and tested for their ability to bind to the CB1 and CB2 receptor orthosteric sites. A competitive [^{3}H]CP-55,940 binding screen revealed five compounds that exhibited >60% displacement at 10 μM concentration. Further concentration-response analysis revealed two compounds, **4k** and **4q**, as potent and selective CB2 ligands with sub-micromolar activities (K_i = 146 nM and 137 nM, respectively). In order to support the potential efficacy and safety of the analogs, the oral and intravenous pharmacokinetic properties of compound **4k** were sought. Compound **4k** was orally bioavailable, reaching maximum brain concentrations of 602 ± 162 ng/g (p.o.) with an elimination half-life of 22.9 ± 3.73 h. Whether administered via the oral or intravenous route, the elimination half-lives ranged between 9.3 and 16.7 h in the liver and kidneys. These compounds represent novel chemotypes, which can be further optimized for improved affinity and selectivity toward the CB2 receptor. **Acknowledgements**: This work is supported by the National Institute of General Medical Science of the National Institute of Health under Award Number P30GM122733.

P-184 – Jonathan Jeyaraj

Molecular Networking of Secondary Metabolites from the Bioactive Chloroform Extract of *Dodonaea viscosa* ssp. *angustifolia* (Sapindaceae)

Jonathan G. Jeyaraj[1], Ines Castro Dionicio[1], Gerardo D. Anaya-Eugenio[1], Tran Ngoc Ninh[2], Djaja D. Soejarto[3,4], A. Douglas Kinghorn[1], and Esperanza Carcache de Blanco[1]. [1]College of Pharmacy, The Ohio State University, Columbus, Ohio 43210, [2]Vietnam Academy of Science and Technology, Hanoi, Vietnam, [3]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, [4]Science and Education, Field Museum, Chicago, IL 60605

Recent development of hyphenated techniques of mass spectrometry with chromatographic and spectroscopic methods has accelerated the screening, dereplication, and identification of potential biologically active novel drug leads from complex mixtures of phytochemical extracts. To identify qualitatively potential novel anticancer natural products and inactive constituents that are known or unknown, LC-MS fingerprints were generated using the Thermo Q-Exactive Orbitrap with Vanquish-H UHPLC. The fingerprints were completed on the chloroform extract and its bioactive fraction, from the Vietnamese flowering plant, *Dodonaea viscosa* Jacq. ssp. *angustifolia* (L.f.) J.G. West [Syn.: *Dodonaea angustifolia* L.f.] (Sapindaceae). This plant is used traditionally for sore throats, cold, fever, digestive issues, and malaria. Global Natural Product Social Molecular Networking (GNPS) and MZmine were utilized for analysis of the data being presented and to confirm the isolation of active secondary metabolites from *D. viscosa*.

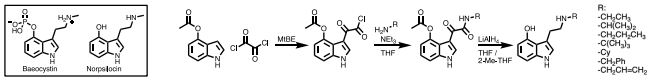
P-185 – Alexander Sherwood

Synthesis of Norpsilocin Derivatives for Pharmacological Evaluation

Elise K. Burkhartzmeyer and Alexander M. Sherwood. Department of Medicinal Chemistry, Usona Institute, Madison, WI 53711

The study of *Psilocybe* "magic mushroom" tryptamine natural products psilocybin, psilocin, baeocystin, and norpsilocin has raised questions about the influence of their terminal amine

substituents on pharmacological activity. Previous observations in rodents have indicated that baeocystin lacked central nervous system (CNS) activity despite potent *in vitro* activity at the serotonin 2A receptor for its dephosphorylated metabolite norpsilocin. We hypothesized that the secondary methylamine in norpsilocin rendered the compound too polar to pass the blood brain barrier (BBB) to elicit CNS effects. This research aims to explore structure activity relationships for a series of norpsilocin derivatives featuring differing substitutions at the terminal amine position to improve CNS bioavailability. Eight novel norpsilocin derivatives were synthesized by a 3-step process from 4-acetoxyindole. The products were fully characterized and obtained with UPLC purity of 96.3 % - 99.6 % by peak area. The calculated partition coefficient (cLogP) for each compound was determined to infer potential BBB penetrability. The compounds are being screened to determine CNS-receptor binding profiles and behavioral properties rodents.



P-186 – Aleksandra Gurgul

Acetogenins and Other Constituents of *Uvaria rufa* (Annonaceae)

Aleksandra Gurgul, Chun-Tao Che, Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, 60612, IL, United States

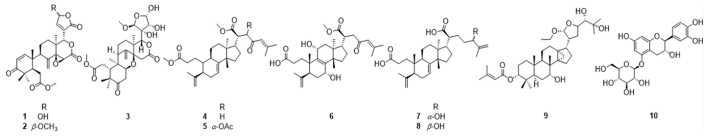
Annonaceae is a large plant family distributed mainly in tropical and subtropical regions. Previous reports have shown a variety of chemical constituents and pharmacological activities of the extracts and compounds of the Annonaceae species. Of particular interest are the Annonaceous acetogenins, polyketide compounds showing strong cytotoxic activity and promising anticancer potential. This project focuses on phytochemical investigation of *Uvaria rufa* Blume from the Annonaceae family. A crude methanolic extract was partitioned and further separated using open column chromatography and semi-preparative HPLC. Structure elucidation of the isolated compounds was performed based on the spectroscopic methods. Compounds belonging to the class of polyoxygenated cyclohexene derivatives, flavonoids and lignans have been identified so far. Most importantly, the representatives of the acetogenin class have been purified as well. To the best of our knowledge, this is the first report of acetogenins from *U. rufa*. The ultimate goal of this study is to identify compounds with new structures and bioactivities. The isolates will be tested for their biological activities, including cytotoxic activity against cancer cells.

P-187 – Aleksandra Gurgul

Chemical Constituents of *Entandrophragma Angolense* and their Activities

Isoo Youn[1], Aleksandra Gurgul[1], and Chun-Tao Che[1].
[1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612

From the stem bark of *Entandrophragma angolense,* ten undescribed compounds were isolated, including limonoids, *seco*-tirucallanes, a glabretal triterpenoid, and a catechin glucoside, along with thirty known structures. All structures were determined by interpretation of spectroscopic and HRMS data, and absolute configuration was confirmed with the aid of electronic circular dichroism. The isolated compounds were tested for LPS-induced NO inhibition in RAW 264.7 macrophages and cytotoxicity assay against cancer cell lines.



P-188 – Cody Earp

Isolation and Characterization of Anti-malarial Compounds from Fungal Isolates

Kristof B. Cank[1], Cody E. Earp[1], Robert A. Shepard[1], Huzefa A. Raja[1], Adriana A. Marin,[2] Steven P. Maher[2], Dennis E. Kyle[2], Blaise A. Darveaux,[3] Cedric J. Pearce[3], Nicholas H. Oberlies[1]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27402-6170, [2] Center for Tropical and Emerging Global Diseases, University of Georgia, 335 Coverdell Center 500 D.W. Brooks Drive, Athens, GA, 30602-7399, [3] Mycosynthetix Inc., Hillsborough, NC, 27278

The primary focus of the Oberlies lab has been on the isolation and identification of cytotoxic compounds from fungal sources, and a new project focuses similar resources towards antimalarial leads. This disease is caused by *Plasmodium falciparum* parasites transferred to humans from infected female *Anopheles* mosquitoes. Infection is widespread across Africa, South America, and Southeast Asia with 241 million cases and 627,000 deaths reported in 2020. The fungal library at Mycosynthetix was screened for antimalaria activity. Of the 40,000 fungal samples screened, 1227 showed greater than 33% inhibition, and 149 showed greater than 67% inhibition. Of those 149, 71 were selected for high priority based on anti-malarial activity and minimal cytotoxicity. The extracts of these fungi were subjected to initial purification using flash chromatography, and daughter fractions were then tested for antimalarial activity. Of the 71 active fungal samples, 107 daughter fractions from 45 parent extracts displayed high anti-malarial activity. These fractions were then analyzed by mass spectrometry and compared to an in-house database for initial dereplication. Purified compounds were sent for activity testing to determine the source of the activity. So far 11 compounds have been found to have unreported antimalarial activity from seven fungal samples. Future work will involve processing the rest of the active extracts in order to uncover novel malaria treatments.

P-189 – Annika Jagels

Myropeptins C-E: Genome Mining, Isolation, Structure Determination, and Bioactivity of Lipopeptides from the Fungus *Myrothecium inundatum*

Annika Jagels[1,3], Donovon A. Adpressa[4], Elizabeth N. Kaweesa[1,3], Mark McCauley[1,3] Benjamin Philmus[5], James A. Strother[2,3], Sandra Loesgen[1,3], [1]Department of Chemistry, [2]Department of Biology, University of Florida, [3]Whitney Laboratory for Marine Bioscience, St. Augustine, FL 32080, [4]Loxo Oncology/Lilly, Louisville, CO 80020, [5]Department of Pharmaceutical Sciences, Oregon State University, Corvallis, Oregon 97331

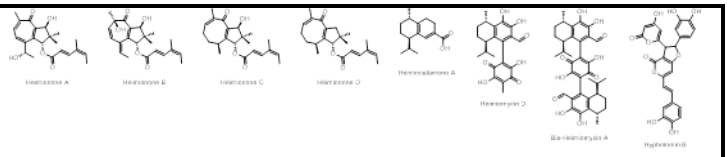
The saprotrophic filamentous fungus *Myrothecium inundatum* represents a chemically underexplored species despite the large number of putative biosynthetic gene clusters found in its genome. Here, we present three new linear lipopeptides along with one known analogue from non-genetic gene activation experiments using nutrient and salt variations. Structures were determined by extensive analysis of NMR and HRMS data, their absolute configuration established by Marfey's analysis, and their helical behavior assessed by ECD. A panel of *in vitro* and *in vivo* assays was employed to examine their biological and cellular mode of action. Myropeptins exhibit congener specific potent, low micromolar cytotoxic activity based on membrane depolarization. Additionally, we identified the putative myropeptin biosynthetic gene cluster consisting of type I PKS and NRPS modules in the fungal genome.

P-190 – Sebastian Pfütze

Chemical Diversity of Sesquiterpenoids Produced by *Heimiomyces* sp.

Sebastian Pfütze[1], Atchara Khamsim[1], Frank Surup[1], Marc Stadler[1]. [1]Department of Microbial Drugs, Helmholtz Centre for Infection Research GmbH, Inhoffenstraße 7, 38124 Braunschweig, Germany

With Heimionone A-E, new terpenoids with unprecedented bicyclo [5.3.0] decane and uncommon [6.3.0] undecane sesquiterpenoids were isolated from shaking cultures of *Heimiomyces* sp., respectively. Furthermore, new calamene-type sesquiterpenoids Heimiocalamene A and B were observed. The metabolite pattern largely changed when the fungus was cultivated in rice standing cultures and novel meroterpenoides Heimiomycin D-E and Bis-Heimiomycin A-D were isolated. Additionally, previously described compounds Hispidin, Hypholomin B, Heimiomycin A and B were observed. Heimionones A and C, Heimiocalamene B, as well as meroterpenoids Heimiomycin D and Bis-Heimiomycins B-D display weak cytotoxic effects against cell lines KB3.1 and L929, respectively.



P-191 – Hadi Pourhadi

Identification of Sporogenic Metabolites from Strains of *Aspergillus flavus* and Close Relatives

Hadi Pourhadi[1], Manuel R. Grimaldo[1], Huzefa A. Raja[1], Tyler N. Graf[1], E. Anne Hatmaker[2,3], Sonja Knowles[1], Rafael W. Bastos[4], Gustavo H. Goldman[4], Antonis Rokas[2,3], Nicolas H. Oberlies[1]. [1]Depatment of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, USA, [2]Department of Biological Sciences, Vanderbilt University, Nashville, TN, USA, [3]Evolutionary Studies Initiative, Vanderbilt University, Nashville, TN, USA, [4] Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil

Aspergillosis and fungal keratitis are two of the most prevalent diseases affecting immunocompromised individuals. These diseases are caused by inhalation of spores or through small wounds on the eye's surface. *Aspergillus flavus* is commonly isolated from patients and is considered as the second leading cause of invasive aspergillosis. Hence, *A. flavus* and close relatives have gained considerable attention in recent years. In this project, we worked with seven strains of the Flavi family (*A. flavus* NRRL 501 and NRRL 1957, *A. parasiticus* NRRL 502 and NRRL 2999, *A. arachidicola* IC26645 and IC26646, *A. nomiae* NRRL 6108) to gain insights into their metabolomic profile. The growing conditions for all the strains were carried out on oatmeal media at 37 °C in the dark. Our investigation focused on the production of fatty acids as the main compounds in all strains, particularly PSI A and PSI B. These metabolites, along with other linoleic acid derivatives, have been reported as sporogenic under the same growing conditions. Such metabolites could be related to the virulence of these strains.

P-192 – Jan-Peer Wennrich

Screening for Biologically Active Agents from Nematode-Associated Fungi

Jan-Peer Wennrich[1], Frank Surup[1], Natalia A. Llanos-Lopez[1], Soleiman E. Helaly[1], Samad Ashrafi[2], Wolfgang Maier[2], Marc Stadler[1]. [1]Department of Microbial Drugs, Helmholtz Centre for Infection Research GmbH (HZI), Braunschweig, Germany.[2]Institute for Epidemiology and Pathogen Diagnostics, Julius-Kühn-Institute Federal Research Institute for Cultivated Plants (JKI), Braunschweig, Germany

Fungi are capable of producing a tremendous diversity of natural products with interesting biological properties, and therefore represents a promising source of new active principles for antibiotic development. This study focuses on nematode-associated fungi, which are isolated from eggs of cyst nematodes, a worldwide pathogen which causes significant losses in agricultur. Based on their sedentary lifestyle, these nematodes are

good targets by parasitism. In some of these interactions, it's associated with the production of nematicidal compounds beside other biologically active secondary metabolites. Some of these compounds could be starting points for the development of antibiotics, pesticides or several other therapeutics. Herein, strains of interest were collected in a recent survey of the cyst nematode *Heterodera filipjevi* from wheat fields in Turkey. Using the state of the art isolation technique, established by our collaboration partners, several new genera and nematode-associated fungi have been found. Moreover, these isolates are currently investigated for the production of secondary metabolites with HPLC-DAD/MS. Promising candidates were selected and after optimization of culture conditions, novel natural products were isolated and characterized by high-resolution mass spectrometry (HR-MS) and nuclear magnetic resonance (NMR) spectroscopy.

P-193 – Menny Benjamin

The Design and Synthesis of Novel Classes of Broad-Spectrum Inhibitors of SARS and MERS Coronaviruses Targeting the Methyltransferase (2′-O-MTase, Nsp10-Nsp16) Viral Protein

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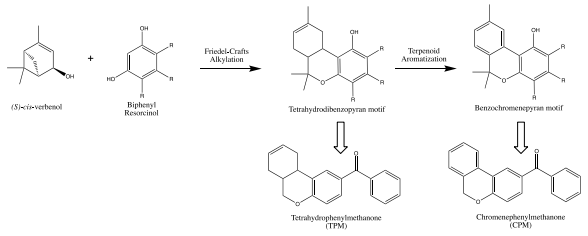
Novel biphenylpyran (BPP) ring systems were chemically synthesized based on *in silico* binding affinities to the 2′-O-MTase protein in SARS-CoV-2 (-9.8 kcal/mol), SARS-CoV (-9.6 kcal/mol), and MERS-CoV (-9.7 kcal/mol). A biphenyl resorcinol was reacted with *(S)-cis*-verbenol via Friedel-Crafts alkylation to produce the tetrahydrophenylmethanone (**TPM**) ring system with a tetrahydrobenzopyran core motif. A secondary reaction followed to aromatize the terpene ring, resulting in the chromenephenylmethanone (**CPM**) ring system with a benzochromenepyran core motif. *In vitro* assays using **TPM** and **CPM** BPPs demonstrated high efficacy against SARS-CoV-2 (98.9% inhibition), as well as no cytotoxicity (>100 μM). Protein-ligand assays are planned for target-validation and assessment of potential off-target effects.



P-194 – Austin Lowry

Creating New Chloramphenicol Derivatives Via a Semi-Synthetic Approach

Austin C. Lowry, Andrew N. Lowell, Department of Chemistry at Virginia Tech

To fight against pathogenic bacteria that have developed resistance to various antibiotics, developing new derivatives from existing scaffolds provides an avenue to next generation of antibiotics that are effective against these resistant pathogens. One antibiotic of interest for derivatization is the broad-spectrum antibiotic chloramphenicol. Chloramphenicol has become a drug of last resort due to its toxicity but synthetic derivatives have shown to be just as effective without being as toxic. We are applying new methodologies to create chloramphenicol derivatives semi-synthetically. This approach allows us to reduce the number of synthetic steps while synthesizing chloramphenicol derivatives with a diverse range of functionality. Previous studies have shown the importance of the diol and dichloro-group. Using this knowledge and investigating ribosomal co-crystal structures allows us to focus on modifying other sites in order to improve activity.

P-195 – Raveena Gupta

Metabologenomic Identification of Bioactive Natural Products and their Biosynthetic Machinery in Fungi using High Throughput Screening

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Fungi are a hyper-diverse group that biosynthesizes natural products (NPs) with a high promise for new bioactivity. Big Data approaches seeking to combine complementary -Omics datasets have the potential to efficiently tap into the underexplored biosynthetic potential of fungi. We recently completed a study in which we correlated biosynthetic gene cluster (BGC) and NP profiles from 111 fungi and revealed thousands of new NP-BGC pairs awaiting discovery. To focus efforts towards the most high-value NP/BGC pairs, we use bioactivity as a key filter to prioritize relevant extracts for further analysis. As a starting point, we tested fungal extracts against a panel of cancer cells via high throughput screening and subsequently used correlative biochemometrics analysis to link bioactivity to a family of NPs contained in our most bioactive strains. Using metabologenomics, we identified the BGC most likely to encode those compounds with bioactivity. Targeted studies are now underway to identify these NPs and dissect their biosynthetic pathways. In addition, we are also screening for anthelmintics in a worm model to discover high-value pharmacophores and identify their molecular target(s).

P-196 – Steven Chamberlin

Untargeted Transcriptomic Analysis of the Effects of *Centella asiatica* in Cortical Neurons

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The water extract of the Ayurvedic plant *Centella asiatica* (CAW) can increase synaptic plasticity and cognitive function, although the exact mechanism by which this occurs is not fully understood. To further explore potential mechanisms of actions we investigated transcriptomic changes that occur in primary cortical neurons treated with CAW or combinations of its constituent compounds. Mouse primary cortical neurons were treated with CAW or 3 different groups of constituent compounds: triterpenes (TT), caffeoylquinic acids (CQA), combined TT and CQA (TT+CQA) at concentrations equivalent to their presence in CAW. Samples were analyzed by RNA-seq. Differential gene expression analyses comparing each of the four treatment groups to control show 2,667 genes that were significantly altered by CAW, 198 for CQA, 1,760 for TT, and 981 for combined TT+CQA. All differences were significant after FDR adjustment. Pathway and network context evaluation is ongoing. While previous work has focused on TT and CQAs as active CAW compounds, the current findings indicate the presence of other active compounds in CAW, as well as potential interactions between the TT and CQA compounds.

P-197 – Kadine Cabey

Withania Somnifera (WS) Extracts Exhibit Extract-Dependent Neurotropic Activities

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The major bioactive compounds of the Ayurvedic herb *Withania somnifera* (WS) associated with cognitive enhancement are believed to be the withanolides, in particular Withaferin A and Withanolide A. It is unknown whether other compounds also mediate these effects. Here we compared the chemistry and neurotropic effects of WS extracts made from different accessions and plant parts. The phytochemical composition of water (WSAq) and 70% ethanol (WSE) extracts of WS was determined. Effects on gene expression and dendritic arborization were evaluated in mouse primary neurons and effects on age-related changes in phototaxis were evaluated in *Drosophila melanogaster*. WSE had approximately 10 times higher levels of withanolides than WSAq. However, WSAq induced gene expression changes and dendritic arborization whereas WSE did not. While both WSAq and WSE improved phototaxis in *Drosophila*, WSAq was effective at lower concentrations. The disparate observations between measured withanolide levels and biological activity suggest that the bioactive principles of the extracts warrant further investigation.

P-198 – Nicholas Chiaramonti

In vivo and *in vitro* Evaluation of Neuroprotective Capacity of Natural Soft Electrophiles

Nicholas I. Chiaramonti, Lukasz Ciesla. Department of Biological Sciences, University of Alabama, Tuscaloosa, AL, 35487

Parkinson's disease (PD) is the second most prevalent neurodegenerative disease and—together with other neurodegenerative diseases—has emerged as one of the greatest medical challenges of the 21st century. The PD pathogenesis is mostly unknown, and currently, no preventions or cures are available or in sight. Numerous recent epidemiological studies have shown that people consuming a diet rich in flavonoids, a subclass of polyphenolic specialized plant metabolites, have been less likely to develop PD. The mechanism by which flavonoids prevent or delay the onset of PD is unknown. Many biologically active flavonoids contain an electrophilic α,β-unsaturated carbonyl group similar to anti-inflammatory oxidation products of essential ω-3 fatty acids. We hypothesize that the α,β-unsaturated carbonyl moiety plays an important role in the neuroprotective potential of flavonoids. Herein we demonstrate the neuroprotective potential of selected natural soft electrophiles in a *Drosophila* model of PD. Further, we apply *in vitro* reactivity assessments to prove the ability of several neuroprotective flavonoids to non-enzymatically interact with cysteine thiolate ions via thia-Michael addition reactions. Lastly, we explore the capacity of xanthohumol (a prenylated chalcone and natural soft electrophile) to interact with cysteine residues in human Keap1 protein *in vitro*. These studies seek to improve our understanding of the molecular mechanism of neuroprotection by natural electrophiles such as flavonoids.

P-199 – Marsha Pierce

Evaluation of Manzamine Compounds for Neuroactivity and Neuritogenesis in Murine Primary Cortical Cultures

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Marine organisms produce a wide variety of primary and secondary metabolites with unique scaffolds that are biologically active. Manzamines are marine-derived polycyclic alkaloids. Approximately 100 manzamine-type alkaloids have been isolated from 16 marine sponge species, and some of these compounds are reported to have anti-inflammatory and neuritogenic properties. The goal of this study was to screen a subset of the manzamine compounds to identify novel neuroactive marine natural products for potential neuroscience drug development. Calcium activity plays an important role in neurite outgrowth and connectivity, so we screened using FLIPR high-throughput assays. Minimal effects were observed on frequency and amplitude of calcium oscillations at 10 micromolar concentration, suggesting the manzamines do not directly modulate ion channels. Initial neurite outgrowth screens identified seven of the 21 compounds evaluated as potentially neuritogenic, based on total neurite outgrowth and complexity. Neurite outgrowth assays identified the following compounds for further analyses: manzamine A, 8-methoxymanzamine A, 12-propoxymanzamine A, 12-isobutoxymanzamine A, ATL 2-97, ircinin-1, and palinurin. Currently, we are assessing dose-response curves in neurite outgrowth assays for these compounds. Future directions include live-dead assays with propidium iodide and fluorescein diacetate using a dose-response curve to assess for neurotoxicity, and further analysis on potential pathways that may be contributing to neuritogenesis. Together, these studies will help identify novel neuroactive manzamine compounds for the marine natural products preclinical pipeline.

P-200 –Mary Foglio

Arrabidaea Chica for Oral Mucositis in Patients with Head and Neck Cancer: A Pilot Randomized Clinical Trial

Núbia de Cassia Almeida Queiroz[1], Michelle Pedroza Jorge[2],Ilza Maria de Oliveira Sousa[2], Carmen Silvia Passos Lima[1], Eduardo Baldon Pereira[1],João Ernesto de Carvalho[2], Tais Freire Galvao[2], Mary Ann Foglio[2]. [1]Faculty of Medical Sciences, State University of Campinas, Sao Paulo, Brazil, [2]Faculty of Pharmaceutical Sciences, State University of Campinas, Sao Paulo, Brazil

Oral mucositis (OM) jeopardize patients' quality of life (QoL) treated for head and neck cancer-undergoing chemotherapy with a platinum derivative, concomitant with radiotherapy. Herein a pilot randomized clinical study is reported that evaluated the therapeutic effect of a 2.5% standardized *Arrabidaea chica* extract gel to treat the side effects compared to low-level laser therapy applied on the affected area during 40 s with infrared radiation at 808 nm (positive control). The test group (TG) (n 5) received *SACEG* whereas the control group (CG) received low- level laser (n 6). The outcome considered the number of days to heal mucositis defined as the mean mucositis score in radiation-induced OM, occurrence of OM, pain, QoL, and adverse effects. No significant group differences occurred in the mucositis score, pain, or QoL. Mucositis occurrence rates were higher in the control group compared with the SACEG group (9.2 days for SACEG and 16.4 days for CG). No adverse effects occurred in either group. The benefit of using SACEG is the convenience of in-house treatment. This protocol is registered at Brazilian Registry of Clinical Trials number CAAE: 55933516.3.0000.5404 from July 2017 until November 2019. Acknowledgements: FAPESP; CNPq, and CAPES agencies.

P-201 – Lee Bum Soo

Ultra-Intimate Hydrogel Hybrid Skin Patch with Asymmetric Elastomeric Spatula-like Cylinders and a Natural Anti-Atopic Agent, Maltol

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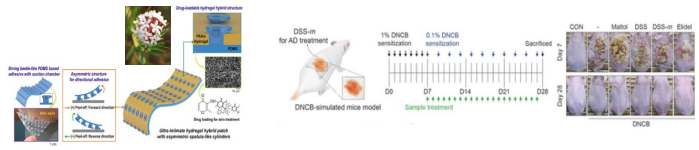
Intelligent bioinspired adhesive devices are attracting attention as a tool for the treatment of various skin diseases. Fully compliant skin contact is crucial for consistent effective therapy through a transdermal interface, for which structured materials for an intelligent adhesion should be developed. It is also important to design such skin patch with non-invasive, human-friendly treatment material and small structural interface for effective treatment of skin disorder. Herein, we fabricated the asymmetric elastomeric adhesive structures that mimics the spatula-like setae of diving beetles capable of directional adhesion and nanoporous hydrogel. Our hybrid skin patch devices demonstrated reversible and directional adhesion to the complex skin surface, while allowing a natural anti-atopic agent, maltol-containing hydrogel to be in ultra-intimate contact with the non-flat skin with hierarchical roughness. With the aid of diving beetle-inspired adhesive, this extraordinary conformal hydrogel interface provides an efficient strategy for the treatment of skin diseases such as atopic dermatitis.



P-202 – Zhenjian Lin

Non-Peptidic Small Molecule Components from Cone Snail Venoms

Zhenjian Lin[1], Joshua P Torres[1], B. Duygu Özpolat[2], Maren Watkins[3], Baldomero M Olivera[3] and Eric W Schmidt[1], [1]Departments of Medicinal Chemistry and Biochemistry, School of Biological Sciences, University of Utah, Salt Lake City, UT, United States. Marine Biological Laboratory, Woods Hole, MA 02543, USA. [3]School of Biological Sciences, University of Utah, Salt Lake City, UT 84112, USA

Venomous animals hunt using bioactive peptides, but relatively little is known about venom small molecules and the resulting complex hunting behaviors. Here, we show that the small molecules found in the *C. imperialis* venom gland are deployed as part of a complex worm-hunting behavioral strategy. We define the chemical structures of several unique small molecules from the *C. imperialis* venom gland and demonstrate that the compounds act as metabolically stable mimics of prey pheromones. The major compounds, conazoliums A and B, are synthesized by epithelial cells in the venom gland. We show that diverse, bioactive small molecules are present in the colored portion of the glands. In a model polychaete, the compounds induce mating behaviors, revealing that they act as pheromones in the predatory strategy. This work demonstrates a role for small molecules in the cone snail venom, reveals that these compounds are structurally diverse yet species specific in distribution, and unveils a complex prey capture strategy in cones.

P-203 – Seo Yeon Seonu

Anti-inflammatory Effects through Inflammasome Inhibition of Bioconversion Product from Korean Traditional Medicinal Plants

Seo Yeon Seonu[1], Eun Bin Kim[1], Min Won Lee[1], [1]Laboratory of Pharmacognosy and Natural Product Derived Medicine, College of Pharmacy, Chung-Ang University, Seoul 06974, Korea*

Acanthopanax and *Kalopanax* species (*Araliaceae*) have widely distributed in Korea and have been used in traditional medicine to treat rheumatoid arthritis. Bioconversion refers to a technology that converts existing materials using biological reactions of microorganisms such as enzymes and strains and is known to increase the content of active ingredients through biotransformation which decomposes sugar bound of glycoside to a dividend into an aglycone by replacing it with a hydrogen atom. Bioconversion of *Acanthopanax sessiliflorus* (AS) and *Kalopanax pictus Nakai* (KP) was performed through Pectinex 3days 37℃ (EAS and EKP). The TLC and HPLC showed that content of glycoside (acanthoside D, **1**) was decreased and the aglycone (syringaresinol, **2**) was increased after enzymatic hydrolysis in EAS and content of kalopanaxsaponin B (**3**) was decreased and kalopanaxsaponin I (**4**) was increased after enzymatic hydrolysis in EKP. Recently, various types of inflammasome have been studied, of which NLRP3 complex is considered very important as a treatment target for inflammatory diseases. NLRP3 inflammasome consists of a sensor (NLRP3), an adaptor (ASC) and an effector (caspase-1). The inflammatory activities on EAS and EKP showed the decrease of inhibitory activities of NLRP3, Caspase-1 and ASC compared with control groups in western blot assay. Therefore, bioconversion of EAS and EKP might have effect on inflammatory diseases such as arthritis.

P-204 – Dhammika Nanayakkara

Natural Molluscicides to Control the Intermediate Host Snails for the Trematode *Bolbophorus damnificus* in Catfish Aquaculture

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The digenean *Bolbophorus damnificus* infection causes substantial economic loss to catfish aquaculture in Mississippi and Louisiana. The catfish acquires the infection from the intermediate hosts, ram's horn snails (*Planorbella trivolvis*) and the invasive snail, *Biomphalaria havanensis,* which are prevalent in catfish production ponds. The infection is currently controlled by reducing snail population mainly by using copper sulfate. Even though copper sulfate is effective in controlling snail population its usefulness is limited due to its accumulation in the environment, toxicity towards phytoplankton, and small margin of safety between molluscicidal and ichthyotoxic concentrations. The objective of this study is to identify inexpensive natural molluscicides with limited toxicity to fish and phytoplankton. Saponins have been shown to possess potent molluscicidal activity. We evaluated the molluscicidal activity of five commercially available saponin extracts from plants (tea, alfalfa, yucca, English ivy, soya) listed by the US Food and Drug Administration as generally recognized as safe (GRAS). One of these commercial extracts showed potent molluscicidal activity and the major compounds isolated from this extract showed activity comparable to that of copper sulfate. The molluscicidal activity of these extracts and compounds and their structure activity relationships will be presented.

P-205 – Danika Boltz

Evaluation of Basil (O*cimum* Spp.) Leaf Extract Minimum Inhibitory Concentrations Against Methicillin-Resistant *Staphylococcus Aureus*

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The *Ocimum* genus, commonly known as basil or Tulsi, is a well-known herb commonly found in culinary dishes as well as personal health and beauty products. With over 150 cultivars distributed across several species, different cultivars have potentially unique chemical profiles that contribute to their biological activity, which includes antimicrobial activity. In this study, leaf extracts from seven different cultivars within three species of basil were prepared using aqueous methanol. Minimum inhibitory concentration assays tested each extract against methicillin-resistant *Staphylococcus aureus* (MRSA, CDC strain 681) to determine the antimicrobial activity. Average MIC values ranged from 312 μg/mL to 1250 μg/mL, revealing

substantial differences between species and cultivars. Metabolome profiling suggested metabolite differences that vary between taxonomically-similar groupings could be responsible for the range of MIC values, and have a large impact on the bioactivity and health properties of the plant.

P-206 – Wook-Bin Lee

Lithospermum erythrorhizon Extract Reduces the Severity of Endotoxin-Induced Uveitis

Tae Kyeom Kang[1], Kyung-A Kim[2], Young-Joo Kim[1], Sang Hoon Jung[1,3], Wook-Bin Lee[1*] [1]Natural Product Research Center, Korea Institute of Science & Technology, Gangneung 25451, Republic of Korea. [2]Division of Medical Oncology, Yonsei Cancer Center, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea [3]Division of Bio-Medical Science & Technology, KIST School, Korea University of Science and Technology, Gangneung 25451, Republic of Korea*

Recent studies have reported the anti-inflammatory effect of *Lithospermum erythrorhizon.* We investigated the effect of ethanol extract of *Lithospermum erythrorhizon* (EELE) on endotoxin-induced uveitis (EIU) in rats and mice. In addition, the endotoxin-induced expression of pro-inflammatory cytokines and activation of transcription factor IRF and NFκB were investigated in human monocyte reporter cell lines (THP1) treated with EELE in vitro, to clarify the anti-inflammatory effect. Endotoxin-induced uveitis was induced in rat and mice by a footpad injection of lipopolysaccharide (LPS). EELE (10 mg/kg) was daily administered for 7 days before LPS injection. After 24 hours of LPS injection, clinical severity and retinal vessel thickness were evaluated. THP1-Blue-ISG and THP1-XBlue cells pretreated with EELE were incubated with LPS for 24 hours. Level of TNFα, IL-6 and IL-8 expression and activation of IRF and NF-κB were investigated. Clinical severity and retinal vessel thickness were significantly decreased in EELE-treated rat than in control group ($P < 0.001$, $P = 0.0167$). EELE down-regulated the production of TNFα, IL-6 and IL-8. And EELE treatment suppressed the activation of NFκB/AP1 and IRF. Orally administrated EELE alleviated the ocular inflammation. These findings demonstrate that EELE could be an effective agent for the control of endogenous ocular inflammatory disease.

P-207 – Eun Jin Park

Insulin Mimetic Activity of 23-Glycosyl Oleanane Triterpenoids Isolated from Gymnema latifolium

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Chemical investigation of the plant *Gymnema latifolium* Wall. ex Wight led to the isolation of seven new 23-glycosyl oleanane glycosides gymlatinosides GLF1-GLF7 (**1**-**7**) and two known compounds gymnemosides D and E (**8** and **9**). The structures of the isolated compounds were elucidated using diverse spectroscopic methods. The extract of *G. latifolium* and all isolated compounds **1–9** enhanced significantly glucose 2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) amino]-2-deoxyglucose (2-NBDG) uptake at 20 μM in 3T3-L1 adipocyte cells. Among them, compounds **2** and **4** showed particularly potential stimulatory effects on glucose uptake in a dose-dependent manner. Further investigation revealed that compounds **2** at 20 μM up-regulated the expression of the phosphorylated AMPK (*p*-AMPK). The results suggested that isolated compound **2** may enhance glucose uptake by regulating the AMPK signaling pathway.

P-208 – Lukasz Cielsa

Dietary Flavonoids – Improbable Metabolic Panaceas or Potentially Essential Soft Electrophiles?

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Phytochemicals abundant in plant-rich diets, have been linked to beneficial and disease-preventive effects of dietary approaches. Numerous recent epidemiological studies have shown that people consuming a diet rich in flavonoids have been less likely to develop neurodegenerative diseases. Despite many years of research on flavonoids, none of the investigated compounds has been successfully registered as a drug. This has led to the classification of these compounds as invalid/improbable metabolic panaceas (IMPs) lacking drug-like characteristics. Additionally, flavonoids have been often classified as pan-assay interference compounds (PAINs) due to their ability to interact with numerous targets in *in vitro* assays. We will present data indicating that certain classes of flavonoids together with *n*-3 fatty acid oxidation products play important role in cellular signaling. These soft electrophilic molecules modulate cellular activity through non-enzymatic post-translational modifications, previously mostly considered as indicators of oxidative/metbolic stress and disease. We will also discuss the possibility of considering certain flavonoids as important or even essential nutrients rather than pursue the development of these molecules as drugs.

P-209 – Devadoss Samuvel

Platanosides (PTS) Decrease Acetaminophen (APAP) Hepatotoxicity by Inhibition of Keap1/NRF2 Complex Formation, c-Jun *N*-terminal Kinase (JNK) Activation and JNK/Sab Interaction

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In this study, we investigated the potential utility of PTS isolated from American sycamore trees in decreasing APAP hepatotoxicity and the mechanisms of action. Mice received APAP (300mg/kg, i.p.) were treated with PTS (isoforms *EE*, *ZZ*, *EZ*, *ZE* 1.9:1.0:1.1:0.5;10mg/kg, *ig*.) immediately (0h) or 2h after APAP. PTS treatment at 0h markedly decreased necrotic areas from 46% to 23% and serum ALT from 11,200U/L to 2,750U/L. PTS and *N*-acetyl-cysteine (NAC, 300mg/kg, ip) treatment at 2h after APAP decreased necrotic areas to 20% and 19% and ALT to 4,500 and 3,800U/L, respectively. PTS also inhibited IL-1β formation and neutrophil infiltration. APAP hepatotoxicity is linked to NAPQI formation, oxidative/nitrative stress, JNK activation and binding to Sab, a mitochondrial protein. *In silico* studies showed that PTS bind poorly to Cyp2E1 but are good ligands for the binding pockets of iNOS, JNK1/2, MMK4/7, and the Keap1/Nrf2 complex, the last likely promoting Nrf2/Keap1 dissociation and subsequent Nrf2 pathway activation. After APAP overdose *in vivo*, iNOS, 3-nitrotyrosine, 4-hydroxynonenal adducts increased, persistent JNK activation occurred, and pJNK/Sab binding increased. PTS (0h) increased thioredoxin-1 expression but decreased 4-hydroxynonenal, iNOS, and 3-nitrotyrosine. PTS also inhibited JNK activation and subsequent binding to Sab after APAP-overdose. In conclusion, PTS represent a promising new class of liver protective agents for prevention and therapy of APAP hepatotoxicity with protective effects comparable to NAC. PTS appear to be protective via a polypharmacological mechanism involving decreasing oxidative/nitrative stress by inhibition of Keap1/NRF2 complex formation and preventing persistent JNK activation/Sab interactions.

P-210 – Sofia Padilla-Mayne

Antinociceptive Activity of Compounds from the Aqueous Extract of *Melampodium divaricatum*

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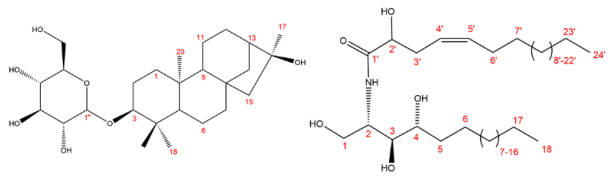
A decoction prepared from the aerial parts of *Melampodium divaricatum* (Rich.) DC. (*Asteraceae*) showed antinociceptive and antihyperalgesic responses when tested in the formalin model in mice. From the CH_2Cl_2 fraction of the decoction, two non-previously reported secondary metabolites, 3-*O*-β-D-glucopyranosil-16-β-hydroxy-*ent*-kaurane (**1**) and melampodiamide (**2**) [-(2′*R**,4′*Z*)-2′-hydrxy-N-[(2*S**, 3*S**, 4*R**)-1,3,4-trihydroxyoctadec-2-yl]tetracos-4-enamide] were separated and characterized by spectroscopic, spectrometric, and computational techniques. The flavonoids isoquercitrin and hyperoside, which possessed noted antinociceptive properties, were obtained from the active AcEOt fraction of the decoction. The chemical composition of the essential oil of the plant was also analyzed by gas chromatography-mass spectrometry. The major constituents were *(E)*-caryophyllene, germacrene-D, *β*-elemene, *δ*-elemene, *γ*-patchulene and 7-*epi*-*α*-selinene. Headspace solid-phase microextraction analysis detected (*E*)-caryophyllene as the main volatile compound of the plant.



P-211 – Kiesha Wilson

Prophylactic CBD Treatment Improves Fatal Inflammatory Response Exhibited in SEB-Induced ARDS

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The novel SARS-CoV-2 virus known to cause the COVID-19 outbreak has resulted in a global healthcare crisis that has persisted the past 3 years. Thus, understanding the mechanisms underlying this disease are vital at this time. While there are issues of research infrastructure to handle the virus and because of the refractoriness of rodents to this disease, the availability of these tools is still limited. The cytokine storm and fatality presented in patients with severe COVID-19 can be mimicked with Staphylococcal enterotoxin B (SEB)-induced Acute Respiratory Distress Syndrome (ARDS). Within ~7 days, the survival rate drops to 0% for C3H/HeJ mice exposed to a dual dose of SEB. In this study, we administered cannabidiol (CBD) intraperitoneally for 3 days pre- and post-SEB dosing and found that the clinical outcomes improved significantly. Initial evaluation of scRNASeq data from lungs comparing naïve to SEB-induced ARDS mice illustrated an increase in infiltrating immune cells, and a loss in pulmonary epithelial cells in the latter group. When evaluating the effect of CBD treatment on SEB-induced ARDS, we were able to demonstrate that CBD reduced the macrophage population. To characterize the mechanism by which CBD treatment ameliorated the inflammatory response, we found that CBD treated mice had significant reduction in infiltrating immune cells and alveolar thickening. This same histology and infiltration is presented in ARDS. MicroRNA expression analysis showed a significant increase in the expression mmu-miR-298-5p and mmu-miR-566 with CBD treatment. Ingenuity Pathway Analysis (IPA) indicated that the dysregulated miRNAs were also implicated in pathways associated with macrophage activation, respiratory disease and inflammation, interferon stimulated genes, as well as genes which have been upregulated in the disease state of this model. These targets include but are not limited to *Cebpb, Efhd2, Stat3, Socs3, Cxcl5, Gbp2, and Birc3.* This finding offers insights for the development of preventive and therapeutic strategies in the treatment of ARDS, including that induced in COVID-19. (Supported by NIH grants P01AT003961, P20GM103641, R01ES003961, R01AI129788, R01AI123947, R01AI160896 to MN and PSN and K99GM147910 to KW)

P-212 – Esperanza Carcache de Blanco

Molecular Networks of Bioactive Extracts from the NCI Natural Products Repository

Eric D. Salinas-Arellano[1], Ines Y. Castro[1], and Esperanza J. Carcache de Blanco[1]. [1]College of Pharmacy, The Ohio State University, Columbus, OH 43210

Natural products (NPs) and their derivatives are one of the major sources of lead candidates for drug development; nevertheless, the frequency of isolation of novel compounds is steadily declining day by day. Hence, early detection of known natural compounds at an early stage is essential to efficiently identify new drug leads and to reduce time, effort, and cost in the drug discovery process. Molecular networking is a well-suited strategy to perform this task. In the present work, 352 plant extracts and 176 microorganism extracts from the NCI Natural Products Repository (NPR) have been screened against human pancreatic (HPAC), thyroid (MDA-T32), breast (MDA-MB-231 and MCF-7) cancer cells. LC-HRMS analysis of the extracts with significant cytotoxic activity were generated using the Vanquish-H UHPLC system coupled to a Q-Exactive mass spectrometer. Molecular Networking (GNPS) platform for the discovery of new potential drug leads is being used to annotate and visualize structurally similar compounds in clusters.

P-213 – Esperanza Carcache de Blanco

Use of Molecular Network Analysis for Prioritization of NCI Natural Products Repository Bioactive Extracts

Ines Y. Castro-Dionicio[1], Eric D. Salinas-Arellano[1], and Esperanza J. Carcache de Blanco[1]. [1]College of Pharmacy, The Ohio State University, Columbus, OH 43210

Natural products (NPs) have inspired the discovery of a high percentage of modern chemotherapeutic agents; however, there is a decreasing trend in the discovery of novel bioactive natural product compounds. The application of new tools, such as molecular networking and other bioinformatics approaches, are essential to increase efficiency during early stages of natural products research. In the present work, a total of 352 plant extracts and 176 microorganism extracts, obtained from the NCI Natural Products Repository (NPR), were submitted to the SRB cytotoxicity assay against the prostate (DU-145 and PC-3) and bladder (HT-1376) cancer cells, as well as one leukemia cell line (BDCM). Extracts with significant cytotoxic activity were injected into a UHPLC-ESI-Q Exactive system and the ESI-MS/MS data was submitted to the Global Natural Product Social Molecular Networking (GNPS) platform to construct molecular families and annotate known compounds. Extracts with the potential of bearing unknown compounds will be prioritized for phytochemical and biological studies.

P-214 – Shengxin Cai

Symetrian™ for Immune Homeostasis

Shengxin Cai, Ping Jiao, Teresa Horm, Mesfin Yimam, Mei Hong, Thida Tea, Shayna Rossiter, Lidia Brownell, Qi Jia, Unigen Inc., 2121 South State Street, Suite 400, Tacoma, WA 98405, USA

Symetrian™ is a novel aloe-based composition composed of plant extracts standardized for polysaccharides and polyphenols from *Aloe barbadensis* (Aloe vera), *Poria cocos* and rosemary (*Rosmarinus officinalis*). Symetrian was tested in multiple animal models for its immune modulation activities. Symetrian was first evaluated for animal survival rate in mice with intraperitoneal injection of lethal dose of lipopolysaccharides (LPS). Seventy-two hours after LPS injection, the survival rates for the groups were determined to be 62.5%, 50% and 12.5% for Symetrian, sodium butyrate (positive control) and vehicle respectively, with all mice in the vehicle control group deceased after 82 hours of LPS injection. In a D-galactose-induced accelerated immunosenescence aging model, Symetrian reduced thymus damage and involution, at 52.9% and 50.6% administered at 400 mg/kg and 200 mg/kg, respectively. From histopathology analysis, a 157.8% increase in senescence cells was observed for the D-gal control mice, while mice treated with Symetrian at 200 mg/kg, showed a 42.7% reduction in senescence cells in comparison to the normal control mice. Symetrian resulted in increased in IgA, NKp46+ Natural Killer cells, CD3+ T cells, CD4+ Helper T cells, CD8+ Cytotoxic T cells, and CD3+TCRγδ+ and CD4+TCRγδ+ gamma-delta T cells, demonstrating that this aloe-based composition primes the inactivated immune system, causes expansion of immune cell populations, and increases immune "readiness". In the same model, Symetrian caused significantly higher SOD activity and Nrf2, indicating an increased capacity to neutralize free radicals. Maltodextrin, and some cheap carbohydrates are common adulterants found in Aloe and Poria. A simple and accurate method to detect and quantify polysaccharides in aloe and Poria, were developed by differentiating between α- and β-anomeric types of polysaccharides and analysis of polysaccharides profile. These pre-clinical studies showed that Symetrian could be potentially utilized as an effective agent to maintain a healthy immunity homeostasis, promote innate and adaptive immunity, and provide strong antioxidant properties.

P-215 – Mrinmay Chakrabarti

Resveratrol Inhibited Aortic Valve Calcification Through Downregulation of TGFβ1 Signaling

Mrinmay Chakrabarti, Henry Helms, and Mohamad Azhar; Department of Cell Biology and Anatomy, University of South Carolina School of Medicine, Columbia, SC 29209

Calcific aortic valve disease (CAVD) is the most common valvular heart disease in the aging population and the third leading cause of heart disease. Surgical specimens from calcific aortic valve disease patients have increased levels of transforming growth factor beta (TGFβ). Unfortunately, there is no

medical treatment, and without surgery, calcific aortic stenosis leads to death. Here we demonstrate that resveratrol, a plant-derived polyphenol very much effectively inhibited calcification *in vitro* and *in vivo*. We have isolated valve interstitial cells (VICs) from 4-6 weeks old Ts(H2-K1-tsA58) mice aortic valves. Our alizarin red staining and qPCR analysis confirmed the calcification of VICs and upregulation of osteogenic markers, respectively in osteogenic media, and resveratrol could significantly inhibit these processes. Our western blotting results confirmed induction of TGFβ signaling pathways and VIC calcification, and resveratrol treatment significantly downregulated the TGFβ signaling resulting inhibition of VIC calcification *in vitro*. We have generated VIC specific *Tgfb1* conditional transgenic *Tgfb1TG*/*PostnCre* mice that develop CAVD and pathogenesis of CAVD increases with age. We treated 8-10 weeks old double transgenic mice for two weeks at an oral gavage dose of 100 mg/kg mice. Live mice were serially followed before and after resveratrol treatment by micro-CT analysis. Finally, immunohistochemical staining confirmed the micro-CT findings. Collectively, the results indicated that resveratrol significantly blocked the development and progression of AV calcification. Our findings suggest that resveratrol is a potential therapeutic agent CAVD treatment.

P-216 – James McAlpine

The Ethics of Natural Product Science

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The essence of science is a search for the truth, one might expect "scientists" to be very conscious and observant of these demands. Unfortunately, that is not universal, and most egregious examples of lack of ethics are driven by money. In 1998, Dr. A. J. Wakefield of the Royal Free Hospital and School of Medicine in London, and 12 colleagues published in Lancet claiming a linkage between autism and the MMR vaccine. This, later retracted, paper was based on *preselected* children. The result: thousands of children died of measles, as their parents were guided by this misinformation. More unethical, in 2013, Newmaster + 4 colleagues at the University of Guelph, published in BMC Medicine on the use of "DNA Barcoding" to QA North American herbal products. Despite rapid rebuffs including from the ABC, the NY AG demanded all herbal dietary supplements have DNA barcoding before sale. Newmaster being entrepreneurial, formed companies offering "quality" endorsements to suppliers at substantial fees. His publications and presentations are replete with fabrications and plagiarisms: as described in (DOI:10.1126/science.ada0801). Patent applications on chemicals with new activities involve ethical conundrums. Patent rules require that the inventor divulge the *best* method to practice the invention. Within entities, IP managers may suggest withholding crucial steps. Don't do so as this can invalidate the patent. But there is a more common conundrum. A researcher's goal is to patent a discovery, the goal of the patent attorney is to gain maximum intellectual property. This commonly leads to an application with a list of mythical analogues or methods. which any experienced scientist will know have not been made/developed yet. While this might not be deceitful, it raises ethical concerns. More deceitful and more common is e.g., article X shows that the claimed activity of compound Y is wrong because the in vitro assays were faulty. Next, another article Z says that compound Y is useful for this bioactivity and, cites article X. This is unethical. In citing an article, one is accepting its conclusion and framework of reasoning, unless providing a reason for disagreeing. All 4 examples highlight the need for ethical conduct in the maintenance of science in NP science.

P-217 – Adéla Čmoková

Ecological Role of Secondary Metabolites in Plant-Fungal Interactions

Adéla Čmoková[1], Clara Chepkirui[2], Frank Surup[3], Tobias Zettler[3], Martina Réblová[4], Miroslav Kolařík[1], Marc Stadler[3]. [1]Laboratory of fungal genetics and metabolism, Institute of Microbiology of the CAS, Prague, Vídeňská 1083, Czech Republic, [2]Institute of Microbiology, Eidgenössische Technische Hochschule (ETH) Zurich, 8093, Zurich, Switzerland, [3]Microbial Drugs, Helmholtz Centre for Infection Research GmbH (HZI), Inhoffenstraße 7, 38124 Braunschweig, Germany, [4]Institute of Botany, Academy of Sciences, CZ-252 43, Průhonice, Czech Republic

Endophytes, which live inside plant tissues, are studied as a promising source of new active secondary metabolites. In a recent study, we have isolated new bisnaphthazarins, perylenequinones, and napthopyrans derivatives from various endophytic fungi. The structures of these compounds were elucidated by NMR spectroscopy and X-ray crystallography. The ecological role of newly described metabolites in plant-fungal interaction is however unknown. A photoinduced phytotoxicity have been reported for some perylenequinones previously. These compounds help pathogens to shed host plant leaves that are exposed by light to allow fungi to feed on plant matter. The discovery of photoinducible toxins in non-pathogenic endophytes, however, points to their additional ecological roles. In the study isolated dark brown binaphtharazins pigments with strong antioxidative activity probably help the fungus to survive harsh conditions inside plant tissues. The role of newly described colourful naphopyranones with broad biological activity is not clear. Understanding the ecological role of these metabolites in nature conditions may lead to better implementation of these metabolites in pharmacognosy research.

P-218 – Kamila Yuyama

Antiprotozoal Activities of the Amazonian Plant *Malouetia tamaquarina* (Apocynaceae) and its Endophytes

Kamila T. Yuyama[1,2], Claudia C. Macedo[1], Weilan G. P. Melo[1], Matheus H. Silva[1], Jaime P. L. Aguiar[4], Ana C. D. Castello[5], Leonardo L. G. Ferreira[6], Adriano D. Andricopulo[6], Gilvan F. Silva[3], Thomas J. Schmidt[2]

and Monica T. Pupo[1], [1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, 14040-903, Ribeirão Preto, SP, Brazil, [2]Institute of Pharmaceutical Biology and Phytochemistry, University of Münster, 48149, Münster, Germany, [3]EMBRAPA da Amazônia Ocidental, 69010-970, Manaus, AM, Brazil, [4]Instituto Nacional de Pesquisas da Amazônia 69067-375, Manaus, AM, Brazil, [5]Universidade Estadual de Campinas, 13083-862, Campinas, SP, Brazil, [6]Instituto de Física de São Carlos, Universidade de São Paulo, 13563-120, São Carlos, SP, Brazil

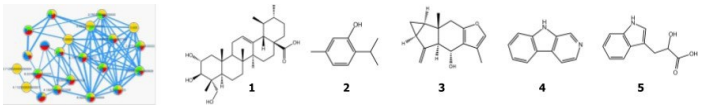
A recent study of a West African plant from Apocynaceae, *Holarrhena africana*, showed promising activity against *Trypanosoma brucei rhodesiense*. *Malouetia tamaquarina* is an Amazonian plant that belongs to the same tribe as *H. africana*. Neither the Amazonian plant nor its endophytes have been chemically studied. The alkaloidal extracts from bark and leaves of *M. tamaquarina* showed activities against *T. brucei rhodesiense* (IC_{50} 0.51, 1.06 μg mL^{-1}) and *Plasmodium falciparum* (IC_{50} 0.47, 6.4 μg mL^{-1}) respectively. Three endophytic fungi (*Cosmospora*, *Byssochlamys* and *Phomopsis*) and two actinobacteria (*Amycolatopsis* and *Nocardia*) isolated from *M. tamaquarina* showed promising antiprotozoal activity, with inhibition of parasites (*T. cruzi* and *Leishmania infantum*) higher than 70% at 20 μg mL^{-1}. The results demonstrate the *in vitro* potential of the plant and its endophytes against the parasites of Neglected Tropical Diseases (NTDs). The isolation and identification of the bioactive metabolites are currently in progress.

P-219 – Dulce Silva

Secondary Metabolites Produced by Endophytic Fungi Strains Isolated from Marine Red Algae *Dichotomaria marginata* Using Factorial Design and GNPS Molecular Networking

Iatã C. Mendonça[1], Victor H.L. Rufino[1], Lucas H.S. Moura[1], Givaldo S. Silva[1], Edelson J.S. Dias[1], Adriely Z. Boller[1], Rafael V. Silva[1], Yan L. Fernandes[1], Dulce H.S. Silva[1]. [1]Nucleus of Bioassays, Biosynthesis and Ecophysiology of Natural Products-NuBBE, Dep. Biochemistry and Organic Chemistry, Institute of Chemistry, São Paulo State University - UNESP, Araraquara - SP, Brazil

Marine endophytes chemodiversity remains largely untapped and represents valuable sources for the development of novel drug candidates. Fungal strains of *Microascus* sp., *Nemania bipapillata* and *Hypomontagnella monticulosa* were isolated from marine red alga *Asparagopsis taxiformis*, and their extracts were prepared using factorial design and analyzed by UPLC-MS/MS. GNPS molecular networks analysis (Figure 1) evidenced pH and temperature-dependent chemical profiles and provided annotation of their chemical constituents, including the triterpene asiatic acid (**1**), dipeptide L-prolyl-L-phenylalanine, monoterpene thymol (**2**), sesquiterpene lindenenol (**3**), a linear diarylheptanoid rubranoside A, in addition to the tryptophan alkaloids β-Carboline (**4**) and 3-Indole-lactic acid (**5**). Such results evidenced that chemical profiles and hence chemodiversity depends on external factors during the growth of the marine endophytes strains under investigation.



P-220 – Kirk Manfredi

Antimicrobial Natural Products from Plant Endophytes and Cave Dwelling Fungi

Kirk P. Manfredi, Kyle Biscoglia, Bridget Shoemaker, and Justin Peters, Department of Chemistry & Biochemistry, University of Northern Iowa, Cedar Falls, IA 50614

Over the last several years this lab has been interested in identifying biologically active natural products from fungi. Our goal is to identify fungi that produce biologically active compounds that inhibit the growth of bacteria and other fungus. Initially our source of fungus were plant endophytes. We have primarily been interested in isolating endophytes from native prairie plants. Further, we wanted to determine if the endophytes were derived from the environment (horizontal) or passed down through seeds (vertical). Therefore, we isolated endophytic fungus from the stems of plant and their seeds. We were also fortunate to partner with other research groups in our department who were studying the speleochemistry at Wind Cave national park. They had access to rarely visited portions of the cave and provided water and soil samples from which we isolated, cultured, and bioassayed for antimicrobial activity. This presentation will discuss the methodologies used in isolating, growing, and assaying the isolated fungi. In addition, we will discuss the methodologies used to identify the fungus through their ITS (internal transcribed spacer) region for the rRNA. Spectroscopic details of purified compounds will also be presented.

P-221 – Zoie Bunch

Antimicrobial Production by Coagulase-Negative *Staphylococcus warneri* from the Healthy Human Skin Microbiome

Zoie L. Bunch,[1] Nadja B. Cech,[1] Alexander R. Horswill[2]. [1] Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, 27412. [2] Department of Immunology and Microbiology, University of Colorado School of Medicine, Aurora, CO, 80045

There is an invisible battle happening on the human skin; with one bacterial army fighting to protect the largest organ of the human body, and the other seeking to infect and destroy. Coagulase-negative staphylococci (CoNS), a class of bacteria that are abundantly present on healthy human skin, have been shown to play a role in protecting the skin from infection and colonization by opportunistic pathogens, such as methicillin resistant *Staphylococcus aureus* (MRSA). One such protective mechanism is thought to be the production of antimicrobial molecules. Using broth microdilution assays, we have established the antimicrobial

activity of spent media from a strain of CoNS *Staphylococcus warneri* against MRSA. Additionally, we have been able to concentrate the activity using aqueous-organic partitioning. Further evaluation is being performed to isolate and identify the antimicrobial molecule(s) produced by the bacterium.

P-222 – Sunghee Bang

Bacterial Immunogens from the Human Gut Microbiomes

Sunghee Bang[1], Sung-Moo Park[2,3,4], Daniel B. Graham[2,3,4], Ramnik J. Xavier[2,3,4], Jon Clardy[1]. [1]Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School and Blavatnik Institute, Boston, MA 02115, USA, [2]Broad Institute of MIT and Harvard, Cambridge, MA 02142, [3]Department of Molecular Biology, Massachusetts General Hospital, Boston, MA 02114, [4]Center for the Study of Inflammatory Bowel Disease, Massachusetts General Hospital, Boston, MA 02114

Human gut microbiota are microorganisms inhabiting the human gastrointestinal tract. Bacteria living in human estimated to exceed one trillion respond to their environment with small molecules. Some of these molecules also influence broadly from their human hosts to surrounding microbes. Human microbiology research has been facing the challenge for deconvoluting the enormous complexity and dynamics of the microbiota and its associated molecules relevant to human health and disease. However, the numerous studies have been restricted to correlating bacterial populations or change in bacterial populations with health or disease. Only a few of the molecules and mechanisms underlying these correlations have been established. Therefore, in this study, we describe about bacterial immunogens from human gut microbiomes.

P-223 – Chase Clark

Sifting Through Haystacks: Large Scale Analysis of Protein Homology for Microbial Drug Discovery

Chase M. Clark[1], Jason C. Kwan[1]. [1]Division of Pharmaceutical Sciences, University of Wisconsin, Madison, WI, 53705 USA

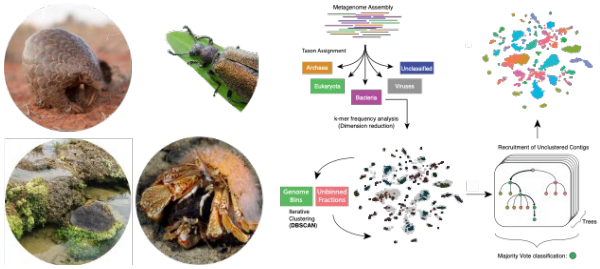
The annotation of function to genes is commonly achieved by the relation of sequence similarity to previously characterized nucleotide or protein sequences. In genomic-based microbial drug discovery this concept extends into the theory that homologous proteins and biosynthetic gene clusters (BGCs) will produce similar natural products (NP). Additionally, while NP drug discovery often focuses on BGCs found in the accessory pangenome, these BGCs are subject to both vertical and horizontal transfer between closely, and sometimes distantly, related organisms where the pairwise sequence identity of functionally-equivalent proteins can become extremely low. To help find proteins of similar function, especially where protein sequence divergence is high, I have created a unified collection of tools (python package, nextflow pipeline, graph database, user interface), called Socialgene. Socialgene attempts to overcome some of the inherent difficulties of searching through large numbers of genomes, while retaining the flexibility of having no inbuilt notion of what a BGC should look like. Precomputing pHMM annotations of non-redundant proteins facilitates searching by domain homology and the discovery of distantly related proteins that may be missed by tools that rely on sequence alignment alone, e.g. BLASTp. While finding homologous proteins sounds simple, the use cases are broad and include discovering BGCs encoding new chemical analogs; strains to screen for increased BGC expression; suitable hosts for heterologous expression; and finding BGCs across fragmented genomes.

P-224 – Evan Rees

Autometa 2.0: A Versatile Tool to Extract Genomes from Highly-Complex Metagenomic Communities

Evan R. Rees, Siddharth Uppal, Chase Clark, Samantha Waterworth, Andrew Lail, Jason C. Kwan. Pharmaceutical Sciences Department, University of Wisconsin – Madison, Madison, WI 53705

Largely the environment is un(der)explored. Autometa is a metagenome annotation package enabling researchers to quickly explore these microbial communities to gain culturing, biosynthesis and evolutionary insights. The Autometa package is provided with multiple metagenome assembly pre-processing utilities with multiple configuration parameters, allowing for an approach that suits any of a panoply of datasets. Autometa has its own workflow enabling scalable and reproducible analyses of up to hundreds of metagenomes per run. Autometa was written to be easily implemented so researchers may extend their own pipelines with its metagenome annotation functions. A companion-user interface is also available, named Automappa, allowing manual refinement, providing biologists with an approachable means to better characterize their system of interest. You may find more information on Autometa and Automappa at autometa.readthedocs.io and github.com/WiscEvan/Automappa, respectively.

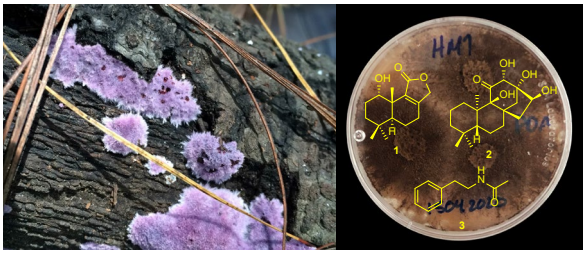


P-225 – Mario Figueroa

New Terpenoids from the Corticioid Fungus *Punctularia atropurpurascens*

Daniel Acero and Mario Figueroa. Facultad de Química, Universidad Nacional Autónoma de México, Ciudad de México, 04510, México

Chemical investigation of *Punctularia atropurpurascens* strain HM1 (Punctulariaceae), a corticioid isolated from a decorticated piece of *Quercus* bark collected in Bosque de Tlalpan, Mexico City, led to the isolation of a new drimane, 1-α-hydroxy-isodrimenine (**1**) and a new tetrahydroxy kauranol, 16-hydroxy-phlebia-nor-kauranol (**2**), together with the known N-phenylacetamide (**3**). Structures of all compounds were elucidated by spectroscopic and spectrometric methods, and the absolute configuration of **1** and **2** was confirmed via single-crystal X-ray crystallography. The isolated compounds showed modest antimycobacterial activity.



P-226 – Osama Mohamed

New Peptaibols Isolated from Michigan Honeybee Entomopathogenic Fungus *Tolypocladium inflatum* NPDC-F280

Osama G. Mohamed[1,3], Thomas Pavey[1], Alden Dirks[4], Timothy James[4], and Ashootosh Tripathi[1,2]. [1]Natural Products Discovery Core, Life Sciences Institute, University of Michigan, MI, USA. [2]Department of Medicinal Chemistry, College of Pharmacy, University of Michigan, MI, USA. [3]Pharmacognosy Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt. [4]Department of Ecology and Evolutionary Biology, University of Michigan, MI, USA

U-M's collection of NPEs is a unique source of novel chemical matter to discover potential leads and chemical starting points for drug discovery. As part of our ongoing effort to curate one of the chemically richest natural product collections in the United States from biodiversity hotspots around the globe. We have developed a custom pipeline that employs both function-centric and data-centric approaches to identify novel biologically active compounds. Biological interactions prevalent in nature are another guiding principle to developing our discovery platform. As a proof of principle, we investigated an entomopathogenic fungus *Tolypolcladium inflatum* (NPDC-F280), found growing on dead honeybee sourced from woods area in Ann Arbor, Michigan. We deployed our cheminformatic pipeline involving molecular networking of features extracted from UPLC-qTOF profiles of extracts obtained from fungus growing on honeybee host and a range of laboratory media. The chemical profile comparison revealed a qualitative and quantitative diversity in the secondary metabolism of the fungus. Interestingly, the chemical profiling directed us to a unique cluster of metabolites that were shared in honeybee fungal extract and rice grain laboratory culture. Scaled-up cultivation of NPDC-F280 yielded 12 new linear 11-residue lipopeptaibols whose structures were assigned by a combination of detailed spectroscopic and C_{18} Marfey's analysis. Efforts to understand the ecological/biological role are still in progress.

P-227 – Christopher Thornburg

National Cancer Institute (NCI) Program for Natural Product Discovery: A Diverse Fungal Extract Library for High-Throughput Screening

Christopher C. Thornburg[1], Suzanne M. Shipley[1], Terri M. Delloyd[1], Joyce A. Darner[1], Jerell R. Thompson[1], Matthew J. Harris[1], Rhone K. Akee[1], Susan M. Ensel[1], John R. Britt[1], Lucero Martinez[2], Jason R. Evans[2], Tanja Grkovic[2,3], and Barry R. O'Keefe[2,3]. [1]Natural Products Support Group, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, Frederick, Maryland 21702-1201, United States. [2]Natural Products Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Frederick, Maryland 21702-1201, United States. [3]Molecular Targets Program, Center for Cancer Research, National Cancer Institute, Frederick, Maryland, 21702-1201, United States

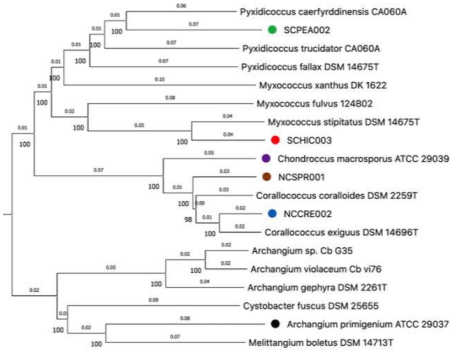
Fungi are an essential resource for natural product-based drug discovery and based on estimates of undescribed species, together with the wealth of putative metabolites that have been revealed through genomic sequencing of single organisms, these workhorses will continue to play a leading role in the discovery of new therapeutic agents. For this reason, the US National Cancer Institute's (NCI) Natural Products Branch recently instituted a new program to expand the microbial strain collection of the NCI Natural Product Repository. With nearly 25,000 new soil and marine derived fungi added to the collection, the need to develop a more cost-effective, scalable fermentation and extraction method was required to include them in the NCI Pre-fractionated Natural Product Extract Library. Herein we describe the use of a unique mixture of adsorbent resins and a simplified recovery procedure to increase extract mass and production titers. The results from a proof-of-concept study containing over 1200 fungal isolates from this new collection, as well as details of brefeldin A and fumitremorgin C production from *Eupenicillium brefeldanium* and *Aspergillus fumigatus*, respectively.

P-228 – Hanan Albataineh

Assessment of Evolutionary Relationships for Prioritization of Myxobacteria for Natural Product Discovery

Hanan Albataineh, Andrew Ahearne, and D. Cole Stevens. Department of BioMolecular Sciences, University of Mississippi, University, MS 38677

Long-read genome sequencing for two myxobacteria previously classified *Archangium primigenium* and *Chondrococcus macrosporus* as well as four environmental myxobacteria were utilized in this study. Average nucleotide identity and digital DNA- DNA hybridization scores suggest previously classified *A. primigenium* to instead be a member of the genus *Melittangium*, *C. macrosporus* to be a member of the genus *Corallococcus*, and the four isolated myxobacteria to be species from *Corallococcus*, *Pyxidicoccus*, and *Myxococcus*. The analysis of the biosynthetic potential of each myxobacterium suggests that genus-level conservation of biosynthetic pathways support this preliminary taxonomic assignment. This highlights the significance of applying modern genomics to revise myxobacterial taxonomy and improve our understanding of the genetic basis of myxobacteria social activities and specialized metabolism.

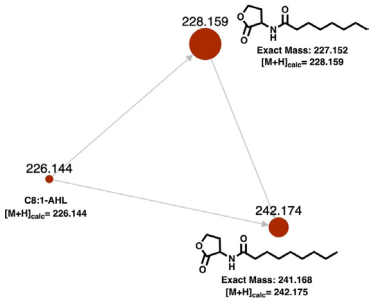


P-229 – Hanan Albataineh

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, University, MS 38677

The mining of different myxobacterial genomes for biosynthetic gene clusters led us to the discovery of a cryptic acyl homoserine lactone (AHL) synthase, *agpI*, encoded in the genome of the myxobacterium *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. 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-230 – Mario Augustinovic

Discovery of New Antimicrobials from a Marine-Derived *Knoellia* sp.

Mario Augustinović[1], Chase C. Clark[1], Maria Sofia Costa[2], Sesselja Ómarsdóttir[2], and Brian T. Murphy[1]. [1]Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL, 60612, USA, [2]Faculty of Pharmaceutical Sciences, University of Iceland, Reykjavik, IS

In 2019, antibiotic resistant infections accounted for over 1.2 million deaths globally, and if left unaddressed, the World Health Organization estimates upwards of 10 million deaths annually by 2050 due to antibiotic resistance. Greater than 70% of all antibiotics used in the clinic are derived or inspired by natural products produced by microorganisms. Most known antibiotic producers belong to the bacterial phylum Actinomycetota, which includes the prolific antibiotic genus *Streptomyces*. However, the reliance on well-studied antibiotic producers has limited our capacity to discover new areas of chemical space. In the current study, we aim to discover new antibiotic leads from understudied bacteria, which we define as bacteria that contain fewer than ten reported natural products in peer-reviewed literature. We hypothesize that this focus on understudied bacteria will allow the discovery for structurally unique antibiotics. Our lab recently reported the discovery of 30 bacterial isolates that represent several understudied genera, many of which have no reported secondary metabolites or ascribed biological activities. Upon initial antibiotic screening of these understudied bacteria against *S. aureus* ATCC 29123, a marine-derived *Knoellia* isolate demonstrated growth inhibition activity. Dereplication implicated that the strain produced no known antibiotics, and a media study determined improved growth and antibiotic production. Optimized larger scale fermentation and antibiotic isolation efforts are currently underway. If successful, this study will be among the first reports of an antibiotic from a *Knoellia* sp., and will contribute to the further expansion of bacterial chemical space.

P-231 – Sandra Bennett

Assessing the Genetic Diversity and Bioactivity of Gar Ectoparasite Isopod-Associated Bacteria

Sandra Bennett[1], Zainab Qazalbash[2], Joshua O. Foster[2], Muzaffar Nazarov[2], Monique van Hoek[3], Yue Xi[4], Andrew Fribley[4], R. Thomas Williamson[5], Julia Buck[6], Wendy K. Strangman[5]. 1. Center for Marine Science, University of North Carolina Wilmington, Wilmington, NC 28409. 2. Department of Biology, George Mason University, Fairfax, VA 22030. 3. School of Systems Biology, George Mason University, Fairfax, VA 22030. 4. Otolaryngology, Wayne State Medical School, Detroit, MI, 48201. 5. Department of Chemistry and Biochemistry, UNC Wilmington, Wilmington, NC 28409. 6. Department of Biology and Marine Biology, UNC Wilmington, Wilmington, NC 28409

More than 35,000 people in the United States and more than 1.2 million globally die each year due to antimicrobial resistant infections; additionally, billions are spent annually in the U.S. to

combat these infections. Misuse of antibiotics and a lack of new compounds complicate this already alarming situation. Studies of the interactions between insects and symbiotic microbes have uncovered new classes of bioactive natural products. Different environmental pressures are placed on marine microbes which could induce the production of unique chemical structures. The longnose gar, common to coastal waters in Southeastern NC, carries the isopod ectoparasite *Anilocra acuta*. First, the biodiversity of bacteria isolated from this isopod was examined through 16S rRNA sequencing and compared to 16S barcoding of culture independent sequencing. Culture media were tailored to the natural environment with the incorporation of river water and chitin. Solidifying agents agar and gellan gum were compared for isolate variability. Chemical extracts of the culture collection were tested for antibiotic activity, screened against multi-drug resistant pathogens, and for cytotoxicity against a panel of human cancer cell lines. Results of the sequencing and bioactivity of the extracts will be presented.

P-232 – Benjamin Blackburn

The Power of Conductive Quinones: The Electron Shuttling Capabilities of Quinone Containing Natural Products and Synthetic Analogs

Benjamin T. Blackburn, Emily Mevers, Department of Chemistry, Virginia Tech, Blacksburg, VA 24061

A dire need for renewable energy sources has come to the forefront with concerns of fossil fuel carbon emissions causing climate change. A promising renewable energy source that has emerged are Microbial Fuel Cells (MFCs) that utilize metal reducing bacteria. One particular bacterium, *Shewanella oneidensis* MR-1, utilizes a polar menaquinone analog 2-amino-3-carboxy-1,4-naphthoquinone (ACNQ) to shuttle electrons to an insoluble terminal electron acceptor, facilitating anaerobic cell growth. In this study, a library of natural product-mimicking quinone-containing metabolites has been assembled through a combination of commercial sources, isolation, and or semi-synthesis. These compounds were given to MR-1 ΔmenC (non-ACNQ producing) strain in liquid media to explore their electron shuttling capabilities. Examining the electron shuttling capabilities to chemical properties, i.e. redox potential, clogP, polarizability, and size, we hope to gain a better understanding of the key properties that lead to efficient activity. This will help answer outstanding questions about electron shuttling mechanisms, substrate specificity, and how to increase MFC energy output to a larger scale.

P-233 – Paul Price

Optimization of Antibiotic Production During Mixed-Culture Fermentation

Lilly Vael[1], Dawit Abebe[1], Khaled Ali[1], Alexis Robles[1], Taye Caperon[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 recently described a modified crowded plate technique (mCPT) that can provide extensive physical and/or chemical contacts leading to the production of natural products from otherwise silent BGCs. Students in out Tiny Earth biology lab courses have used this method to isolate over 4500 antibiotic-producing microbes, most of which produce little to no antimicrobial compounds when grown axenically under more traditional laboratory fermentation conditions. We are currently utilizing principles of microbial and chemical ecology to help inform the optimization parameters required to increase/induce the production of antibiotic compounds during mixed-culture fermentation. By identifying and adjusting a couple of core inducing parameters while removing suppressing parameters, we have generated baseline parameters that result in the production of antimicrobial compounds for over 80% of our identified isolates on average. Global Natural Products Social (GNPS) molecular networking of a small sample (n=26) of Gram-negative active extracts have not yielded any known bioactive compounds in the public databases.

P-234 – Luis Prieto-Costas

Center for Tropical Biodiversity, a Program from the Puerto Rico Science, Technology and Research Trust

Luis A. Prieto-Costas[1], Sebastián Sagardía[2], Matías Cafaro[3], Abel J. Baerga-Ortiz[1,4]. [1]Center for Tropical Biodiversity, Puerto Rico Science, Technology and Research Trust, San Juan, Puerto Rico. [2]Huerto Rico LLC, Bayamón, Puerto Rico. [3]Department of Biology, University of Puerto Rico, Mayagüez Campus, Mayagüez, Puerto Rico. [4] Department of Biochemistry, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico

Puerto Rico is the site of numerous biodiversity research efforts aimed at delineating the interactions between organisms and their tropical environment.The Puerto Rico Science, Technology and Research Trust has established a Center for Tropical Biodiversity (CTB), focused on the protection of biodiversity resources of the island, as well as sharing benefits that arise from commercial development of these assets. Herein, we will present projects developed by the CTB. Among them, is the creation of the Natural Product Repository of Caribbean Natural Products, whose goal is to document natural products and biodiversity from across the Caribbean and to promote collaboration among researchers in the region. We also collaborate with local company *Huerto Rico* for the development of therapeutic products from Puerto Rican

Ganoderma mushrooms. Furthermore, we have engaged with research efforts from the University of Puerto Rico toward the discovery of new natural products. For instance, we are identifying metabolites from termite-associated *Streptomyces* found in the dry forest ecosystems of Puerto Rico. These collaborations enabled us to develop untargeted LC/MS methods to construct molecular networks for these Caribbean species using our facilities that include high-end mass spectrometry and NMR instrumentation.

P-235 – Timothy Bushman

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, Lukasz Ciesla, Department of Biological Sciences, University of Alabama, Tuscaloosa, AL, 35487

One of the main challenges of natural product discovery from microbial cultures is the isolation of large quantities of secondary metabolites. In our work 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. However, the method of isolation from spent media requires large culture volumes and a cumbersome filtration process and yields minute amounts of active compound. To solve this issue, we developed a novel method for extraction and isolation of the metabolite of interest through the utilization of accelerated solvent extraction on the bacterial biomass itself. This technique decreases the time required and increased metabolite recovery per unit of culture. 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-236 – Ian Tietjen

Ellagitannins Isolated from the Medicinal Plant *Gunnera perpensa* Synergistically Inhibit Multiple SARS-CoV-2 Variants of Concern

Ian Tietjen [1], Luke Invernizzi [2], Phanankosi Moyo [2], Joel Cassel [1], Emery T. Register [1], Frederick Keeney [1], Ephraim Felix Marondedze [3], Krishna Kuben Govender [3,4], Penny Poomani Govender [3], Joseph M. Salvino [1], Freddie J. Isaacs [4], Vinesh Maharaj [2], Luis J. Montaner [1]. [1], The Wistar Institute, Philadelphia, PA, 19104, USA, [2], Department of Chemistry, University of Pretoria, Pretoria, South Africa, [3], Department of Chemical Sciences, University of Johannesburg, Johannesburg, South Africa, [4], Pure Herbal Medicine, Uitenhage, South Africa

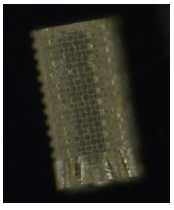
Antivirals are urgently needed to supplement SARS-CoV-2 vaccines and target SARS-CoV-2 variants of concern, particularly in resource-limited regions that lack access to existing therapies. Here we show that punicalin (PC) and punicalagin (PG) isolated from the medicinal plant *Gunnera perpensa*, already in use as a general antiviral in humans by traditional health practitioners in the Eastern Cape Province of South Africa, target SARS-CoV-2 entry and replication *in vitro*. Using an established AlphaScreen-based assay (PMID: 34543092), PC and PG inhibited binding of parental, beta, delta, and omicron spike to host ACE2 protein with IC_{50}s of 6.6 – 13.3 nM (compared to 2.1 – 10.6 nM for control therapeutic antibody REGN10987 vs. parental, beta, and delta spike and > 700 nM vs. omicron). Consistent with these data, computational modeling suggested that PC and PG interact with spike in regions distinct from those under selection pressure in SARS-CoV-2 variants. Experimentally, PC and PG further inhibited all variants in established pseudovirus and live virus assays (PMID: 34543092) with EC50s of 6.7 – 11.8 μM and 36.4 – 46.8 μM, respectively, in contrast to an EC50 of 3.0 μM for licensed antiviral remdesivir. When combined in a 10:1 molar mixture, PC and PG exhibited synergistic activity in virus assays (EC50 = 5.0 μM), which was statistically significant as measured by the Bliss Independence model and almost on par with remdesivir. Taken together, results indicate that PC, PG, and associated medicinal plant extracts are highly active and promising new leads for SARS-CoV-2 antivirals in resource-limited regions.

P-237 – Christopher Cartmell

Microfabrication of a Micron-scale Microbial-Domestication Pod for *In-Situ* Cultivation of Marine Bacteria

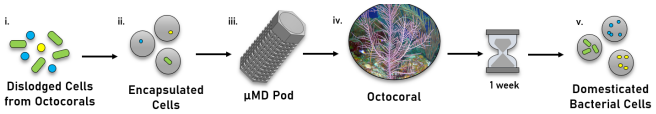
Christopher Cartmell[b]†, Sydney K. Wheatley[a]†, Bradley A. Haltli[c,d], Russell G. Kerrb,c,d and Ali Ahmadi[a,d]. Faculty of Sustainable Design Engineering, University of Prince Edward Island, 550 University Avenue, Charlottetown, PE, C1A 4P3, Canada. Department of Chemistry, University of Prince Edward Island, 550 University Avenue, Charlottetown, PE, C1A 4P3, Canada. Nautilus Biosciences Croda, Regis and Joan Duffy Research Centre, 550 University Avenue, Charlottetown, PE, C1A 4P3, Canada. Department of Biomedical Science, University of Prince Edward Island, 550 University Avenue, Charlottetown, PE, C1A 4P3, Canada. † Sydney K. Wheatley and Christopher Cartmell are considered joint first authors on this publication*

Currently around only 1% of bacteria are cultivatable using existing methods leaving a vast untapped supply of bacteria as an exciting resource for the discovery of new therapeutics. We currently find ourselves in a discovery void, with antibiotic resistance rising and the entry of new therapeutics into clinical trials declining. Culture-independent studies have shown that the 'Great Plate Count Anomaly' still comes into effect with only an incredibly small fraction of bacteria isolated from all environments being accessible through present cultivation methods.



It is currently unknown why the majority of microbes are unable to be cultured on artificial media, but it is believed to be a result of an absence of chemical signaling the microbe would be subjected to within its own natural environment from other neighboring

microbes. Current *in-situ* methods include that of diffusion chambers and the iChip which suffer from low throughput and a lack of chemical communication respectively with neither suitable for cultivation within octocorals. Through the hyphenation of bio-fabrication and microbial encapsulation, we can increase the throughput, whilst allowing for chemical communication to still occur, harnessing host-symbiont relationships. This process has the potential to create a new platform for natural product discovery, allowing access to a vast array of chemical space currently unattainable, leading to the much-needed discovery of new bioactive compounds.

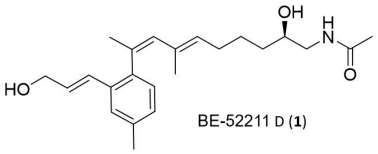


P-238 – Ama Boamah

Structure Elucidation and Genetic Basis of Novel Beta-Hydroxy Acetamides Isolated from Great Salt Lake-Derived Actinomycetes

Ama Boamah, Guangwei Wu, Jaclyn M. Winter, University of Utah, Department of Medicinal Chemistry, Salt Lake City, UT 84112

Environmental pressures have been shown to influence the structural diversity of compounds produced in Nature, and microorganisms thriving in extreme environments often produce chemical agents not observed in their terrestrial counterparts. The Great Salt Lake, also recognized as "America's Dead Sea," is an endorheic hypersaline lake located near the University of Utah. While seawater has an average salinity of ~3.3%, Great Salt Lake ranges between 8-28%. Recently, our lab started a natural products drug discovery campaign aimed at interrogating halophilic bacteria isolated from this unique environment. One of our isolates, *Streptomyces* sp. GSL-15 was shown to produce BE-52211 D (**1**), a new beta-hydroxy acetamide belonging to the rare class of trialkyl-substituted aromatic acids and amides produced by *Streptomyces* spp.



BE-52211 D (**1**)

While it is reported that these other *Streptomyces* spp, produce trialkyl-substituted benzenes constitutively, *Streptomyces* sp. GSL-15 must be challenged with *S. aureus* in order for **1** to be detected. Following de novo genome sequencing and assembly, we identified the 57 kb type I polyketide biosynthetic cluster responsible for the synthesis of this unique metabolite. Feeding experiments with various ^{13}C-labeled precursors revealed how the backbone of **1** is biosynthesized as well as its offloading mechanism. The discovery and characterization of **1**, its corresponding biosynthetic machinery, and the discovery of two additional beta-hydroxy acetamide producing Great Salt Lake organisms will be presented.

P-239 – Johanne Gerstel

β-lactam Antibiotic and Potentiation Constituents from the Botanical, *Larrea tridentata*

Keely Puchalski[1], Tiffany Turner[1], Guillermo Ruiz[1], Johanne Gerstel[1], Charles Veltri[2] and Jeffrey Langland[1]. [1]Southwest College of Naturopathic Medicine, The Ric Scalzo Institute for Botanical Research, Tempe, AZ 85282, USA, [2]College of Pharmacy, Midwestern University, Glendale, AZ 85308, USA

β-lactam antibiotics are a class of broad-spectrum antibiotics consisting of all antibiotic agents that contain a β-lactam ring in their molecular structures. β-lactam antibiotics are only known to be isolated from fungi and bacteria. We have shown that botanical extracts prepared from *Larrea tridentata* have strong antimicrobial activity against several bacteria, including members of *Staphylococcus* and *Streptococcus* genera. Previous studies have suggested that nordihydroguaiaretic acid (NDGA) may be the major antimicrobial compound in *L. tridentata* extracts. However, through resistance studies, inhibitor assays, ELISA testing and fractionation analysis, we demonstrated that extracts of *L. tridentata* likely contain a β-lactam type antibiotic and that this antibacterial activity is not associated with NDGA. Based on the estimated β-lactam concentration within the extract, the antimicrobial activity of the *L. tridentata* extract was approximately 2,000-8,000-fold greater against *Staphylococcus* as compared to other β-lactams, penicillin or ampicillin. In the *L. tridentata* extract, this increased activity was found to be associated with the presence of a cofactor leading to increased activity or potentiation of the β-lactam compound, as well as increasing the activity of exogenously added natural penicillin antibiotics.

P-240 – Katharine Watts

Swapping Amino Acid Specificity and Facilitating Intermodular Interactions of a Non-Ribosomal Peptide Synthase

Wilson Yeung, Chris Cummings, Jack Reynolds, Claire Meeds, Ava Sanderson, Nicole Ozawa, Gabriela Pinzon, Carson Cable, Anthony Chacon, Nicholas Wauer, Madeline Dennis, Anna Klavins, Katharine Watts, California Polytechnic State University, Department of Chemistry and Biochemistry California Polytechnic State University, Center for Applications in Biotechnology

Epoxomicin is a potent and selective proteasome inhibitor naturally synthesized by the bacterial Actinomycete strain classified as *Goodfellowiella coeruleoviolacea*. Chemical modifications of the tetrapeptide backbone of epoxomicin has yielded synthetic derivatives YU101 and Carfilzomib which display increased proteasome inhibition, selectivity, and solubility in water. Carfilzomib is FDA-approved and marketed as Krypolis™ for treatment of multiple myeloma relapse. The high cost of Krypolis™ is attributed to the laborious process of its chemical synthesis. We believe that harnessing the biosynthetic pathway that produces epoxomicin may lower the cost to patients. The

assembly of epoxomicin is catalyzed by a hybrid non-ribosomal peptide synthetase (NRPS) and polyketide synthetase (PKS) mega-enzyme. Modifying the amino acid specificity of the adenylation domains within epoxomicin NRPS modular protein may instead allow assembly of the YU101 derivative, which differs only in the tetrapeptide core. We hypothesize that modification of the mega-enzyme can be achieved by dissecting the synthase into individual modules and installing communication mediating domains that allow protein-protein interactions between consecutive modules. Previous efforts in our lab to heterologously express the first dissected NRPS module resulted in low yield and significant fragmentation using a *lac*-operon based promoter. Thus, the gene was cloned into pBAD33 with an arabinose inducible promoter, resulting in improved yield and purity of the *holo-* and *apo*protein. Modular enzymes with differing adenylation domains are currently being assessed for amino acid substrate specificity, as well as for protein-protein interactions with subsequent modules in the synthase.

P-241 – Rita Kidner

Uncovering the Molecular Cues that Drive the Symbiosis between *Capsaspora owczarzaki* and *Biomphalaria glabrata*: A potential Agent Against Schistosomiasis

Ria Kidner[1], Henry Rodefeld[1], Nuria Ros-Rocher[2], Catherine Gerdt[1], Inaki 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

Each year, ~291 million people suffer from the neglected tropical disease schistosomiasis. This disease is caused by a parasitic flatworm called a schistosome. One such schistosome, *Schistosoma mansoni*, is transmitted by the freshwater snail *Biomphalaria glabrata*. The snail also hosts another microbe, *Capsaspora owczarzaki*. Remarkably, this protozoan can swarm and kill parasitic schistosomes *in vitro*. Because of this observed swarming behavior, *Capsaspora* has potential as an alternative biocontrol agent against the spread of schistosomes inside snails. However, not all snails in their native habitat naturally contain *Capsaspora*, and the molecular mechanisms by which *Capsaspora* colonizes snails are unclear. We have discovered 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 to uncover signaling pathways between these organisms may help to develop *Capsaspora* as a biocontrol agent against schistosomiasis.

P-242 – Lesley-Ann Giddings, Brian Murphy and Christine Salomon (ASP DEI Committee)

Equity in Action: The ASP Summer Research Fellowship Program

Lesley-Ann Giddings[1], Brian Murphy[2], and Christine Salomon[3]. [1]Department of Chemistry, Smith College, Northampton, MA 01063, Department of Pharmaceutical Sciences, [2]University of Illinois at Chicago, Chicago, IL 60607, [3]Center for Drug Design, University of Minnesota, Minneapolis, MN 55405

One critical challenge facing STEM fields in the US, which is reflected within the ASP, is a lack of racial and ethnic representation among our membership, leadership, award recipients, and meeting speakers. To correct for the underrepresentation of Black, Indigenous and Latinx (BIL) students in our field, the ASP DEI and Executive Committees, ASP Foundation, and ASP Fellows collaborated to develop the Summer Research Fellowship (SRF) program. The program offers 1) a 2.5 month stipend for students to engage in research under a mentor in the natural product sciences; 2) 12 weekly online professional development workshops focused on science communication as well as exposure to graduate programs and careers in natural products; and 3) a special online ASP webinar for students to present their research to an international audience. The first cohort (2021) was highly successful, with at least one student accepted to a natural products graduate program and several others receiving prestigious research fellowships and awards (remainder of the cohort are still engaged in undergraduate studies). Importantly, most students in the first cohort are continuing to pursue research in the field of natural products chemistry. Students in the second cohort (2022) have begun their research, participating in the weekly workshops and preparing for their presentations. Several students in both cohorts are attending the 2022 ASP meeting, so please be sure to visit their posters and welcome them. The DEI committee is is seeking additional support through grants and donations to continue the successful SRF program.

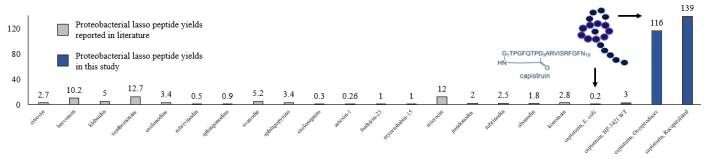
P-243 – Rita Kidner

Reverse Engineering High Yield Lasso Peptide Production by a *Burkholderia* Bacterial Host

Hannah N. Fernandez, Ashley M. Kretsch, Douglas A. Mitchell, Alessandra S. Eustaquio. Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL 60607, Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801

The goal of this study is to determine the basis of high-yield lasso capistruin production by a stochastic overproducer clone identified while testing *Burkholderia* sp. FERM BP-3421 as a bacterial host. Lasso peptides are a class of compounds with a specialized knotted configuration that confers potent target

affinity and makes this class of compounds excellent drug leads. Investigation of the underlying molecular mechanisms of capistruin overproduction led to the recapitulation of high yield capistruin production by up to 120%. The capistruin yields garnered with FERM BP-3421 are greater than any reported yields for the heterologous production of a proteobacterial lasso peptide. FERM BP-3421 as a heterologous host was then used to express two novel lasso peptides from *Burkholderia* sp. B13.



P-244 – Margaret Hill and Melany Puglisi

The URI College of Pharmacy's Pharmacognosy Club – a model for ASP Student Chapters?

Margaret Hill[1], Melany Puglisi[2], Amy Wright[3], Kerry McPhail[4], David Rowley[1], Matthew Bertin[1]. [1]Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island, Kingston, RI, USA 02881, [2]Department of Pharmaceutical Sciences, Chicago State University, Chicago, IL, USA 60628, [3]Harbor Branch Oceanographic Institute, Florida Atlantic University, Boca Raton, FL, USA 33431, [4]Marine Studies Initiative, Oregon State University, Corvallis, OR 97331

The University of Rhode Island has a wealthy history of pharmacognosy research, dating back to the College of Pharmacy's founding dean, Dr. Hebert W. Youngken Jr. who established a medicinal plant garden that would be used by faculty members and students for many years to come. The Pharmacognosy Club was established by founding members, Dominic DeFilipi and Julia V. Law, to provide students with an opportunity to explore their interests in traditional medicine systems, herbal medicine, and pharmacognosy. In more recent years, the main initiative of the Pharmacognosy Club has shifted to introducing students to natural products research. The current executive board has implemented teaching lab environments that have 1) educated individuals on research opportunities and provided them with laboratory techniques that are necessary in pharmacognosy related research, 2) connected students with principal investigators at the university, and 3) have helped bridge the gap between those who have had access to opportunities such as these, and those who haven't. If the American Society of Pharmacognosy were to create student chapters and induct our club as the first, we would be able to expand our network of student-run organizations and create more opportunities for the next generation of pharmacognosists.

P-245 – Anthony Mena

Alkaloid Distribution in North American Columbine Species using LC-MS Metabolomics

Anthony Mena[1] Yi Zhao,[2,3] and Edward J. Kennelly[2,3]. [1]Department of Chemistry Lehman College, City University of New York, Bronx, NY, [2]Department of Biological Sciences, Lehman College, City University of New York, Bronx, NY, [3]Biology PhD program, The Graduate Center, City University of New York, New York, NY

The genus *Aquilegia* (columbine) includes many medicinal species that produce bioactive alkaloids. Previous investigations of *Aquilegia* have reported significant antibacterial and antispasmodic activities. Although valued as ornamental in North America, *A. caerulea* is also used medicinally for gallbladder disorders and general stomach and intestinal problems. Some North American species have been chemically analyzed and were found to contain bioactive alkaloids such as magnoflorine and berberine. We hypothesize that North American *Aquilegia* species produce isoquinoline or related bioactive alkaloids that make them useful as medicinal plants. To test this, methanol extracts from all plant parts (flowers, aerial, and roots) of four North American *Aquilegia* species, *A. chrysantha*, *A. caerulea*, *A. canadensis* var. little lantern, and *A. chrysantha* var. *chaplinei*, were prepared. Using liquid chromatography-quadrupole time-of-flight mass spectrometry the alkaloid composition of each species was determined. Orthogonal projections to latent structures discriminant analysis (OPLS-DA), and principal component analysis (PCA) were used for untargeted analysis. The PCA analysis of the flowers shows *A. caerulea, A. chrysantha,* and *A. canadensis* var. little lantern to be chemically different, with closer similarities between the latter two species. Further PCA and OPLS-DA analyses of other *Aquilegia* plant parts are ongoing, as well as marker compound identification.

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