ASP 2026
Annual Meeting

Denver

Elevating Natural Products

American Society of Pharmacognosy

Annual Meeting

Elevating Natural Products

Denver, Colorado
July 26–29, 2026

By the 2026 ASP Organizing Committee

The 2026 Organizing Committee of The American Society of Pharmacognosy (ASP) is delighted to welcome you to the Mile High City. You will be participating in a meeting located one mile above sea level!

We have strived to create a scientific program representative of our society's myriad foci, including work from industry, government, and academia. We have symposia addressing cancer, infectious disease, biosynthesis, screening technologies, clinical applications, and more. Please also note that we have employed a new schedule this year. There is no programming Saturday, and Sunday will be a full day of science with our traditional opening reception in the evening. Our workshops, the Younger Members Career Fair and the Primarily Undergraduate Institution session, will be held on Tuesday afternoon. The Executive Committee meeting will also occur on Tuesday afternoon.

The Denver Marriott Tech Center is located off I-25 and the E light rail line/Belleview station for easy access to downtown areas. Across from the hotel are several restaurants and a beer garden. The venue also houses a large restaurant and bar area, in addition to a grab and go market, perfect for a quick breakfast. Please check the meeting website for our Denver Fun guide with listings of all the Front Range and mountain areas have to offer.

We are here to help facilitate the most enjoyable and productive meeting possible. Please don't hesitate to reach out to us with any questions or if we can assist you in any way. Wishing all of you a wonderful stay in the Mile High City!

Check out Denver Activity Guide and Visit Denver

We want to hear from you #ASP2026

2026 ASP Annual Meeting

Organizing/Scientific Committee

Amy Keller, Chair - (University of Colorado)
Kerry McPhail, Chair **-** (University of Utah)

Donovon Adpressa (Eli Lilly and Company)
Allegra Aron (University of Denver)
Gil Belofsky (Central Washington University)
J.P. Gerdt (Indiana University)
Sandra Loesgen (University of Florida)
Vanessa Phelan (University of Colorado, Anschutz)
Tarek Sammakia (Eli Lilly and Company)
Eric Schmidt (University of Utah)

Meeting Planner

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. 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.

NIH Reporting for Harassment

Thank you to the 2026 ASP Annual Meeting Sponsors!

Funding for this conference was made possible (in part) by 1R13CA314207-01 from the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases (NIAID). The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. government.

Thank you to the 2026 Annual Meeting Exhibitors!

ASP Awards

2026 ASP Norman R. Farnsworth Research Achievement Award

Matthias Hamburger (University of Basel)

Norman R. Farnsworth received both baccalaureate and master's degrees under the tutelage of Professor Heber Youngken at Massachusetts College of Pharmacy, and a doctorate from the University of Pittsburgh (Pitt) in 1959. At Pitt, he helped institute the Pharmacognosy Ph.D. program and served as its first chair. In 1970, he left Pitt to become head of the Department of Pharmacognosy and Pharmacology in the College of Pharmacy at the University of Illinois at Chicago (UIC). Instrumental in shaping the modern field of pharmacognosy, he was a founding member of the American Society of Pharmacognosy, and founding director of the Program for Collaborative Research in the Pharmaceutical Sciences at UIC — a multidisciplinary program that brought together, for the first time, scientists in numerous fields of medicinal plant research to collaborate on both basic and clinical research on natural products. He established the Norman R. Farnsworth endowed Professorship in Pharmacognosy at UIC, where over the course of his tenure he mentored more than 100 doctorate and 30 graduate students, as well as numerous post-doctoral fellows. In 1975, back in the "dawn of the computer age", Professor Farnsworth created NAPRALERT, the world's first computerized database on the ethnobotany, chemistry, pharmacology, toxicology, and clinical trials of natural products. NAPRALERT evolved from several generations of natural product bibliographic references, including the Lynn Index, a seven-volume bibliography of phytochemistry developed by Professor Eldin V. Lynn at MCP, followed by Pharmacognosy Titles, a nine-volume periodical reference (1966-1974) documenting literature sources for global natural product investigations. The NAPRALERT database represents one of Professor Farnsworth's most important scientific contributions, and his enthusiasm for- and dedication to- the database remained steadfast throughout his career.

2026 ASP Varro E. Tyler Prize

Michael Heinrich (University College London)

Varro E. (Tip) Tyler was one of those unique individuals who cast a long shadow in life having had a profound impact on pharmacy education, natural product science, and the use of herbal medicine by the American public as well as the worldwide community. As a broad view of some of his accomplishments, he was a renowned educator serving Purdue University as Dean of Pharmacy for twenty years before his selection as executive vice president for academic affairs. While a professor at the University of Washington, he conducted a distinguished research career focused on the chemistry of toxic mushrooms and other fungi. He was the senior author of what was for years the most widely used text in pharmacognosy in the United States. He was recognized as one of the nation's leading experts on herbal medicine, an endeavor he was actively engaged in at the time of his death. In philately, he was the world authority on Japanese stamp forgeries, and his signature of authentication is recognized worldwide as without equal. Concerning the American Society of Pharmacognosy, we owe Tip a tremendous debt. He served as its first president, guiding the organization through the critical first two years (1959-1961) of its existence. He was the principal force in the negotiations to obtain Lloydia (The Journal of Natural Products) as the official publication of the Society. In addition, he played a major role in forging the friendly ties our Society has with the Gesellschaft fur Arzneipflanzenforschung (Society for Medical Plant Research) which has resulted in our joint international meetings every four to five years starting with Vienna in 1970. Tip was so highly regarded by the Gesellschaft that they elected him to their Board of Directors and to honorary membership. Tip thoroughly enjoyed sharing his knowledge, and he was a master at communication in both the written and spoken word. After he retired as executive vice president at Purdue in 1991, he devoted his efforts to the area of herbal medicine. He wrote four well received books on the subject as well as numerous articles in the scientific and lay press, including a regular column in Prevention magazine. It became clear that he was a voice of reason in an area fraught with misinformation and hyperbole. As a consequence, he was in great demand as a speaker at conferences and continuing education programs. He appeared on national radio and television programs. As his fame grew, he became inundated with requests for information from the news media and from interested individuals. Although he had an extremely busy schedule and was dealing with personal health problems, he was always generous with his time and answered each query with his usual detailed kindly manner; something a less patient man would have refused to do. In recognition of his accomplishments, Tip received many honors and accolades; however, he stated more than once that even though these meant a lot to him, what he cherished most was the many friendships he established during his life's work.

2026 ASP Matt Suffness (Young Investigators Award)

Jie Li (The University of Texas at Austin)

Matthew Suffness served as the Society's President in 1989-1990, during which time he initiated the "Young Investigator's Symposium" which now bears his name. Born in Staten Island, N.Y., Dr. Suffness received his B.S. degree in Pharmacy from Howard University and a Ph.D. in Pharmaceutical Chemistry from the University of Wisconsin under the mentorship of the late natural products authority, Dr. S. Morris Kupchan. In 1970-71, he did postdoctoral work at Stanford University with Prof. E.E. van Tamelen. After beginning his career as an Assistant, then Associate Professor at Ohio Northern University, Dr. Suffness joined the Natural Products Branch in the Developmental Therapeutics Program of the National Cancer Institute in 1976. In 1981 he became chief of the Natural Products Branch and was responsible for the major collection contracts that were initiated by the NCI. He also served as the first coordinator for the National Cooperative Natural Product Drug Discovery Group Program. He is best known for his commitment to the development of taxol as an anticancer drug. He edited the book entitled "Taxol—Science and Applications," which was published shortly before his death in 1995 (of pneumonia secondary to leukemia). Friends and colleagues remember his tireless support of natural product research, his efforts to facilitate multidisciplinary research efforts and his accessibility and sound advice. He was particularly helpful to younger investigators trying to establish a successful research program and career.

2026 Phillip Crews Mentoring Award

Rachel Mata (Universidad Nacional Autónoma de México)

Phillip Crews received his undergraduate degree in chemistry from the University of California, Los Angeles, and completed his Ph.D. in organic chemistry at the University of California, Santa Barbara. Following postdoctoral work at Princeton University, he joined the faculty at the University of California, Santa Cruz (UCSC), where he built a pioneering program in marine natural products chemistry. A leader in the discovery of bioactive compounds from marine sponges, Crews' research combined rigorous chemical analysis with a commitment to training the next generation of scientists. At UCSC, he mentored over 40 graduate students, over 45 postdoctoral fellows, and well over 200 undergraduate students, emphasizing hands-on oceanographic fieldwork and interdisciplinary collaboration. Deeply committed to diversity and outreach, Crews was the program director for the NIH-funded Bridges to the Baccalaureate (ACCESS) program at UCSC for 30 years, which provided intensive research opportunities to students from underrepresented backgrounds. In addition to his research and mentorship, he co-authored the widely used textbook *Organic Structure Analysis*, which has trained countless students in the interpretation of spectroscopic data for structural elucidation. In recognition of his scientific and educational contributions, Crews received numerous awards, including the Journal of Natural Products, Arthur E. Schwarting Award, Norman R. Farnsworth ASP Research Achievement Award, Paul J. Scheuer Award for Marine Natural Products, and the Ernest Guenther Award in the Chemistry of Natural Products. Crews also served as the vice president and president of ASP. Throughout his career, he remained dedicated to expanding the boundaries of marine natural products research while championing equity and excellence in scientific training. As a result, ASP established the Phillip Crews Mentorship Award in 2025.

ASP 2026 Award Winners

Research Starter Grant
Richard Tehan, Utica University
Vikram Shende, Occidental College

Student Research Award
Christina McBride, University of Michigan

Undergraduate Research Award
Anna Erdos, University of Michigan

D. John Faulkner Travel Award
Jayho Lee, Seoul National University
Sung Chul Park, University of Wisconsin-Madison

Member Travel Award
Jianying Han, The University of Queensland
María del Carmen Osorio Ramírez, Universidad Nacional Autónoma de México
Hyeongju Jeong, Kyung Hee University,
Byeol Ryu, University of California-San Diego

Waqar Bhatti Student Travel Award
Alexandria Evans, University of Arizona

Lynn Brady Student Travel Award
Courtney Clevenger, University of North Carolina at Wilmington
Margaret Hill, University of Illinois Chicago
Pearl Lee, University of the Pacific
Cleo Oralndo, Virigina Tech
Rafiul Noyon, University of North Carolina at Greensboro
Jennifer Nguyen, University of Michigan
Alana Ponte, University of Michigan
Alyssa Rodriguez, University of Michigan
Raima Sen, University of Alabama
Emma Swystun, University of North Carolina at Greensboro

David Carew Student Travel Award
Natalia Makaro, University of Illinois Chicago

Jerry McLaughlin Student Travel Award
Gabriela Garcia Marin, Universidad Nacional Autónoma de México
Sahar Mofidi, University of Kentucky

ASP 2026 Award Winners Continued

Sheo and Sushila Singh Travel Award
Diego Rangel Rodriguez, Universidad Nacional Autónoma de México

2026 Arthur E. Schwarting Award
Title: Neuromodulating Alkaloids from Millipede Defensive Secretions
Authors: Carla Menegatti, Jared S. Wood, Paige Banks, Kenneth Knott, Jonathan S. Briganti, Anthony J. Briganti, Samuel V. G. McNally, Paul E. Marek, Anne M. Brown, Tappey H. Jones, R. Thomas Williamson, **Emily Mevers***
Reference: J. Nat. Prod. 2025, 88, 110-118.
http://pubs.acs.org/doi/10.1021/acs.jnatprod.4c01162

2026 Jack L. Beal Award
Title: Cyclic Peptide Natural Product Inspired Inhibitors of the Free-Living Amoeba *Balamuthia mandrillaris* Authors: Chenyang Lu, Samantha Nelson, Gabriela Coy, Chris Neumann, Elizabeth I. Parkinson,* **Christopher A. Rice***
Reference: *J. Nat. Prod.* 2025, *88*, 274-281.
https://pubs.acs.org/doi/10.1021/acs.jnatprod.4c00834

2026 A. Douglas Kinghorn Award
Title: Machine-Readable Structural Information Is Essential for Natural Products Research Authors: **Karin Steffen**,* Nicholas H. Oberlies,* Antonis Rokas* Reference: *J. Nat. Prod.* 2025, *88*, 2815-2821
https://doi.org/10.1021/acs.jnatprod.5c00836

2026 Audrey S. Bingel Fellowship
Skylar Carlson (University of the Pacific)
Amy Lane (Rose-Hulman Institute of Technology)
Olha Mykhailenko (National University of Pharmacy)

2026 Student Chapter Presentation Competition Award
Victor Olaoye (University of Rhode Island)

American Society of Pharmacognosy

Annual Meeting

July 26 – 29, 2026

Denver, CO

Elevating Natural Products

Program Schedule

Sunday July 26, 2026

7:00 AM – 6:00 PM **Registration** – *Rocky Mountain Event Foyer*

Welcoming Remarks and Announcements

Rocky Mountain Event

8:00 AM – 8:30 AM **Robert Cichewicz** (ASP President), **Amy Keller** (University of Colorado) and **Kerry McPhail** (University of Utah)

Symposium I – Leveraging Natural Products for Infectious Disease

Rocky Mountain Event

Chair: **Tim Bugni** (University of Wisconsin, Madison)

8:30 AM – 9:05 AM **PL-01 - Carole Bewley** (NIDDK)
Chemical Mechanisms of Natural Product Antibiotics:Targets, Enzymes, and Self-Resistance

9:05 AM – 9:40 AM **PL-02 – Jason Crawford** (Yale University)
Mode of Action for Translational Inhibitory Nucleotides Encoded in the Human Microbiome

9:40 AM – 10:00 AM **C-01** – **Dmitrii Travin** (University of Illinois at Chicago)
Tiarins – Novel Natural Trojan-Horse Inhibitors of Aminoacyl-tRNA Synthetases Discovered by Genome Mining

10:00 AM – 10:30 AM **Break** – *Rocky Mountain Event Foyer*

Symposium II – Technologies to Accelerate Natural Products Research

Rocky Mountain Event
Chair: **Donovon Adpressa**

10:30 AM – 11:05 AM **PL-03 - Jessica Prenni** (Colorado State University)
The Periodic Table of Food Initiative: Mapping the Chemistry of Food

11:05 AM - 11:40 AM **PL-04 – Cassandra Quave** (Emory University)
Development of a MicroED-Enabled Discovery Platform for Rapid Identification of Bioactive Natural Products

11:40 AM – 12:00 PM **C-02 – Ashley Kretsch** (Corteva Agriscience)
An Integrated Informatics-Driven Platform for Natural Product Discovery and Analog Generation in Crop Protection

12:00 PM – 1:30 PM **Journal of Natural Products Board Meeting** (Invitation Only) *Cottonwood*

Session S-PM1 – Chemical Ecology and Symbioses

Evergreen Ballroom A
Chair: **J.P. Gerdt** (Indiana University)

Sponsored by: DEPARTMENT OF CHEMISTRY COLLEGE OF ARTS + SCIENCES

1:30 PM – 2:00 PM **I-01** -**Pierre Stallforth** (Hans Knöll Institute)
Natural Products in Space and Time: from Ancient Molecules to Microbial Arms Races

2:00 PM – 2:30 PM **I-02 - Justin Silpe** (Princeton University)
Pectin-Based Formulation Protects Milk Fat Globule Membranes in Stored Human Milk

2:30 PM – 2:45 PM **C-03 – Marina Luccioni** (Stanford University)
Chemical Ecology of the Sonoran Desert Toads

2:45 PM – 3:00 PM **C-04 – Nicole Kanya** (University of South Florida)
Terpenoid-Mediated Defense in Caribbean Gorgonian Corals: Insights into Predator Deterrence and Metabolite Diversity

3:00 PM – 3:15 PM **C-05 – Jack Ganley** (Princeton University)
Ecology-Guided High Throughput Elicitor Screening (Eco-HiTES) for Discovery of Natural Products

3:15 PM – 3:30 PM **C-06 – Arden Hatch** (Virginia Tech)
Evaluation of the Chemical Secretions and Their Ecological Role of the Millipede Brachycybe

Session S-PM2 – Botanicals and Mushroom Functional Foods

Evergreen Ballroom B
Chair: **Mario Figueroa** (Universidad Nacional Autónoma de México)

1:30PM – 2:00PM **I-03 - Tiffany Weir** (Colorado State University)
The Gut Microbiome as an Important Determinant of Dietary Polyphenol Bioavailability

2:00 PM – 2:30 PM **I-04 – Milton Drott**
Microevolutionary Reservoirs of Fungal Natural Products: From Aspergillus to Invasive Mushrooms

2:30 PM – 2:45 PM **C-07 – C. Benjamin Naman** (San Diego Botanic Garden)
Natural Products Research Is Better In Situ – A Case Study on Yerba Santa (Eriodictyon)

2:45PM – 3:00 PM **C-08 – Patrick Still (**National Center for Complementary and Integrative Health)
A Holistic Approach to Study Non-Addictive Natural Products for Pain Management

3:00 PM – 3:15 PM **C-09 – Wilmer Perera** (CAMAG Scientific, Inc.)
Advancing HPTLC Botanical Authentication from Visual Evaluation to Chemometric-Driven Data Intelligence

3:15 PM – 3:30 PM **C-10 – Alana Pontev** (University of Michigan)
Gut Microbiome-Mediated Transformation of Mangosteen Xanthones and its Impact on Breast Cancer Bioactivity

3:30 PM – 4:00 PM **Break**

Session S-PM3 – Natural Products Biosynthesis

Evergreen Ballroom A

Chair: **Taifo Mahmud** (Oregon State University)

4:00 PM – 4:30 PM **I-05 -Filipa Pereira** (University of Michigan)
Optimizing Microbial Hosts for Sustainable Production of Natural Products

4:30 PM – 5:00 PM **I-06 - Jonathan Chekan** (University of North Carolina at Greensboro)
Aromatic Side Chain Crosslinking and Macrocyclization in RiPP Biosynthesis

5:00 PM – 5:15 PM **C-11 – Antonio Del Rio Flores** (University of Colorado, Boulder)
Mechanistic Analysis of Programmed Iteration by Module 5 of the Nocardiosis-Associated Polyketide (NOCAP) Synthase

5:15 PM – 5:30 PM **C-12 – Shogo Mori** (Augusta University)
Harnessing Natural Enzymatic Pathways for Amino Acid Homologation

5:30 PM – 5:45 PM **C-13 – April Lukowski** (University of California, San Diego)
An Emerging Family of Efficient Cyanobacterial Halogenases: Discovery, Function, and Evolution

5:45 PM – 6:00 PM **C-14 – Chung Sub Kim** (Sungkyunkwan University)
Stress-Induced Metabolites from Bacteria

Session S-PM4 – Natural Products Discovery and High Throughput Screening

Evergreen Ballroom B

Chair: **Sandra Loesgen** (University of Florida)

Sponsored by: CORTEVA™ agriscience

4:00 PM – 4:45 PM **A-01 – Michael Heinrich** (University College London)
Tyler Prize 2026
'... Inspired by Diversity: A Biological and Chemical Journey from (Medical) Anthropology to Ethnopharmacology.'

4:45 PM – 5:15 PM **I-07 - Qihao Wu** (University of Pittsburgh)
Metabolomics-Guided Mapping of Chemical Interactions at the Diet–Microbiome Interface

5:15 PM – 5:30 PM **C-15 –Dong-Chan Oh** (Seoul National University)
Integrated Metabologenomic and Chemical Approaches for Drug Lead Discovery from Actinomycetes

5:30 PM – 5:45 PM **C-16 – Laura Sanchez** (University of California, Santa Cruz)
A High-Throughput Biocatalytic Platform for Screening Isomeric Kainoid Natural Products

5:45 PM – 6:00 PM **C-17 – Nathan Wlodarchak** (University of Colorado, Anschutz)
Designing and Executing Successful High Throughput Screening Assays for Drug Discovery

6:30 PM – 9:30 PM **President's Opening Reception –** *Atrium* ***(Ticketed Event)***

Monday July 27, 2026

8:00 AM – 4:00 PM **Registration** – *Rocky Mountain Event Foyer*

Symposium III - Integrated Omics for Natural Products Discovery

Rocky Mountain Event
Chair: **Allegra Aron**

8:30 AM – 9:05 AM **PL-05 – Allison Walker** (Vanderbilt University)
Machine Learning Strategies for Natural Product Discovery and Engineering Biosynthesis

9:05 AM – 9:40 AM **PL-06 – Jason McDermott** (Pacific Northwest National Laboratory)
Understanding the Dark Matter of the Metabolome Using Multi-Omic Characterization: Can AI Save Us? Maybe

9:40 AM – 10:00 AM **C-18** – **Kalindi Morgan** (University of Northern British Columbia)
Integrating Genomics and Nitrogen-15 NMR for Natural Product Discovery from Northern Canadian Bark Beetle-Associated Bacteria

10:00 AM – 10:30 AM **Break** – *Rocky Mountain Event Foyer*

Symposium IV - Natural Products and Molecular Targets for Cancer

Rocky Mountain Event
Chair: **Joanna Burdette** (University of Illinois, Chicago)

10:30 AM – 11:05 AM **PL-07 – Xue (Sherry) Gao** (University of Pennsylvania)
Engineering CRISPR Systems for Precision Therapeutics and Molecular Innovation

11:05 AM – 11:40 AM **PL-08 - Daniel Labarbera** (University of Colorado)
The Mechanism of Action of Small-Molecule CHD1L Inhibitors

11:40 AM – 12:00 PM **C-19** – **Luis Prieto-Costas** (Puerto Rico Science, Technology and Research Trust)
Screening Natural Products Protein Targets Using the HuProtTM Proteome Microarray

12:00 PM – 2:30 PM Presenters for Poster Session I Set up Posters
Atrium

12:00 PM – 1:30 PM **Fellows Meeting (Invitation Only)** – *Cottonwood*

Session M-PM1 – Early Career

Evergreen Ballroom A
Chair: **Joe Egan** (Ometa Labs)

1:30 PM – 2:00 PM **I-08 -Vitor Lourenzon** (Univeristy of Illinois at Chicago)
Selective Antibiotic Antidotes Produced by Marine Sponge-Associated Bacteria

2:00 PM – 2:30 PM **I-09 – Jerry Carr** (University of Arizona)
Terpenes from Cannabis sativa Relieve Neuropathic Pain in Mice via the Adenosine A2a Receptor Expressed in Pax2+ Spinal Inhibitory Interneurons

2:30 PM – 2:45 PM **Break**

2:45 PM – 3:00 PM **C-20 – Alyssa Rodriguez** (University of Michigan)
A Metabolite Prioritization Pipeline for Antifungal Drug Discovery from Microbial Symbioses

3:00 PM – 3:15 PM **C-21 – William Crandall** (Emory University)
Energy Resolved Ion Mobility Mass Spectrometry of Natural Product Diastereomers

3:15 PM – 3:30 PM **C-22 – Hyomoon Cho** (NIH)
Multi-Level Relative Mass Defect Analysis for Natural Product Classification

3:30 PM – 3:45 PM **C-23 – Victor Olaoye** (The University of Rhode Island)
Thiamine Reverses Dormancy in Uropathogenic Escherichia coli

Session M-PM2 – Marine Natural Products

Evergreen Ballroom B
Chair: **Wendy Strangman** (University of North Carolina at Wilmington)

1:30 PM – 2:00 PM **I-10 -Aaron Puri** (University of Utah)
Connecting Genes to Molecules Using Inverse Stable Isotopic Labeling (Inversil)

2:00 PM – 2:30 PM **I-11 – Shaun McKinnie** (University of California, Santa Cruz)
The Chemoenzymatic Syntheses of 'Clickable' Kainoid Derivatives for Chemical Neuroscience Applications

2:30 PM – 2:45 PM **Break**

2:45 PM – 3:00 PM **C-24 – Byeol Ryu** (University of California, San Diego)
Unraveling the Structural Complexity of a Bastimolide A–Like Antitrypanosomal Macrolide

3:00 PM – 3:15 PM **C-25 – Chase Clark** (Evoquant)
A Platform for the Discovery of Novel Microbial Natural Product Chemical Scaffolds and Their Biological Targets

3:15 PM – 3:30 PM **C-26 – Cleo Orlando** (Virginia Tech)
Understanding the Role of Bacterial Glycoside Hydrolase Present in the Microbiota of Moon Snail Egg Masses

3:30 PM – 3:45 PM **C-27 – Barry O'Keefe** (National Cancer Institute)
Isolation and characterization of an antiviral protein from the soft coral Alertigorgia sp., derived from the NCI marine aqueous extract library

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3:45 PM – 4:00 PM **Break –** Bar Open During Break – *Atrium*

4:00 PM – 6:00 PM **Poster Session I** *–Atrium* *Sponsored by:*
Poster #'s: P-001 – P-077
All posters need to be picked up by Tuesday 9:00 AM
ASP is not responsible for lost or damaged posters.

COLLEGE OF PHARMACY
UNIVERSITY OF UTAH
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Session M-PM3 – Taking Action with the ASP

Evergreen Ballroom A

6:00 PM – 6:45 PM *This informal workshop and discussion will provide an overview of the ASP and how it functions led by two long time members, a discussion by the incoming ASP President on ways to get involved through committees, and an update on ASP student chapters and their impact led by a PhD student with a history of engagement in the society.*

7:00 PM – 10:00 PM **Early Career Event** (Ticketed Event) – *Pikes Peak*

Sponsored by: Lilly

Tuesday July 28, 2026

8:00 AM – 12:00 PM **Registration** – *Rocky Mountain Event Foyer*

Symposium V - Synthetic Strategies for Natural Product Lead Development

Rocky Mountain Event
Chair: **Tarek Sammakia (Eli Lilly and Company)**

8:30 AM – 9:05 AM **PL-09 – Richmond Sarpong** (University of California, Berkeley)
Break-it-to-Make-it Strategies and Methods for Chemical Synthesis Inspired by Complex Natural Products

9:05 AM – 9:40 AM **PL-10 - Mingji Dai** (Emory University)
Chemistry Innovation and Biological Discovery through Natural Product Total Synthesis

9:40 AM – 10:00 AM **C-28 – Sian Marin** (University of South Florida)
Growing Yeast for a Semi-synthetic Approach to the Core of Eleutherobin

10:00 AM – 10:30 AM **Break** – *Rocky Mountain Event Foyer*

Symposium VI - Synthetic Biology for Natural Products Production and Engineering

Rocky Mountain Event
Chair: **Eric Schmidt** (University of Utah)

10:30 AM – 11:05 AM **PL-11 – Bruno Perlatti** (Hexagon Bio)
Resistance-Gene Guided Genome Mining and Heterologous Expression of Fungal Biosynthetic Gene Clusters for Discovery of Bioactive Compounds

11:05 AM – 11:40 AM **PL-12 - Carrie Eckert** (Oak Ridge National Laboratory)
Development and Implementation of High Throughput Genetic Tools for Gene Discovery and Microbial Engineering

11:40 AM – 12:00 PM **C-29 – Elizabeth Skellam** (University of North Texas)
Complete Biosynthesis of Penicillin G in the Plant Host Nicotiana Benthamiana

12:00 PM – 5:00 PM **Executive Committee Meeting** (Invitation Only) – *Cottonwood*

1:30 PM – 3:30 PM **PMWS1** – *Evergreen E-F*
Career Fair - The Early Career Committee is hosting a career fair! Be sure to stop by to expand your network, learn about various career opportunities, and potentially find your next role.

1:30 PM – 3:30 PM **PMWS2** – *Aspen*
Natural Products Research and Teaching at Primarily Undergraduate Institutions
Workshop Leaders: **Christine Theodore** (The University of Tampa) and **Daniel May** (Washington College)

4:00 PM – 6:00 PM **Poster Session II** – *Atrium*
Poster's: P-078 – P-156
All posters need to be picked up by Wednesday 9:00 AM
ASP is not responsible for lost or damaged posters.

6:00 PM – 8:00 PM **Elevate Your Network** – *Pint Brothers*
Don't take your time at the meeting for granite … or be too in-tents … be boulder and peak your sense of community. This informal mix and mingle event will be held in the lobby bar area but is open to all. We just want to provide a space for new members to network, established members to reconnect, and everyone to enjoy a bit of good conversation and fun. Bring a favorite easy card game or join in a game with some new friends. Build collaborations in science or to plan a hike.

Wednesday July 29, 2026

8:00AM – 2:00PM **Registration** – *Rocky Mountain Event Foyer*

Award Symposium I
Rocky Mountain Event
Chair: **Cindy Angerhofer**

8:15 AM – 9:00 AM **A-02 - Rachel Mata** (Universidad Nacional Autonoma de Mexico)
Phillip Crews Mentoring Award 2026
Malbranchea Fungi: Key Discoveries Shaping the Future of Bioprospecting

9:00 AM – 9:45 AM **A-03 - Matthias Hamburger** (University of Basel)
Farnsworth Award 2026
Musings of a Pharmaceutical Biologist

9:45 AM – 10:30 AM **A-04 - Jie Li** (The University of Texas at Austin)
Suffness Award 2026
Mining Immunomodulatory Metabolites at the Human-Microbe Interface

10:30 AM – 11:00 AM Break – *Rocky Mountain Event Foyer*

Session W-AM1 – Animal and Environmental Microbiomes in Health and Disease

Rocky Mountain Event

Chair: **Vanessa Phelan** (University of Colorado, Anschutz)

11:00 AM – 11:30 AM **I-12** - **Manuela Raffatellu** (University of California, San Diego)
Host-Microbe Competition for Iron in the Inflamed Gut: From Basic Discoveries to Translational Applications

11:30 AM – 11:45 AM **C-30 – Reed Stubbendieck (**Oklahoma State University)
Dynamic Secondary Metabolite Production Mediates Interactions That Structure the Cystic Fibrosis Lung Microbiota

11:45 AM – 12:00 PM **C-31 – Tribute and Open Remembrance: In Memory of Lukasz Ciesla**
This slot is reserved for those who wish to step forward and share a personal or professional memory of Lukasz

Session W-AM2 – Clinical Translation

Pikes Peak

Chair: **Amy Keller** (University of Colorado)

11:00 AM – 11:30 AM **I-13 – Emily Lindley** (University of Colorado, Anschutz)
Exploring the Therapeutic Potential of Cannabinoids for Chronic Musculoskeletal Pain

11:30 AM – 11:45 AM **C-32 – Veronika Butterweck** (Max Zeller Soehne AG)
Exercise-Associated Metabolic Effects of the Cimicifuga racemosa Extract Ze 450 in a High-Fat Diet Model

11:45 AM – 12:00 PM **C-33 – James Hassell** (University of Colorado, Anschutz)
Blocking Microglial Endogenous Fructose Production with Green Tea Catechin Prevents Metabolic Reprogramming

Session W-PM1 – Animal and Environmental Microbiomes in Health and Disease

Rocky Mountain Event

Chair: **Vanessa Phelan** (University of Colorado, Anschutz)

1:30 PM – 2:00 PM **I-14** – **Andrew Goodman** (Yale University)
Drug-Microbiome Interaction

2:00 PM – 2:15 PM **C-34 – Jennifer Nguyen** (University of Michigan)
Integrated Multi-omics Analysis Reveal Role of Strain Specific Bacterial Metabolites in Colorectal Cancer Pathogenesis

2:15 PM – 2:30 PM **C-35 – Gisele Rodriguez** (University of Utah)
The Filamentous Gut-Fungus Basidiobolus as a Reservoir for Biologically Relevant Peptidic Natural Products

Session W-PM2 – Clinical Translation

Pikes Peak

Chair: Amy Keller (University of Colorado)

1:30 PM – 2:00 PM	**I-15 – Andrew Novick** (University of Colorado) *Effects of Psilocybin on Anhedonia in Treatment-Resistant Major Depressive Disorder*
2:00 PM – 2:15 PM	**C-36 – Ester Oh (**University of Colorado, Anschutz) *Acute Effects of Equol on Vascular Endothelial Dysfunction in Postmenopausal Women and Mice*
2:15 PM – 2:30 PM	**C-37 – Alpna Tyagi** (University of Colorado Anschutz) *Honokiol Hexafluoro Administration in Mice Enhances the Brain Mitochondrial Functions*

3:00 PM – 5:00 PM	**ASP Business Meeting** – *Rocky Mountain Event* All ASP Members Welcome (Associate Members may attend but Voting Privileges are for Full Members Only)
6:30 PM – 7:00 PM	**Closing Reception** – ***Atrium***
7:00 PM – 10:30 PM	**Banquet and Closing Program** – *Rocky Mountain Event* (Ticketed Event)

****Program Subject to Change****

Thank you for your participation in the 2026 ASP Meeting!

See you in Orlando for ASP2027!

American Society of Pharmacognosy

Award Speakers

A-01 – Michael Heinrich

… inspired by diversity: A Biological and Chemical Journey from (Medical) Anthropology to Ethnopharmacology.

Michael Heinrich[1,2] *[1] Pharmacognosy and Phytotherapy Group, UCL School of Pharmacy WC 1N 1AX, United Kingdom. [2] Chinese Medicine Research Centre, College of Chinese Medicine, China Medical University, Taichung, Taiwan*

In this presentation I look back and forth on an academic and personal journey which started in earnest around 1980 and with Bernard Ortiz de Montellano (1936 – 2016), an organic chemist and a Chicano supervising me in the middle of Detroit at Wayne State University, Michigan This has taken a German suburban kid on a journey driven by some key questions and changing challenges. Most recently we have focused in considerable detail on climate changes. With human activities severely impacting plants and ecosystems, threatening biodiversity, healthcare resources, and sustainable development, medicinal plants offer one opportunity within ecosystem services including climate mitigation, and for their socio-economic role (Takubessi et al., 2025). Back to the start of this journey: B. Ortiz de Montellano (1975) had asked a simple and crucial question, how can we assess the effects of plants used by the Aztecs (México), if we assess them according to their therapeutic concepts. This in combination with the international drive to develop the new antimalarials medicine artemisinin led to a project which sought to find new leads for anti-malarial leads from Mexican indigenous plants, The idea ultimately failed and instead a long series of studies resulted from fieldwork in México, first on my own for the PhD and then with students co-supervised by Otto Sticher (Zürich) and Horst Rimpler (Freiburg). The therapeutic focus shifted to anti-inflammatory and anti-infective agents also with an emphasis on a new innovative target – NF-κB (joint with Lienhard Schmitz, now Giessen, Germany (Heinrich et al 2014). With a move to a chair at the School of Pharmacy, Univ London, UK at the turn of the millennium (now UCL School of Pharmacy), a range of new exciting lines of research and development were possible including more work on anti-inflammatory agents and on Mediterranean food plants, funded through the European continued some of these interests, with novel foci developing on the quality and authenticity of herbal medicines, their safety and potential. More and more the fast emerging role of plants from Asia moved centre stage as well as most recently the challenges linked to climate change (Mykhailenko et al 2025). What continues throughout this journey has been an enthusiasm for understanding and supporting biocultural diversity and to work in multicultural and transdisciplinary contexts – '….inspired by diversity'

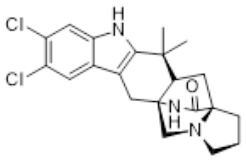
Heinrich, M. , Leonti, M.,. Frei Haller, B. 2014. A perspective on natural products research and ethnopharmacology in México. The eagle and the serpent on the prickly pear cactus. Journal of Natural Products 77: 678–689. dx.doi.org/10.1021/np4009927 Ortiz de Montellano BO. Empirical Aztec medicine. 1975, Science. 188(4185):215-20. doi:10.1126/science.1090996. Mykhailenko O, Jalil B, McGaw LJ, Echeverría J, Takubessi M, Heinrich M. 2025. Climate change and the sustainable use of medicinal plants: a call for "new" research strategies.Front Pharmacol. 15:1496792. doi: 10.3389 /fphar.2024.1496792. Acknowledgements: Thanks to all who were a part of this journey and esp. to Doug Kinghorn (Ohio) present here)

A-02– Rachel Mata

Malbranchea Fungi: Key Discoveries Shaping the Future of Bioprospecting

Rachel Mata and coworkers. Departamento de Farmacia, Facultad de Química, Universidad Nacional Autónoma de México, Ciudad de México 04510, México

The genus Malbranchea has emerged as a fertile and underexploited source of structurally diverse natural products with clear pharmacological potential. Across multiple species, we have isolated distinct classes of bioactive metabolites: Some display complementary activities relevant to cardiometabolic diseases. These activities include calmodulin modulation and vasorelaxation, inhibition of carbohydrate-hydrolyzing enzymes (a-glucosidase), allosteric inhibition of protein tyrosine phosphatase 1B (PTP1B), and insulinotropic/insulin-sensitizing effects. Malbrancheamide (**1**) and gymnoascolide A (**2**) are the flagship compounds from this work. Altogether, the evidence supports advancing translational efforts through several parallel pathways, while highlighting that training many graduate students and postdoctoral fellows has been the most significant outcome.



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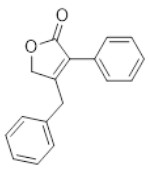

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A-03– Matthias Hamburger

Musings of a Pharmaceutical Biologist

Matthias Hamburger, Department of Pharmaceutical Sciences, University of Basel, 4050 Basel, Switzerland

The lecture will provide a journey through my scientific career. I will pay tribute to the scientists and mentors who were important in shaping my decision to embark on this journey. Overarching aspects that have been a common thread throughout my work will be addressed, and my fascination with specialized metabolites and their amazing structural diversity exemplified with selected cases.I will describe specific areas where, together with my respective teams in industry and academia, I was able to make important contributions to the natural products field, including bioautographic methods, HPLC-PDA-MS based dereplication, instrumented extraction technologies, HPLC-based activity profiling for a miniaturized localization and identification of bioactive compounds in extracts, high content screening utilizing biological probes and imaging technologies, and biopharmaceutical evaluation of natural products. Aspects of library-based discovery in academia, and multidisciplinary collaboration with other academic groups and with pharmaceutical industry will also be addressed.

A-04 – Jie Li

Mining Immunomodulatory Metabolites at the Human-Microbe Interface

Jie Li, Conor Pulliam, Michael Madden, Hanyu Xiao, Dan Xue, Mingming Xu, Paige Ellingson, Leilei Gou, and Katherine Holandez-Lopez. Division of Chemical Biology and Medicinal Chemistry, College of Pharmacy, University of Texas at Austin, Austin, TX 78712

The human microbiome—comprising trillions of microorganisms and their genetic material—is a critical modulator of health and disease, influencing conditions ranging from inflammation to cancer. Despite this established link, the specific molecular mechanisms by which the microbiome mediates disease outcomes remain largely unknown. A primary interface of this interaction involves microbiome-encoded functional metabolites, which maintain direct and constant contact with host cells. This talk presents an integrated, multi-omics approach to mining immunomodulatory metabolites at the human-microbe interface. By further leveraging a biosynthetic enzyme-disease correlation strategy, we have established direct links between microbiome-encoded metabolites and specific disease conditions, providing a roadmap for their discovery and biological evaluation. Our efforts have discovered microbiome-derived mimics of human endogenous metabolites that exhibited dual immunomodulatory activities, offering new insights into the chemical modulation between the microbiome and the host.

PLENARY SPEAKERS

PL-01 –Carole Bewley

Chemical Mechanisms of Natural Product Antibiotics:Targets, Enzymes, and Self-Resistance

Carole Bewley, Gengxiang Zhao, Victoria Klein, Hongbing Liu, Shannon Ohlemacher. Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health, Bethesda, MD 20892

Structurally complex natural products remain a rich source of antibiotics and powerful probes of cellular vulnerabilities and function. Our laboratory integrates natural products chemistry, structural biology, and mechanistic enzymology to identify how these molecules interact with bacterial targets and how producing organisms manage their biosynthesis and self-protection. This talk highlights complementary studies spanning these themes. For example, recent studies in our laboratory sought to determine the mechanism by which marine pyrrole–imidazole alkaloids such as sceptrin, exert antibiotic activity and act as antibiotic adjuvants that restore susceptibility in drug-resistant strains. We found that sceptrin specifically targets negatively charged lipids in the bacterial membrane and induces adaptive lipid remodeling responses that reinforce outer-membrane integrity in *Escherichia coli*. Structural investigations of ATP-grasp ligases that install ω-lactone and ω-lactam crosslinks during graspetide maturation have illuminated substrate recognition and macrocyclization mechanisms in RiPP biosynthesis, and functional studies have uncovered a potential regulatory mechanism. Finally, studies of the desert-derived aridomycins identify reversible glycosylation as an unusual self-resistance strategy and define a new acyltransferase specificity motif associated with hydroxymalonyl-ACP incorporation in Type I polyketides. Together, these examples illustrate how mechanistic studies of natural product antibiotics reveal targets, biosynthetic logic, and resistance strategies.

PL-02 –Jason Crawford

Mode of Action for Translational Inhibitory Nucleotides Encoded in the Human Microbiome

Emily Reagle[1,2] and Jason M. Crawford[1,2,3] [1]Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT 06510, [2]Institute of Biomolecular Design & Discovery, Yale University, West Haven, CT 06516, [3]Department of Chemistry, Yale University, New Haven, CT 06511

We previously characterized a translational inhibitory nucleotide featuring an orthoester moiety that was encoded in the human vaginal microbiome member *Lactobacillus iners*. Lipidation of the molecule by an atypical nonribosomal peptide synthetase (NRPS) enzyme in the *L. iners* pathway led to compound inactivation, supporting a prodrug mechanism for translational inhibition. However, the mode of action remained unknown. In this study, we characterized related pathways in gut *Enterococcus cecorum* and soft tissue *Mycobacterium decipiens*, and collective analysis of the three microbiome-encoded pathways and their products supported selective inhibition of the tyrosyl-tRNA synthetase, a required component for protein translation. Intriguingly, a mis-annotated "abortive" tRNA synthetase contributes to the synthesis of the nucleotide and orthoester linkage, whereas a separate atypical tRNA synthetase serves a self-resistance enzyme (SRE) role. Biochemical and binding studies further validated the tyrosyl-tRNA synthetase as the target for these unusual nucleotide pathways found across several body sites and other environmental microbiomes.

PL-03 –Jessica Prenni

The Periodic Table of Food Initiative: Mapping the Chemistry of Food

Jessica E. Prenni[1], Ming Wang[2], Melanie Odenkirk[1], Rachel Jones[1], Jacqueline Chaparro[1], Katie Fromuth[1], Chi-Ming Chien[3], Steve Watkins[3], Tracy Shafizadeh[3], Sarah Brinkley[4], Jillian Pavich[4], Nile Nair[4], John de la Parra[5], Selena Ahmed[4]. [1]Department of Horticulture and Landscape Architecture, Colorado State University, Fort Collins, CO, [2]University of California Riverside, Riverside, CA, [3]Verso Biosciences, Inc., Davis, CA, [4]The American Heart Association, Dallas, TX, [5]The Rockefeller Foundation, New York, NY

What is in our food, and how much of it have we actually characterized? Conventional food composition databases capture only a fraction of the chemical complexity of foods, typically reporting fewer than 160 components. Leveraging advances in mass spectrometry, the Periodic Table of Food Initiative (PTFI) is a global effort to systematically map the chemical composition of the world's edible biodiversity using standardized, high-resolution analytical workflows. Here, we present a comprehensive molecular characterization of 500 foods spanning 250 species and diverse ontologies, including plants, animals, fungi, algae, and processed foods. Using harmonized protocols across multiple laboratories, we applied untargeted mass spectrometry approaches to profile the small molecule composition of the foods. Nontargeted LC–MS workflows incorporated a novel retention time indexing system and consensus-based feature annotation. These data reveal extensive, previously underappreciated chemical diversity across foods, including both known compounds and structurally unresolved "known unknowns." Deeper exploration of the data using open-source tools within the GNPS2 environment enabled putative annotation through characterization of structural analogues. By establishing a scalable and standardized framework for food composition analysis, PTFI is generating a foundational resource for natural products discovery and enabling new connections between food chemistry, human health, and environmental sustainability.

PL-04 – Cassandra Quave

Development of a MicroED-Enabled Discovery Platform for Rapid Identification of Bioactive Natural Products

Lewis Marquez[1], Ella Vardeman[1], William J. Crandall[1], Hailey Swaldi[1], Diandre Slusarek[1], Cassandra L. Quave[1], Emory University School of Medicine, Atlanta, GA 30322, USA

Natural products offer unparalleled chemical diversity for drug discovery, yet discovery pipelines remain constrained by slow, iterative workflows requiring repeated purification prior to structure elucidation. To address this bottleneck, we developed a microcrystal electron diffraction (MicroED) enabled discovery platform integrating semi-preparative HPLC fractionation, bioactivity screening, and mass spectrometry to enable rapid structural determination of bioactive small molecules from complex mixtures. Crude plant extracts are fractionated to generate high-resolution libraries (up to 188 fractions) arrayed into 96-well plates. Fractions are arrayed into 96-well plates dedicated to bioactivity screening, LC–MS/MS dereplication, and MicroED analysis. Active wells are prioritized using assay-driven heatmaps and selectively analyzed by LC–MS/MS and MicroED, with plates screened for microcrystalline material (~500 nm). Microcrystal structures are then solved directly by MicroED using a Rigaku XtaLAB Synergy-ED electron diffractometer, eliminating iterative purification and enabling rapid transition from bioactive fraction to molecular identification. This workflow provides a scalable framework that can be extended to fungal and marine natural product discovery. Applications to antimicrobial and anti-inflammatory discovery will be presented, including assays against *Candida albicans* and *Gardnerella vaginalis*, enabling rapid prioritization and structural characterization of active compounds from complex extracts. Proof-of-principle studies using COX-2 inhibition assays in 96-well plates further demonstrate the utility of this approach for identifying analgesic and anti-inflammatory natural products. Together, this work establishes a generalizable framework for rapid, scalable identification of bioactive small molecules across diverse chemical space and advances a new paradigm linking chemical structure to biological function from complex mixtures.

PL-05 – Allison Walker

Machine Learning Strategies for Natural Product Discovery and Engineering Biosynthesis

Allison S. Walker[1,2] [1]Department of Chemistry, Vanderbilt University, 1234 Stevenson Center Lane, Nashville, TN 37240, United States [2]Department of Biological Sciences, Vanderbilt University, VU Station B, Box 35-1634, Nashville, TN 37235, United States

Natural products play an important role in drug discovery. However, they are often discovered serendipitously and there is a lack of tools that enable prioritization of organisms that are likely to produce active and structurally novel compounds. In addition, natural products often need to be modified in order to be developed as therapeutics, but total synthesis of natural products is challenging. My lab aims to develop AI-guided genome mining techniques to enable the discovery of natural products with therapeutically-relevant bioactivities and the engineering of biosynthetic machinery to produce new natural product-like compounds. In this presentation, I will discuss my group's recent progress in these areas. Specifically, I will focus on strategies to predict natural product bioactivity from biosynthetic gene cluster sequences and experimental validation of this approach. In addition, I will discuss recent developments in creating a pretrained model for prediction of both bioactivity and structural features from biosynthetic gene cluster sequence.

PL-06 – Jason McDermott

Understanding the Dark Matter of the Metabolome Using Multi-Omic Characterization: Can AI Save Us? Maybe

Jason McDermott, Yannick Mahlich, Dylan Ross, Sutanay Choudhury, Lummy Monteiro

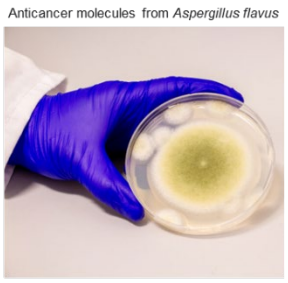
Despite continuing advances in sequencing and computational function determination, large parts of the studied gene, protein and metabolite space remain functionally undetermined. Most function assignment is driven by homology searches and annotation transfer from known and extensively studied molecules, which limits function prediction for genes and proteins when homology can't be established, and is impossible for metabolites and lipids. Alternate function prediction methods have been developed but do not make use of available experimental omics data generated via technologies like mass-spectrometry, which represents a rich source of unrealized functional information. The VaLPAS (Variation Leveraged Phenomic Association Screen) framework is an approach to shed light on the functional dark matter of molecular space by elucidating previously unknown functions of proteins and metabolites via statistical association metrics (correlation, mutual information) and novel unsupervised ML approaches to better capture non-linear associations between molecules. Furthermore, we have implemented supervised methods if known relationships are available, and these are used to calculate confidence metrics for predictions in a report format. We benchmark VaLPAS on multiomic data from oleaginous yeasts and bacterial datasets using KEGG module and pathway membership. Our results show that VaLPAS is able to assign KEGG module membership with high confidence for a large number of proteins and metabolites that have no known functional labels. Tracking metabolites across MS experiments has allowed us to assign putative functional annotation for a large number of small molecules from bacterial systems that were previously unknown. In this study we show the applicability of using experimental abundance data from detectable metabolites and proteins (extendable to other modes of experimental data) to infer protein functionality and metabolite annotation for as of yet unannotated data.

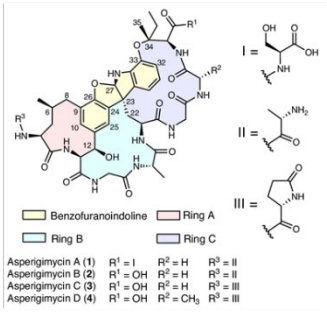
PL-07 – Xue Gao

Engineering CRISPR Systems for Precision Therapeutics and Molecular Innovation

Xue Gao[1, 2, 3]. [1]*Department of Chemical and Biomolecular Engineering, University of Pennsylvania, Philadelphia, PA 19104, United States.* [2]*Center for Precision Engineering for Health, University of Pennsylvania, Philadelphia, PA 19104, United States.* [3]*Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104, United States*

CRISPR genome editing has transformed our ability to interrogate and reprogram biological systems, opening new opportunities for drug discovery. In this talk, I will present our recent efforts to engineer next-generation CRISPR platforms with improved precision and multiplexing capabilities, enabling systematic and scalable exploration of biosynthetic pathways. We apply these tools to fungal genome engineering to uncover cryptic biosynthetic gene clusters and access previously hidden small-molecule diversity, leading to the discovery of novel compounds with therapeutic potential.





PL-08 – Daniel LaBarbera

The Mechanism of Action of Small-Molecule CHD1L Inhibitors

Daniel V. LaBarbera, Qiong Zhou, Hector Esquer, and Paul Awolade. The CU Anschutz Center for Drug Discovery, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

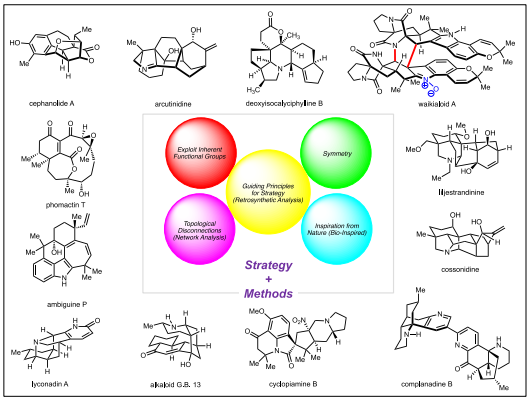
Chromodomain Helicase DNA-binding Protein 1-Like (CHD1L), also known as ALC1, is a PAR-regulated chromatin remodeling enzyme amplified and overexpressed across multiple cancer indications, where it promotes tumor progression, metastasis, and therapeutic resistance. CHD1L orchestrates oncogenic transcriptional and stress-response programs that enable tumor cell adaptation, manifested in phenotypes including epithelial–mesenchymal plasticity and cancer stem cell states. More fundamentally, CHD1L functions as a master regulator of tumor cell survival under cellular stress and immune pressure through coordination of DNA damage response and repair (DDR), G1. OTI-611 binds allosterically to CHD1L, inhibiting its ATPase and chromatin remodeling activity. In cells, this interaction entraps CHD1L onto chromatin, thereby suppressing malignant gene expression and DDR signaling while inducing G1 cell cycle arrest. Furthermore, CHD1L acts as a gatekeeper of PARthanatos, a programmed cell death pathway driven by fragmentation of poly(ADP-ribose) (PAR) and nuclear translocation of apoptosis-inducing factor (AIF), leading to large-scale DNA fragmentation. The mechanism of action of OTI-611 overcomes apoptosis and necrosis-associated cell death evasion and strongly synergizes with chemotherapy and targeted therapies across multiple cancer types, producing order-of-magnitude improvements in therapeutic response in preclinical models. These findings position CHD1L as a precision oncology target and redefine combination therapy by eliminating tumor cells via PARthanatos rather than cytotoxic damage.

PL-09 – Richmond Sarpong

Break-it-to-Make-it Strategies for Chemical Synthesis Inspired by Complex Natural Products

Richmond Sarpong, Department of Chemistry, University of California–Berkeley, Berkeley, CA 94720, United States of America

Natural products continue to inspire and serve as a basis of new medicines. They also provide intricate problems that expose limitations in the strategies and methods employed in chemical synthesis. Several strategies and methods that have been developed in our laboratory and applied to the syntheses of architecturally complex natural products will be discussed. In particular, new ways to employ the cleavage of core bonds such as C–C and C–N bonds (i.e., break-it-to-make-it strategies) to achieve skeletal editing will be presented.



PL-10 – Mingji Dai

Chemistry Innovation and Biological Discovery through Natural Product Total Synthesis

Mingji Dai[1]. [1]Department of Chemistry and Department of Pharmacology and Chemistry Biology, Emory Univeristy, 1515 Dickey Drive, Atlanta, GA

Our recent efforts focus on function and efficiency-driven total synthesis of medicinally important natural products. Herein, case studies on the curcusone diterpene and the veragranine steroidal alkaloid will be used to highlight how we use natural product total synthesis to achieve synthetic strategy and methodology innovation and biological discovery. The latter includes biological evaluation and target identification of the selected natural products and their analogues via collaborations, which have led to novel protein targets and promising lead compounds for the treatment of glioblastoma and chronic pain.

PL-11– Bruno Perlatti

Resistance-Gene Guided Genome Mining and Heterologous Expression of Fungal Biosynthetic Gene Clusters for Discovery of Bioactive Compounds

Bruno Perlatti, Colin J.B. Harvey. Hexagon Bio, Menlo Park, CA, 94025

Fungal natural products remain one of the most prolific sources of bioactive small molecules, yet traditional discovery workflows are often hindered by frequent rediscovery, limited capacity of unlocking full biosynthetic potential of wild type strains, and a lack of early-stage mechanistic insight. To address these challenges, we have developed a genome-centric platform to accelerate the identification of novel leads with predefined modes of action (MOA). By leveraging a global collection of > 120,000 fungi and a database of > 90,000 genomes and over 4 million biosynthetic gene clusters (BGCs), we employ a proprietary algorithm to identify "R-genes", resistance-gene homologs co-localized within BGCs that serve as internal maps to a compound's predicted biological target. This "target-first" approach allows for the prioritization of clusters likely to yield inhibitors for high-value and/or "hard-to-drug" proteins. To overcome the limitations of native fungal production, we utilize a high-throughput heterologous expression framework in *Aspergillus nidulans*, enabling the stable production and structural characterization of novel metabolites, used for downstream assays and MOA validation. The utility of this platform is demonstrated through several successful discovery cases. This integrated workflow combining resistance-gene guided genome mining, advanced synthetic biology, high throughput metabolomics, precise natural products chemistry and orthogonal MOA determination provide a scalable path for discovering the next generation of bioactive compounds for applications in oncology, infectious disease, and agriculture.

PL-12– Carrie Eckert

Development and Implementation of High Throughput Genetic Tools for Gene Discovery and Microbial Engineering

Margaret Bales[1,2,3], Jiwoo Kim[1,2], Yasemin Kaygusuz[1,2], Andrea Garza Elizando[1], Rebecca Wilkes[1,2], Ilenne del Valle Kessra[1], William Alexander[1,2], Adam Guss[1,2], Carrie A. Eckert[1,2]. [1]Biosciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831, USA, [2]Center for Bioenergy Innovation, Oak Ridge National Laboratory, Oak Ridge, TN, 37831, USA, [3]Bredesen Center for Interdisciplinary Research and Graduate Education, University of Tennessee, Knoxville, TN, 37996

The ability to effectively engineer microbes for the conversion of cheap feedstocks to a variety of performance-advantaged chemicals and products is key for achieving economically viable and scalable platforms for an emerging bio-based economy. Even the most studied chassis, *E. coli* and *S. cerevisiae,* are still limited in application due to a lack of functional understanding of all genes in their genomes and how to effectively engineer complex phenotypes (e.g. tolerance) and heterologous production pathways. There are many non-model microbes with natural capabilities for key bioconversion processes, but lagging genetic tool development slows engineering efforts. Approaches for accelerated microbial engineering rely on the development of enabling genetic toolsets across a broader range of microbial species and the deployment of these tools in a Design-Build-Test-Learn (DBTL) research cycle to expand generation of datasets, both global and targeted, to reveal underlying design principles to address engineering challenges. The application of CRISPR-Cas has enabled library based high-throughput and multiplexed experiments for genotype-phenotype mapping, protein engineering, strain engineering, and novel gene discovery in model microbial systems. Here I will discuss recent advances and future applications of genetic tool development towards engineering and high throughput functional genomics platforms for a broader array of microbes.

INVITED SPEAKERS

I-01 –Carole Bewley

Natural Products in Space and Time: from Ancient Molecules to Microbial Arms Races

Pierre Stallforth[1,2]. [1]Leibniz Institute for Natural Product Research and Infection Biology – Leibniz-HKI, [2]Friedrich Schiller University, Jena, Germany

Microbial natural products are a critical source of therapeutic agents. These compounds are shaped by intricate ecological interactions. Predator–prey dynamics between amoebae and bacteria represent particularly rich reservoirs of these secondary metabolites. Amoebae, as ubiquitous bacterivores, exert strong selective pressure, driving bacterial defenses against grazing and, in turn, amoebal counter-adaptations.[1] We investigate the biosynthesis and diversification of amoebicidal natural products, including polymicrobial modifications that expand their chemical repertoire. Extending this perspective into the past, we exploit ancient bacterial DNA to identify and reconstruct biosynthetic genes, providing access to previously untapped natural product diversity.[2] References: [1] S. Zhang, K. Schlabach, V. H. Pérez Carillo, A. Ibrahim, S. Nayem, A. Komor, R. Mukherji, S. Chowdhury, L. Reimer, F. Trottmann, A. C. Vlot, C. Hertweck, U. A. Hellmich, P. Stallforth *Cell* **2025**, *188*, 2495. [2] M. Klapper, A. Hübner, A. Ibrahim, I. Wasmuth, Maxime Borry, V. G. Haensch, S. Zhang, W. K. Al-Jammal, H. Suma, J. A. Fellows Yates, J. Frangenberg, I. M. Velsko, S. Chowdhury, R. Herbst, E. V. Bratovanov, H.-M. Dahse, T. Horch, C. Hertweck, M. R. González Morales, L. G. Straus, I. Vilotijevic, C. Warinner, P. Stallforth *Science* **2023**, *380,* 619.

I-02 – Justin Slipe

Pectin-Based Formulation Protects Milk Fat Globule Membranes in Stored Human Milk

Justin E. Silpe[1], Hyesoo Kim[1,2], Anjali ShahLyng[1], Yi-Ting Tsai[2], Kelsey E. Johnson[3], Bum Jin Kim[4], Jennifer Branson[4], Carolyn M. Slupsky[5], Ameer Y. Taha[5], David C. Dallas[6], Itay Budin[2], and Bonnie L. Bassler[7,8,]. [1]PumpKin Baby Inc., Princeton, NJ; [2]University of California San Diego; [3]University of Southern California; [4]Oregon State University; [5]University of California Davis; [6]Oregon State University; [7]Princeton University; [8]Howard Hughes Medical Institute*

During household storage, expressed human milk can develop odor and flavor changes that trigger infant refusal and milk waste. We investigated whether this deterioration reflects disruption of the milk fat globule membrane (MFGM), the protective interface surrounding milk fat, and whether a low-methoxy pectin-based formulation (PBF) containing vitamins C and E preserves this structure. Using Di-4-ANEPPDHQ imaging, we found that storage at 4 C or -20 C progressively disrupted MFGM-localized fluorescence and increased dye penetration into the milk fat core, whereas PBF-treated milk retained peripheral MFGM signal during storage and after mammalian or bacterial lipase challenge. Natural variation in CEL and LPL transcript abundance correlated with measured lipase activity, supporting endogenous lipolysis as a contributor to stored-milk deterioration. PBF-treated samples showed lower glycerol in all 12 non-baseline donor-condition comparisons, with a maximum 16.8-fold reduction, and lower butyrate and caprate/caprylate signals in 11 of 12 and 10 of 12 comparisons, respectively. PBF also reduced oxidation-associated free oxylipins, including lower 13-HODE and 9-HODE in all 12 comparisons and lower 12(13)-EpOME in 11 of 12 comparisons. Proteomic profiles, bulk macronutrients, and culturable microbial burden showed no major PBF-associated shifts. In blinded olfactory testing, 36 of 44 adult evaluators identified PBF-treated, lipase-challenged milk as smelling more similar to fresh milk than lipase-only controls. These findings identify MFGM destabilization as a measurable mechanism of stored-milk deterioration and suggest that food-compatible pectin-based stabilization can preserve human milk sensory and lipid quality during routine storage.

I-03 – Tiffany Weir

The Gut Microbiome as an Important Determinant of Dietary Polyphenol Bioavailability

Jessica Prenni[1], Kelly Wrighton[1], Sarah Johnson[2], Anandh Babu Pon Velayutham[3]. Tiffany Weir[1]. [1]Colorado State University, [2]Florida State University, [3]University of Utah

Dietary polyphenols are extensively transformed by the gut microbiota, generating a diverse array of metabolites with distinct bioavailability and biological activities. These microbially derived transformations represent a critical, yet poorly understood, source of inter-individual variability in responses to polyphenol-rich foods. Blueberries are a well-characterized source of complex polyphenols whose metabolic fate is highly dependent on gut microbial composition and function. In this work, we use blueberry consumption as a model system to investigate how inter-individual differences in gut microbial polyphenol-metabolizing pathways shape circulating polyphenol metabolites and downstream host responses. By integrating multi-omics approaches—including metagenomics, metabolomics, and targeted bioinformatics analyses—we aim to identify specific microbial pathways and taxa responsible for polyphenol biotransformation in humans. This framework will advance mechanistic understanding of diet–microbiome interactions and support the development of precision nutrition strategies that account for microbial contributions to polyphenol metabolism and function.

I-04 – Milton Drott

Microevolutionary Reservoirs of Fungal Natural Products: From Aspergillus to Invasive Mushrooms

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Fungal natural products are typically studied at the species level, with one or a few isolates treated as representative of an organism's chemical potential. However, recent population genomic work suggests that substantial biosynthetic diversity exists within species and may reflect local adaptation, ecological interactions, and ongoing evolutionary processes. Using *Aspergillus flavus* as a model, we have demonstrated that more than 25% of biosynthetic gene clusters in the species pangenome exhibit population-specific patterns of presence, absence, or divergence, and that these genomic differences correspond to measurable differences in metabolite production. These findings suggest that fungal secondary metabolism is shaped by microevolutionary processes operating within genetically structured populations, with important implications for ecology, evolution, and natural product discovery. These processes extend far beyond *Aspergillus*: the invasive "death cap" mushroom (*Amanita phalloides*) similarly shows dynamic evolution of MSDIN toxin genes, including strong differentiation between invasive and native populations and evidence that toxin repertoires are maintained by natural selection. Intraspecific variation is not limited to secondary metabolite gene content; a newly discovered class of leaderless ribosomally synthesized and post-translationally modified peptides (RiPPs) varies by several orders of magnitude in expression between native and invasive populations of *A. phalloides*. Together, our work suggests that a population-genomic view of fungal secondary metabolism reveals a hidden reservoir of chemical diversity with broad relevance to ecology, invasion biology, and pharmacognosy-driven natural product discovery.

I-05 – Filipa Pereira

Optimizing Microbial Hosts for Sustainable Production of Natural Products

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Microbes are a rich source of natural products with significant pharmaceutical potential. Discovery and diversification of bioactive scaffolds remains an essential route to new therapeutics, yet complex microbial natural products have been largely inaccessible due to low production titers and synthetic challenges. Advances in genomic technologies, such as whole-genome sequencing and mining, have uncovered the full biosynthetic potential of microbes, revamping the search for novel natural products. However, to access those unexplored biosynthetic pathways we need to address limitations in microbial cultivation and uncontrolled expression of secondary metabolic pathways. Metabolic engineering approaches can tackle those challenges, enabling access to Nature's hidden chemistry. Here, by combining genome mining, engineering, and metabolomics, we provide scalable access to two structurally complex compounds from families of bioactive natural products, the plecomacrolides and cyclic prodiginines. Taken together, we show that coupling strain engineering with late-stage semi-synthetic and biocatalytic diversification expands chemical space.

I-06 – Jon Chekan

Aromatic Side Chain Crosslinking and Macrocyclization in RiPP Biosynthesis

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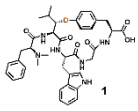
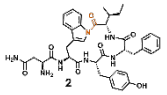
Peptide cyclization is a defining feature of many in RiPP natural products. A diverse array of new cyclases have been recently discovered that perform aromatic side chain crosslinking or macrocyclization. For example, we uncovered a new class of copper-dependent cyclases responsible for crosslinking observed in the burpitide family of plant RiPPs. Study of a burpitide cyclase (BpC) that installs a Tyr-O-Leu ether bridge from *Coffea arabica* (**1**) has given fundamental insights into the biochemical details of the BpC enzyme family. Separately, we have examined the ThiF-like protein family which is known to catalyze a variety of diverse reactions, such as phosphoramidate bond formation in microcin C7. Using genome mining, we uncover a gene cluster in the pathogen *Streptococcus pneumoniae*. In vitro reconstitution and product elucidation revealed an indolylamide macrocyclization (**2**) catalyzed by a member of the ThiF-like protein family, Together, these results expand our understanding of the diverse biosynthetic pathways and mechanisms responsible for aromatic side chain crosslinking and macrocyclization in RiPPs.





I-07 – Qihao Wu

Metabolomics-Guided Mapping of Chemical Interactions at the Diet–Microbiome Interface

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Diet-derived molecules represent a large and chemically diverse substrate space for gut microbial metabolism, yet these transformations remain difficult to map systematically. Here, we developed a repository-scale metabolomics framework to connect food-associated chemical features with microbiome-regulated metabolites across public food and biological datasets.

By integrating large-scale spectral organization, comparative metabolomics, and experimental prioritization, the framework recovered established microbial transformations and identified previously uncharacterized chemical interactions at the diet-microbiome interface. Prioritized candidates were investigated through structural validation, mouse metabolomic profiling, strain-resolved microbial assays, biochemical characterization, and activity profiling across human G protein-coupled receptors. These studies revealed previously unrecognized microbial activities that reshape diet-derived metabolites and alter the abundance and biological properties of molecules encountered by the host.

I-08 – Vitor Lourenzon

Selective Antibiotic Antidotes Produced by Marine Sponge-Associated Bacteria

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Pseudovibriamides B (PB) are depsipeptides isolated from the marine sponge-associated bacterium *Pseudovibrio brasiliensis* Ab134 that act as selective antidotes to the broad-spectrum antibiotic blasticidin S, an analog of P10 previously isolated from a marine sponge. To explore the ecological roles of PB, we engineered *P. brasiliensis* to optimize PB production and developed an assay to evaluate antidote activity. This assay revealed that PB selectively protects *Bacillus cereus* and a marine sponge–isolated *Bacillus* sp., but not pathogens or other sponge-associated bacteria, demonstrating narrow antidote activity. The optimization of PB production, the characterization of its biological activities and ecological role, and progress toward translating the antidote activity towards human health and elucidating its mechanism of Action will be presented.

I-09 – Jerry Carr

Terpenes from *Cannabis sativa* Relieve Neuropathic Pain in Mice via the Adenosine A2a Receptor Expressed in Pax2+ Spinal Inhibitory Interneurons

Jerry E. Carr, Caleb Seekins, Emily Forrest, Dea Kobeci, and John M. Streicher, Department of Pharmacology and the Comprehensive Center for Pain and Addiction, College of Medicine, University of Arizona, Tucson AZ USA

Chronic pain is a debilitating condition that affects one in five people in the United States adult population. Limited efficacy and/or harsh side effects limit many pain drugs, driving the need for alternative analgesics. In our past research, we showed the terpenes geraniol, linalool, β-pinene, α-humulene, and β-caryophyllene are efficacious in the treatment of mouse chemotherapy-induced peripheral neuropathy (CIPN). However, the cell type and spinal circuitry for A2aR-induced antinociception by terpenes are unknown. Given the known role of the A2aR as a stimulatory GPCR, we hypothesized that the A2aR is localized in inhibitory interneurons in the spinal dorsal horn and acts by inhibiting neuronal pain transmission. For our model, we used CD- 1 mice treated with paclitaxel (2 mg/kg) to induce CIPN. Using immunohistochemistry, we found that A2aR is strongly colocalized with neurons and is localized to 75% of Pax2 inhibitory interneurons. We then used Pax2+ cell-selective CRISPR knockdown of the A2aR gene, which resulted in a complete loss of terpene antinociception in CIPN, strongly suggesting that terpenes work through the A2aR in this specific cell population to relieve pain. To further confirm these findings, we used Fos staining in spinal cord, showing that Fos activation was increased by CIPN and repressed by terpene treatment. Taken together, we show that terpenes have antinociceptive effects in neuropathic pain via the A2aR on Pax2+ inhibitory interneurons in the mouse spinal cord. With this work, we aim to identify the detailed mechanism by which terpenes relieve neuropathic pain and establish a scientific basis for their use as a novel non-opioid pain therapeutic. Acknowledgments: This work was funded by R01AT011517 and a generous donation from The J. D. Simmons Endowment. JMS is an equity holder for Teleport Pharmaceuticals, LLC and Botanical Results, LLC. The funders and companies noted had no role in study design or conduct.

I-10 – Aaron Puri

Connecting Genes to Molecules Using Inverse Stable Isotopic Labeling (Inversil)

Jose Miguel D. Robes, Mike Wallace, Tashi C. E. Liebergesell, and Aaron W. Puri. Department of Chemistry and the Henry Eyring Center for Cell & Genome Science, University of Utah, Salt Lake City, UT 84112

The rapid expansion of bacterial genomic data has revealed substantial unexplored biosynthetic potential for discovering new natural products. Isotopic labeling is a powerful strategy for linking biosynthetic genes to the natural products they encode by identifying compounds that incorporate isotopically distinct precursors predicted to participate in biosynthetic pathways. However, in many cases, the required precursors are not commercially available or readily synthesized. We use an inverse stable isotopic labeling (InverSIL) approach to identify natural products that contain precursors of interst by growing bacteria on a ^{13}C-substitued carbon source and detecting incorporation of unlabeled precursors by mass spectrometry. This strategy enables the use of any unlabeled compound as a precursor, bypassing limitations in precursor availability. Here, I will present applications of InverSIL that link predicted biosynthetic gene clusters to their products, including quorum-sensing signals and siderophores across diverse bacterial systems.

I-11 – Shaun McKinnie

The Chemoenzymatic Syntheses of 'Clickable' Kainoid Derivatives for Chemical Neuroscience Applications

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Nature is a remarkable chemist capable of assembling structurally diverse compounds, many of which possess therapeutically useful bioactivities. The McKinnie lab uses an interdisciplinary approach to better understand the role of natural product enzymology within natural product biosynthesis and adapt it to complement conventional organic chemistry. The kainoid synthases are a group of non-heme iron (II) a-ketoglutarate-dependent dioxygenases from marine algae that catalyze the enantioselective C-H activation and oxidative cyclization of *N*-prenylated L-glutamic acids to form bioactive pyrrolidine rings. Kainoid natural products have affinity towards the kainate subtype of ionotropic glutamate receptors in the mammalian central nervous system, whose neuropharmacological study have been hampered by the lack of selective tools. We have explored the biocatalytic potential of these synthetically powerful enzymes using a combination of organic chemistry to access non-native substrates and kainoid synthase directed evolution to generate diverse structural and functional variants. This has been further enhanced through a recently established collaborative high-throughput screening platform with the Sanchez lab that uses matrix assisted laser desorption/ionization-based trapped ion mobility spectrometry-mass spectrometry (MALDI-tims-MS) for rapid, chromatography-free separation and analysis of screening assays. We have successfully engineered kainoid synthases to accept novel substates with bioorthogonal handles, and these 'clickable' kainoids maintain the neurologically active pharmacophore and demonstrate kainate receptor binding and agonistic activity. These cumulative efforts highlight our work to better understand and apply biosynthetic enzymology towards the construction of bioactive natural products and their derivatives.

I-12 – Manuela Raffatellu

Host-Microbe Competition for Iron in the Inflamed Gut: From Basic Discoveries to Translational Applications

Manuela Raffatellu, Division of Host-Microbe Systems and Therapeutics, Department of Pediatrics, University of California San Diego, La Jolla, CA 92093, USA

Iron is an essential metal nutrient for both the host and most bacterial pathogens, making competition for this metal a defining feature of host-microbe interactions. During infection, many pathogens secrete siderophores, high-affinity iron-chelating molecules that scavenge iron from the host. In response, the host restricts iron availability through a process known as nutritional immunity. A central component of this defense is lipocalin-2, a host antimicrobial protein that sequesters enterobactin, the major siderophore produced by commensal and pathogenic *Enterobacteriaceae*, including *Escherichia coli* and *Salmonella*. As a result, commensal *E. coli* strains that rely solely on enterobactin are susceptible to lipocalin-2-mediated growth inhibition. In contrast, pathogens such as *Salmonella*, uropathogenic *E. coli*, and the adherent-invasive *E. coli* pathovar associated with inflammatory bowel disease evade lipocalin-2 by producing "stealth siderophores" such as salmochelin, a C-glucosylated derivative of enterobactin that is not bound by lipocalin-2. In this talk, I will discuss the ongoing battle for iron among the host, enteric pathogens, and the gut microbiota during intestinal inflammation, with a focus on *Salmonella* and adherent-invasive *E. coli*. I will then describe our efforts to translate these fundamental discoveries into novel therapeutic approaches. By engineering catecholate siderophores conjugated to carrier proteins, we have developed immunization strategies that elicit antibodies targeting these siderophores. Mice immunized against siderophores exhibit reduced intestinal colonization by pathogens and attenuated inflammation in experimental colitis. Together, these findings establish siderophore-targeted immunization and the development of anti-siderophore antibodies as promising strategies to combat enteric pathogens by exploiting their dependence on iron acquisition.

I-13 – Emily Lindley

Exploring the Therapeutic Potential of Cannabinoids for Chronic Musculoskeletal Pain

Emily M. Lindley PhD, University of Colorado, Anschutz

Over the past two decades, cannabis has increasingly become recognized as a potential alternative therapeutic for a number of health conditions, including chronic pain. Although high-quality clinical data on the treatment efficacy of cannabis for chronic pain has historically been limited, largely due to complex regulations associated with studying Schedule I drugs, research in this area has accelerated in recent years. This presentation provides a window into the establishment of a cannabis clinical research laboratory in Colorado and details the hurdles we overcame to study the health effects of cannabinoids. Our research includes clinical trials of acutely administered vaporized cannabis versus oxycodone and long-term daily use of oral cannabinoids for chronic neck and back pain. We also use observational methods to study the efficacy of real-world topical cannabinoid preparations using our Mobile Pharmacology Laboratory, which allows us to bring the research clinic to participants and avoid the regulatory restrictions of bringing dispensary products onto our university campus. Upcoming projects include a collaborative multi-PI NIH-funded study examining the effects of perioperative cannabis use on endocannabinoid levels, postoperative pain and opioid use, and functional recovery after total knee arthroplasty.

I-14 – Andrew Goodman

Drug-Microbiome Interaction

Andrew L. Goodman. Department of Microbial Pathogenesis and Microbial Sciences Institute, Yale School of Medicine, New Haven, CT 06510

Oral medicinal drugs can exhibit incomplete absorption in the upper gastrointestinal tract or reach the gut after enterohepatic circulation. In these circumstances, drugs encounter commensal microbes that encode many drug-metabolizing enzymes, suggesting that the microbiome could modulate exposure to drugs and drug metabolites in the GI tract and in circulation. These enzymes could also determine whether and how non-antibiotic drugs alter microbiome composition. This seminar will discuss efforts to map the breadth of microbiome-mediated drug metabolism and to understand the consequences of these activities

I-15 – Andrew Novick

Effects of Psilocybin on Anhedonia in Treatment-Resistant Major Depressive Disorder

Andrew Novick, MD, PhD. Department of Psychiatry, University of Colorado, Anschutz Medical Campus, Aurora, Colorado 80045

Anhedonia, defined as diminished capacity to experience pleasure or motivation, is a core feature of major depressive disorder (MDD) and remains inadequately addressed by existing pharmacologic treatments. Psilocybin has shown promise as a novel therapeutic for MDD, but its effects on anhedonia and related neurobehavioral processes remain incompletely characterized. This pilot study represents a multimodal investigation of psilocybin's effects on anhedonia in treatment-resistant depression, incorporating self-report measures, behavioral paradigms, and functional neuroimaging. Importantly, the protocol was designed to evaluate feasibility in individuals both on and off concurrent antidepressant therapy. Twenty participants were randomized to receive psilocybin 25 mg or 1 mg with psychological support. The primary outcome was change in Dimensional Anhedonia Rating Scale (DARS) scores at one week. Secondary outcomes included the Snaith–Hamilton Pleasure Scale (SHAPS), Montgomery–Åsberg Depression Rating Scale (MADRS), neural activation in the nucleus accumbens during reward anticipation on the Monetary Incentive Delay task, and behavioral indices of reward responsiveness using the Probabilistic Reward Task. Preliminary results indicate that participants receiving 25 mg psilocybin demonstrated greater reductions in anhedonia at one week compared to the 1 mg group, as measured by the DARS. Consistent with prior studies, psilocybin was also associated with reductions in overall depressive symptoms on the MADRS. These findings support further investigation of psilocybin as a mechanism-informed intervention targeting anhedonia in treatment-resistant depression.

CONTRIBUTED SPEAKERS

C-01 – Dmitrii Travin

Tiarins – Novel Natural Trojan-Horse Inhibitors of Aminoacyl-tRNA Synthetases Discovered by Genome Mining

Dmitrii Travin[1], Alexei Livenskyi[2], Dmitry Bikmetov[2], Constantine Pavlov[2], Marina Serebryakova[3], Konstantin Gilep[2], Feng-Jie Wu[4], Delphine Naquin[5], Tatiana Timchenko[5], Guy Lippens[6], Séverine Zirah[7], Peter Mergaert[5], Svetlana Dubiley[6]. [1] Department of Pharmaceutical Sciences, University of Illinois Chicago, USA, [2] Institute of Gene Biology, Russian Academy of Science, Russia, [3] Lomonosov Moscow State University, Russia, [4] University of Basel, Switzerland, [5] Université Paris-Saclay, Institute for Integrative Biology of the Cell, Gif-sur-Yvette, France, [6] Toulouse Biotechnology Institute, Toulouse, France, [7] Unit Molecules of Communication and Adaptation of Microorganisms, Alliance Sorbonne University, France

Trifolitoxin (TFX) is a ribosomally synthesized and post-translationally modified peptide antibiotic produced by *Rhizobium anhuiense* T24. Although TFX was discovered more than half a century ago, its mechanism of action remained unknown. We discovered that trifolitoxin inhibits bacterial arginyl-tRNA synthetase, an essential translation enzyme. Notably, TFX acts as a Trojan-horse antibiotic: it enters cells via the inner membrane oligopeptide transporter and then undergoes partial proteolysis by cellular aminopeptidases to release a "warhead" that binds ArgRS and arrests translation. Our systematic analysis of prokaryotic genomes uncovered a widespread previously overlooked family of trifolitoxin-like modified peptides that we named tiarins. The tiarin family includes compounds that specifically target at least seven different aminoacyl-tRNA synthetases. These findings define a novel family of natural antibiotics and provide a framework for developing a new class of inhibitors targeting various tRNA synthetases.

C-02 – Ashley Kretsch

An Integrated Informatics-Driven Platform for Natural Product Discovery and Analog Generation in Crop Protection

Ashley Kretsch[1], Matt Chase[1], Krishna Madduri[1], Deepa Acharya[1]. [1]Crop Health R&D, Corteva Agriscience, 9330 Zionsville Road, Indianapolis, Indiana 46268

Corteva Agriscience™ maintains a biorepository of hundreds of thousands of microbial strains, currently undergoing metabologenomics characterization to drive discovery of new crop protection solutions. Molecular networking is central to this effort — organizing repository-scale, untargeted metabolomics datasets into interpretable chemical families for efficient mining of novel bioactive molecules. However, translating a bioactive hit into a crop protection product is challenging, requiring the generation of diverse analogs for robust structure-activity relationship (SAR) studies. To address this, we have developed an integrated platform uniting discovery microbiology, synthetic chemistry, synthetic biology, and bioprocess, bolstered by LCMS-based metabolomics, to rapid discover and characterize novel analogs. Microbial biotransformation leverages a dedicated microbial collection to rapidly screen exogenous compounds to generate a rich diversity of structural analogs around an active natural product scaffold. Complementarily, cell-free protein synthesis enables complex biosynthetic and/or stereoselective transformations, and through introduction of non-native substrates can facilitate the production of naturalogs. Underpinning these approaches is robust LCMS-based metabolomics, coupled with molecular networking, which is deployed to deconvolute complex mixtures and exploits structural relatedness of analogs to identify candidates for SAR. Together, this work showcases informatic approaches deployed to an integrated platform that dramatically accelerates natural product crop protection pipeline from initial hit to lead optimization.

C-03 – Marina Luccioni

Potential Enzymatic Pathways for 5-MeO-DMT Production in Toad Secretions Detected by HRMS Screening of Tryptamine Derivatives

Marina Luccioni[1], Megan Danielewicz[2]. [1] Stanford University, Biology Department. [2] Stanford University, Vincent Coates Mass Spectrometry Laboratory (SUMS)

Psychedelic indolethylamines have gained attention for their therapeutic potential in treating neuropsychiatric disorders. Among these, **5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)** is uniquely concentrated in the parotoid gland secretions of the Sonoran Desert toad (*Incilius alvarius*). While the biosynthesis of 5-MeO-DMT has been hypothesized to follow a pathway from serotonin through bufotenine via specific methyltransferases, the identity and activity of the enzymes involved—whether endogenous to the toad or produced by skin microbes —remains largely uncharacterized. In this study, we employed **High-Resolution Mass Spectrometry (HRMS)** screening to characterize and quantify tryptamine derivatives in the secretions of wild *I. alvarius* compared to secretions from two sympatric anurans: the Red-Spotted toad (*Anaxyrus punctatus*) and the Great Plains toad (*Anaxyrus cognatus*). By evaluating the presence, absence, and relative abundance of intermediate metabolites, we infer the potential enzymatic logic required for 5-MeO-DMT production. Our comparative analysis suggests that *I. alvarius* may possess specialized enzymatic adaptations or microbial symbioses not present in sympatric species, allowing for the specific O-methylation or N-methylation patterns observed. These findings offer preliminary insights into the in-vivo production of potent tryptamines in *I. alvarius*. While further proteomic and genomic validation is required to definitively identify the enzymes responsible, this chemical screening provides a necessary foundation for understanding the natural synthesis of 5-MeO-

DMTemical ecology of desert anurans.

C-04 – Nicole Kanya

Terpenoid-Mediated Defense in Caribbean Gorgonian Corals: Insights into Predator Deterrence and Metabolite Diversity

Nicole Kanya[1], Paul Scesa[1]. [1]Department of Chemistry, University of South Florida, Tampa, FL 33620

Octocorals possess a significant number of secondary metabolites that play a role in chemical defense and communication. Three gorgonian genera known for chemical antifeedant activity were focused upon for this study, *Antillogorgia, Briareum,* and *Plexaura.* Antifeeding behavior of fractionated extracts was examined through usage of live assays with the common reef predator, *Thalassoma bifasciatum.* High-resolution mass spectrometry was employed to examine molecular relationships and fragmentation patterns of associated active and nonactive fractions. Further purification was utilized to hone in on specific compounds that contribute to a feeding deterrent response. These analyses provide insight into the chemical ecology of gorgonian corals and the structural diversity of their terpenoid metabolites. The findings presented will aim at contributing to a broader understanding of metabolite function and lay the groundwork for future investigations into gene expression and environmental factors influencing metabolite production.

C-05 – Jack Ganley

Ecology-Guided High Throughput Elicitor Screening (Eco-HiTES) for Discovery of Natural Products

Jack G. Ganley (Princeton University, Department of Chemistry, USA, Mohammad R. Seyedsayamdost (Princeton University, Departments of Chemistry and of Molecular Biology, USA

High-throughput elicitor screening (HiTES) is a chemical genetics approach that uses small molecules to activate silent or cryptic biosynthetic gene clusters (BGCs), enabling the discovery of otherwise inaccessible natural products. Here, I present Eco-HiTES, an ecology-guided extension of this platform that leverages metabolites from a bacterium's native environment as targeted elicitors. By repurposing ecological signals as chemical probes, Eco-HiTES enables the discovery of new compounds while simultaneously revealing their functional roles *in situ*. Using a marine bacterium as a proof of principle, I demonstrate that algal-derived flavonoids induce the production of a previously uncharacterized class of ceramide lipids, highlighting how host-associated metabolites can regulate bacterial secondary metabolism. Building on this framework, I have expanded Eco-HiTES to plant root and human gut microbiomes, uncovering cryptic metabolites with bioactivities relevant to their respective ecosystems. Together, these results establish Eco-HiTES as a broadly applicable platform for linking natural product discovery with ecological function across diverse microbiomes.

C-06 – Arden Hatch

Evaluation of the Chemical Secretions and Their Ecological Role of the Millipede *Brachycybe*

Arden Hatch[1], Anne Jones[2], Luisa Vasquez Valverde[2], Paige Banks[1], Isabel Gooding[1], Lisa Markoff[1], Paul Marek[2], and Emily Mevers[1]. [1]Departments of Chemistry and [2]Entomology, Virginia Polytechnic Institute & State University, Blacksburg, VA, 24061

Brachycybe is a genus of the millipede subterclass Colobognatha, a group that exhibits rare social characteristics, including species aggregations and male brood care. Although it has been hypothesized that alkaloid-based defensive secretions may also serve as pheromones, no studies have examined the chemical mechanisms underlying these traits. Here, we evaluated the chemical secretions of six species, two of which were previously unstudied, and conducted Y-tube pheromone assays. Chemical investigations led to the structure elucidation of three new metabolites, each containing a carboxylic acid, a functionality previously unobserved in millipede secretions. A molecular phylogeny of this clade, based on whole-genome sequencing, clarified the evolution of these metabolites. Y-tube pheromone assays revealed that Brachycybe producta is significantly attracted to conspecifics ($p = 0.0428$) and is deterred by a different species of alkaloid-producing millipede ($p = 0.0161$). The former assay was repeated using a mixture of the crude ($p = 0.0428$) and purified ($p = 0.0433$) chemical defense secretion from B. producta. This study provides the first evidence that the colobognath millipede's chemical secretions function as both defensive agents and pheromones.

C-07 – C. Benjamin Naman`

Natural Products Research Is Better *In Situ* – A Case Study on Yerba Santa (*Eriodictyon*)

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As part of an ongoing effort to enhance the opportunity for and effectiveness of medicinal plant research, San Diego Botanic Garden has created a national medicinal plants collection and local research consortium to catalyze and conduct multi-omics natural products discovery. This effort aims to address some of the major challenges of international phytochemistry, including sustainable resupply, dereplication and natural product rediscovery, batch to batch variation of metabolites, and other compounding factors of complexity, including the chemical impacts of different methods for harvesting, processing, and extracting. To demonstrate the efficiency and effectiveness of using a living plant collection or repeated visits to nearby field collection sites rather than single time point expeditions, a multi-omics study was initiated that focused on the storied and well-studied California native medicinal plant, *Eriodictyon californicum* (California yerba santa), and related species of the yerba santa genus. The results of targeted and untargeted LC-MS

metabolomics have highlighted significant plant-to-plant variation, within-plant seasonal variation, and even within-individual-plant local variation such as between different leaves collected from the same organism at the same time. In some cases, these variances reach 2 log-fold differences, lending credence to the traditional knowledge about these medicinal plants and offering new productive avenues for the study of pharmacognosy in these species and others. Genomic data has been collected for *E. californicum*, and transcriptomic analysis is ongoing.

C-08 – Patrick Still

A Holistic Approach to Study Non-Addictive Natural Products for Pain Management

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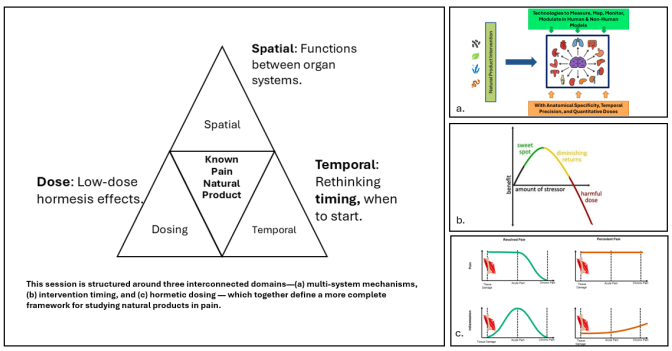
Chronic pain is increasingly recognized as a dynamic, systems-level condition that arises from coordinated interactions among the nervous system, vascular and metabolic tissues, and musculoskeletal structures. Yet much of analgesic development, including components of the NIH HEAL Initiative® portfolio, has historically centered on single molecular targets within isolated pathways. Natural products, widely used by the U.S. public for pain management, often exert pleiotropic effects across multiple biological systems and may engage adaptive stress-response networks rather than single receptor pathways. This session presents a holistic, systems-level framework focused on three interconnected domains: (1) multi-organ and multi-system mechanisms of action, (2) optimization of dosing based on the principle of hormesis and (3) identification of optimal intervention timing to align with the dynamic phases of pain and inflammation. This focus complements HEAL funding announcements centered on single-target drug optimization and IND-enabling efforts, by generating foundational mechanistic knowledge that can inform future therapeutic development, without centering on product advancement itself. Together, these domains provide a translational bridge from genome-enabled discovery and chemical characterization to mechanism-informed intervention design to accelerate development of safe, non-addictive interventions for pain consistent with whole-person health.



C-09 – Wilmer Perera

Advancing HPTLC Botanical Authentication from Visual Evaluation to Chemometric-Driven Data Intelligence

Wilmer Perera, CAMAG Scientific, Inc.

High-Performance Thin-Layer Chromatography (HPTLC) has long been established as a robust and reproducible technique widely used for the authentication of botanicals. The most common approach relies on the visual comparison of the fingerprint of a sample with a botanical reference material, focusing on band patterns such as color, position, and intensity. HPTLC is one of the most widely used techniques for the authentication of botanicals in compendial settings, where this classical workflow remains subjective and dependent on analyst experience when working with complex mixtures. Recent advances in chemometric tools integrated into HPTLC workflows are transforming botanical authentication into a more objective and data-driven process. Various algorithms have been implemented, enabling the extraction of hidden information from peak profiles derived from images or scanner data. This improves discrimination between closely related species, aids in the detection of adulteration, and supports batch-to-batch consistency assessment among other applications. These approaches reduce reliance on visual interpretation and enhance the analytical power of HPTLC without compromising its inherent simplicity. This presentation compares traditional HPTLC evaluation with modern strategies. Case studies will illustrate how chemometric integration enhances specificity, supports regulatory compliance, and strengthens quality assurance in complex botanical matrices. The transition from subjective interpretation to data-driven classification represents a significant step forward in the evolution of HPTLC as a gold-standard technique in herbal authentication and quality control.

C-10 –Alana Ponte

Gut Microbiome-Mediated Transformation of Mangosteen Xanthones and its Impact on Breast Cancer Bioactivity

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Alana Ponte Abstract

C-11 – Antonio Del Rio Flores

Mechanistic Analysis of Programmed Iteration by Module 5 of the Nocardiosis-Associated Polyketide (NOCAP) Synthase

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Assembly-line polyketide synthases (PKSs) possess multimodular architectures in which each module harbors the requisite protein domains to catalyze a single round of polyketide chain elongation and post-elongation modifications. Exceptions to this paradigm are modules that catalyze multiple elongation cycles, a phenomenon referred to as "programmed iteration". The molecular mechanism that allows PKS modules to iterate remains poorly understood. For example, Module 5 of the nocardiosis-associated polyketide (NOCAP) synthase catalyzes three elongation cycles during the biosynthesis of its undecaketide product, although in the absence of downstream modules, it has been shown to catalyze five elongation cycles. To understand the context-dependent control of its iterative capacity, we combined in vitro analysis of purified Module 5 of the NOCAP synthase with in vivo studies in E. coli. Our findings reveal that, while the ability to iterate is an inherent property of Module 5, protein-protein interactions with its downstream module (Module 6) are key determinants of the number of elongation cycles catalyzed by Module 5 within the context of the complete assembly line. We also show that the intrinsic ability of Module 5 to iterate can be strongly influenced by the identity of its substrate. Our findings highlight the potential of Module 5 of the NOCAP synthase to reveal fundamentally new insights into the mechanistic differences between iterative and assembly-line PKSs..

C-12 – Shogo Mori

Harnessing Natural Enzymatic Pathways for Amino Acid Homologation

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Homologation of amino acids generally refers to a chemical transformation to elongate their side chain. Homologated amino acids (homoAAs) are not common non-proteinogenic amino acids found in natural products but are present in several peptide drugs Although homoAA building blocks are believed to enhance amide bond stability in biological systems, their potential has not been fully utilized due to limited knowledge of their biosynthesis and the cost of some homoAAs. This presentation will focus on the characterization and/or engineering of two of the three novel enzymes, HphA and HphB, involved in the homologation pathway for l-Phe and l-Tyr. We biochemically characterized these enzymes by investigating their proposed reactions, substrate profiles, and kinetics. HphA was found to be highly selective and acts as a gatekeeper of the pathway, while HphB displayed extreme promiscuity. Bioinformatics and site-directed mutagenesis in the HphA active site identified an amino acid residue that plays a critical role in its substrate selection. One of the mutations on this residue made HphA promiscuous and accept non-canonical substrates. The newly active substrate included the Trp counterpart, whose homologated derivative is not seen in nature. These studies will lead to the development of enzymatic tools for producing homoAAs, which can be applied for derivatization of bioactive molecules.

C-13 – April Lukowski

An Emerging Family of Efficient Cyanobacterial Halogenases: Discovery, Function, and Evolution

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Cyanobacteria are prolific chemists capable of producing a myriad of halogenated natural products. Halogen atoms serve as both a chemical and genetic hook for identifying novel enzyme chemistry. In complex chemical mixtures, halogen atoms are easily identifiable via their isotope patterns in untargeted metabolomics studies. In genomes, several classes of halogenases can be identified based on signature motifs. However, not all halogenated metabolites and halogenases are able to be effectively linked with the current state of knowledge we have on halogenated natural product metabolism. In recent years, we have identified an emerging novel family of flavin-dependent halogenases that are distinct at phylogenetic and mechanistic levels. These enzymes are capable of halogenating terminal alkynes, a previously unknown reaction in enzyme chemistry, and we have more recently identified enzymes capable of efficiently polyhalogenating indole-containing molecules. These enzymes open the door for exploration in biocatalytic applications, comparative enzymology, and genome mining. Our most recent work focuses on understanding the fundamental enzymology of these halogenases guided by structural biology, ancestral sequence reconstruction, and machine learning. Analysis of the genomic contexts of emerging halogenases, particularly within cyanobacteria, will also be discussed.

C-14 – Chung Sub Kim

Stress-Induced Metabolites from Bacteria

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Bacteria utilize specialized metabolites to adapt to environmental challenges. This study demonstrates how external stressors drive both structural and functional diversity in bacterial metabolites. In gut bacteria, oxygen pressure induced the production of bioactive metabolites. Enterozoliums in *Enterococcus faecalis* disrupt the bacterial proton motive force. Furthermore, we identified a unique biosynthetic mechanism for scalemic *N*-acyl amides in marine *Pseudovibrio denitrificans* induced by aminoglycosides antibiotics. We characterized the *pdf* gene cluster, where the adenylyltransferase PdfB mediates downstream racemization through carboxyl activation. This process creates stereochemically labile intermediates, leading to the formation of racemic and scalemic mixtures. Our findings reveal that environmental stressors are key drivers of chemical complexity, expanding the known framework of bacterial metabolic and stereochemical adaptation.

C-15 – Dong-Chan Oh

Integrated Metabologenomic and Chemical Approaches for Drug Lead Discovery from Actinomycetes

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Actinomycetes from diverse ecological niches, including insect-associated microbiomes and terrestrial environments, remain a prolific source of structurally diverse natural products and promising drug leads. An integrated discovery strategy combining chemical investigation, genomics, and metabologenomic targeting enabled the identification of multiple bioactive scaffolds from distinct actinomycete strains. Chemical exploration of *Micromonospora* sp. from a blister beetle gut yielded arenicolide macrolides with potent activity against multidrug-resistant and extensively drug-resistant *Mycobacterium tuberculosis* via ATP depletion and cell wall disruption. Investigation of termite-associated *Kitasatospora* sp. led to the discovery of spirosnuolides, type I/III hybrid polyketide spiro-macrolides; spirosnuolide B showed strong antiproliferative activity against non-small-cell lung cancer through AMPK activation and apoptosis induction. In parallel, a metabologenomic approach leveraging genomic (TfuA) and metabolomic (sulfur isotopic) hallmarks enabled the discovery of thiogochangamides from *Streptomyces*. Thiogochangamide B exhibited potent activity against drug-resistant pancreatic cancer by suppressing Wnt/β-catenin signaling.

C-16 – Laura Sanchez

A High-Throughput Biocatalytic Platform for Screening Isomeric Kainoid Natural Products

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The growing field of biocatalysis relies on the generation of large, genetically diverse libraries. However, challenges remain when assessing enzyme variants in a high-throughput manner whose transformations yield isomeric low molecular weight products. The kainoid synthase subfamily of Fe/αKG-dependent dioxygenases produce the isomeric neurochemicals kainic acid (KA) and kainic acid lactone (KAL) in ranging yields and ratios. To enable an improved throughput screening of engineered kainoid synthases, we developed a matrix-assisted laser desorption/ionization–trapped ion mobility spectrometry–mass spectrometry (MALDI-TIMS-MS) platform to directly detect regioisomeric products with near-baseline resolution from bacterial colonies. Screening of 1054 genetically diversified KabC variants identified seven with improved KAL formation, while retaining favorable expression profiles and improved in vitro stabilities. We identified seven KabC variants with improved conversion to KAL relative to GfKabC. Notably, two shuffled variants exhibited an almost complete shift toward KAL production, accompanied by enhanced substrate consumption. Importantly, the assay with enzyme engineering leverages the convenience and speed of direct colony MS analysis without sacrificing detailed analytical information, decreases reliance on LC, and enables the rapid assessment of large libraries for natural product production. Further, PRM-PASEF enables the simultaneous analysis of multiple analytes with distinct mobility values, offering improved sensitivity and multiplexing capabilities for isomeric products. We established MALDI-TIMS-MS as a platform for high-throughput isomeric product screening and provided a platform to probe structure–function relationships.

C-17 – Nathan Wlodarchak

Designing and Executing Successful High Throughput Screening Assays for Drug Discovery

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Tuberculosis is the deadliest infectious agent worldwide, with a quarter of the population latently infected and 1.25 million annual deaths. Standard-of-care treatment requires long regimens of toxic drugs and resistance is increasing significantly. Thus, new drugs against new targets are desperately needed to improve treatment outcomes. High-throughput screening (HTS) remains central to drug discovery, and machine learning (ML) is increasingly streamlining this process by reducing the number of compounds that must be tested. We developed robust automated biochemical HTS assays for two novel *M. tuberculosis* targets: a focused kinase inhibitor library (1,100 compounds) for a serine threonine kinase, PknB, and a broad library (100,000 compounds), including natural product derivatives, for a serine threonine phosphatase, PstP, yielding hit rates of 1.9% and 0.4%, respectively. ML approaches retrospectively (PknB) and semi-prospectively (PstP) identified most HTS hits. A prospective ML screen for PknB selected 96 compounds and achieved an 85% hit rate (82 compounds), outperforming prior HTS efforts. Inhibitors were validated biochemically and tested against a BSL-2 *M. tuberculosis* strain, with twelve PknB and eleven PstP inhibitors showing promising microbiological activity. This work demonstrates the value of curated HTS assays and ML to accelerate discovery of inhibitors targeting novel *M. tuberculosis* targets.

C-18 – Kalindi Morgan

Integrating Genomics and Nitrogen-15 NMR for Natural Product Discovery from Northern Canadian Bark Beetle-Associated Bacteria

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Bacterial specialized metabolism remains vastly underexplored, particularly in insect-associated microbiomes where ecological pressures drive the evolution of secondary metabolites. Bark beetle-associated bacteria from northern Canadian forest ecosystems represent a promising yet largely untapped source of genetically-encoded chemical diversity. Here, we present an integrated strategy that combines genome mining, bioactivity screening, and nitrogen-15 NMR spectroscopy to direct investigation toward high-value nitrogen-containing natural products. Bacterial isolates obtained from multiple bark beetle species were first prioritized using antifungal challenge and disc-diffusion assays against phytopathogenic fungi. Whole-genome sequencing of bioactive strains followed by antiSMASH and BiG-SCAPE analysis revealed over 200 biosynthetic gene clusters (BGCs), including numerous nonribosomal peptide synthetases (NRPS), NRPS–polyketide synthase hybrids, and RiPP pathways. A substantial proportion of these clusters encode predicted nitrogen-rich scaffolds and display low homology to characterized pathways, indicating strong novelty potential. To bridge the gap between genomic prediction and chemical access, we implemented natural-abundance $^{1}H–^{15}N$ HSQC NMR as a rapid, non-destructive prioritization tool. Nitrogen NMR directly reports on amides, amines, heterocycles, and non-proteinogenic amino acid motifs within crude extracts, enabling early confirmation of nitrogen-rich chemistry without isotopic labeling. Coupled with OSMAC-based cultivation strategies, this approach allows biosynthetic output to be steered toward desired chemical features and reduces time spent on low-value strains. Together, these results demonstrate a practical framework for natural product discovery by integrating ecological context, BGC-level prediction, and nitrogen spectroscopic signatures. This workflow accelerates access to novel nitrogen-containing natural products with relevance to antifungal and agrochemical development while advancing strategies for rational exploration of an underexplored microbial niche.

C-19 – Luis Prieto Costas

Screening Natural Products Protein Targets Using the HuProt™ Proteome Microarray

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Secondary metabolites or natural products are molecules synthesized by organisms that have a benefit for human health. However, the discovery of bioactive compounds can be hindered by the limited understanding of their mechanism of action and/or protein targets. Known methods to assess these targets (e.g. activity-based protein profiling, compound-centered chemical proteomics) are limited by the range of targets that can be studied in a single experiment, considering that bioactive compounds can have multiple targets. An alternative approach utilizes proteome arrays, enabling the simultaneous examination of multiple targets for natural products in a single experiment. CDI has developed a platform termed HuProt™ Proteome Microarray for high-throughput analysis of 21,000+ human proteins. With this technology, we envision the detection of targets from natural products extracts through a strategy we term Proteome Array Target Screening (PATS). Herein, we will show our proof-of-concept experiment, where we stain the proteins in the microarray with a common dye (i.e., congo red) and identify the targets of erianin, a natural product known to have anticancer properties, through a fluorescence displacement assay in a high-throughput manner. We will compare this strategy with complementary methodologies such as biotin-streptavidin based detection (i.e., biotin-labeled erianin) and fluorescent-labeled erianin via click chemistry. We will report the effectiveness of the strategy addressing the targets revealed by each strategy. Future work will focus on the discovery of protein targets in complex natural products extracts to accelerate the development of new therapeutics.

C-20 – Alyssa Rodriguez

A Metabolite Prioritization Pipeline for Antifungal Drug Discovery from Microbial Symbioses

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Fungal pathogens are attributed to nearly 2.5 million deaths worldwide each year. Rising incidence and mortality rates associated with fungal pathogens due to underdiagnoses antifungal resistance presents an urgent need for new antifungal treatments. Natural products are rich sources of structurally diverse bioactive molecules, although linking their biosynthesis to biological activity remains a critical bottleneck in discovery efforts. We developed a pipeline that connects predictions of specialized metabolite biosynthesis to potential antifungal activity of microbial metabolites using *Bombella apis* as a model for antifungal molecule discovery. Previous work showed that *B. apis* inhibited the growth of two fungal pathogens, *Aspergillus flavus* and *Beauveria bassiana*, and genomic analyses of four *B. apis* strains identified conserved biosynthetic gene clusters (BGCs). Using a metabolomic-based stable isotope labeling (SIL) platform, *B. apis* metabolites were linked to these conserved BGCs by aligning experimental isotopic labeling patterns determined by liquid chromatography tandem mass spectrometry (LC-MS/MS) to theoretical isotopic labeling patterns. *B. apis* cultures were then challenged by two environmentally or clinically relevant fungal pathogens to induce antifungal metabolites and subsequently analyzed using LC-MS/MS. Our newly developed R-based package identified LC-MS/MS features shared between SIL and fungal induction experiments which were prioritized for isolation. Future work will be directed toward identifying prioritized metabolites and assessing their antifungal activity, providing a new pipeline for antifungal lead molecule discovery.

C-21 – William Crandall

Energy Resolved Ion Mobility Mass Spectrometry of Natural Product Diastereomers

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Structural determination of small bioactive molecules is principal in the understanding of their pharmacological actions. Stereochemical differences can greatly affect receptor binding affinity, as shown by mitragynine, a natural product, and its diastereomers, which have different affinities for human opiate receptors. A chromatographic method was developed to separate the diastereomers mitragynine (MG), speciogynine (SG), speciociliatine (SC), and mitraciliatine (MC). Energy-resolved collision-induced dissociation of the precursor ion across a range of normalized collision energies was conducted to statistically identify distinguishing product ions of the diastereomers using a two-way analysis of variance (ANOVA). Product ions capable of differentiating the C3 and C20 stereocenters were identified, providing an LC-MS method for stereochemical identification. Ion mobility measurements were taken on an Agilent 6560B to determine the precursor collision cross section (CCS). Computational modeling using UFM (universal fragment model) combined with ion mobility of fragments measured on a Waters Cyclic IMS provided detailed mechanistic insights into fragmentation energetics, with novel rearrangement structures proposed. Overall, energy-resolved and ion mobility mass spectrometry enabled the stereochemical assignment of MG, SG, SC, and MC in the gas phase.

C-22 – Hyomoon Cho

Multi-Level Relative Mass Defect Analysis for Natural Product Classification

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Natural product-derived molecules remain a critical source of therapeutics. In parallel, advances in high-resolution mass spectrometry (HRMS) have enabled rapid identification of known compounds in complex natural product extracts. However, discovering new compounds remains challenging because complex HRMS datasets contain thousands of molecular features, making it difficult to determine which features are chemically related and which molecules are most strongly associated with the observed bioactivity and should be prioritized for follow up studies. Methods that can translate complex mass data into chemically meaningful insights are therefore needed. Here we asked whether simple mass-based properties can be used to reveal hidden structural patterns within complex metabolomic datasets. We hypothesized that relative mass defect values capture conserved chemical features and enable rapid grouping of related natural product classes without requiring full structural determination at the initial screening stage. Relative mass defect visualization revealed clear and reproducible pattern signatures, visible groupings in mass data, that reflect shared core chemical scaffolds and capture pattern differences arising from chemical modifications. Compounds within the same chemical class formed highly similar visual patterns, while chemically distinct metabolites separated into clearly different pattern groups. Importantly, this pattern-based representation enabled rapid recognition of compound classes and

highlighted features that deviated from established patterns, flagging candidates likely to represent chemical novelty. This approach has been validated by the discovery of several new antibiotic and antitumor natural products. Together, these results demonstrate that relative mass defect analysis provides an intuitive and efficient strategy for converting complex mass spectrometry data into chemically interpretable insights. By enabling rapid classification and prioritization of metabolites, this approach supports natural product discovery efforts and helps bridge the gap between mass spectrometry expertise and discovery driven research.

C-23 – Victor Olaoye

Thiamine Reverses Dormancy in Uropathogenic *Escherichia coli*

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Recurrent urinary tract infections (UTIs) are frequently caused by uropathogenic *Escherichia coli* (UPEC) that persist in a dormant, quiescent state. Quiescent bacteria exhibit reduced metabolic activity and antibiotic tolerance, contributing to treatment failure and infection recurrence. While prior studies have characterized mechanisms governing entry into and exit from bacterial quiescence, experimental approaches to identify dormancy-reversing molecules have relied largely on agar-plate assays. These platforms are inherently low throughput, limited in sensitivity, poorly suited for systematic small-molecule screening, and unable to efficiently generate quantitative dose–response relationships. To address this gap, we developed a novel, high-throughput, fluorescence-based quiescence reversal assay compatible with 96-plate formats. This platform enables sensitive, quantitative measurement of metabolic reactivation, supports rapid determination of concentration-response relationships and EC_{50} values, and provides improved statistical power for compound screening. Using this assay, 130 compounds, including TCA cycle metabolites, amino acids, and small molecules, were screened for their ability to restore metabolic activity under quiescent conditions, with known quiescence-reversing metabolites validating assay performance. Thiamine (vitamin B1) exhibited exceptional potency, with sub-nanomolar activity (EC_{50} = 0.3 nM). Thiamine is an essential cofactor for pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, enzymes that regulate carbon entry and flux through the TCA cycle. Consistent with prior evidence linking TCA cycle flux to bacterial exit from quiescence, these findings identify thiamine as a potent chemical driver of dormancy reversal and highlight metabolic cofactors as tractable intervention points for targeting dormancy-driven recurrent UTIs caused by UPEC.

C-24 – Byeol Ryu

Unraveling the Structural Complexity of a Bastimolide A–Like Antitrypanosomal Macrolide

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Structural elucidation of the new antitrypanosomal bastimolide-type polyhydroxylated macrolide was complicated by severe NMR signal congestion arising from multiple contiguous polyol motifs. High-resolution pure shift HSQC and HSQC-TOCSY experiments enabled reconstruction of overlapping spin systems and establishment of the macrocyclic backbone. Relative configurations within the polyol segments were assigned using empirical NMR approaches, including Kishi's universal NMR database for 1,3,5-triol motifs and the Aggarwal-Butts empirical rule for 1,5-diols. To address stereochemical ambiguity introduced by *tert*-butyl-substituted 1,5-diol motifs, comparisons with synthetic model fragments were performed. In addition, base-mediated macrolactone hydrolysis to generate a *seco*-derivative followed by PGME derivatization enabled the determination of the absolute configuration. This work highlights both a new antitrypanosomal macrolide and an integrated strategy for resolving highly congested polyol-rich natural products.

C-25 – Chase Clark

A Platform for the Discovery of Novel Microbial Natural Product Chemical Scaffolds and Their Biological Targets

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For nearly a century, microbially-produced natural products (NPs) have been a prolific source of antibiotic, anticancer, and immunomodulatory small molecules. Despite advances in genomics and the availability of hundreds of thousands of public genomes, the field of NP drug discovery remains hampered by multiple challenges that include, but are not limited to, the frequent rediscovery of known compounds and the blind selection of bioassays, particularly for eukaryotic targets. These

contribute to a high failure rate in NP discovery pipelines, with many potential therapeutics failing to be discovered or advanced due to early-stage misdirection. Evoquant is working to address these challenges with a discovery platform that leverages >5 million biosynthetic gene clusters (BGCs) from >750 thousand diverse genomes/metagenomes, alongside a curated chemical and disease-relevant dataset. In the short term Evoquant is working on validating its thesis for discovery with a set of 30 microbes predicted to produce small molecules that affect specific protein targets. Evoquant's long term goal is to have a reliable, efficient, best-in-class platform for discovery and commercial development of chemical scaffolds against diverse disease targets through microbial strain procurement and heterologous expression. Here I will present the platform and progress, including the discovery of novel proteasome inhibitors.

C-26 – Cleo Orlando

Understanding the Role of Bacterial Glycoside Hydrolase Present in the Microbiota of Moon Snail Egg Masses

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Moon snails are marine mollusks that, when reproducing, suspend their eggs in a matrix of secreted mucus and environmental sand. These egg masses harbor a distinct microbial community, and their texture degrades as they age. The interactions between the animal host and the dominant symbiont, *Flavobacteriaceae*, are of particular interest, as the ecological role of *Flavobacteriaceae* remains unclear. We hypothesize that *Flavobacteriaceae* are enriched in the microbiome of moon snail egg masses because they degrade carbohydrates in the mucus, potentially helping liberate eggs from the sand-mucus matrix. Analysis of Metagenome Assembled Genomes (MAGs) from *Flavobacteriaceae* reveals they are enriched with glycoside hydrolases (GHs) and are likely capable of degrading the carbohydrates found in the egg masses. One GH, a β-*N*-acetylhexosaminidase from GH family 20, was selected for purification because it prefers the substrate *N*-acetylglucosamine, an important component of bacterial biofilms. Treatment of the egg mass with a community of Flavobacteriaceae or purified GH20 causes the tertiary structure of the egg mass to degrade. These visual changes were quantified by analyzing the egg masses on a rheometer. As the egg masses degrade, they become stiffer and more fragile, exhibiting reduced elasticity overall. This research lays the foundation for future studies on how mucus degradation affects biofilm formation and the bacterial community in this animal system.

C-27 – Barry O'Keefe

Isolation And Characterization of an Antiviral Protein from the Soft Coral *Alertigorgia sp.*, Derived from The NCI Marine Aqueous Extract Library

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The NCI Natural Products Repository Discovery contains a large library of marine aqueous extracts. Initial method development studies towards the creation of a pre-fractionated marine aqueous fraction library, evaluated various purification strategies and resulted in the identification of antiviral activities within the initial test set of fractions. Here we report the isolation and characterization of a new antiviral protein from the soft coral *Alertigorgia* sp. which was found to bind to the HIV-1 Envelope glycoprotein gp120 and inhibit the infection of target lymphoblasts by HIV-1. The protein, determined to have a M.W. = 11,657 Da and no disulfide bonds, was sequenced by a combination of LC-MS/MS and Edman degradation. DNA was isolated from a frozen sample of *Alertigorgia* sp. and the gene responsible for the production of the antiviral protein was established.

C-28 – Sian Marin

Growing Yeast for a Semi-Synthetic Approach to the Core of Eleutherobin

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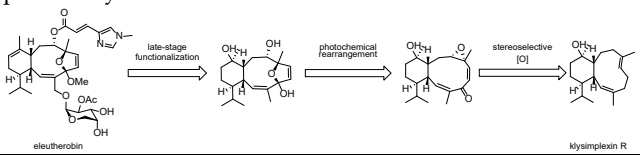
This synthesis mimics the 'oxidase phase' in the production of terpenoids and is based on our ability to produce klysimplexin R on a gram-scale through the heterologous expression of the coral terpene cyclase EcTPS 1 in yeast S. cerevisiae. This molecule is one of the simpler eunicellane skeletons, making it a common precursor and intermediate to many diterpenoids. Several oxidative steps open the pathway to the synthesis of the anti-mitotic molecule eleutherobin in a more cost-effective and efficient manner than compared to a total synthesis. Although eleutherobin is the main target, certain reactions in the synthesis have yielded closely related, but different terpene skeletons. These divergences provide opportunities for access to new and potentially more bioactive molecules.



C-29 – Elizabeth Skellam

Complete Biosynthesis of Penicillin G in the Plant Host *Nicotiana Benthamiana*

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Since the discovery of penicillin in 1928, and the development of fermentation technologies in the 1940s, many microbially-derived essential medicines are manufactured commercially using deep vat fermentation. Here, we engineered the plant *Nicotiana benthamiana* to produce penicillin G in its leaves by transient Agrobacterium-mediated expression of up to seven fungal biosynthetic genes (*pcbC, penDE, npgA, paaT, penM, penV, phl*), including *pcbAB* which encodes a non-ribosomal peptide synthetase (NRPS) enzyme not known in plants. Production of penicillin G was optimized through investigating phosphopantethienyl transferases, accessory enzymes, the necessity of transporters, and supplementing precursors which enable the production of penicillin V; each enzymatic step was validated through confocal microscopy and LC-MS/MS-based metabolite characterization. Non-targeted metabolomics enabled the detection of a variety of plant-metabolites produced after infiltration of penicillin G, many involved in defense and stress responses, although primary metabolism remained unaffected. Although non-ribosomal peptide synthetases (NRPS) occur widely in fungi and bacteria for the production of a plethora of specialized metabolites, their evolutionary distribution does not extend to plants, opening up a new metabolic frontier. This proof of concept study provides opportunities to address global health concerns by offering an alternative sustainable biotechnology platform for pharmaceutical production.

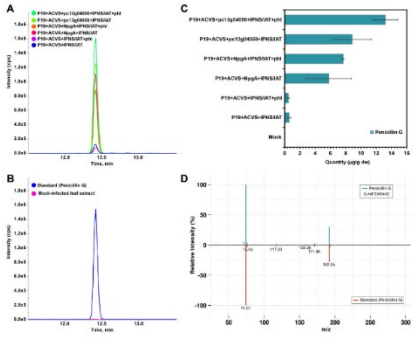

Figure 1 *– LC-MS/MS characterization of penicillin production in the plant N. benthamiana. A) Extracted ion chromatogram (XIC) detecting penicillin G in plant leaves co-infiltrated with different fungal genes; B) XIC of a standard of penicillin G; C) Absolute concentrations of penicillin G detected in plant leaves (per gram of dry weight leaf); D) Mirror plot of penicillin G detected in plant leaves vs. a synthetic standard of penicillin G.*

C-30 – Reed Stubbendieck

Dynamic Secondary Metabolite Production Mediates Interactions That Structure the Cystic Fibrosis Lung Microbiota

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Cystic fibrosis (CF) is a multisystem disease characterized by the accumulation of thick mucus in the lungs that promotes pathogen colonization, leading to respiratory exacerbation, lung failure, and death. Culture-independent approaches have revealed that the CF lung harbors a complex microbiota, including opportunistic pathogens and aerodigestive tract bacteria, both of which produce secondary metabolites. Here, we reanalyzed 5,260 16S rRNA gene microbiota datasets to predict interactions between members of the CF microbiota. We determined that increasing diversity and bacterial interactions are each positively associated with improved lung function. While oral anaerobes were positively correlated with each other, pathogenic bacteria were negatively correlated with most other members of this microbiota. To validate these predictions, we cultured 1,597 bacterial isolates from 96 people with CF and performed 12,542 coculture assays with eight ecologically relevant CF bacterial species. Approximately one-fourth of interactions resulted in growth inhibition, and while *Pseudomonas* isolates were broadly the most inhibitory, bioactivity was variable among isolates. We confirmed that *Pseudomonas* isolates, even from the same donor and timepoint, exhibited significantly different secondary metabolite production profiles and bioactivity. Together, our results demonstrate that secondary metabolite production is variable, even among closely related isolates, and highlight that characterizing multiple isolates is necessary to capture the full chemical landscape of interactions within microbial communities.

C-31 – Lukasz Ciesla

Dietary Soft Electrophiles Drive Lipid Mediator Class Switching Toward Resolution of Inflammation

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Chronic inflammation and impaired resolution are hallmarks of neurodegenerative diseases. Although dietary phytochemicals (such as vitamin E vitamers, carotenoids, or flavonoids) are linked to improved health, their molecular mechanisms of action remain unclear. We introduce dietary soft electrophiles as a unifying concept explaining how abundant dietary molecules promote lipid mediator class switching from pro-inflammatory to pro-resolving pathways. These compounds, characterized by

electrophilic motifs (e.g., α,β-unsaturated carbonyls), modulate redox-sensitive signaling and regulate oxylipin biosynthesis. Selected plant-derived soft electrophiles enhance production of pro-resolving lipid mediators from essential fatty acids *in vivo*, shifting inflammatory responses toward active resolution. This challenges the traditional antioxidant paradigm and identifies controlled electrophilic reactivity as a key determinant of bioactivity. Additionally, we highlight spatial mass spectrometry approaches for mapping pro-resolving lipids in *Drosophila melanogaster* heads in a paraquat-induced neuroinflammation model, revealing tissue-specific lipid mediator dynamics. Together, these findings establish dietary soft electrophiles as a new class of bioactive molecules linking diet to resolution of inflammation.

C-32 – Veronika Butterweck

Exercise-Associated Metabolic Effects of the *Cimicifuga racemosa* Extract Ze 450 in a High-Fat Diet Model

Veronika Butterweck[2], Elisabeth Habersatter[1], Siyu Chen[1], Jürgen Drewe[2], Georg Boonen[2], Patrick Diel[1]. [1]German Sport University Cologne, Institute of Cardiology and Sports Medicine, 50933 Cologne, Germany, [2]Max Zeller Soehne AG Switzerland, Medical Department, 8590 Romanshorn, Switzerland

Physical inactivity and high-calorie diets are major drivers of obesity and metabolic disease. In a previous pilot study, the *Cimicifuga racemosa* extract Ze 450 reduced visceral adiposity and circulating leptin levels in female rats, suggesting exercise-associated metabolic effects. Here we examined whether these effects persist under diet-induced metabolic stress. Female Wistar rats were fed a high-fat (HF) diet for 12 weeks and treated with Ze 450 (130 mg/kg), voluntary running activity, or their combination. HF feeding induced weight gain, visceral fat accumulation, adipocyte hypertrophy, and hyperleptinemia. Ze 450 significantly reduced visceral fat mass, adipocyte size, and circulating leptin levels, effects comparable to voluntary running and independent of caloric intake. Molecular analyses revealed distinct regulatory patterns: while voluntary running induced a classical lipolytic transcriptional response in adipose tissue, Ze 450 suppressed adipogenic signaling and reduced hepatic fatty acid synthase protein levels despite similar transcriptional responses. The results support further investigation of *Cimicifuga racemosa*–derived preparations as natural product–based metabolic modulators with exercise-associated physiological effects.

C-33 – James Hassell Jr.

Blocking Microglial Endogenous Fructose Production with Green Tea Catechin Prevents Metabolic Reprogramming

James E. Hassell, Jr[a], Annalise M. Sturno[a] Katelyn M. Baker[a], Garrett J. Potter[a], Dean Oldham[a], Jenna Banh[a], Miguel A. Lanaspa[b], Kimberley D. Bruce[a]. [a]Division of Endocrinology, Metabolism and Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO 80045, USA. [b]Division of Renal Diseases and Hypertension, University of Colorado Anschutz Medical Campus, Aurora, CO 80045, USA

Aldose reductase (AR) is a rate-limiting key enzyme in the reduction of glucose to sorbitol, which subsequently is oxidized to fructose. Notably, within the central nervous system (CNS), microglia—the resident immune cells—predominantly express AR. In aging and disease, microglia are metabolically reprogrammed from oxidative phosphorylation to glycolysis, driving neuroinflammation, cellular dysfunction, and disease risk. Although AR-mediated fructose metabolism is known to promote metabolic reprogramming in peripheral tissues, its role in microglial dysfunction within the brain remains poorly understood. Here, we hypothesized that blocking the polyol pathway in microglia could prevent metabolic reprogramming. To test this, we employed both genetic and pharmacological approaches, including AR knockout (AR-KO) mice and primary microglia, as well as treatment with the AR inhibitor sorbinil and the green tea–derived AR inhibitor epigallocatechin gallate (EGCG). We found that aged AR-KO mice exhibited significantly fewer dysfunctional microglia throughout the brain. In vitro, AR deficiency or pharmacological inhibition of AR conferred resistance to lipid accumulation and microglial activation. Moreover, EGCG attenuated or blocked inflammation-induced microglial activation. Collectively, these findings identify AR-mediated fructose metabolism as a key regulator of microglial metabolic reprogramming and highlight the utility of targeting the polyol pathway with ECGC to mitigate age- and disease-associated neuroinflammation and to preserve brain health.

C-34 – Jennifer Nguyen

Integrated Multi-omics Analysis Reveal Role of Strain Specific Bacterial Metabolites in Colorectal Cancer Pathogenesis

Jennifer N. T. Nguyen[1], Ivan Anterola[2], Kathryn R. McBride[3], Marcy J. Balunas[1,2,3,] [1]Department of Medicinal Chemistry, University of Michigan, Ann Arbor, MI, USA; [2]Program in Chemical Biology, University of Michigan, Ann Arbor, MI USA; [3]Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI USA*

Colorectal cancer (CRC) ranks as the second leading cause of cancer-related deaths worldwide and is increasingly linked to gut microbiome dysbiosis, yet the therapeutic potential of microbiome-derived metabolites remains largely untapped. Using functional analysis of paired metagenomic and metabolomic data from a clinical cohort (30 healthy, 30 adenoma, and 30 CRC), we aimed to identify keystone gut microbiome-derived bacteria and associated metabolites that drive CRC pathogenesis. Metagenomic analysis revealed enrichment of *Fusobacterium*, *Parasutterella*, and *Parvinomas* in the carcinoma group., with five bacterial genera that strongly

correlated with specific metabolomic features in the fecal samples. Anaerobic cultivation and subsequent antiproliferation testing of the crude extracts from these bacterial hits resulted in inhibition of multiple CRC cell lines and common human pathogens. Interestingly, the activity was found to be inducible when strains were co-cultured with common biofilm co-inhabitants, suggesting potential microbe-microbe interactions that drive host responses. Ongoing research will focus on identifying metabolites responsible for the observed bioactivity. Ultimately, successful characterization of those biomarkers will offer transformative insights into host-microbiome interactions and facilitate early clinical adoption of microbiome-targeted therapy in CRC.

C-35 – Gisele Rodriguez

The Filamentous Gut-Fungus Basidiobolus as a Reservoir for Biologically Relevant Peptidic Natural Products

Gisele J. Rodriguez[1], Elizabeth McGurk[1], Kimberly C. Syring[2], Lluvia Vargas-Gastelum[2], Daniel Farthing[2], Joseph W. Spatafora[2], and Kerry L. McPhail[1]. [1]Department of Medicinal Chemistry, University of Utah, Salt Lake City, UT, USA. [2]Department of Botany and Plant Pathology, Oregon State University, Corvallis, OR, USA

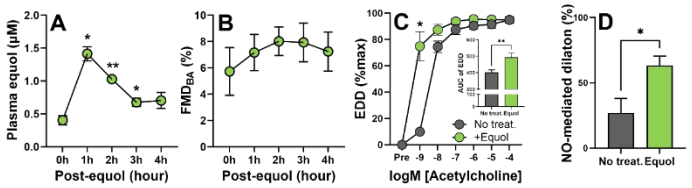
The filamentous fungus, *Basidiobolus* (Order Entomophthorales), lives saprophytically in leaf litter, is a ubiquitous member of reptile and amphibian gut microbiomes (collectively referred to as herptiles), and can infect humans (basidiobolomycosis). *Basidiobolus* fungi have an enhanced genetic capacity for specialized metabolite production, with signatures of horizontal gene transfer. As part of a collaborative herptile microbiome project, we have investigated the differences in specialized metabolite production of *Basidiobolus* across three known species clades: *B. meristosporus*, *B. ranarum*, and *B. haptosporus*. Pure cultures of 68 field collected *Basidiobolus* isolates from varying herptiles hosts were cultured aerobically on 2 different media types. Chemical extracts were profiled using liquid chromatography tandem mass spectrometry (LCMS^2) and spectral networking combined with cheminformatic analyses of the data were used to annotate the observed MS features. The distribution of known and putative antibacterial and immunomodulatory metabolites was documented.

C-36 – Ester Oh

Acute Effects of Equol on Vascular Endothelial Dysfunction in Postmenopausal Women and Mice

Ester Oh[1], Kristen Nowak[1], Vienna Brunt[1]. [1]Division of Renal Diseases and Hypertension, University of Colorado Anschutz Medical Campus, Aurora, CO 80045

endothelial function with chronic supplementation, but its acute effects remain unclear. In a single-arm, open-label, pilot study, healthy postmenopausal women (N=5; age 62±1 y) received a single oral dose of 30 mg equol, and brachial artery flow-mediated dilation (FMD_{BA}) was measured at baseline and at 1, 2, 3, and 4 hours post-ingestion. Secondly, ovarian depletion was induced in female C57BL/6J mice (N=8) using 4-vinylcyclohexene diepoxide (VCD). At 22 weeks after VCD, carotid arteries were isolated, and *ex vivo* EDD to acetylcholine was assessed ±1-hour equol pre-treatment, with NO-mediated EDD determined using L-NAME. In women, plasma equol increased (peak 1 h; **Fig A**) and showed a trend toward higher FMD_{BA} (peak 2 h; **Fig B**). In mice, equol improved EDD (**Fig C**), mediated by enhanced NO bioavailability (**Fig D**). These findings suggest equol may improve endothelial function and could be a potential alternative to estrogen therapy.



C-37 – Alpna Tyagi

Honokiol Hexafluoro Administration in Mice Enhances the Brain Mitochondrial Functions

Alpna Tyagi[ab], Samar Rao[a], Jack Arbiser[c] and Subbiah Pugazhenthi[a] . [a] Rocky Mountain Regional VA Medical Center, Aurora, CO, USA, [b] Department of Medicine, University of Colorado-Anschutz Medical Campus, Aurora, [c] Emory University School of Medicine, Atlanta, GA, US

Alzheimer's disease (AD) is a highly prevalent and complex neurodegenerative disorder affecting millions of elderly people worldwide. Metabolic syndrome (MetS) in midlife has been shown to drive AD progression. Deficiency of SIRT3, a mitochondrial deacetylase enzyme is associated with the development of MetS. We previously reported that Sirt3 deletion in an AD mouse model worsens amyloid plaque accumulation, mitochondrial dysfunction and neuroinflammation. We hypothesize that SIRT3 is a potential therapeutic target for AD. Honokiol, a naturally occurring SIRT3 activator has been shown to be present in all parts of *Magnolia* genus plants. Structural modifications of honokiol have resulted in synthetic analogues with improved biological activity. We tested the effects of one such analog, namely, hexafluoro honokiol (Hexa) on brain mitochondrial function by *in vitro* and *in vivo* studies. Hexa increased SIRT3 levels and decreased in lysine acetylation of mitochondrial proteins, a marker for SIRT3 activation in mouse microglial cells. Administration of Hexa in C57/BL6 mice increased the levels of SIRT3 as well as its key mitochondrial target proteins in the brain resulting in improved mitochondrial respiration. Furthermore, Hexa decreased the levels of BACE1, an enzyme that generates Aβ from APP and COX-2, an inflammatory marker. The effects of Hexa were lost in Sirt3$^{-/-}$ mice suggesting that this drug molecule acts through SIRT3. Together, our results strongly support the therapeutic potential of Hexa in AD. Our future studies will test this drug molecule in Alzheimer's transgenic mice.

Poster Presentations – Session I

P-001 – Shiwei Chen

Specialized Sesquiterpene Lactones (STLs) in *Liriodendron*: Species-Specific Chemistry & Plant Defense

Shiwei Chen,[1] Sarah Al Kinani,[2] Oli Horyn,[2] Colin Galliano,[2] David C. Rowley,[2] Kathryn M. Ramsey,[2,3] Divita Mathur,[1] Matthew J. Bertin[1,]. [1]Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106, USA. [2]Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, Kingston, RI 02881, USA. [3]Department of Cell and Molecular Biology, College of the Environment and Life Sciences, University of Rhode Island, Kingston, RI 02881, USA*

Tulip trees (*Liriodendron tulipifera* and *Liriodendron chinense*), members of the Magnolia family, are known for their distinctive morphology, yet their chemical diversity remains underexplored. Comparative profiling revealed that *L. tulipifera* contains a broader and distinct suite of specialized metabolites than *Magnolia species*. Several features detected in tulip were not observed in the *Magnolia* extracts analyzed, underscoring specific chemical diversification. In this study, we identified and characterized several sesquiterpene lactones (STLs) produced by *L. tulipifera* using high-resolution mass spectrometry and nuclear magnetic resonance spectroscopy. Notably, one STL with antibiotic activity was unique to *L. tulipifera* and absent in *L. chinense*. Additionally, some STLs showed strong deterrent effects on herbivory, suggesting a defensive ecological role. These findings highlight the species-specific chemical defenses of *Liriodendron* and point to potential applications of these metabolites in pharmaceuticals and agriculture.

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P-002 – Hyomoon Cho

Exploring Natural Product Structural Space through Multi-Level Mass Defect Analysis

Hyomoon Cho and Carole A. Bewley. Laboratory of Bioorganic Chemistry, 8 Center Drive, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892, USA

A central challenge in natural product discovery is extracting chemically meaningful information from the thousands of molecular features detected in high-resolution mass spectrometry (HR-MS) datasets. We examined whether relative mass defect values capture conserved structural features that enable the classification of compounds directly from complex MS data. Relative mass defect values derived from precursor ions separated metabolites into distinct superclass level regions of chemical space, enabling broad categorization across diverse metabolite families. RMD analysis of fragment ions provided finer resolution resolving compounds at the class and subclass levels based on scaffold-specific fragmentation patterns. Together, MS^1 and MS^2 relative mass defect analysis provide complementary classification at two levels of chemical resolution, enabling broad superclass grouping and finer-scale class and subclass discrimination, both without reliance on spectral library matching. Features deviating from established signatures were flagged as candidates for chemical novelty. When applied to complex microbial extracts, this multi-level RMD strategy contributed to the identification of several new natural products with antibiotic and antitumor activities. Hierarchical RMD analysis, integrating MS^1-based superclass assignment with MS^2-based class and subclass resolution, thus offers a practical and efficient approach for metabolite prioritization in early-stage natural product discovery.

P-003 – Richard Fitch

Tandem Mass Spectra as a Common Fingerprint in GC-MS and LC-MS Data

Richard W. Fitch[1], Luke M. Bloebaum[1], Xianghu Wang[2] and Mingxun Wang[2]. [1]. Department of Chemistry and Physics, Indiana State University, Terre Haute, IN 47809 [2]. Department of Computer Science and Engineering, University of California at Riverside, Riverside, CA, 92507

Hyphenation of chromatography and mass spectrometry (MS) is commonly used to initially characterize the numerous secondary metabolites and complex mixtures commonly encountered in natural extracts. A wealth of gas chromatography-mass spectrometry (GC-MS) data is documented in the literature and in databases for natural products of various classes. However, most of that archival data is from electron ionization (EI), for which there are no commercially available analogs for liquid chromatography-mass spectrometry (LC-MS), which generally uses electrospray (ESI). This is a significant limitation as compound isolation is typically performed using LC rather than GC and a positive ID/correlation of components for tracking and dereplication during the isolation process would be most helpful. ESI is a form of chemical ionization (CI) and should be comparable with GC-MS using CI with an appropriate reagent gas to correlate data for the two modes of separation. Unfortunately, CI or ESI typically gives protonation $[M+H]^+$ without significant fragmentation thus limiting the confidence of correlations, especially in the presence of isomeric or isobaric mixtures. Tandem mass spectrometry (MSn) can address the need for a common fingerprint in these circumstances, allowing high confidence correlation of compounds in the two modes. Alkaloids perform well correlated spectra, provided collision energies are matched. Here, we will present our findings to date for various compound classes using GC-CI-MS using different reagent gases (NH3 and CH_4) as well as LC-MS using ESI and atmospheric pressure chemical ionization (APCI).

P-004 – Pearl Lee

Isolation of Aquatic Fungal Secondary Metabolites with Antimicrobial Properties

Pearl Lee and Skylar Carlson. Department of Chemistry, University of the Pacific, 3601 Pacific Ave., Stockton, CA 95211

Aquatic fungal strains have the potential to provide an prolific source of novel natural products (Gao LW., Zhang P., *Phytochem Review*, 2023). Fungi have provided antibacterial drugs such as penicillin, which have proven to be broad spectrum inhibitors of pathogenic bacteria. Fungal secondary metabolites were significant contributors to the golden age of antibacterial drug discovery, yet with the rise of antimicrobial resistance, demand for new drug leads is at an all time high (V. Antonio, *Biomedicines*, 2023). Strains were isolated from collection sites across North America, grown in PDB, cryopreserved, and extracted with ethyl acetate to create a fungal strain library and corresponding extract library. These were then tested for antimicrobial properties against bacterial and fungal human pathogens. Antibacterial screening against both gram-positive and gram-negative human pathogens resulted in significant inhibition against gram-positive bacteria from the strains Y034 and Y052. When screening for antifungal activity against human pathogen *Candida albicans*, strain, Z021, showed antifungal activity only when grown in presence of the highest dose of sodium butyrate (100 μM), a methyltransferase inhibitor (Beau J., *Marine Drugs*, 2012). Fungi have complex genomes that are tightly regulated resulting in the silencing of some biosynthetic pathways. These can be manipulated by inhibiting DNA methyl transferase through treatment with sodium butyrate to increase the production of secondary metabolites. By July, it is anticipated that the conclusions to both projects will be presented with the identity (via 18s rRNA sequencing) of the fungi and any known or novel compounds responsible for both activities.

P-005 – Zijian Rong

Research on *Aspergillus*: Annotation of Mycotoxins by NMR and MS

Zijian Rong[1], Kelsey E. Custer[1], Tyler N. Graf[1], Huzefa A. Raja[1], Nicholas H. Oberlies[1]. Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC 27412

Aspergillus fungi are well known to have both beneficial properties (i.e., commercial applications in cheese and alcohol industries) and detrimental properties (i.e., infections of animals and plants). While the main players in those specific areas are well studied, many species across the 26 different sections of Aspergillus are not well investigated. As part of a collaboration to examine the evolution of pathogenicity in Aspergillus, we are working with colleagues to examine both the genomic and metabolomic properties of representative species in each of the sections of Aspergillus. In most cases, spectral data for the compounds from these fungi are either nonexistent or incomplete. Thus, we are using a systematic approach to identify these compounds with both MS and NMR data. First, we obtained cultures of representative species from different sections of Aspergillus fungi, where they were grown at 25 ℃. A standard procedure was used for the extraction and fractionation of each culture. Based on the MS profile of these extracts, we built a molecular network to visualize the differences between these species, leveraging a dereplication protocol and database that our lab has assembled over 15 years (using Mzmine), that include retention time, UV spectra, high resolution MS data, and MS fragmentation patterns. As an auxiliary tool, we also use ACD Labs to establish a simulated MS database. Additionally, NMR spectra were searched in our database, examining literature-simulated data. The end goal of the research is to connect the genomic and metabolomic data, and we plan to share these data with the research community.

P-006 – Melina Tamang

Wheldone, a Cytotoxic Compound from Fungal-Fungal Co-Culture

Melina Tamang[1], Manuel Rangel-Grimaldo[2], Huzefa Raja[1], Tyler N. Graf[1], and Nicholas H. Oberlies[1] [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, NC 27402, [2]Departamento de Productos Naturales, Instituto de Química, Universidad Nacional Autónoma de México, Ciudad Universitaria 04510 Ciudad de México, México*

Recent genomic studies suggest that fungi, especially in the Ascomycota, are capable of biosynthesizing an average of 40-50 distinct secondary metabolites per species. However, when fungi are grown in the lab, most of the time only dozen or so compounds are produced. One way to stimulate their biosynthetic machinery is to have them fight for limited resources in culture. Fungal-fungal co-culturing is growing two different fungal species together with limited nutrients, triggering cryptic biosynthetic gene clusters and stimulating biosynthesis of novel scaffolds as a defense mechanism in a competetive environment. From fungal-fungal co-culture of Aspergillus fischeri (strain NRRL181) and Xylaria flabelliformis (strain G536), a new compound, wheldone, was isolated that showed micromolar cytotoxic activity against breast, ovarian and melanoma cancer cell lines. Since the discovery of wheldone in 2020, we have significantly improved the scaleup methodology. During initial studies, we isolated 9 mg of wheldone. Our new method now allows us to routinely isolate ~ 100 mg of wheldone. These scaleup efforts have also led to the discovery of four additional wheldone analogues. Here we present structure elucidation of these analogues along with our most recent data from our scaleup studies on the gram scale, which will significantly help with ongoing pharmacology and semisynthetic work to advance this molecule to further drug discovery endeavors.

P-007 –Courtney Clevenger

Multi-Year Investigation of Benthic Cyanobacteria Accumulation in Stormwater Ponds Using Mass Spectrometry and Chemoinformatics

Courtney Clevenger[1], Stuart Oehrle[2,3], Avery Tatters[4], Wendy Strangman[1], [1]University of North Carolina Wilmington; [2]Northern Kentucky University, [3]Waters Corporation, [4]United States Environmental Protection Agency

Cyanobacterial Harmful Algal Blooms (CHABs) are increasing in urban freshwater systems, driven by nutrient input, rising temperatures, and anthropogenic pressures. CHABs produce well known toxins such as hepatotoxins and potent neurotoxins, as well as a broader suite of secondary metabolites with potential threats for human and ecosystem health. Large proliferations of benthic cyanobacterial mats were observed in a stormwater retention pond network, located in northwest Florida, during late summer of 2021-2024. Weekly sampling across the pond system and was employed each year. Microscopy and both targeted and untargeted LC-MS/MS analyses were conducted to assess the presence of toxin-producing cyanobacteria, associated cyanotoxins, and other potentially bioactive cyanobacterial metabolites at various sites within the pond network and surrounding watershed. To support compound identification, we analyzed in-house cyanobacterial cultures in parallel with the pond samples, using them as reference nodes within the molecular network. These culture extracts allowed us to annotate many features not represented in existing Global Natural Product Social Networking (GNPS) libraries. Aligning culture and environmental profiles provides a more confident framework for interpreting metabolite diversity across the pond system.

P-008 – Younghoon Kang

LITMass: A Taxonomically Informed Pipeline for HRMS Annotation Using LiteratureCurated Natural Product Data

Younghoon Kang[1], Myeongji Kim[1], KyuHyeong Lee[1], Jiin Park[1], Hyunwoo Kim[1]. [1]College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University-Seoul, Goyang 10326, Republic of Korea*

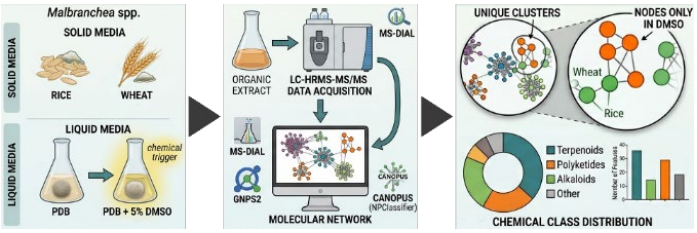
To overcome the bottleneck of re-identifying known compounds, we developed LITMass, an informatics pipeline that integrates genus-level taxonomic filtering with the COCONUT database for HRMS annotation. Validated against an in-house reference set of 1,463 compounds, LITMass achieved a 53.7% recognition rate, significantly exceeding the 48% benchmark for constrained searches. In a large-scale benchmark of 200 crude extracts, the workflow prioritized candidate structures for 2,810 unique features missed by public MS/MS libraries, demonstrating its high complementary to existing methods. As a application, LITMass guided the targeted isolation and structural elucidation of Physalin A from Physalis alkekengi. These results highlight the value of taxonomic information as a critical constraint for improving the precision and efficiency of natural product annotation in complex metabolomic datasets.

P-009 – Alan López-Martínez

Metabolomic Diversity of *Malbranchea* spp. Under OSMAC Conditions Revealed by Molecular Networking and In Silico Annotation

Alan López-Martínez, Alan G. Hernández-Melgar, Mario Figueroa, and Rachel Mata. Facultad de Química, Universidad Nacional Autónoma de México, Ciudad de México, 04510, México

Filamentous fungi are well-known sources of secondary metabolites; however, many biosynthetic pathways remain silent under standard laboratory conditions. In this study, the metabolomic diversity of several *Malbranchea* species was evaluated using an OSMAC approach. The strains were fermented in both solid (rice and wheat) and liquid (PDB and PDB + 5% DMSO) media, and their organic extracts were analyzed by LC-HRMS-MS/MS. Subsequently, the MS/MS data were processed using MS-DIAL and exported to GNPS2 for FBMN analysis. CANOPUS was employed to perform chemical classification within the NPClassifier hierarchy, and metabolite distribution across conditions was visualized using Cytoscape. Distinct metabolomic profiles and chemical classes were observed across culture conditions; in particular, several features were unique to the DMSO-supplemented cultures. These results illustrate the significant impact of culture conditions on fungal metabolite diversity and support the use of molecular networking for prioritizing metabolites for further investigation.



P-010 – Carla Menegatti

Industrial-Scale Metabolomics Strategies for Sustainable Crop Protection Solutions

Carla Menegatti[1], Amanda Rosier[1], Cecilia Chagas deFreitas[1], Christine Kraus[1], Vera Bonardi[1], Deepa Acharya[1]. [1]Crop Health R&D, Corteva Agriscience, 9330 Zionsville Road, Indianapolis, Indiana 46268

Crop health faces escalating challenges from plant diseases and increasing pest pressure, posing significant risks to global food security. These threats are further intensified by climate change, rapid pest and pathogen evolution, and the growing emergence of resistance to existing crop protection products.

Identifying bioactive metabolites with strong and reproducible activity is therefore a critical step in addressing these challenges. Natural products are known for their unique chemical complexity and broad biological activity and represent a rich source of novel crop protection solutions. Corteva Agriscience™ maintains a large microbial biorepository containing hundreds of thousands of strains, which serves as a foundation for industrial-scale natural products discovery. At this scale, discovery efforts rely on modern metabolomics techniques to organize massive untargeted datasets into interpretable chemical information. Through integrated omics tools, including molecular networking and comparative genomics and metabolomics, combined with biological screening-based activity profiling, this resource is used to efficiently identify bioactive metabolites and advance new biological crop protection solutions that promote sustainable agricultural practices. Close collaboration across integrated biological discovery groups enables the rapid discovery of compounds that can directly control plant pathogens or serve as the active component of live microbial products.

P-011 – Raima Sen

Development of a Novel Analytical Technique to Assess Anti-AGE Properties of Dietary Polyphenols in *Drosophila* Hemolymph

Raima Sen[1], Zana Norton[1], Isabella Lange[1], Christian Landry[1], Zhao Zhitao[2], Si Wu[2], Lukasz Ciesla[1] [1]Department of Biological Sciences, and [2] Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa AL

Polyphenols are a structurally diverse class of natural products widely studied for their antioxidant properties. Research suggests that polyphenol-rich diets may promote healthspan and reduce in-vivo buildup of harmful compounds like Advanced Glycation End Products (AGEs) and Advanced Lipoxidation End Products (ALEs). AGEs/ALEs form when sugars or lipid-derived molecules react with proteins under persistent metabolic stress, accumulate with age, and drive inflammation. Despite extensive structural characterization of polyphenols, precise mechanisms of their protective actions remain obscure. The α,β-unsaturated carbonyl motifs of polyphenols confer soft electrophilic properties, enabling covalent modification of nucleophilic residues of diverse biomolecules, and thereby possibly modulating multiple biochemical pathways. This further hinders a precise mechanistic understanding of the molecular modes of action of polyphenols. To address this gap, the project develops a targeted mass spectrometry based approach to quantify systemic AGE/ALE levels in *Drosophila melanogaster* hemolymph following dietary polyphenol intervention. Using hemolymph as a physiologically relevant matrix, this work aims to identify biomarker/s analogous to human HbA1c, enabling quantitative assessment of systemic AGEs /ALEs burden. This platform distinguishes between preventative, rescue, and stress-response mediated effects of polyphenols, advancing understanding of natural products beyond the one-drug, one-target approach in an ageing relevant biological context.

P-012 – Joshua Tennant

Metabolomic Changes of Flavobacteria when Grown on Various Complex Carbohydrates

Joshua Tennant, Rose Campbell, Karla Piedl, Emily Mevers. Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA, 24061, USA

Natural products have a well-documented history of use in pharmaceuticals, with approximately 65% of drugs classified as natural products or structural derivatives. This includes complex biosynthetic pathways in marine organisms that generate skeletal structures that are favorable for various therapeutic applications. Recently, our research group has been studying moon snails (Nacticidae), a family of marine snails that lay egg masses that exhibit resistance to predation and biofouling. Egg masses are formed by binding eggs and sediments with host-derived mucin (glycosylated protein). We demonstrated that the microbiota of egg masses from SW Florida are dominated by Flavobacteriia and contain Alpha- and Gammaproteobacteria. As moon snail egg masses age, Flavobacteriia abundance increases to nearly 69% of all sequences. Flavobacteriia produce glycoside hydrolases that are likely capable of degrading the complex carbohydrates within the host-derived mucin. Little is known about the relationship between carbohydrate degradation and bacterial community composition, let alone the regulation of bacterial natural product production on the egg masses. Here, we aim to investigate metabolomic changes associated with growth on different carbohydrates, using liquid chromatography-mass spectrometry (LC-MS). Alterations in natural product production by Flavobacteria, Alpha- and Gammaproteobacteria when cultured on various complex carbohydrates have been identified, and work is ongoing to elucidate their structures.

P-013 – Johnny Tran

Untargeted Metabolomics of Marine-Dependent Lichen via QTOF-LC/MS and Genomic Sequencing

Johnny Tran[1], Shelia Podell1, and April L. Lukowski1,[2]. [1]Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA, 92037, USA, [2]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, CA, 92037, USA

Symbiotic organisms take part in unique chemical ecological relationships, making these organisms an excellent target for natural product discovery. Lichen, which are symbiotic composites of fungi and green algae, have been of interest for natural product research for several decades. Although thousands of natural products have been reported from lichen, lichens that acquire a majority of their water and nutrients from coastal spray (marine-dependent lichen) have been generally overlooked in this regard. In this study, marine-dependent lichens were collected from the Cabrillo National Monument (San Diego, USA) and evaluated for their potential to produce unique natural products distinct to the

coastal ecosystem. We identified the lichen as belonging to the *Vermilicinia* genus, and initial identification of metabolites of the lichen was conducted using QTOF-LC/MS, and the results will be presented. The biosynthetic gene clusters and natural product connection will also be highlighted.

P-014 – Warren Vidar

LC–MS/MS and Molecular Networking Demonstrate Indole Alkaloid Diversity in Leaves and Fruits of *Voacanga globosa* and *Voacanga megacarpa*

Warren S. Vidar[1], John Henry C. Casao[2], Zander Louis O. Ongpeng[2], Nadja B. Cech[1], and Hilbert D. Magpantay[2]. [1]Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro NC 27402. [2]Department of Chemistry, De La Salle University, Manila 0922, Philippines

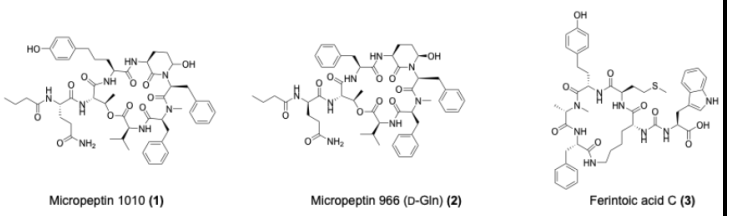
The genus *Voacanga* (Apocynaceae) is known to produce structurally diverse monoterpene indole alkaloids with a wide range of reported biological activities. While several compounds have been isolated from *Voacanga globosa* (locally called bayag usa), the chemical composition of its fruits, as well as that of the related species *Voacanga megacarpa* (locally called bayag aso), remains underexplored. In this study, we aimed to explore and compare the indole alkaloid diversity in the leaves and fruits of both *Voacanga* species using liquid chromatography–tandem mass spectrometry (LC–MS/MS) and feature-based molecular networking to guide targeted purification and structural elucidation of prioritized metabolites. LC–MS/MS data were processed to generate molecular networks, enabling the visualization of structurally related indole alkaloids and the annotation of known compound classes. Several clusters consistent with indole alkaloid scaffolds were observed, along with multiple unannotated features that may represent new or underreported analogs. These features will be prioritized for isolation based on their distribution across plant parts and their connectivity within the molecular network. This work demonstrates the broader applicability of LC–MS/MS–based molecular networking for uncovering and prioritizing structurally related monoterpene bisindole alkaloids in chemically complex natural product systems.

P-015 – Runjie Xia

New Micropeptins and Generalizable MS/MS Workflows for Cyanopeptide Annotation

Runjie Xia[1], Lindsey Ahn[1], Michaela Burkhauser[1], Ross Youngs[2] and Matthew J. Bertin[1]. [1]Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106, USA, [2]Biosortia, Inc., Columbus, OH 43235, USA

Cyanobacterial harmful algal blooms (cyanoHABs) are a major ecological and public health concern. While four metabolites are recognized by WHO, the broader suite of bioactive metabolites remains under characterized. Here, we interrogated a chromatography fraction library from a cyanoHAB in Muskegon, Michigan, leading to the isolation of two new micropeptins (**1** and **2**) and the structural confirmation of ferintoic acid C (**3**). One of the new micropeptins (**1**) exhibited moderate inhibition of neutrophil elastase, suggesting potential human and ecological relevance. To expand chemical space coverage beyond isolated compounds, LC–MS/MS data were analyzed using the GNPS2 Analysis Hub query language for product ion searching, enabling annotation of cyanopeptide classes and class-specific modifications across the fraction set. Analysis of field samples from Lake Erie showed recurring micropeptins but no evidence of microcystins. Together, the LC–MS/MS workflows are valuable in compound discovery and environmental monitoring.



P-016 – Marquis Yazzie

Potential Roles for a Metallophore in Lanthanide Homeostasis in *Methylobacterium mesophilicum* A47

Marquis T. Yazzie[1], Ram Ambre[1], Charlie Mineo[2], Alexa M. Zytnick[2], Colin Brady[1], Zachary Reitz[3], N. Cecilia Martinez-Gomez[2], Brady T. Worrell[1], Allegra T. Aron[1]. [1]Department of Chemistry and Biochemistry, University of Denver, Denver, CO, USA, [2]Department of Plant and Microbial Biology, University of California Berkeley, Berkeley, CA, USA. [3]Department of Ecology, Evolution and Marine Biology, University of California Santa Barbara, CA, USA

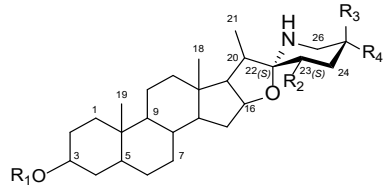
Lanthanide (Ln) elements are increasing in demand for various technologies, however Lns are difficult to separate using traditional extraction methods. Ln-binding proteins and small molecules have emerged as a potential method for Ln separation. This project aims to investigate the role of a novel metallophore produced by the Ln utilizing *M. mesophilicum* A47. We have identified a novel putative A47-produced metallophore structure from a metal-limited extract. We are in the process of verifying the structure of the metallophore by NMR. Moreover, the metallophore has been found to have preliminary lanthanide binding using a mass spectrometry method. Finally, we are developing a novel total synthesis to obtain metallophore for metal binding assays. Future work will investigate the metallophore's role in Ln uptake.

P-017 – Dong Hyuk Baek

New Steroidal Glycoalkaloids from *Solanum lycopersicum* var. *cerasiforme* Varieties

Dong Hyuk Baek[1], Hee Jung Yang[2], and Sang Hee Shim[1]. [1]Natural Products Research Institute, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea. [2]College of Pharmacy, Kangwon National University, Chuncheon 24341, Republic of Korea

Steroidal alkaloids and glycoalkaloids are major secondary metabolites in cherry tomato (*Solanum lycopersicum* var. *cerasiforme*), contributing to plant defense mechanisms and pharmacological potential. In this study, four new steroidal glycoalkaloids esculeoside E (**8**), E2 (**9**), esculeoside F (**10**), and F2 (**11**) along with seven known compounds were isolated from cherry tomato using various chromatographic methods. Their chemical structures were elucidated through 1D/2D NMR and high-resolution mass spectrometry, identifying them as derivatives with spirosolane and solanocapsine skeletons. Additionally, quantitative profiling of these metabolites was conducted across commercial cherry tomato varieties. As the discovery and structural elucidation of novel tomato-derived glycoalkaloids are challenging due to their low natural abundance and high structural similarities, the characterization of these derivatives provides a fundamental basis for future phytochemical research.



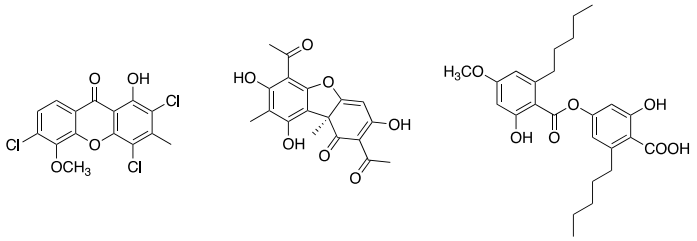
	R_1	R_2	R_3	R_4	C-25
8	β-lycotetraosyl	-OAc	-H	-COOH	*(R)*
9	β-lycotetraosyl	-OAc	-COOH	-H	*(S)*
10	β-lycotetraosyl	-OAc	-H	-COOMe	*(R)*
11	β-lycotetraosyl	-OAc	-COOMe	-H	*(S)*

P-018 – Leng Chee Chang

Constituents of Hawaiian Lichen *Cladonia skottsbergii* and its Antimicrobial Properties

Marvin J. Rositzki[1], Achara Raksat[1], Charles J. Simmons[2], Clifford Smith[3], Reverend Danette V. Choi[4], Supakit Wongwiwatthananukit[5], and Leng Chee Chang[1]. [1]Department of Pharmaceutical Sciences, The Daniel K. Inouye College of Pharmacy, University of Hawai'i at Hilo (UHH), Hilo, HI, 96720, USA. [2]X-ray diffraction Laboratory, Department of Chemistry, UHH, Hilo 96720. [3]Department of Botany, University of Hawai'i at Manoa, Honolulu 96822, USA.[4] Priest of Bang San Ho Temple Yun Hwa Denomination of World Social Buddhism dba Lotus Buddhist Monastery, Mountain View, HI, 96720. [5]College of Pharmacy, Rangsit University, Pathum Thani 12000, Thailand

Three compounds were isolated and characterized: clarosione (**1**), a newly identified trichlorinated xanthone, and two known metabolites, (*S*)-usnic acid (**2**) and perlatolic acid (**3**). Compounds **2** and **3** have exhibit potent antimicrobial activity, strongly inhibiting both MRSA and MSSA, with minimum inhibitory concentrations (MICs) of 2 to 4 μg/mL, compared to 0.5–1 μg/mL for vancomycin. Furthermore, cytotoxicity assays indicated a higher sensitivity in A549 cells than in Vero E6 cells. These results gave favorable selectivity indices for the active compounds, indicating potential therapeutic relevance. Further studies are ongoing and will be presented in the meeting.



Clarosione (**1**) (*S*)-Usnic acid (**2**) Perlatolic acid (**3**)

P-019 – John Cort

How an NMR Knowledgebase and Data Repository Facilitates Natural Products Research: Natural Products Magnetic Resonance Database (NP-MRD)

John R. Cort[1,5], Jessica L. Bade[1], Giselle Miralles[1], Roger G. Linington[2], Matthew Pin[2], Ella F. Poynton[2], Lloyd W. Sumner[3], James T. Koller[3], Ronald Myers[3], Zachary M. Tretter[3], David S. Wishart[4], Mark Berjanskii[4], Scott MacKay[4], Eponine Oler[4], Harrison Peters[4], Tanvir Sajed[4]. [1]Biological Sciences Division, Pacific Northwest National Laboratory, Richland WA, 99354, USA, [2]Department of Chemistry, Simon Fraser University, Burnaby BC, V5A 1S6, Canada, [3]Department of Biochemistry, University of Missouri, 65211, Columbia MO, USA, [4]Department of Biological Sciences, University of Alberta, Edmonton AB, T6G 2E9, Canada, [5]Institute of Biological Chemistry, Washington State University, Pullman WA, 99164, USA

The Natural Products Magnetic Resonance Database (NP-MRD, np-mrd.org), established in 2020, is a comprehensive knowledgebase and data repository for NMR spectroscopic data of natural products and specialized metabolites. NP-MRD is a free and open resource with structures, raw data (FIDs), curated literature data, predicted data (from DFT and AI/ML), simulated spectra, chemotaxonomy, synonyms, links to other databases, search tools, chemical shift prediction tools, and a deposition system wherein users can deposit raw data to satisfy publishing requirements. The mission of NP-MRD is to benefit research through engagement and partnership with the worldwide natural products community. In this presentation we will look back over the more than five years that NP-MRD has been operating, and look forward through the next five years and beyond, to assess 1) how it is being used currently to facilitate research and what may be done to make the resource more

useful, 2) how it has grown (in terms of both users and content) and what the prospects for continued growth are, and 3) how it can be sustained over the long term and become an enduring scientific resource that will continue to benefit the natural products field for decades to come.

P-020 – Yumin Dai

Identification, Enrichment and Structural Elucidation of Two Trace Colored Degradants from White *N*-Pyridinyl-3-Amino-2-Pyridone via Traditional Natural Products Approach

Yumin Dai[1], Hao Li,[1] Yuning Chang,[1] Yoshiyuki Takeda,[2] Raymond Turro,[2] Zhipeng Lu,[2] Tatsuaki Matsubara,[2] Yanmei Lan,[1] Izumi Takagi,[1] Kazunobu Moriguchi,[1] Mark J. Milton,[1] Mark T. Zell,[1, 1]Analytical Development Synthetic Molecules, [2]Synthetic Molecule Process Development, Takeda Development Center Americas, Inc., Cambridge, MA 02142

Traditional natural products research provided extensive methodology to solve the structures of unknown compounds, including the isolation of sample with trace quantity, LC-MS or NMR-based structural elucidation without a molecular template. In pharmaceutical industry, these techniques are extremely crucial for the investigation of unknown impurity or degradant during drug development. Among them, color degradant identification has become one of the challenging subjects as the presence of trace amount of color may impact the quality of drug. In this study, two unknown-colored degradants were identified as the major degradants by using white *N*-pyridinyl-3-Amino-2-Pyridone motif as the material. To understand their structures, full structural characterization was performed by following an established workflow by combining a traditional natural products structural elucidation and forced degradation method. In brief, the colored impurity was identified by a UV-Vis guided LC-MS analysis. With the purpose of facile isolation and purification, various photodegradation conditions were screened to enrich the desired colored impurity to a decent level. Following isolation by prep-HPLC, 1D and 2D NMR studies and HRMS characterization. In addition, plausible mechanisms of formation were also proposed.

P-021 – William Gerwick

'SPECTRE: A Multimodal Spectral Transformer for Small Molecule Annotation

Wangdong Xu,[1] Byeol Ryu,[2] Anthony Tong,[1] Huanru Henry Mao,[3] Hyunwoo Kim,[4] James Jialun Zhao,[1] Chen Zhang,[2] Yiran Xu,[1] Mingxun Wang,[5] William H. Gerwick,[2,6] Garrison W. Cottrell[1.] [1]Department of Computer Science and Engineering, University of California San Diego, La Jolla, CA 92093; [2]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA 92093; [3]Smithery, Singapore 409053, Singapore; [4]College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University-Seoul, Goyang 10326, Republic of Korea; [5]Computer Science & Engineering Department, University of California Riverside, Riverside, CA 92521; [6]Skaggs School of Pharmacy and Pharmaceutical Science, University of California San Diego, La Jolla, CA 92093

Nuclear magnetic resonance (NMR) spectroscopy is an essential tool for elucidating the chemical structure of Natural Products (NPs). However, interpreting NMR spectra is a time-consuming process that requires considerable domain expertise. This has led to the development of computational tools that directly annotate structures from NMR spectra, accelerating this elucidation and discovery process. Here we introduce SPECTRE, a state-of-the-art transformer-based model for structure dereplication and annotation. Key contributions of this tool include (1) a novel, transformer-based structure annotation method that accepts several types of NMR data for flexible annotation; (2) a novel, entropy-optimized, and collision-free molecular binary fingerprint that enhances the accuracy when retrieving molecular candidates. SPECTRE achieves a new state of the art 80% top-1 annotation accuracy using a challenging search space of 526,163 molecules. SPECTRE is also the first tool to provide fine-grained similarity maps between predicted and retrieved structures. These maps enable substructure-level interpretation, offering interpretable visual cues that highlight matched chemical fragments. Even in cases where overall molecular similarity is low, these fragment-level hints offer valuable insights to chemists, guiding hypothesis generation and accelerating the structure elucidation process

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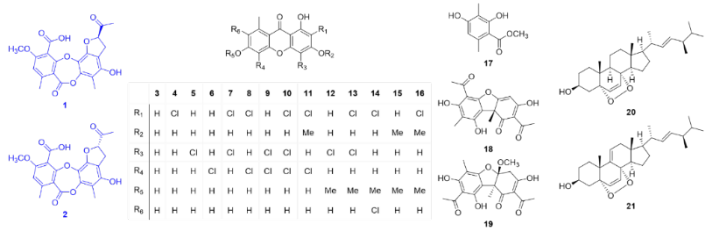
P-022 – Sunbeom Kwon

Novel Enantiomeric Depsidone Derivatives from the Antarctic Lichen *Haematomma erythromma* and Their Anticancer Potential

Sunbeom Kwon[1], Seulah Lee[1,. 1] Department of Convergent Biotechnology and Advanced Materials Science, College of Life Sciences, Kyung Hee University, Yongin 17104, Republic of Korea*

Chemical investigation of the acetone extract of the Antarctic lichen *Haematomma erythromma* afforded two new enantiomeric depsidone derivatives (**1** and **2**) and nineteen known compounds (**3**–**21**). The new compounds were resolved by chiral HPLC into (*R*)-erythrommic acid (**1**) and (*S*)-erythrommic acid (**2**), and their absolute configurations were unambiguously assigned by ECD spectroscopy. Network pharmacology and molecular docking analyses suggested the anticancer potential of **1** and **2**. Based on these findings, further experimental investigation into the anticancer activity of these compounds is required.



P-023 – Natalia Makaro

Novel Class of Anti-Cancer Metabolites from Cyanobacterium *Cylindrospermum* sp. UIC12000

Natalia Makaro, Aleksej Krunic, Jimmy Orjala[1]. [1]Department of Pharmaceutical Sciences, Retzky College of Pharmacy, University of Illinois at Chicago

Cyanobacteria, also known as "blue-green algae," are photosynthetic, gram-negative autotrophs that have been the focus of many recent drug discovery efforts due to their production of diverse secondary metabolites with unique chemical scaffolds. *Cylindrospermum sp*. UIC12000 is a strain of interest due to strong activity in preliminary biological testing against melanoma cancer cell line MDA-MB-435 and ovarian cancer cell line OVCAR3. Using a bioactivity guided approach, compounds of interest were identified and isolated through multiple chromatographic steps. Structural elucidation was done through mass spectrometry (MS), nuclear magnetic resonance (NMR) spectroscopy, and chemical derivatization. Although a current project, preliminary information reveals the structure is novel and unusual; there is a highly functionalized conjugated system and aliphatic macrocycle. The pure compound was submitted for biological evaluation. A metabolomics investigation was initiated to further evaluate the biosynthetic capacity of *Cylindrospermum sp*. UIC12000. It has been shown that cyanobacterial growth and amount of metabolite production are dependent on the presence or absence of nutrients like nitrogen, phosphorus, and iron. The strain was grown in multiple media conditions and etxtracts from these growths were analyzed via LC-MS and platforms like GNPS and MetaboAnalyst, leading to the identification of a cluster of analogs related to the initial compound. We are in the process of elucidating one analog, which will be used to inform initial structure activity relationships for this class of novel metabolites. Overall, a novel metabolite with potent anti-cancer activity was identified using a bioactivity guided approach, and further discovery of analogs was guided through metabolomics.

P-024 – Kanchan Sonkar

Enabling High-Throughput Natural Product Identification through Structure-Validated Molecular Rotational Resonance (MRR) Spectral Libraries

Kanchan Sonkar, Christopher Thompson, Reilly E. Sonstrom, and Justin L. Neill, BrightSpec, Inc., 770 Harris St., Charlottesville, VA 22903

Natural products, particularly terpenoid-rich extracts, represent a structurally diverse chemical space central to drug discovery and pharmacognosy. However, reliable identification of closely related compounds, especially isomers, remains a bottleneck in high-throughput workflows, where conventional approaches depend on chromatographic separation or reference-based spectral matching. Molecular rotational resonance (MRR) spectroscopy enables direct, structure-specific identification by measuring rotational transitions uniquely defined by molecular geometry. This provides reference-free identification, allowing unambiguous differentiation of structurally similar compounds without separation or spectral libraries. We present an automated workflow that integrates quantum-predicted spectra with experimental MRR measurements for rapid structure validation and iterative, de novo library generation, enabling high-confidence, high-throughput identification of natural products across complex extracts.

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P-025 – Kanchan Sonkar

Standards-Free Structural Elucidation of Natural Products Using Molecular Rotational Resonance (MRR) Spectroscopy

Kanchan Sonkar, Christopher Thompson, and Justin L. Neill, BrightSpec, Inc., 770 Harris St., Charlottesville, VA 22903

The characterization of minor components and impurities in natural product systems remains a key challenge in pharmacognosy, particularly in complex mixtures relevant to human health. These systems often contain structurally similar species at low abundance, where conventional workflows rely on reference standards and multiple orthogonal techniques, limiting throughput and slowing discovery. We present molecular rotational resonance (MRR) spectroscopy as an emerging, standards-free approach to support structural identification in complex natural product matrices. Recent advances in instrument sensitivity and data analysis workflows have enabled the use of MRR for rapid structural interrogation of low-level components. By directly probing molecular three-dimensional structure through moments of inertia, MRR provides highly discriminative information that can distinguish closely related isomeric species without requiring prior experimental reference spectra. Coupled with computational chemistry, MRR supports confident structural

assignment where traditional analytical methods may be inconclusive. This approach offers a pathway to accelerate dereplication, impurity assessment & profiling, and early-stage characterization, positioning MRR represents a complementary analytical tool to streamline structural elucidation workflows in complex natural product environments.

P-026 – José D. D. Cediel-Becerra

Integrating Targeted Genome Mining and Structure-Guided Modeling Reveals Unexplored 7-Deazapurine-Containing Pathways

José D. D. Cediel-Becerra[1], Marc G. Chevrette[1,2], Valérie de Crécy-Lagard[1,2], and Raquel Dias[1]. [1] Department of Microbiology and Cell Science, University of Florida, Gainesville, FL, USA, [2] University of Florida Genetics Institute, University of Florida, Gainesville, FL, USA

7-deazapurines are nucleoside analogs that play key roles in nucleic acid modification and can serve as building blocks for diverse, bioactive secondary metabolites. Despite their biological significance, their biosynthetic diversity, distribution, and enzymatic determinants of structural diversification remain poorly understood. Here, we leverage large-scale targeted genome mining, phylogenetic, and network analysis to explore 7-deazapurine-containing pathways across ~2 million bacterial genomes. We identified over 900 candidate biosynthetic gene clusters (BGCs), grouped into more than 100 families, most of which remain uncharacterized. These GATOR-GC-predicted BGCs are predominantly found in *Streptomyces*. We then examined enzyme-substrate interactions in three representative pathways: (i) peptidyl-deazapurines, (ii) huimycin, and (iii) dapiramicin A. Molecular docking and molecular dynamics (MD) simulations recapitulated known enzyme-substrate interactions and highlighted candidate catalytic residues governing amide bond formation, methylation, and glycosylation. Using this genome- and structure-guided framework, we identified a candidate BGC for dapiramicin A and proposed tailoring steps, including scaffold methylation and deoxy-sugar formation. These findings expand the known diversity of 7-deazapurine-containing BGCs and demonstrate how integrating genome mining with structural modeling can link BGCs to chemical function, providing a foundation for discovering and characterizing 7-deazapurine-containing secondary metabolites.

P-027 – Rachel Johnson

Phylogeny of Asparagine synthetase-like Genes in Type II Polyketide Biosynthesis

Rachel A. Johnson[1], Megan Hasbrooke[1], and Katharine Watts[1]. [1]Department of Chemistry and Biochemistry, California Polytechnic State University, San Luis Obispo, CA 93407

Type II polyketide synthase (PKS) biosynthetic gene clusters (BGCs) utilize a minimal synthase heterodimer for initiation, extension, and determining carbon chain length, termed the ketosynthase–chain length factor (KS–CLF) complex. Phylogenetic studies by Charkoudian and team showed that CLF sequences clade by polyketide (PK) carbon length and that a key roster of type II PKS tailoring genes evolved with CLF, introducing PK chemical diversity. Our group took note of the presence of asparagine synthetase-like (AsnB-like) genes in several known type II BGCs, including those that make the fredericamycins, the pradimicins, and TLN-05220, and wondered if these genes evolved with PK size and/or modifications. We obtained a list of 5552 genomes containing type II PKS from the Charkoudian group and used GATOR-GC as an initial tool to search for AsnB-like genes within 70 kb of the KS–CLF gene pair. From a condensed list of 325 genomes, the presence of AsnB-like genes within type II PKS BGC bounds were confirmed through antiSMASH analyses with relaxed strictness. We are currently investigating coevolution of the type II PKS associated AsnB-like genes with the KS, CLF, and other tailoring enzymes through pairwise amino acid identity plots. To more broadly probe the evolutionary origin of AsnB-like genes in secondary metabolism, we have pulled >10,000 unique AsnB-like genes from UniProt using JackHMMER and are conducting phylogenetic analyses to probe ancestry. These studies may reveal evolutionary mechanisms that introduced AsnB-like genes to the type II PKS BGC roster and highlight essential residues that differentiate enzyme functions in primary and secondary metabolism.

P-028 Nicholas Oberlies

Machine-Readable Structural Information is Essential for Natural Products Research

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As part of a collaboration to examine the evolution of pathogenicity in *Aspergillus* filamentous fungi, our team has been examining the genomic and metabolomic properties of representative species in each of its taxonomic sections. There are approximately 200 genomes of *Aspergillus* species in the literature, and it is rather straightforward to download all of them for additional analyses. However, if you wanted to catalogue all the compounds that have been reported from *Aspergillus*, which is arguably the most well investigated fungal genus, you would find it remarkably difficult to download the structures readily. Even with a suite of public/free databases available, there is not a universal solution. As we reported recently as a Perspective in the *Journal of Natural Products*, we believe that there is a simple solution, publishing machine-readable text descriptors for new secondary metabolites. Requiring such descriptors will be straightforward to implement for both authors and publishers and will help derive even greater value from the efforts expended to understand the chemistry of Nature. This presentation will highlight some examples that are illustrative of both the problem and the potential solutions.

P-029 – Sam Waterworth

Coupled MS1-PDA Feature Extraction and Clustering for NP-HTS Project Prioritization

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Screening complex natural mixtures often results in large lists of active fractions. These are prioritized using dereplication, so that efforts can be focused on novel molecules. To streamline this process, we developed a two-stage computational methodology that leverages mass spectrometry (MS1) and photodiode array (PDA) data to characterize extract fractions. Stage one utilizes a custom feature extraction algorithm to parse coupled MS1 and PDA data from known pure compounds previously isolated at the NCI. This establishes a reference database of multidimensional metrics, including exact mass detected, MS and UV retention times, peak intensities, PDA peak counts, and UV maxima wavelengths and intensities. Stage two deploys a complementary clustering algorithm to identify similar feature sets from experimental mixtures. By aligning these experimental metrics against the established database, known masses are identified, correlated with biological activity, which enables prioritization of isolation chemistry efforts. Recognizing the inherent variability in MS instrumentation, chromatography, and handling protocols across different laboratories, this approach is intended not as a universal database resource, but rather as a useful methodological framework. This strategy provides a highly adaptable methodology to streamline dereplication efforts and accelerate discovery pipelines.

P-030 – Mohammed Ahmed

Functional Characterization of Myxobacterial Terpene Synthases Reveals Enzyme Plasticity and Expands Terpenoid Diversity

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Myxobacteria possess large genomes enriched in biosynthetic gene clusters, yet their terpenoid biosynthetic potential remains underexplored. In this study, we functionally characterized a panel of myxobacterial terpene synthases (TSs) to assess their product diversity and catalytic behavior. Eighteen TSs were heterologously expressed in engineered *E. coli* strains optimized for terpene precursor overproduction (C-15, C-20, and C-25), and their products were analyzed by GC-MS. Screening identified 12 diterpene synthases and 8 sesquiterpene synthases, while no sesterterpene activity was detected. One enzyme (TS3) exhibited the highest product yield and was selected for detailed investigation. Structural and biochemical characterization revealed TS3 as an isobonnadiene synthase (IbdS) that produces isobonnadiene and five minor diterpenes. Comparative analysis with a homologous bonnadiene synthase (BdS), combined with site-directed mutagenesis, demonstrated that product selectivity can be altered by a single amino acid substitution, providing insight into the mechanistic basis of terpene cyclization. Expanding this analysis to selected sesquiterpene synthases resulted in the identification of 15 sesquiterpenes, including three previously unreported compounds. These findings expand the known terpenoid chemical space of myxobacteria and highlight the functional diversity of their TS enzymes. This work underscores the value of genome-guided enzyme discovery coupled with metabolite profiling for uncovering new natural products and informs future efforts in enzyme engineering and terpene diversification.

P-031 – Matthew Bertin

Shared Biosynthetic Architectures Generate Diverse β-amino Polyketide Residues in Cyanobacterial Peptides

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Cyanobacteria generate structurally complex peptides with diverse biological functions and vast chemical diversity, yet the enzymatic logic that produces their many documented unusual β-amino acid–containing polyketide units remains incompletely understood. Here we show that the recently described genus Floridanema harbors biosynthetic systems that unify the production of tychonamides and pahayokolide-like peptides, including the assembly of the signature residues 3-amino-2,5,7-trihydroxy-8-phenyloctanoic acid (Atpoa) and 3-amino-2,5,7,8-tetrahydroxy-10-methylundecanoic acid (Athmu). Using an integrated "pathways-to-products" strategy combining comparative genomics, bioinformatics analyses, and structure elucidation by NMR and MS, we link previously cryptic gene clusters to new metabolites and define shared architectural features across these pathways. Furthermore, we identified a ketoreductase in multiple pathways predicted to reduce α-keto acids and generate the starting unit in the Athmu moiety. These results support a common evolutionary origin or convergent phenomenon for constructing β-amino polyketide building blocks within cyanobacterial hybrid assembly lines. Together, our findings reposition *Floridanema* as a central source organism for these peptide families and establish generalizable biosynthetic principles that can be leveraged to predict, discover, and engineer related natural products.

P-032 – Chase Clark

A Platform for the Discovery of Novel Microbial Natural Product Chemical Scaffolds and Their Biological Targets

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For nearly a century, microbially-produced natural products (NPs) have been a prolific source of antibiotic, anticancer, and immunomodulatory small molecules. Despite advances in genomics and the availability of hundreds of thousands of public genomes, the field of NP drug discovery remains hampered by multiple challenges that include, but are not limited to, the frequent rediscovery of known compounds and the blind selection of bioassays, particularly for eukaryotic targets. These contribute to a high failure rate in NP discovery pipelines, with many potential therapeutics failing to be discovered or advanced due to early-stage misdirection. Evoquant is working to address these challenges with a discovery platform that leverages >5 million biosynthetic gene clusters (BGCs) from >750 thousand diverse genomes/metagenomes, alongside a curated chemical and disease-relevant dataset. In the short term Evoquant is working on validating its thesis for discovery with a set of 30 microbes predicted to produce small molecules that affect specific protein targets. Evoquant's long term goal is to have a reliable, efficient, best-in-class platform for discovery and commercial development of chemical scaffolds against diverse disease targets through microbial strain procurement and heterologous expression. Here I will present the platform and progress, including the discovery of novel proteasome inhibitors.

P-033 – Nadia Diaz

Prioritizing Bacterial Strains Derived from *Ariolimax* spp. (banana slug) and Assessing Their Natural Product Potential Using MALDI MS

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The slime of the banana slug (*Ariolimax* spp.) is known to exhibit both analgesic and antimicrobial properties. The exact molecular components that drive this activity remain uncharacterized. We aimed to investigate the slime associated microorganisms to identify the molecules responsible for these biological properties. We employ a Matrix Assisted Laser Desorption/Ionization Mass Spectrometry *(MALDI MS)*-based workflow for the direct analysis of microbial strains isolated from the slime of the banana slug and its environmental surroundings. My mentor and I have isolated a total of 104 strains and analyzed them directly from colonies using this workflow designed to generate three datasets per strain. These datasets include a protein fingerprint at the MS1 level and small molecule fingerprints at both the MS1 and MS2 levels. These three datasets are processed to (i) generate a protein MS dendrogram to resolve protein-based phylogenetic relationships among isolates and the library, and (ii) build Molecular Association Networks (MANs) and (iii) Molecular Networks (MNs) to assess shared and unique metabolite production across microbial isolates. The protein dendrogram and the small molecule analyses in both MS1 and MS2 levels, have allowed for the prioritization of 17 unique microbial strains derived from the slime of the banana slug. These strains were prioritized for whole genome sequencing. I will analyze these genomes to assess the biosynthetic potential pairing it with our metabolomics data.

P-034 – Alan Hernández-Melgar

Deep Mining of Marine *Plantactinospora* Using a Metabologenomics Approach

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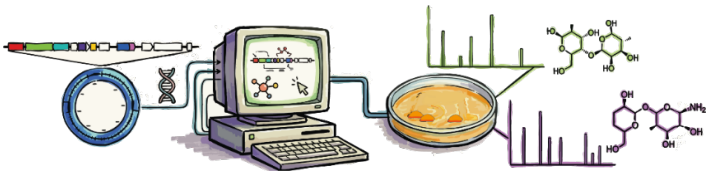
Actinomycetes are prolific sources of natural products; however, the study of marine microorganisms, especially the genus *Plantactinospora*, remains poorly characterized. This study combines genomics and metabolomics to investigate the biosynthetic potential of the marine isolate *Plantactinospora* sp. BC1 from the Gulf of California. Genome mining identified 26 BGCs, mainly NRPs, PKS, and terpenes. BiG-SCAPE analysis showed that 88% of these clusters are singletons with substantial divergence from characterized GCFs in the BiGFAM database. On the other hand, FBMN and CANOPUS identified and classified a broad spectrum of alkaloids and fatty acyls. MetaMiner and Seq2Saccharide linked mass spectra to genomic regions encoding novel RiPPs and aminoglycoside structures. Overall, this is the first report of a metabologenomics study of a *Plantactinospora* strain.



P-035 – Erik Jakubec

Structural and Mechanical Elucidation of Genome Encoded *Neo*-Dolabellane Soft Coral Diterpene Cyclase

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In this study, we described the biochemical characterization of the first dolabellane and *neo*-dolabellane scaffolds producing diterpene cyclase (DTC), EcTPS4, from an animal.

This gene belongs to the Western Atlantic octocoral *Erythropodium caribaeorum* and was discovered to be a cryptic dolabellane scaffold producer, previously unknown to contain these types of compounds. The sequence of this gene was described previously but challenges with cloning prevented full characterization. With the heterologous expression approach in mind, the tandem gene duplicate was synthesized and expressed in *Escherichia coli* and *Saccharomyces cerevisiae*. From this, the corresponding enzyme mechanisms were investigated through isolation and structural elucidation of three major products with the use of spectroscopic and spectrometric data, *in-vitro* protein assays, and site-directed mutagenesis. Further structural diversity was generated via deliberate epoxidation resulting in a crystal structure that was used to derivatize the absolute stereochemistry of the terpenes via x-ray crystallography.

P-036 – Hyeongju Jeong

Cebulassopins, Antiproliferative Lasso Peptides from a Split Biosynthetic Operon

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Lasso peptides are a class of ribosomally synthesized and post-translationally modified peptides distinguished by their lasso-like, threaded topology. Common to all lasso peptides biosynthetic gene clusters examined so far is an arrangement whereby the precursor peptide is encoded adjacent to the macrolactam synthetase and other modification genes. Here we report the cebulassopins A–D (**1**–**4**), the first example of lasso peptides synthesized by a split operon whereby multiple precursors are encoded several Mbps distant from the modification enzymes. Aside from characterizing their structures and calculating the three-dimensional topology of **1** and **2**, we also find that the cebulassopins are potent antiproliferative agents with sub-μM inhibitory concentrations against human lung carcinoma cells. These results set the stage for further biological examination and exploration of other split lasso peptide gene clusters.

P-037 – Sangwook Kang

Discovery of Two Novel Cinnamoyl-Containing Nonribosomal Peptides via Genome Mining and Regulator Overexpression

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Cinnamoyl-containing nonribosomal peptides (CCNPs) are actinobacterial secondary metabolites characterized by unique chemical structures and diverse biological activities. The biosynthetic gene clusters of CCNPs encode highly reducing type II polyketide synthases, nonribosomal peptide synthetases, and conserved cluster-situated LuxR-family regulators. Bioinformatic analysis of cinnamoyl isomerases classified CCNPs into three major types based on their cinnamoyl substructures: Z-type (2-((1Z)-alkenyl)-cinnamoyl), E-type (2-((1E)-alkenyl)-cinnamoyl), and M-type (2-methylcinnamoyl). Overexpression of cluster-situated regulators activated the production of cryptic CCNPs across two different types, leading to the discovery of two novel CCNPs (**1** and **2**). **1** is an M-type CCNP bearing a 2-methylcinnamoyl moiety, closely related to a previously reported synthetic-bioinformatic natural product, but differs in its amino acid composition. **2** is an E-type CCNP featuring a 2-((1E)-propenyl)-cinnamoyl moiety and a distinctive bicyclic scaffold in which hydroxyphenylglycine is bridged via biaryl ether and ester linkages. Their structures were elucidated by NMR spectroscopy and advanced Marfey's method. **2** exhibited antibacterial activity against Staphylococcus aureus.

P-038 – Mo Aqib Raza Khan

High-Throughput Media Screening for Modulating Production of Secondary Metabolites in Actinomycetes

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Antimicrobial resistance (AMR) is an escalating global health crisis, projected to impose more than USD 1 trillion in healthcare costs by 2050. Thus, developing new antibiotics is essential. Actinomycetes have long been recognized as prolific producers of clinically important antibiotics, including streptomycin, tetracycline, vancomycin, and neomycin. However, recent genomic analyses reveal that many biosynthetic gene clusters (BGCs) remain transcriptionally silent or poorly expressed under standard laboratory conditions. We hypothesize that cryptic BGCs can be activated by altering nutritional and environmental conditions. To test this, we employed a robotic high-throughput media screening (HTMS) platform programmed to generate1,025 unique growth conditions in a 96-well format. By systematically varying carbon, nitrogen, and trace element sources, this approach aims to stimulate the expression of silent pathways and enhance secondary metabolite production. Three actinomycete strains were selected to validate the approach they include the well-studied model bacterium *Streptomyces coelicolor*, and an unexplored soil isolate *Streptomyces* GA7, and *Amycolaptosis keratiniphila*, specifically chosen to test whether HTMS could awaken silent

biosynthetic gene clusters and stimulate antibiotic production. *A keratiniphila* has been shown to have a cryptic metabolite produced only in the presence of a specific elicitor. This approach yielded three key findings: first, *S. coelicolor* produced actinorhodin and undecylprodigiosin under specific media formulation, second, in *Streptomyces* GA7, optimal media formulations result led to a 17-fold increase in the production of coproporphyrins, and third, we, detected a novel member of the cryptic glycopeptide antibiotic family, keratinimicin C1, in *A. keratiniphila* in limited media formulations. These results demonstrate that HTMS is a powerful tool for affecting secondary metabolism in actinomycetes and may accelerate the discovery of novel bioactive compounds. In addition, HTMS can serve as a rapid bioactivity test platform for identifying the optimal media formulation for a given strain against targeted pathogens.

P-039 – Gyu Sung Lee

Discovery of Scalemic *N*-acyl Amides in a Marine Bacterium Illuminates a ThiF-like Enzyme-Mediated, Stereodivergent Biosynthesis

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Scalemic natural products, which contain unequal proportions of two enantiomers, remain biosynthetically poorly understood. Here, we isolated eight *N*-acyl amides (**1**–**8**) from *Pseudovibrio denitrificans* and elucidated their structures and biosynthetic origin through 1D and 2D NMR, HR-ESI-MS, isotope-labeling, heterologous expression, and in vitro enzymatic assays. Our results support a pathway in which enantiomerically pure and racemic congeners arise from distinct branches, yielding an overall scalemic outcome. This pathway proceeds without dirigent proteins or radical-mediated transformations and instead depends on PdfB, a ThiF-family adenylyltransferase. To the best of our knowledge, this is the first bacterial example of this biosynthetic pathway and the second known case of non-peptidic small molecules produced by a ThiF-family enzyme. (*S*)-**6** suppressed HIF-1α protein expression and downregulated VEGF and GLUT-1 mRNA expression in vitro.

P-040 – Jayho Lee

Discovery of Cryptic Cyptide-type RiPP Donghaeamides A–C through Heterologous Expression in *Streptomyces coelicolor* and Enhanced Production by stnYp Promoter

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Natural products remain a major source of therapeutics, yet many biosynthetic gene clusters (BGCs) are silent under laboratory conditions. Cytochrome P450-associated cyptides, a subclass of RiPPs, feature oxidative crosslinks that generate structurally constrained scaffolds with potential bioactivity. Genome mining of an in-house database identified candidate cyptide BGCs, prioritizing *Streptomyces* sp. SUD119 for its predicted novelty. Native expression was inactive, but heterologous expression in *Streptomyces coelicolor* enabled production. While initial use of the ermE* promoter gave low yields, replacement with the stnYp promoter increased production up to ten-fold. This led to the discovery, isolation, and structural elucidation of three new cyptides, donghaeamides A–C. These findings highlight promoter engineering as an effective strategy to activate cryptic RiPP pathways and accelerate discovery of novel cyptides.

P-041 – Ana Rodriguez

Oxidative Sesquiterpenoid Tailoring in a Mediterranean Gorgonian

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Marine invertebrates are prolific producers of natural products which play an important role in their ecology and have a significant potential in drug discovery. In particular, corals produce terpenoids, a type of secondary metabolite that originates from five-carbon isoprene units. They function as allelopathic agents, enabling corals to deter predators and inhibit competing organisms. However, accessing coral biomass is challenging, making heterologous expression a suitable alternative over wild harvest which may potentially damage marine ecosystems. Here we studied the *Leptogorgia* genus composed of colorful sea fans that produce a diverse suite of biologically poorly understood, yet chemically complex metabolites. Although some pathways have been characterized and biosynthetic gene cluster have been identified, many oxidative enzymes remain uncharacterized. By using an established animal enzyme expression strategy in *P. pastoris,* we expressed multiple oxidative genes simultaneously, allowing multi-step chemical pathways to be reconstructed. The production of resulting metabolites was scaled, and compounds were isolated from *P. pastoris*, allowing for access to these molecules at a scale necessary for bioassay screening.

P-042 – Shaz Sutherland

Kibdelomycin Biosynthesis and Resistance Mechanism to Guide the Engineering of the Next-Generation Antibiotic Analogs

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This project investigates Kibdelomycin (KBD), a potent natural product antibiotic with a hybrid glycosylated polyketide/non-ribosomal peptide structure. KBD inhibits bacterial DNA gyrase and topoisomerase IV through a unique dual binding mode, making it a promising candidate against drug-resistant pathogens. This presentation highlights its biosynthetic pathway, focusing on the enzymatic steps involved in pyrrole ring formation, particularly halogenation selectivity and methyltransferase activity. Additionally, we explore the self-resistance mechanisms employed by Kibdelosporangium sp., using biophysical characterizations to compare resistance strategies across gyrase-targeting antibiotics. Future work will involve engineering microbial strains for enhanced KBD analog production and identifying key enzymes, such as a putative Diels-Alderase, for tetramic acid core biosynthesis. This research advances our understanding of KBD biosynthesis while providing valuable insights for the development of novel antibiotics with improved therapeutic potential.

P-043 – Jake Wilson

Genomics Guided Discovery of Molecular Glues from Bacteria

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The majority of the human proteome is considered "undruggable" due to the absence of defined small-molecule binding pockets. Molecular glues offer an alternative strategy by stabilizing protein–protein interactions at otherwise flat interfaces. The recently identified immunophilin-binding molecular glue WDB002, which targets the coiled-coil protein CEP250, highlights the potential of rapamycin-like compounds (rapalogs) to access this space. Rapalog immunophilin binding is enabled by a conserved pipecolic acid moiety. Here, we describe a genome-mining–guided approach to identify rapalog biosynthetic gene clusters in public sequencing data and to detect their products. Actinobacterial strains from culture collections were analyzed by LC-HRMS/MS for pipecolic acid-derived signatures, but these experiments were confounded by background signals in this low *m/z* range. Therefore, we developed an NMR-based strategy using stable-isotope labeling. Lysine cyclodeaminase, which catalyzes the production of pipecolic acid, is known to retain the amino group at the epsilon position of lysine. Strains were cultured with ε-^{15}N-lysine, and extracts were analyzed by ^{1}H-^{15}N gHMBC to selectively detect pipecolic acid-containing metabolites. Using this approach, we identified a pipecolic acid–derived spin system in extracts of *Streptomyces* sp. NPDC. This signal provides a handle for NMR-guided isolation and characterization of a putative rapamycin-like polyketide.

P-044 – Enrique Aguilar Ramírez

Activating Silent Biosynthetic Gene Clusters through Transcription Factor Overexpression in Transcriptionally Permissive Landscapes

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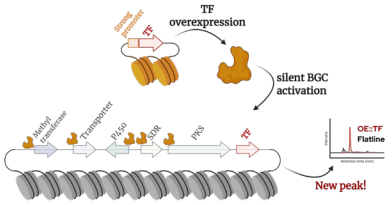
Our group recently engineered a *Penicillium expansum* flatline strain that revealed an unusual depsipeptide incorporating two units of the rare amino acid pipecolic acid, assembled by a five-module nonribosomal peptide synthetase (NRPS). Motivated by this discovery, we performed a genome-wide analysis of this strain to identify novel biosynthetic gene clusters (BGCs). This analysis revealed at least 14 putative novel BGCs, each associated with a predicted cluster-specific transcription factor (TF) located proximal to core biosynthetic genes. In addition, several known BGCs were identified and subsequently inactivated to streamline the flatline chassis. Here, we explored strategies for targeted overexpression (OE) of cluster-specific TFs in transcriptionally permissive or epigenetically optimized backgrounds, aiming to activate silent BGCs.



P-045 – Sebastian Ashcraft

Development of a One-Pot Prenyltransferase Reaction for the Biocatalytic Synthesis of Indole Diketopiperazine Alkaloids

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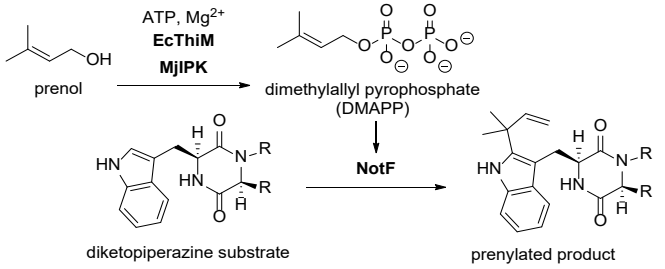
Prenyltransfer is an enzymatic C–H bond functionalization catalyzed by prenyltransferase (PT) enzymes that is widespread in the biosynthesis of biologically active diketopiperazine (DKP) alkaloids. PTs utilize dimethylallyl pyrophosphate (DMAPP) as a prenyl donor, and engineered kinases EcThiM and MjIPK enable the sequential phosphorylation of commodity chemical, prenol, to

produce DMAPP in situ. We sought to develop a biocatalytic cascade using the well-characterized PT, NotF, to generate prenyl indole DKP products in a chemoenzymatic step. Optimization of this one-pot reaction will enable efficient and scalable access to prenylated DKPs scaffolds for the biocatalytic synthesis of complex DKP alkaloids.



P-046 Yness Benzari

Engineering Pictet-Spenglerase, KslB, for Improved Activity with Structurally Diverse Aldehydes

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The tetrahydro-β-carboline scaffold is present in hundreds of characterized natural products with a strong representation in marine natural products in particular. Synthetic chemistry and biosynthesis have adopted the same approach to the construction of this motif, the Pictet-Spengler reaction. Recently, KslB, has been identified as a diastereoselective Pictet-Spenglerase from the kitasetaline biosynthetic pathway, catalyzing the formation of tetrahydro-b-carboline, kitasetalic acid, from tryptophan and α-ketoglutarate. We leveraged structure guided mutagenesis to expand the substrate scope of KslB to include diverse aldehydes and enable the construction tetrahydro-β-carboline scaffolds that can serve as intermediates for the construction of structurally complex bioactive natural products and analogues thereof.

P-047 – Carole Bewley

Culture-Dependent Modulation of Tailoring Reactions Redirects Production of Bioactive Ansamycins

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Culture-dependent variation in natural product biosynthesis can shift metabolite profiles, yet the regulatory basis of these changes is poorly understood. Analysis of a *Streptomyces* strain producing naphthomycin-type ansamycins revealed a striking medium-dependent switch in the dominant metabolite governed by substitution at C-30. Depending on culture conditions, the major product contained either a methylthio substituent or a C-30 chloro group. Remarkably, the chlorinated analog exhibited strikingly enhanced anticancer activity across multiple cancer cell lines. This observation suggested that medium-dependent regulation of tailoring reactions controls production of the biologically active metabolite. Transcriptomic analysis across culture conditions revealed that expression of genes within the naphthomycin biosynthetic gene cluster, including a halogenase responsible for C30 chlorination, increased under conditions favoring production of the chlorinated analog, whereas candidate sulfur-related modification enzymes showed reduced expression. These results indicate that culture-dependent modulation of competing tailoring pathways controls substituent installation at C30 and alters the dominant metabolite profile. Together, these findings demonstrate that targeted adjustment of culture conditions can shift biosynthetic output toward more potent analogs and provide a strategy for enhancing production of bioactive natural products through pathway-level regulation.

P-048 – Sam Catania

Molecular Cloning, Expression, and Purification of a Ketosynthase-Like Decarboxylase for Analysis of Substrate Preference

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TLN-05220 (TLN) is a natural product antibiotic produced by several species of Actinobacteria with activity against many antibiotic-resistant pathogens. The biosynthesis of TLN involves a hybrid Type 1/Type 2 Polyketide Synthase (T1/T2 PKS) pathway. The T1 PKS is comprised of a loading and extension module that make a 2-methylbutyrate starter unit. The TLN T1 PKS contains a ketosynthase-like decarboxylase (KS_Q) domain which catalyzes the decarboxylation of a malonyl or methylmalonyl substrate, an acyltransferase (AT) domain that selects the extender unit, and an acyl carrier protein (ACP) that delivers the substrate to the KS_Q. Based on sequence prediction, the TLN KS_Q putatively selects for methylmalonyl-CoA, but to synthesize the 2-methylbutyrate starter unit it must select malonyl-CoA instead. Other KS_Q domains have been reported with different predicted and in vitro substrate preferences, so specificity of the TLN KS_Q for malonyl-CoA would support the production of a 2-methylbutryate starter unit. We cloned the KS_Q-AT as a didomain due to the insolubility of the KS_Q and performed site-directed mutagenesis to inactivate the AT to avoid testing its activity instead. A High-Performance Liquid Chromatography (HPLC) kinetic assay will be used to determine the substrate preference of the KS_Q. Hybrid T1/T2 PKS pathways produce unique complex polyketide products, so

investigation of the TLN pathway provides insight that may lead to the engineering of new antibiotics.

P-049 – Joshua Hamlett

Progress Towards the Biocatalytic Synthesis of Diketopiperazine Dimer, Luchunazine D

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Dimeric diketopiperazine (DKP) alkaloids are a large family of bioactive natural products with incredible structural diversity in direct contrast to their simple cyclic dipeptide core. To date, the biosynthesis of tryptophanyl-DKP dimers from bacteria and fungi has been solely attributed to the oxidative activity of "Nature's blowtorch" cytochromes P450 (P450s). Which have significant drawbacks to their use in late-stage biocatalytic syntheses, such as the requirement for cognate electron transfer protein partners and their high selectivity often results in the formation of only a single constitutional isomer from two DKP monomers. Our synthetic approach leverages the substrate flexibility of engineered tryptophan synthases to enable the efficient and versatile biocatalytic construction of regioisomeric Csp^2–Csp^2 linked DKP dimers, and applied this approach to the synthesis of DKP dimer, luchunazine D.

P-050 – Jeffrey Jean-Joseph

Structural Diversity of Cytochrome P450 and Compatibility of Heterologous Redox Partners

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Ribosomally synthesized and post-translationally modified peptides (RiPPs) are a diverse class of secondary metabolites that serve specialized biological functions. Biarylitides are a class of RiPPs characterized by their unique C-C biaryl cross-linkages. The catalytic process of the cross-linkage is driven by cytochrome P450 enzymes. The enzyme requires a continuous supply of electrons and is shuttled via a redox partner chain. This study identifies P450 homologs involved in biarylide synthesis, investigate their structural diversity, and discern compatible heterologous redox partners needed for catalysis. Genome mining and bioinformatic analysis were used to identify precursor peptide motifs similar to P450 homologs. Solid-phase microwave peptide synthesis was used to generate putative substrates. LC-MS (Liquid Chromatography-Mass Spectrometry) and NMR (Nuclear Magnetic Resonance) were utilized for confirmation. Molecular cloning, heterologous expression, and recombinant protein purification were used to isolate the P450 enzyme and the redox partner. Enzyme and substrate compatibility were assessed through in vitro enzymatic reactions and reverse-phase LC-MS analysis.

P-051 – Lucas Johnson

Uncovering Structural Determinants of Substrate Scope in a Peptide Cyclase Enzyme Family

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Cyclic tetrapeptides (CTPs) are a class of macromolecules that have received increasing interest due to their therapeutic potential. Compared to linear tetrapeptides, CTPs have increased proteolytic stability, enhanced membrane permeability, and more defined structural conformations. However, traditional chemical methods to access CTPs often have restrictions that limit the scope of CTPs that can be produced, necessitating the development of an alternative route for accessing a broad range of CTPs. Previous work has identified a class of enzymes, penicillin-binding protein-type thioesterases (PBP-TEs), that can efficiently catalyze the macrocyclization of tetrapeptides in vitro, but the structural features of these enzymes that determine their substrate scopes are largely unknown. This project is focused on further investigating this family and using mutagenesis techniques to pinpoint structural features that guide their substrate specificities. Through this work, we have identified a residue of the PBP-TE Ulm16 that plays a key role in determining substrate tolerance. Overall, this work aims to guide future engineering efforts to make a broadly useful biocatalyst for accessing a diverse range of CTPs.

P-052 – Jonghwan Kim

Novel Threoninol-Containing Lipopeptides from Marine Bacterium, *Aquimarina muelleri*

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The marine bacterium Aquimarina muelleri harbors diverse biosynthetic gene clusters yet remains underexplored. Small-scale cultures produced ten related metabolites (**1**–**10**), comprising six isomers (m/z 472) and four isomers (m/z 458) with identical MS/MS fragmentation, indicating a common scaffold; however, these metabolites disappeared upon scale-up, suggesting regulated biosynthesis. Compound **1** was purified and identified as a novel threoninol-containing lipopeptide, whose origin from threonine

was confirmed by isotope feeding and further validated by total synthesis. Comparative isotope feeding studies revealed that compounds **2–10** differ in amino acid composition and/or ester linkage position. These results highlight a cultivation-dependent pathway and a rare enzymatic reduction of threonine to an amino alcohol.

P-053 – Reese Le

Investigating Asparagine Synthetase Homologs in TLN-05220 Biosynthesis

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TLN-05220 is a bioactive natural product produced by *Micromonospora echinospora* that demonstrates potent activity against antibiotic-resistant human pathogens. The molecule consists of a polyketide backbone that incorporates amino acid-derived functionality, a rare modification in Type II polyketide biosynthesis that suggests involvement of enzymatic ligases. While prior studies have identified PLP-dependent enzymes in the pathway, the mechanisms responsible for incorporating these intermediates into the final structure remain unclear. Asparagine synthetase homologs encoded within the gene cluster are proposed to mediate key ligation reactions, yet their biochemical functions have not been characterized. To investigate their role, heterologous expression and purification were conducted; however, the enzymes were predominantly insoluble. Complementary approaches, including CAPTURE cloning of the TLN-05220 biosynthetic gene cluster and targeted gene inactivation, have been implemented to assess in vivo enzyme function. These efforts aim to define the role of asparagine synthetase homologs in amino acid incorporation during TLN-05220 biosynthesis and expand the utility of natural product biosynthesis for therapeutic discovery.

P-054 – Tilly Lobdell

A Biocatalytic Approach to the Diastereoselective Synthesis of 3-Hydroxypyrroloindolines

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The 3-hydroxypyrroloindoline (HPI) motif is present in many structurally complex and biologically active natural products (NPs) produced by organisms across the kingdoms of life. Despite the widespread prevalence of the HPI motif in diketopiperazine (DKP) alkaloids in particular, there is no general method for the efficient and diastereoselective synthesis. To overcome this current limitation in synthetic methods, we sought to develop a general, scalable, and diastereoselective biocatalytic approach to the synthesis of HPI NPs and analogs thereof using flavin monooxygenases (FMOs). Wild-type, mutant, and chimeric FMOs were expressed, and their activity assayed with synthetic DKP substrates in vitro. Active site mutagenesis identified residues governing substrate recognition and catalysis as well as guided engineering efforts to expand substrate scope, improve catalytic efficiency, stability, and turnover number.

P-055 – Christina McBride

Sustainable Production and Evolution of Prodiginines as Next-Generation Therapeutics

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The prodiginines are a class of microbial natural products that exhibit broad anticancer, antimicrobial, and antiparasitic activities. Despite their promise as therapeutics, much of prodiginine chemical space remains underexplored due to the inherent structural complexity of these highly conjugated, tripyrrole-based scaffolds. Herein, we merge synthetic biology, biocatalysis, and semi-synthesis to rationally design and sustainably produce a diverse set of prodiginine scaffolds, providing renewed access to these promising therapeutics. By pairing metabolic engineering with fermentation optimization in *Streptomyces* hosts, we engineer robust strains that enable scalable prodiginine production. Tailoring these scaffolds using *de novo* pathway engineering, biocatalysis, and semi-synthesis further expands their structural complexity. We have leveraged this approach in *Streptomyces eitanensis* to enhance production of the potent antimalarial premarineosin A over 500-fold to over 100 mg/L, enabling the synthesis of a suite of analogs with improved potency and selectivity against drug-resistant and drug-sensitive malaria parasites. Our ongoing efforts take advantage of the modularity of this strategy to engineer additional strains that enable high-yield production of other native, non-native, and unnatural prodiginine analogs, facilitating the systematic exploration of these previously inaccessible scaffolds and accelerating their development as therapeutics.

P-056 – Rafiul Noyon

Identification and Characterization of New ThiF-like Enzymes and Biosynthesis of RiPP Natural Products from Bacteria

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Ribosomally synthesized and post-translationally modified peptides (RiPPs) are a rapidly growing class of natural products with broad structural diversity and bioactivities. The advancements in bioinformatics tools and techniques have facilitated the discovery and biosynthesis of this class of natural products. ThiF-like enzymes are present in diverse RiPP biosynthetic pathways and are known to catalyze reactions such as thiolactone, phosphoramidate, and indolylamide bond formation. To discover new chemistry for ThiF-like enzymes, we used a global genome-mining approach and identified a new ThiF-containing gene cluster, which we named Lac, in the human pathogen *Streptococcus pneumoniae*. The AlphaFold3 model of the dimeric precursor peptide LacA, the enzyme LacF, ATP, and Mg^{2+} has shown the C-terminal arginine in an interesting position in the enzyme's active site. The in vitro characterization of LacF indicated the first cyclization of the C-terminal arginine residue in a RiPP pathway and a new reaction type catalyzed by the ThiF enzyme.

P-057 – Anshul Rajput

Discovery and Characterization of a *Coffea canephora* RiPP-Cyclopeptide

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Burpitides are a newly described class of cyclopeptides derived from BURP-domain post translational modification formed by burpitide cyclases (BpCs) in plants. BpCs are classified as copper-dependent peptide cyclases responsible for generating the oxidative side chain cross-links in plant peptidic natural products. These enzymes have been reported to be associated with a variety of cyclization such as C-O, C-C and C-N crosslinks across the plant kingdom. Recently, our group identified and isolated a cyclopeptide alkaloid named arabipeptin A from the well-known plant *Coffea arabica,* also demonstrated the involvement of its BpC in the formation of a Tyr-phenol-O to Leu-C_δ bond. Here, guided by our bioinformatic based discovery, we identify a new split BURP peptide cyclase gene cluster from *Coffea canephora*. This cluster comprises BpC and its nearby dedicated RiPP precursor peptides and hypothesized to be responsible for macrocyclization of its precursor peptide. Successful heterologous expression of found BpC and in vitro enzymatic activity assay revealed the formation of a new Trp-Leu cross link, confirmed by LC-MS analysis. Further detailed studies to confirm the type of cross-link (Trp-indole-C to Leu-C or Trp-indole-N- to Leu-C) are still undergoing. *C. canephora* BpC displayed extremely high sequence identity (97.09%) with *C. arabica* BpC (ArbB2) that allows us to probe the determinants that control substate crosslink specificity. This ongoing study not only expands the known diversity of BURP-domain-mediated cyclization but also aims to provide new insights into whether substrate sequence or intrinsic enzyme features dictate cross-link formation in plant RiPP biosynthesis.

P-058 – Fatma Al-Awadhi

Synthesis and Characterization of Natural Product-Based Steroid-Triazole Hybrids via Click Reaction and Evaluation of Their Anticancer and Antibacterial Activities

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Two highly significant classes of natural and heterocyclic compounds, steroids and triazoles, are pivotal in numerous biological processes, and several steroid conjugates and triazole hybrids exhibiting anticancer and antibacterial activities were reported. In this work, a series of 47 new triazoles based on steroid moieties were synthesized via click chemistry. The effective click reaction of steroid propargyl ethers and steroid acetylenic esters with aryl azides provided quantitative yields of the desired steroid-triazole conjugates. The new compounds were fully characterized based on spectral data, including NMR, HRMS, FT-IR, and single X-ray diffraction analysis. The biological activity of the new steroid-triazole hybrids was evaluated through assessments of their anticancer and antibacterial activities. The screen identified three hits with selective antibacterial activity against the Gram-positive Staphylococcus aureus (MIC 12.5–50 μM; IC_{50} 8.9–41.5 μM), and one compound was weakly cytotoxic against the triple-negative breast cancer cells MDA-MB-231.

P-059 – Joel Yoder

Total Synthesis of Colletotrichone A Utilizing a Pharmacophore-Directed Retrosynthetic Approach

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The total synthesis of the antimicrobial natural product colletotrichone A (**1**) has been achieved utilizing a "Pharmacophore-Directed" retrosynthetic approach Lessons learned from an unsuccessful route were applied to a .2nd generation synthesis proved fruitful wherein known azaphilone **10** was elaborated to tricyclic epoxides **7-9.** A subsequent oxa-Michael cascade furnishes the tetracyclic core of **1**, **6**, and **7**.

Synthetic details and antimicrobial efficacies of designed intermediates will be presented.

P-060 – Lin Du

Cinctinine A, a Bryozoan-derived Macrocyclic Alkaloid with an Unprecedented Adenine-sesquiterpene Hybridized Skeleton

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Recently, the Molecular Targets Program (MTP) at the NCI has used the NCI Program for Natural Product Discovery prefractionated library as a source of test samples for high throughput screening campaigns. In each screen, up to 500,000 natural product fractions are screened. Subsequently 1 mg of confirmed active fractions are further simplified into 22 semi-pure HPLC fractions and re-screened. The Natural Products Chemistry Section of MTP has been developing a chemoinformatic pipeline for effective dereplication and project prioritization of active samples in MTP screens. During this process, an unusual triply charged MS pattern corresponding to cancer cell cytotoxic activity was identified from early-eluting HPLC fractions of the bryozoan species *Cinctipora elegans*. A novel macrocyclic alkaloid, cinctinine A, was identified as the active natural product. The cinctinine A structure comprises three adenine units and three linear sesquiterpene units which are interlinked to form a novel macrocyclic skeleton. The compound showed cytotoxic activity against two Diffuse Pleural Mesothelioma (DPM) cell lines MB24 and MB52 with IC_{50} values in the low-micromolar range. Semi-synthetic (e.g. amides at adenine N-6) and oxidized (on the terpene chains) analogues of cinctinine A showed distinct cytotoxic potencies providing hints about preliminary structure-activity relationships (SARs).

P-061 – Elizabeth Mumby

Conformational Flexibility and Divergent Biological Functions of a Family of Cyclic Heptapeptides from *Paraisaria* fungi

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The genus *Paraisaria* hosts several species of insect-pathogenic fungi that prey on a variety of host insects. These species produce unique natural products that may facilitate infection of their hosts. Published prior work characterized the paraisariamide (Psd) molecular family from three different *Paraisaria* species. Paraisariamides are *N*-methylated cyclic heptapeptides that are known to inhibit mammalian protein secretion. Some members of this molecular family are several orders of magnitude more potent than their congeners. Different degrees of *N*-methylation across congeners of this family influence the number of conformers each compound can adopt and, hence, likely the degree of membrane permeability. Here, we present a comparison of NMR-based solution structures for two natural products, Psd A and Psd F, and the synthetic analogue, *N*-MePsdA. NMR data were collected in a mixture of acetonitrile and water to mimic biological conditions. These NMR data were used to derive spatial constraints for computing 3D structures of each compound using CREST.

P-061B – Shugeng Cao

Fusaric Acid Analogs and Dimers from Marine-Derived *Fusarium* sp.: Biosynthetic Insights and Chloramphenicol-Enhanced Antibacterial Activity

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An investigation of the Hawaiian marine-derived fungus *Fusarium* sp. strain FM701 led to the isolation of two new pyridinium-containing fusaric acid dimers (**1**, **2**), fusaric acid (**3**), and two known fusaric acid derivatives (**4**, **5**), beauvericin (**6**), beauvericin J (**7**), and desferricrocin (**8**). Structures of **1** and **2** were elucidated by NMR spectroscopy, GIAO NMR calculations, HRESIMS, and electronic circular dichroism analyses. Genome mining revealed putative biosynthetic gene clusters for fusaric acid, beauvericin, and desferricrocin.

Chemical synthesis of 9,10-dehydrofusaric acid (**4**) and racemic fusarinolic acid (**5**), combined with feeding experiments, supported their plausible biosynthetic relationship and potential roles as biosynthetic building blocks of dimeric metabolites **1** and **2**. Compounds **1**, **2**, **6**, and **7** exhibited potent antibacterial activity against Gram-positive bacteria, and all compounds (**1**–**8**) showed 2- to 4-fold enhanced activity when combined with a subinhibitory concentration of chloramphenicol. Beauvericin (**6**) also displayed strong antiproliferative activity against human breast (MCF-7) and prostate (DU145) cancer cell lines, with low micromolar IC_{50} values. Together, these findings expand the chemical diversity of fusaric acid metabolites and the biological potential of marine fungal metabolites.

P-062 – Aaditi Chopade

Specialized Metabolome of the Genus Trichodesmium within the Global Cyanobacterial Metabolite Universe: Species-Specific Diversity and Biosynthetic Capacity

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Trichodesmium, an open ocean cyanobacterial genus, plays a pivotal role in influencing biogeochemical cycles in the nutrient-poor oligotrophic ocean. It is estimated that *Trichodesmium* fixes 60-80 Tg of nitrogen out of the 100-200 Tg biologically fixed marine nitrogen. In addition, certain species of *Trichodesmium* also produce a diverse range of specialized metabolites. The overarching goal of this research is to understand the ecological role and the species-specific composition of *Trichodesmium* metabolites - how these specialized metabolites influence the ecological distribution of the genus, and further our understanding about the biosynthetic pathways that are responsible for the synthesis of these specialized metabolites. To understand the *Trichodesmium* metabolites in the context of other cyanobacterial metabolites, a computational method was developed to visualize and classify 3085 cyanobacterial molecules using different similarity metrics. We propose that *T. thiebautii* is a more prolific producer of specialized metabolites than *T. erythraeum* because of its greater biosynthetic capacity. We also demonstrate that potential clades or 'ecotypes' of *T. thiebautii* have distinct specialized metabolite profiles. As evidence, we show that samples of *T. thiebautii* collected in the Gulf of Mexico show prolific production of metabolites in the smenamide group, while those in the Atlantic Ocean produce malyngamides. These results add new context to species-specific specialized metabolism and how specialized metabolites may confer an ecological advantage.

P-063 – Christine Theodore

In Situ Small Molecule Capture from Marine Sponge Microbiomes Using a Redesigned Artificial Sponge

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In situ capture of small molecules using artificial sponge devices offers an alternative to traditional sponge sampling techniques by enabling direct collection of bioactive compounds from the environment while bypassing the need for traditional isolation and cultivation. Previous artificial sponge designs require multi-day incubation on the sea floor which is a costly and cumbersome process. Here we describe a redesigned artificial sponge-like *in situ* resin capture system. Small, hollow-fiber bioreactors were inoculated with marine sponge-derived microbial populations and set up inside our marine field station to allow sea water to continuously flow through each unit. A resin cartridge was attached to each bioreactor to capture small molecules produced by the resident microbial community. The resin was extracted and the crude extract analyzed using UPLC-HRMS.

P-064 – Karissa Trannguyen

Unmasking New Anti-TB Agents From Antarctic Biodiversity

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Mycobacterium tuberculosis remains one of the leading causes of death from infectious disease worldwide. This airborne pathogen primarily targets the lungs and poses an increasing global health threat due to the emergence of antibiotic-resistant strains, particularly against frontline therapies such as rifampin. Antarctica represents a largely untapped source of chemical diversity, where extreme environmental conditions drive the production of unique and structurally diverse secondary metabolites. In this study, a library of over 100 extracts derived from Antarctic organisms was screened for bioactivity against *M. tuberculosis*. Bioactive extracts were prioritized by assessing their cytotoxicity to A549 human lung cancer cells and subsequently fractionated using chromatographic techniques. Dereplication of known metabolites was performed using SMARTNMR, DEEPSAT, SPECTRE, and GNPS, enabling the identification of promising candidates for further investigation.

P-065 – Savannah Anez

Metabolomic Annotation of the Analgesic Medicinal Plant *Monotropa uniflora*

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Monotropa uniflora, commonly known as "ghost pipe," is a plant with a long history of traditional medicinal use in the United States. More recently, ghost pipe has become popular for its reported analgesic properties on social media and the internet. Using the traditional practices surrounding ghost pipe as a guide, we have investigated these reports by conducting *in vivo* bioassays of ghost pipe extracts in mice. The results demonstrated a significant decrease in sensitivity due to chemotherapy-induced neuropathy compared to the negative control, providing preliminary support for ghost pipe's reported medicinal effects. However, there is still almost no literature documenting the phytochemistry, active compounds, or safety of ghost pipe. To address this knowledge gap, I am analyzing extracts of ghost pipe with UPLC-MS using both targeted and untargeted metabolomics approaches and compound annotation tools such as GNPS and SIRIUS to begin profiling the major specialized metabolites in ghost pipe. Preliminary results include a significant absence of grayanotoxin, a neurotoxin that was once reportedly identified in ghost pipe in 1889, but which has not been followed up on since. Future directions will be to pair both the metabolomics data and the bioactivity data in multivariate models to identify putatively active compounds.

P-066 – Gil Belofsky

Antimicrobial Phenolic Constituents of *Dalea Candida* Var. *Oligophylla*, Including New 3-Hydroxyflavanones, a New Flavanone, and a New Pawhuskin

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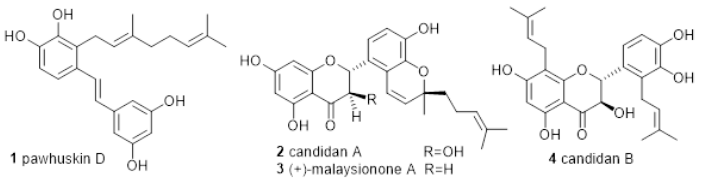
The phytochemical investigation of *Dalea candida* var. *oligophylla* revealed pawhuskin D (**1**), a new geranylated stilbene, two new 3-hydroxyflavanones (**2** and **4**), and a new flavanone (**3**). Compounds **2**-**4** are prenylated or contain a cyclized geranyl group and were summarily named candidans A-C. A suite of known phenolic compounds (**5**-**10**) was also isolated, and all compounds were evaluated for activity against the pathogens methicillin resistant *Staphylococcus aureus*, Vancomycin resistant *Enterococcus faecalis*, *Cryptococcus neoformans*, and *Candida albicans*. Compound **3** was the most active against MRSA, with an MIC value of 8.4 mM. Pawhuskin D was also evaluated for broad opioid receptor affinity in a competitive binding assay with [^{3}H]-naloxone but was found to be less active than pawhuskins A-C that were earlier proven to be in vitro k-opioid antagonists.



P-067 – Brian Doyle

Toxicity of American Mayapple Fruit, *Podophyllum peltatum* L. (Berberidaceae)

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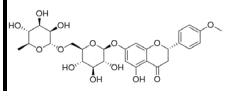
The American mayapple, *Podophyllum peltatum* L. (Berberidaceae), is an herbaceous plant native to Eastern North America. It is a relative of the Himalayan mayapple, *P. hexandrum*, which is the source of podophyllotoxin, a cytotoxic lignan used in the topical treatment of genital warts. Podophyllotoxin is also the precursor to the cancer chemotherapeutic drugs etoposide and teniposide. Though the American mayapple produces podophyllotoxin to a lesser extent than its Asian counterpart, it has nonetheless been investigated as an alternative source of the toxin. Surprisingly, very little attention has been paid to the fruit of the plant, which folk wisdom suggests is edible only when ripe. We aimed to test the hypothesis that, like the rhizome and above ground stems and leaves, green fruits contained podophyllotoxin that diminished as the fruit ripened. Fruits were wild harvested in Michigan at various stages of ripening from early June through late July. Crude methanolic extracts were analyzed by HPLC. Unlike other parts of the plant, podophyllotoxin could not be detected in the fruit at any stage of ripening. Work is underway to evaluate the toxicity of American mayapple fruit and to characterize its phytochemical composition.

P-068 – Gabriela Garcia Marin

Antinociceptive Activity, Toxicological Evaluation, and Chemical Characterization of Two *Clinopodium* Species

Gabriela García-Marín[1], Valeria Reyes-Pérez[1], Sol Cristrians[1], Omar Emiliano Aparicio-Trejo[2], Isabel Rivero-Cruz[1], Rachel Mata[1]. Universidad Nacional Autónoma de México, Ciudad de México, 04510, México. [4]Instituto Nacional de Cardiología "Ignacio Chávez", Ciudad de México, 14080, México

Clinopodium macrostemum (CMC) and *C. mexicanum* (CMX) (Lamiaceae) are traditionally used to treat pain and gastrointestinal disorders; CMC also has edible and eremonial uses. This study evaluated their antinociceptive activity, toxicity, and chemical profiles. Acute toxicity was assessed in mice using Lorke's test and in rats by measuring hepatic and renal markers, while antinociceptive effects were measured in the formalin model. Glycosylated flavones were identified in both species, particularly 1-3, and an UHPLC method was validated in accordance with ICH guidelines. Despite no lethality (LD_{50} > 5 g/kg), both species caused acute renal injury and showed moderate antinociceptive effects. Further safety studies are in progress.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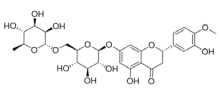
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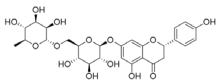
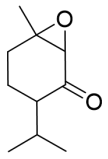

Narirutina (3)

P-069 – Gabriela Garcia Marin

Volatilome and Nutritional Composition of the Traditionally Used Plant *Clinopodium macrostemum*

Gabriela García-Marín, Sol Cristrians, Isabel Rivero-Cruz, Rachel Mata. Universidad Nacional Autónoma de México, Ciudad de México, 04510, México

Beyond its well-recognized medicinal value, Clinopodium macrostemum is also consumed as a food plant; its cooked leaves are eaten directly or used as a seasoning because of their pleasant aroma. This study focused on profiling the plant's volatile compounds through essential oil analysis and HS-SPME coupled with GC–MS. Piperitone oxide (**1**), piperitenone oxide (**2**), and menthone (**3**) were identified as the major constituents of the essential oil, together accounting for 62.3% of the total composition. These findings were confirmed by HS-SPME analysis. Nutritional evaluation revealed a high crude fiber content (74.44 ± 0.29%) and substantial levels of potassium (1193.08 ± 6.07 mg/100 g) and calcium (887.60 ± 37.84 mg/100 g).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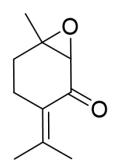
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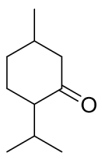
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P-070– Joshua Kellogg

Chemical Characterization of Botanicals to Develop Dermal Toxicity Assessments

Stefan Gafner[1], Joshua J. Kellogg[2], Constance A. Mitchell[3]. [1]ABC, Austin, TX 78723, USA [2]Department of Veterinary and Biomedical Sciences, Pennsylvania State University, University Park, PA 16802, USA, Health and Environmental Sciences Institute, Washington, DC 20005, USA

Until the late 20th century, the safety of botanicals was largely evaluated based on their history of use. However, this presumption lacks comprehensive toxicological evaluation, and there is a need for reliable bioassays that can screen for potential adverse effects. One crucial toxicological endpoint is dermal toxicity, as the skin serves as the body's first line of defense against chemical exposure and toxicity can occur locally at the site of contact. To evaluate assays for skin irritation, phototoxicity, and skin sensitization, well characterized botanical case studies are needed. As part of the Botanical Safety Consortium, 10 plant species were selected to assess the reliability of dermal toxicity assays. The selected plants have documented (positive controls) or are devoid of (negative controls) dermal toxicity. To support the authentication of the materials, characterization of key constituents was carried out using various analytical techniques. Several toxicological assays were selected to evaluate their utility for botanicals as complex mixtures. For example, in an in vitro skin irritation assay, a human epidermis model was exposed to classify materials as irritant or non-irritant. Poison ivy (*Toxicodendron radicans*) was found to be an irritant. Neat lavender (*Lavandula angustifolia*) essential oil was an irritant, so a dilution study was conducted. Only at the 1% concentration was it a non-irritant. These results show promise for predicting ingredients for which dermal use may carry the risk of skin irritation.

P-071 – MyeongJi Kim

Hydrolysis Patterns of Enzymatically Modified Steviol Glycosides

Myeong Ji Kim[1], Jeong-Eun Lee[2], Young-Sam Keum[2], Hyunwoo Kim[1] College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University-Seoul, Goyang, Republic of Korea

Enzymatically modified steviol glycosides (EMS) are structurally enhanced derivatives designed to improve palatability. This study investigates the acidic degradation of EMS, revealing a significant alternative pathway compared to natural stevia. While natural glycosides primarily yield isosteviol, acid-hydrolyzed EMS produces a distinct byproduct identified as *ent*-13-hydroxykaur-15-en-19-oic acid (**1**). Structural characterization via HRMS, NMR, and X-ray diffraction confirmed its identity, with formation being highly pH and time-dependent. Comparative HPLC analysis showed that while compound **1** is minimal in natural stevia, it is substantially pronounced in EMS. These findings indicate that extensive glucosylation alters the chemical behavior of the steviol backbone under acidic conditions. These results suggest that incorporating this byproduct into the current analytical framework for steviol equivalents could provide a more precise assessment for products containing EMS. **Reference -** Myeong Ji Kim, Jeong-Eun Lee, Young-Sam Keum, Hyunwoo Kim, Hydrolysis patterns of enzymatically modified steviol glycosides, *Food Chemistry*, Volume 512, 2026, 148935, ISSN 0308-8146.

P-072 – Jotham N'Do

Nitrogen and Phosphorus Regulation of Flavonoid Biosynthesis *in Acanthospermum hispidum*

Jotham Yhi-pênê N'do[1], Renuka Sankaran[2], Chinenyenwa Erwueme[2], Edward J. Kennelly[2]. [1]Laboratory of Biochemistry and Applied Chemistry Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso; [2]Department o Biological Sciences, Lehman College, City University of New York, Bronx, NY, USA

Acanthospermum hispidum DC (Asteraceae) is a medicinal plant used for the management of liver diseases and produces flavonoids, known for their hepatoprotective properties. In Burkina Faso, fresh *A. hispidum* plant material is not available throughout the year due to overharvesting and habitat destruction. Efficient cultivation of *A. hispidum* could be a useful alternative to optimize the yield of metabolites of interest, such as flavonoids, and obtain a uniform and high-quality product. The uptake of nitrogen and phosphorous can induce significant changes in secondary metabolism. This study investigates the influence of nitrogen and phosphorous on flavonoid content in *A. hispidum*. Seeds of *A. hispidum* from three pedoclimatic regions of Burkina Faso were cultivated in a greenhouse, and subjected to six treatments with varying concentrations of nitrogen and phosphorous. Agronomic measurements, including the number of leaves, stem diameter. and number of nodes per plant, were recorded. Plants were harvested after six weeks, and three parts were separated, extracted and analyzed by UPLC-qToF-MS. Changes in flavonoid composition will be analyzed using Progenesis QI.

P-073 – Carolina Saucedo Cervantes

Metabolic Investigation of Specialized Phytochemical Variation in *Eriodictyon californicum* Extracts Produced from Different Parts of the Same Individual Plants

Carolina N. Saucedo Cervantes[1], Robyn Johanna Araiza[1,2], Alli J. Adams[1], Lisa Cumper[3], Richard Lee Bugbee[4], Mei Wang[5], Pamela Maher[6], Clinton C. Shock[7], C. Benjamin Naman[1]. [1]Department of Science and Conservation, San Diego Botanic Garden, [2]Department of Chemistry and Biochemistry, California State University San Marcos, [3]Tribal Historic Preservation Office, Jamul Indian Village of California, [4]Kumeyaay Community College, El Cajon, CA, [5]Natural Products Utilization Research Unit, Agricultural Research Service, United States Department of Agriculture, University, MS 38677, [6]Cellular Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, CA, [7]Scientific Ecological Services, Inc., Ontario, OR

Yerba Santa (*Eriodictyon californicum*), a shrub endemic to the California floristic province, holds great importance through its traditional medicinal uses and modern implementation as an approved dietary supplement and natural flavor ingredient. Recently, it has been of interest in neurodegenerative disease research for its potential neuroprotective and anti-inflammatory properties. This study investigated how phytochemical composition varies in leaves from different vertical quarters of the same individual *E. californicum* plants. Liquid chromatography (LC) and mass spectrometry (MS) were applied for qualitative untargeted analysis of the phytochemicals present and quantitative targeted analysis using a limited set of available analytical standards: eriodictyol, homoeriodictyol, and sterubin.

P-074 – Velindel Esnard

The Antioxidant Activity and Total Phenolic Content of the Endophytic Fungi *Penicillium* sp. UWISTA-TuR7 associated with *Tillandsia utriculate*

Velindel Esnard[1], Anna Ali[1], Jayaraj Jayaraman[2] and Petrea Facey[1]. [1]Department of Chemistry, The University of the West Indies, St. Augustine, Trinidad and Tobago, [2]Department of Life Sciences, The University of the West Indies, St. Augustine, Trinidad and Tobago

Endophytic fungi are recognized as prolific producers of bioactive secondary metabolites with significant pharmaceutical potential. However, the fungal communities associated with the *Tillandsia* genus in the Caribbean region remain largely unexplored. In this study, the antioxidant activity, total phenolic content, and secondary metabolites of the endophyte *Penicillium* sp. UWISTA-TuR7 isolated from *Tillandsia utriculata* in Trinidad and Tobago, were investigated. The fungal strain was cultured on three different media: Cassava (*Manihot esculenta*) Dextrose Broth (CDB), Dasheen (*Colocasia esculenta*) Dextrose Broth (DDB) and rice. Antioxidant activity was assessed using the DPPH radical scavenging and CUPRAC assays, while total phenolic content (TPC) was determined using the Folin–Ciocalteu method. The antioxidant activity measured using the DPPH assay ranged from 12.22- 63.42 % inhibition. In the CUPRAC assay, antioxidant activity ranged from 11.12–346.6 mg/g Trolox equivalents, while total phenolic content ranged from 24.83–93.79 mg/g gallic acid equivalents. The highest antioxidant activity and total phenolic content across all assays were observed in the water phase extract derived from the DDB medium. The fungal strain was subsequently subjected to scaled-up fermentation on rice medium. Chromatographic separation followed by spectroscopic analysis resulted in the isolation of six compounds: methyl-8-hydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate, isorhodoptilometrin, emodin, citreorosein, 4-methoxy-2-methylisoquinolin-1(2*H*)-one and ergosterol peroxide.

P-075 – Dong Hyun Kim

Structure-Dependent Membrane-Targeting Antibacterial Compounds from an Endophyte of a Wild Ginseng

Dong Hyun Kim[1], Cao Yu Ying[1], Jin Woo Lee[2], Sang Hee Shim[1]. [1]Natural Product Research Institute, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea. [2]College of Pharmacy, Duksung Women's University, Seoul, 01369, Republic of Korea

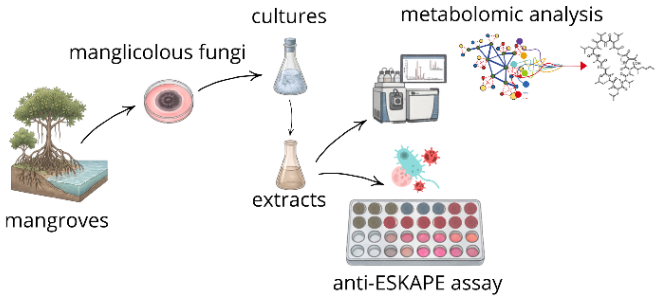
We report the isolation and structural elucidation of 14 new compounds from the endophytic fungus WSG12-RF2, which was isolated from wild ginseng (*Panax ginseng* C. A. Meyer). The structures of these compounds were determined using a combination of chemical reactions and spectroscopic methods. In antibacterial assays, some compounds exhibited potent activity against MRSA, while others showed strong biofilm inhibition at sub-MIC levels. Mechanistic studies revealed distinct membrane-permeabilization kinetics depending on structural features, suggesting different modes of membrane interaction. A detailed discussion of the structural elucidation, modes of action, and structure–activity relationships will be presented.

P-076 – María del Carmen Osorio Ramírez

Bioprospecting Manglicolous Fungi from Mexico: Chemical Profiling and Anti-ESKAPE Potential

María del Carmen Osorio-Ramírez, Alan G. Hernández-Melgar, Carlos A. Fajardo-Hernández, Mario Figueroa [1]Facultad de Química, Universidad Nacional Autónoma de México, CDMX, 04510, México*

Antimicrobial resistance caused by the ESKAPE group of pathogens is a critical public health concern; therefore, the search for novel bioactive compounds from underexplored sources is imperative. In this study, 21 endophytic fungi isolated from three mangrove species (*Rhizophora mangle*, *Laguncularia racemosa*, and *Avicennia germinans*) in Tabasco, Mexico, were bioprospected. Organic extracts were evaluated against 14 ESKAPE strains. The results showed significant activity against *Staphylococcus aureus* and *Enterococcus faecalis*. Metabolomic analysis using GNPS2, SIRUS, and CANOPUS revealed several chemical families, primarily polyketides and macrolides, and the identified metabolites explain the observed antimicrobial effects. These findings highlight mangrove-derived endophytic fungi as a promising source of chemically diverse metabolites with potential against drug-resistant pathogens.

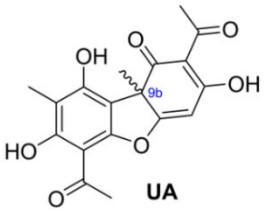


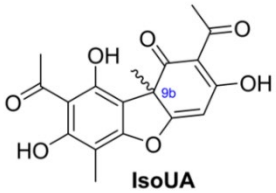
P-077 – Maia Biwersi

Exploring Phylogenetic Patterns of Usnic Acid Isomers in *Cladonia* Lichens

Maia Biwersi[1], Maonian Xu[1], Starri Heiðmarsson[2], Snæbjörn Pálsson[3], John L. Sorensen[4], and Elín S. Ólafsdóttir[1].[1]Faculty of Pharmaceutical Sciences, University of Iceland, Reykjavík, Iceland, [2]Northwest Iceland Nature Research Centre, Sauðárkrókur, Iceland, [3]Faculty of Life and Environmental Sciences, University of Iceland, Reykjavík, Iceland, [4]Department of Chemistry, University of Manitoba, Winnipeg, Canada

Usnic acid (UA) is a secondary metabolite with notable bioactivity, including antimicrobial, anti-inflammatory and antitumor properties. It occurs in lichens as (+) and (−) UA as well as (+) and (-) isoUA, but its stereoselective biosynthesis remains poorly understood. The lichen genus *Cladonia* exhibits substantial chemical and genetic diversity, making it a useful system to examine links between secondary metabolites and evolutionary relationships. Whether stereoisomer patterns relate to phylogeny was analyzed using 197 *Cladonia* specimen with multilocus markers (nrITS, RPB2, MCM7, mtSSU) and chiral HPLC to resolve UA stereoisomers. Chemical profiles were mapped onto phylogenetic trees to explore patterns across lineages, suggesting that closely related taxa often share stereoisomeric states despite multiple transitions across the phylogeny.





Poster Presentations Session II

P-078 – Barbara Adaikpoh

A Lanthipeptide Biosynthetic Gene Cluster Activated by a Plant Stress Signal

Jacob K. Lee, Barbara I. Adaikpoh. Department of Pharmaceutical Sciences, and Center for Biomolecular Sciences, Retzky College of Pharmacy, University of Illinois Chicago, Chicago, IL 60607, USA

Microbial natural products have long been a major source of antimicrobial agents, which are essential for maintaining the health of humans, animals, and plants. Historically, beneficial bacteria associated with plants have been documented to enhance plant defense mechanisms against pathogens. Under pathogenic stress, plants alter their microbiota populations via root exudates, thereby modifying the microbial metabolome. In the metabolomic and transcriptomic analyses of a non-model, plant-associated *Chryseobacterium* strain, a biosynthetic gene cluster was identified, predicted to encode a lanthipeptide that was transcriptionally upregulated in response to a plant stress signal. Crude extracts from these cultures also demonstrated some antifungal activity against *Aspergillus fumigatus*. By employing bioactivity-guided fractionation and genetic engineering techniques, we aim to characterize the antifungal metabolite and correlate it with the biosynthetic genes. In addition to isolating natural products from this strain, this project intends to develop genetic engineering tools to facilitate the discovery of novel natural products from *Chryseobacterium*.

P-079 – J.P. Gerdt

Secondary Metabolites Control Bacterial Immunity Against Bacteriophage Viruses

Joseph P. Gerdt. Department of Chemistry, Indiana University, 800 E. Kirkwood Ave., Bloomington, IN 47405, USA

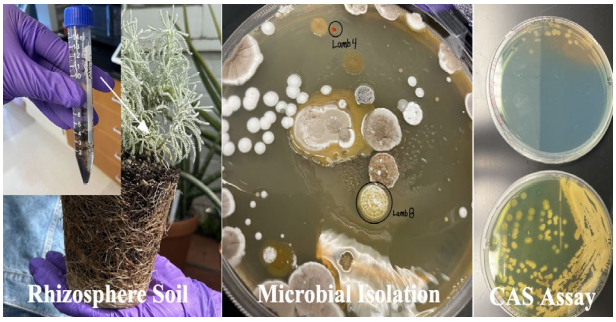
Viruses infect bacteria, too. These viruses (called bacteriophages or 'phages') are major drivers of bacterial mortality and horizontal gene transfer. To defend themselves from phages, bacteria have evolved myriad immune systems—many of which have only recently been reported. These bacteria-phage interactions naturally occur in diverse chemically complex environments. It is plausible that their chemical environments control the efficacy of anti-phage immunity in bacteria. Indeed, we have first found that iron-chelating siderophores can promote or inhibit phage infections (depending on the specific bacteria-phage pair). Furthermore, we have found that the metabolite nicotinamide—along with other pyridine-containing molecules—can inhibit anti-phage immune systems containing Toll/interleukin-1 receptor/resistance protein (TIR) domain-containing enzymes. These discoveries add to a growing number of natural product influences on phage-bacteria interactions.

P-080 – Lesley-Ann Giddings

Mining the Rhizosphere: Student-Led Discovery of Novel Siderophores and Siderophore-Producing Bacteria Within A Course-Based Undergraduate Research Experience

Adline Dely[1], Phoebe Dennison[1], Robert Samples[2], Riccardo Racicot[2], and Lesley-Ann Giddings[1,2]. [1]Department of Chemistry, Smith College, Northampton, MA, USA, 01063, [2]Biochemistry Program, Smith College, Northampton, MA, USA, 01063

Course-based undergraduate research experiences (CUREs) train undergraduates to solve complex, real-life scientific problems. Here, we describe the findings of a new Smith College course, CHM 350 Chemical Ecology: Catch Fe If You Can, in which undergraduates use genomics, microbiology, and (bio)chemical techniques to explore the chemistry organisms use to navigate their environments. Throughout the semester, students explored the rhizospheres in the Smith College Botanic Garden for bacteria that produce iron-chelating molecules or siderophores. Students isolated 30 actinomycetes using heat treatment, plating on glucose, yeast extract, and malt extract (GYM) agar with nalidixic acid and cycloheximide, and Chrome Azurol S overlay assays to detect siderophore activity (see inset). Genomic DNA was extracted for whole genome sequencing and isolates were cultivated in GYM media with or without the rare earth element cerium for metabolomics analyses. Twelve genomes were sequenced, revealing most isolates as *Streptomyces*. Notably, all isolates produced desferrioxamines, and increased levels of desferrioxamines and new desferrioxamines were exclusively detected in cerium-treated cultures, indicating a correlation between cerium and hydroxamate siderophore biosynthesis. Importantly, two students published their results in peer-reviewed journals, demonstrating that this course builds research skills while yielding isolates with the potential to bioremediate metal pollution.

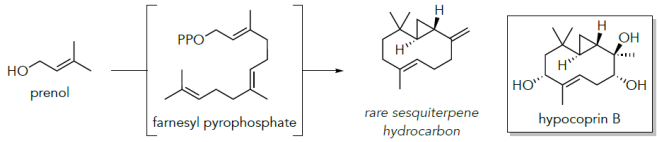


P-081 – Rachel Khavinson

Sesquiterpene Synthase Discovery Enabled By Synthetic Biology and In Vitro Biocatalysis

Rachel F. Khavinson,[1] Kyle Z. Share,[1], Jeffrey S. Cannon,[1] and Vikram V. Shende[1] Department of Chemistry, Occidental College, Los Angeles, CA 90041

Terpenes and oxidized terpenoids are the largest and most structurally diverse family of natural products, with many members possessing pharmaceutical or agricultural potential and/or ecological significance in niche environments. Filamentous fungi are historically abundant sources of bioactive terpenoids, and traditional genome mining has uncovered a vast array of well characterized terpene synthases that construct intricate hydrocarbon scaffolds from linear diphosphate precursors. Engineered kinases capable of constructing isopentenyl diphosphates from prenols have unlocked our ability to rapidly characterize new terpene synthases and the scalably produce of valuable terpene products from inexpensive, commodity chemical feedstocks. We leveraged both *in vivo* and *in vitro* approaches to uncover a new terpene synthase from *Hypocopra rostrata* which produces a rare sesquiterpene scaffold, and propose a mechanism for this enzyme informed by computational calculations.



P-082 – Emily Mevers

Ecological Role of Flavobacteriia within the Moon Snail Egg Mass Microbiota

Karla Piedl[1], Caitlyn O. Agee[2], Anthony G. Tarulli[1], R. Thomas Williamson[2], Emily Mevers[1]. [1]Department of Chemistry, Virginia Tech, Blacksburg, VA 24061; [2]Department of Chemistry and Biochemistry, University of North Carolina Wilmington, Wilmington, NC 28403

Microorganisms wage constant chemical battles against one another as they compete for space and scarce nutrients, particularly within animal-associated habitats. Studying the natural products that mediate these interactions has led to the discovery of bioactive natural products. Here, we studied the microbiota of moon snails (Naticidae) from SW Florida. Previous work revealed that the core microbiota of *Neverita delessertiana* is dominated by Flavobacteriia, which represent up to 69% of sequences as the egg masses age. We hypothesized that Flavobacteriia likely use small molecules to gain a competitive advantage within egg masses. To probe this, we performed binary assays with Flavobacteriia isolated from the egg masses. Analysis of 140 distinct pairings revealed eight that exhibited growth-inhibitory activity. Chemical evaluation of the crude extract from *Cellulophaga omnivescoria* EM610, which inhibited the growth of three other Flavobacteriia, resulted in the isolation of bacillimidazoles A and E, two previously characterized metabolites isolated from a marine *Bacillus* species. Further work demonstrated that these compounds are readily formed spontaneously by condensation of 2,3-butanedione with phenethylamine and/or tryptamine. Tandem mass spectrometry analysis of the chemical extracts of individual moon snail egg masses revealed the presence of bacillimidazole A in 62% of the egg masses.

P-083 – Jotham N'Do

Ethnobotany, Quality Control, and Sustainability of Medicinal Plants in Burkina Faso

Jotham Yhi-pênê N'do[1], Edward J. Kennelly[2], Renuka Sankaran[2], Paulin Wendsom Savadogo[1], Adama Hilou[1], Martin Kiendrébéogo[1]. [1]Laboratory of Biochemistry and Applied Chemistry, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso; [2]Department of Biological Sciences, Lehman College, City University of New York, Bronx, NY 10468, USA

From our ethnobotanical survey on medicinal plant consumption Ouagadougou, Burkina Faso, thirteen plant parts were identified as the most widely used and economically significant. Samples of these plant parts were collected in the field, and their commercial equivalents were purchased from three markets. A total of 104 samples were collected and underwent a comparative analysis of their respective microbiomes. Furthermore, the impact of storage conditions on the phytochemical composition and antioxidant properties of these samples was studied. Microbial colony counts revealed low microbial loads on the medicinal plant parts stored under laboratory conditions (e.g., *Adansonia digitata* (AdT): $0.02 \pm 0.0001 \times 10^6$ CFU/g) compared to those acquired from the various markets (e.g., *A. digitata* (Ad1): $73.07 \pm 1.42 \times 10^6$ CFU/g). Extracts of *A. digitata* obtained from Markets 1 and 3 showed lower total polyphenols and tannins. The storage conditions of medicinal plants significantly impact their secondary metabolite composition, antioxidant properties, and microbiome.

P-084 – Emily Giedraitis

Statistically Informed Molecular Networking Resolves Species-Specific Metabolites

Emily C. Giedraitis[1] and Vanessa V. Phelan[1] 1. Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado-Anschutz Medical Campus, Aurora, CO, 80045, USA

Chronic airway infections in cystic fibrosis (CF) are sustained by complex metabolic exchange among co-colonizing microorganisms. While untargeted LC–MS/MS enables broad detection of metabolites in polymicrobial systems, assigning features to their producing organisms remains challenging due to sparse spectral libraries and shared chemistry. Here, we developed a systematic metabolomics workflow to address this limitation using a synthetic CF microbial community composed of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus sanguinis*, and *Prevotella melaninogenica.* Species were grown as monocultures or as a mixed community in synthetic CF medium, followed by methanol extraction and LC–MS/MS analysis. Statistically informed feature-based molecular networking (FBMN) enabled species-level metabolite attribution. Multivariate analysis distinguished mono- and mixed-species cultures, with the community metabolome strongly influenced

by *P. aeruginosa*. This approach resolved species-specific metabolites associated with virulence and interspecies competition.

P-085 – Margaret Hill

An Intracellular Self-Sensing Circuit in *Listeria monocytogenes* Integrates Carbon Metabolism, Stress Responses, and a Novel Bacteriocin

Margaret L. Hill, Diandra M. Vaval Taylor, Alberto E. Lopez, and Nancy E. Freitag*. Department of Pharmaceutical Sciences, Retzky College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA

Listeria monocytogenes (*Lm*) shifts from an environmental bacterium to an intracellular pathogen after ingestion, requiring host-cell invasion, vacuole escape, and cytosolic replication. Here, we examined the role of the peptide pheromone pPplA, derived from the signal sequence of lipoprotein PplA. Unlike canonical quorum-sensing peptides, pPplA is required for bacteria trapped within host vacuoles, and its loss triggers compensatory mutations, indicating a role in bacterial homeostasis. Transcriptomic analysis of Δ*pplA* strains revealed the significant upregulation of iron acquisition genes from the *svpA-srtB* locus and repression of the glycerol utilization (*gol*) operon, which includes a pediocin-like bacteriocin immunity protein identified by BAGEL4. Adjacent to the immunity gene, lies a divergently oriented open reading frame encoding a leaderless 62-amino-acid peptide with similarity to the class IID bacteriocin lactococcin972, which we termed listeriocin10403S. Ongoing work aims to confirm toxin-antitoxin complex formation through biochemical co-purification, and to define toxin activity using inducible expression systems. Together, these findings support a model in which pPplA functions as an intracellular self-sensing signal that links carbon metabolism to bacteriocin regulation, stress responses, and potential prophage control.

P-086 – Sandra Loesgen

Natural Products Discovery from American Basidiomycetes

Sandra Loesgen[1], Bastien Petit[1], Ines Machrafy[1], Jordan Nafie[2], Grayce E. Dyer[1], Erin M. Marshall[1], Cristian Riquelme[3], Jaime R. Cabrera Pardo[3], James A. Strother, Jason C. Slot[4], [1]University of Florida, Whitney Laboratory, [2]BioTools Inc., [3]Universidad del Bío-Bío, Chile, [4]The Ohio State University

Fungal natural products continue to inspire chemists and drug development. Around 30,000 fungal secondary metabolites (SM) are known, mainly from filamentous fungi of the phylum Ascomycota. Only 5% of all fungal species are described today and even fewer have been cultured or chemically screened, which make fungi an untapped reservoir for chemical discovery. The phylum Basidomycota harbors chemically talented fungi like the psilocybin producer *Psilocybe*, but other members like the genera *Anthracophyllum* or *Athelia* remain largely genetically and chemically underexplored. Here, we present the chemical and bioactivity exploration of a Chilean *Anthracophyllum discolor* fungus. We discovered anthacaurisin A, the first fungal *nor*-sesquiterpene homodimer and atropisomers, with potent cytotoxic activity *in vitro* and *in vivo*, along with some new and known illudins. From the termite associated fungus *Athelia thermitophila*, also known as the 'cuckoo fungus' with its termite-egg-mimicking sclerotia, we discovered a potent serotonergic alkaloid we named atheliapyrrolidine A, and explored its application for human health and its function in the ecosystem.

P-087 – Osama Mohamed

Omics Deployment for Crop Protection Discovery from Natural Products

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Natural products have been a rich source in delivering novel modes of action and sustainable chemistry for crop protection discovery. Corteva Agriscience leverages over 25 years of natural products research experience and a biorepository containing hundreds of thousands of unique microbial isolates, creating a strong need for advanced new tools to effectively mine this extensive collection for innovative solutions. A platform combining high throughput metabolomics, genomics, chemistry, and synthetic biology has been developed and used to mine this large collection of microbes to revive industrial Natural Product discovery for crop protection and biologicals. Deploying this platform led to the identification of a promising herbicidal natural product with putative novel mode of action for dicot weed control. In addition, a combination of fermentation optimization and strain analoging led to 35 fold titer improvement showing promise as a potential future crop protection agent.

P-088 – Olivia Schwartz

Bacteroides Fragilis Modulates Microbiome and Metabolites in Mouse Model of Alzheimer's Disease Pathologies

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Alzheimer's disease (AD) is a neurodegenerative disease and the leading cause of dementia. AD pathology is associated with shifts in the gut microbiome over time with differentiating abundance of taxa including *Bacteroides spp.* [1,2] In collaboration with the Cope Lab, we investigated effects *Bacteroides* has on transgenic mice modeling AD pathology (3xTg-AD) using the model organism *Bacteroides fragilis* (Bf). We identified metabolites which change in abundance upon Bf treatment using ultra high liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Compounds we have identified as changing with Bf treatment include amino acids, which are important as protein building blocks and many other metabolic processes, and bile acids, which are involved in the body's process to eliminate excess cholesterol. [1] Alzheimer's Association. Alzheimer's & Dementia. 2024. [2] Chandra, et. al. Molecular Neurodegeneration.*2023*.

P-089 – Jessia Raherisoanjato

Elucidation of Polysaccharides Variability of *Ruminococcus gnavus* Isolates, Potential Pathobionts in Inflammatory Bowel Disease

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Ruminococcus gnavus is a prevalent gut microbe at low abundance in healthy individuals (~0.1%) but can dominate the gut in Inflammatory Bowel Disease patients (up to 70%). IBD is a lifelong, immune assault of the gut and doesn't have a cure nor a known cause. It has previously been shown that *R. gnavus* isolates display a cell-surface rhamnan polysaccharide that activates mouse Bone Marrow Dendritic Cells (mBMDC) with pro-inflammatory properties. The gene clusters of the polysaccharides all have rhamnose encoding genes but different number of glycosyltransferases (enzyme responsible for adding monosaccharide units), which suggests that different isolates display different structures. To gain a better understanding of the saccharides' roles in disease, this study shows structures variability of the rhamnan between isolates by pairing NMR and GC-MS methods as well as their inflammatory properties.

P-090 – Hyemin Kim

Discovery of Antifungal Metabolites from the Human Gut Bacteria, Butyricimonas paravirosa and Bacteroides uniformis

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Human gut bacteria inhabit the gastrointestinal tract and play important roles through dynamic interactions with the host. Butyricimonas paravirosa and Bacteroides uniformis are obligate anaerobes commonly isolated from human fecal samples. In this study, we investigated the secondary metabolites produced by these two strain and identified eight previously undescribed compounds (**1**–**8**). Their chemical structures were elucidated through NMR, MS, computational analysis, and single crystal X-ray crystallography. The biosynthetic pathway of compounds **1**–**8** was proposed through biomimetic total synthesis, isotope-labeling experiments, and gene knockout study. Among the isolated compounds, compound **7** showed the most notable antifungal activity against multiple invasive fungal pathogens, with MIC values ranging from 3.125 to 25 μg/mL depending on the strain and susceptibility testing method. These findings expand the chemical diversity of human gut bacteria-derived metabolites and identify compound **7** as a promising antifungal lead.

P-091 – Erin Marshall

Exploration of Skin-Resident Bacteria Towards the Discovery of Clinically Relevant Antifungals

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Serious fungal infections impact over 150 million individuals globally and are often accompanied by mortality rates exceeding 50%. This issue is compounded by the emergence of novel and drug-resistant fungal pathogens including *Candida auris*, which has been shown to persist on human skin and engage in asymptomatic transmission. The skin microbiome is home to a diverse population of both skin-resident and pathogenic microbes existing in a dynamic environment showcasing both inter- and intra-species interactions. As these microbes are essential to maintaining skin homeostasis and have been shown to engage in defensive symbiosis, antibiotics derived from naturally colonizing microbes may show enhanced clinical efficacy. Our lab has built a repository of bacteria isolated from different body sites and, through iterative testing of these isolates against microbial human pathogens, many promising skin-resident bacteria from genera including *Staphylococcus*, *Kocuria*, and *Rothia* have shown complete inhibition of *Candida* species in contact-independent cross streak assays. Organic extracts from several of these underexplored bacteria were screened for chemical novelty and were further characterized by MS-based metabolomics revealing no correlation to known antibiotics. With further exploration of these strains, we will isolate and characterize the novel antifungal compounds with the aim of conducting preclinical studies.

P-092 – Martin Aborah

Phytochemicals from Cranberry Leaves Inhibit Bacterial Quorum Sensing Communication

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The opportunistic pathogen *P. aeruginosa* is responsible for causing infections related to indwelling medical devices, such as urinary-tract infections (UTI), that are regulated by quorum sensing communication (QS). The development of QS interfering agents is one of the strategies to reduce multidrug-resistant bacterial virulence. Phytochemicals in cranberry leaves are yet to be exploited for their anti-QS activity. Polyphenol-rich fractions derived from cranberry leaf extracts were incubated with *P. aeruginosa* PAO1 resulting in a significant decrease in QS and virulence activity at 100-200 μg/mL. Further investigations suggest that the fractions inhibited AHL synthesis and activity. By culturing *E. coli* pSB1142 as a reporter activity and adding 10 μM exogenous 3-oxo-C12 AHL either before or after adding the fractions, we observed a time-dependent inhibition of QS, suggesting a competitive binding to the LasR receptor of PAO1. These results indicate that cranberry leaf isolates are potential QS inhibitors against *P. aeruginosa*, encouraging further study for pharmaceutical applications. Molecular docking studies will be performed to evaluate possible competitive binding of specific leaf constituents with LasR, LasI, Vfr, RhlR, PqsA, and PqsR targets.

P-093 – Ermias Mekuria Addo

Rocaglate Derivatives, Sesquiterpenoids and Triterpenoids from Bioactive Partitions of the Branches of *Aglaia perviridis*

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As part of our anticancer drug discovery efforts from biomass of diverse natural origin, this study was aimed at isolating cytotoxic secondary metabolites from the branches of *Aglaia perviridis* (Meliaceae). Previous studies from other parts (e.g., roots, leaves, and twigs) of this plant have led to the isolation of numerous bioactive compounds including the eIF4A inhibitors silvestrol and episilvestrol. For the current study, partitioning of the cytotoxic methanol extract of its branches provided active chloroform and ethyl acetate partitions. While analysis of these partitions with the LC-MS/MS-based molecular networking indicated silvestrol and other rocaglates to be present, further fractionation using column chromatography and HPLC purification led to the isolation of a new sesquiterpenoid and a new triterpenoid along with three known analogs. This presentation will discuss their structural elucidation and biological activities.

P-094 – Evelyn Andrade

The Metabolome of Gram-Negative Bacteria Associated with Brazilian Propolis

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Propolis is a honeybee-derived product known for its several health benefits. Although many secondary metabolites have been isolated from propolis preparations, the process underlying its production is not yet well understood. As such, there is limited information on how microorganisms (fungi and bacteria) participate (or not) in the secondary metabolite composition of different kinds of propolis. We have isolated more than 140 Gram-negative bacterial strains from distinct types of propolis. Growth of these bacteria in appropriate media were processed for LC-MS/MS metabolomics analysis. The results indicated a very high chemical diversity, including previously unreported metabolite clusters. Extracts also exhibited promising bioactivity in different bioassays. Our integrated metabolomic and bioactivity-guided approach reveals propolis-associated Gram-negative bacteria as a rich source of bioactive secondary metabolites.

P-095 – Roberto Berlinck

Chemical Weapons of the Marine Sponge *Monanchora arbuscula*

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Monanchora arbuscula is a sponge species of wide occurrence in the Atlantic Ocean. It is a well-known source of guanidine alkaloids, including various batzelladins, ptilocaulins and crambescidins. We performed a metabolomics and biological activity

investigation of *M. arbuscula* fractions obtained by orthogonal chromatography separations. Fractions with distinct alkaloid compositions presented different profiles of potent antiplasmodial, anti-*Leishmania*, anti-*T.cruzi*, cytotoxic, antibacterial (Gram-positive and Gram-negative) and antifungal activity.

P-096 – Esperanza Carcache De Blanco

Screening NPR-NCI for Rare Cancer Drug Discovery

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Natural products have historically been a rich source of new anticancer drugs. To contribute with the search for novel, safe, and effective anticancer drugs with potentially novel mechanism of action, the Program Project Grant (P01CA125066) is focusing on blind screening of botanically authenticated samples from the Natural Product Repository (NPR), NCI. Rare cancer cell lines selected for screening include HPAC (pancreatic adenocarcinoma), BDCM (acute myelogenous leukemia), HT-1376 (urinary bladder), and MDA-T32 (thyroid) cancer cells. Active plant extract samples are submitted to LC-HRMS using the Thermo UltiMate 3000 system coupled with a Q-Exactive mass spectrometer. Molecular Networking platforms (e.g., GNPS) allows us to analyze, connect, and network based on fragmentation patterns to discover pockets of potential new bioactive molecules and categorize structurally similar compounds in clusters. Hence, LC-MS with GNPS analysis help to identify new phytochemicals with potential novel chemical scaffolds among the bioactive extracts to prioritize samples, based on novelty and potency, for further studies. Thus, promising samples will be phytochemically studied to structurally elucidate bioactive compounds with potential novel mechanisms of action.
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P-097 – Christopher Cartmell

SAGE: A Microfluidic, Disease Agnostic, Natural Product Discovery Engine

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Natural products remain one of the most productive sources of therapeutics, yet discovery efforts are constrained by limited access to microbial diversity, rediscovery of known compounds, and, either access to or inefficiency of screening technologies. To address these challenges, we developed SAGE (Small-molecule Analysis via Generated Emulsions), a modular droplet microfluidic platform that integrates microbial cultivation, multiplexed functional screening, and downstream chemical analysis into a unified discovery workflow. SAGE enables encapsulation of individual environmental microbial cells into picoliter droplets, allowing metabolite production in isolated microenvironments that preserve slow-growing species, enhance cultivation of previously inaccessible microbes, and promote expression of silent biosynthetic gene clusters. Following cultivation, pico-injection is used to introduce assay-specific reporter cells or indicator organisms into pre-formed droplets, enabling flexible and high-throughput functional screening. Fluorescence-based readouts generated by microbial metabolite activity are then used for fluorescence-activated droplet sorting (FADS), allowing recovery of producing strains for downstream chemical analysis and dereplication. This modular architecture supports multiple complementary screening modalities within the same platform. For anticancer discovery, SAGE incorporates engineered pancreatic cancer reporter cells in which caspase-3/7 activation during apoptosis triggers bright fluorescence, enabling direct identification of microbial metabolites that induce cancer cell death. The system is compatible with difficult-to-culture models such as PANC-1 pancreatic ductal adenocarcinoma cells, demonstrating robustness for therapeutically relevant phenotypic screening. In parallel, the platform supports receptor-based discovery through droplet-adapted β-arrestin recruitment assays targeting orphan GPCRs implicated in non-opioid pain pathways, enabling functional deorphanization of receptors through microbial metabolite production. Importantly, SAGE incorporates multiplexed differential antimicrobial screening to prioritize selective activity early in discovery. Fluorescently labeled Gram-negative and Gram-positive indicator strains are co-encapsulated within droplets, allowing immediate visualization of spectrum specificity. Loss of signal from one organism while the second remains viable identifies narrow-spectrum antimicrobial activity, while dual signal loss indicates broad-spectrum or non-specific toxicity. This differential screening strategy enables prioritization of pathogen-selective compounds and reduces downstream attrition associated with broadly cytotoxic metabolites. Preliminary studies demonstrate stable generation of ~50 μm droplets, successful single-cell microbial encapsulation, long-term colony growth within droplets, and viability of mammalian reporter cells following pico-injection. Microfluidic encapsulation enhances both microbial diversity and metabolite production relative to traditional cultivation approaches, expanding the chemical space available for screening. Positive hits are isolated by FADS, validated and then followed by scale-up, bioassay-guided fractionation, and structural elucidation using UHPLC-HRMS, molecular networking, and NMR spectroscopy. By integrating single-cell cultivation, multiplexed phenotypic assays, and differential antimicrobial screening within a miniaturized microfluidic format, SAGE provides a scalable and versatile

platform for natural product discovery. This unified approach enables simultaneous exploration of microbial "dark matter" while accelerating identification of selective bioactive small molecules across oncology, infectious disease, and pain therapeutics. Together, SAGE establishes a generalizable microfluidic discovery engine designed to expand accessible chemical diversity and improve the efficiency of functional natural product discovery.

P-098 – Andres Cumsille

Interspecies Chemical Elicitation. Bacterial Interactions for Natural Products Discovery

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Despite several efforts, the discovery of novel Natural Products (NPs) has been hindered by frequent rediscoveries. Microorganisms dwell in diverse ecosystems, where multiple species compete and cooperate, and where community dynamics, and NP production are tightly interconnected. To better understand how community dynamics influence life cycle and NP production in bacteria, this study examined a 12-member bacterial community. Using pairwise interactions in an all-vs-all setup, we investigated how "elicitor" strains induce changes in "focal" strains. These interactions were further tested by incorporating bacterial supernatants into culture media in a high-throughput elicitation setup. Several interaction phenotypes were observed, in addition, LC-MS/MS metabolomics revealed differences in the production of key NPs. Some examples include differential production of: violacein, actinorhodin, prodigiosines, hygromycin, desferrioxamines, surfactines, and chloramphenicol, among others. These conditions were also observed in antimicrobial activity being elicited against human and plant-associated pathogens. These results underscore the potential of microbial interactions as a model for high-throughput screening in NP discovery, where integrating community and environmental context could help develop more rational, ecology-informed strategies for eliciting NPs in the laboratory.

P-099 – Lydia Davis

Nature, Networks, and New Medicines: Cheminformatics Strategies in Natural Products Drug Discovery

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The development of cheminformatic tools and the emergence of artificial intelligence (AI) have created new avenues in natural products drug discovery. At Enveda, we drive the future of pharmacognosy discovery by leveraging powerful instrumentation, cutting-edge data science, and high-throughput screening to discover promising drug leads from Nature. Using diverse algorithms, machine learning approaches, and AI-informed cheminformatics, we analyze high-resolution mass spectrometry data to annotate of the chemical library of Life and discover first-in-class medicines. However, the key paradigm of cheminformatics-guided small molecule discovery is accessible to both industry and academic researchers alike. This work explores how molecular networking, custom database searches, and structure prediction tools expedite the identification of novel and potentially therapeutic secondary metabolites from natural sources, highlighting that from the smallest culture collection to the world's most advanced pharmacognosy company, endless discoveries await.

P-100 – Kenya DeBarros

MoMo30: A Potential Therapeutic for COVID-19

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MoMo30 is an antiviral protein isolated from aqueous extracts of *Momordica balsamina L.* (Senegalese bitter melon). Previously, we demonstrated MoMo30's antiviral activity against HIV-1. Here, we explore whether MoMo30 has antiviral activity against the COVID-19 virus, SARS-CoV-2. MLV particles pseudotyped with the SARS-CoV-2 Spike glycoprotein and a Luciferase reporter gene (SARS2-PsV) were developed from a three-way co-transfection of HEK293-T17 cells. MoMo30's inhibition of SARS2-PsV infection was measured using a luciferase assay and its cytotoxicity using an XTT assay. Additionally, MoMo30's interactions with the variants and domains of Spike were determined by ELISA. We show that MoMo30 inhibits SARS2-PsV infection. We also report evidence of the direct interaction of MoMo30 and SARS-CoV-2 Spike from WH-1, Alpha, Delta, and Omicron variants. Furthermore, MoMo30 interacts with both the S1 and S2 domains of Spike but not the receptor binding domain (RBD), suggesting that MoMo30 inhibits SARS-CoV-2 infection by inhibiting fusion of the virus and the host cell via interactions with Spike.

P-101 – Emma Ellis

Characterization of Dapalides D and E and Metagenomic Comparison of the Two Co-occurring Dapalide Producing *Dapis* spp.

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Marine cyanobacteria are a rich source of diverse bioactive natural products, targeting proteins involved in many diseases. Here, we combined metagenomic analysis to enhance the structure elucidation process of two new cyclodepsipeptides named dapalides D (**1**) and E (**2**) from a collection of a cyanobacterial mat containing multiple *Dapis* species from Guam. Dapalides D-E are composed of eleven amino acids, including multiple identical ones with different configurations. Enantioselective amino acid identification of the acid hydrolysate established the identity of amino acids including configuration of α- and β-stereogenic centers. Identification and analysis of the dapalides D-E biosynthetic gene cluster from a metagenome-assembled genome aided the elucidation of α-configuration and establishment of the order of individual building blocks, collectively revealing the total structure. Phylogenomic analysis indicates that the dapalides D-E producer belongs to *Dapis* sp. (*Dapis* sp. VPG23–80 MAG-2), which shares a 95.2 % average nucleotide identity to *Dapis* sp. VPG23–80 MAG-1, the producer of dapalides A–C that cooccurs in the assemblage. Dapalide D (**1**) showed moderate growth inhibitory activity against various cancer cell lines. This work expands the dapalide structure class and further highlights the use of combined chemical and metagenomic analyses for natural product structure elucidation.

P-102 – Riley Greenleaf

SAGE: A Natural Product Microfluidic Discovery Engine

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Termed the "Great Plate Count Anomaly," only 0.01–1% of microbes found in our natural environment can be cultured under standard lab techniques, resulting in an abundance of microbes that we are yet to gain access to with untapped therapeutic potential. Small-molecule Analysis via Generated Emulsion (SAGE) presents itself as a workaround: a low-cost, high- throughput natural product discovery system, SAGE allows bacteria that would have been outcompeted to proliferate inside liquid microdroplets. Through pico-injection technology,fluorescent reporter cells can be introduced to observe natural product bioactivity within the droplet across a range of disease states--from differential antimicrobial screening with GFP-expressing *E. coli* and mCherry expressing *S. aureus*, to engineered Panc-1 reporter cells that fluoresce yellow upon apoptosis. Current proof of principle employs polymyxin B, a Gram-negative-selective antibiotic produced *by Paenibacillus polymyxia*, and doxorubicin, an anticancer natural product produced by *Streptomyces peucetius*, as positive controls. Co-encapsulation with *E. coli* resulted in absence of GFP associated fluorescence but presence of mCherry over one week, while exposure of Panc-1 reporter cells to doxorubicin produced a robust apoptotic fluorescent signal, demonstrating that SAGE is a functional and versatile platform for natural product drug discovery.

P-103 – Jiyeon Hwang

Unlocking Actinomycete Metabolic Potential through Genomic and Cultivation Strategies

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Actinomycetes are an important source of structurally diverse secondary metabolites with significant biological activities. In this study, we investigated the metabolic potential of marine-derived actinomycete strains by combining genomic, microbiological culture, and metabolomic techniques. Through the analysis of predicted biosynthetic gene clusters (BGCs) and taxonomic novelty (ANI < 95%), we selected 51 strains with high BGC contents and potentially unusual taxonomy. These strains were cultured in different media to compare their secondary metabolic profiles. The cytotoxic activities of the associated organic extracts were tested against Diffuse Pleural Mesothelioma (DPM) cell lines. Adding trace element solution (TES) to the culture media significantly affected the balance between the production of siderophores and other types of metabolites. During this medium optimization process, two previously unreported catecholate-type siderophores were identified from a *Streptomyces albus* (55348_A269). Comparative metabolomic analysis of strains with unique secondary metabolic profiles that corresponded to cancer cell cytotoxicity resulted in the identification of a group of new glycosylangucycline-type polyketides from *Streptomyces* sp. 030010625 (A363_S67).

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P-104 – Joshua Kellogg

Synergy of Botanicals for Anti-Inflammatory Modulation in Gut: Beyond One Drug-One Target

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Inflammatory bowel disease (IBD) is a chronic gastrointestinal inflammatory disorder with no definitive cure. This project aims to develop a multi-component botanical mixture that acts synergistically to target inflammation, gut barrier integrity, and microbial dysbiosis simultaneously as a novel therapeutic strategy for the management of IBD. *Artemisia dracunculus*, *Cannabis sativa*, and *Diplacus aurantiacus* were three plants of interest to advance to a heightened botanical mixture. Beginning with screening the plant extracts for aryl hydrocarbon receptor (AHR) activity, this study employed *in vitro* cell-based checkerboard assays to evaluate the interaction of the botanicals for anti-inflammation activity. The bioactive synergists will be investigated using a novel biochemometric machine learning approach, integrating high-resolution liquid chromatography-mass spectrometry (LC-MS) metabolomics data, bioassay datasets, and compound interaction terms (CITs) of all combinations in the effective mixtures. Identified synergists will be further evaluated to understand their effects on gut inflammation and relevant biochemical pathways in an *in vivo* model, including a functional microbiome. This project will lay the groundwork for multi-target therapeutics for inflammation, highlighting novel biochemometric tools in natural product research.

P-105 – Jackson Killian

From Millipede to Pharmacy: Efforts to Develop Terpenoid Alkaloids into Pain Relievers

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Colobognatha, a subterclass of millipedes, produces complex terpenoid alkaloids commonly used as chemical defenses. Previously, our group discovered the ischnocybines, oxidized alkaloids, in the defensive secretions of *Ischnocybe plicata*, a millipede found in the Pacific Northwest. We previously demonstrated that ischnocybine A potently and selectively binds the sigma-1 receptor (σ_1R; K_i = 13.6 nM) over the sigma-2 receptor (σ_2R; K_i = 1,292 nM). σRs are chaperone proteins that modulate ion channels such as Na^+, K^+, and Ca^{2+} upon activation; thus, they play a pivotal role in pain sensing and transduction in both the central nervous system and peripheral sites. Antagonists of both σRs have been implicated in the treatment of various neurological disorders, including neuropathic pain. To investigate the utility of the ischnocybines in the treatment of neuropathic pain, we have initiated a structure-activity relationship (SAR) study using isolated material for semi-synthesis. Large-scale collection efforts have afforded >100 mg of the previously described alkaloids (ischnocybine A-C and ischnocybinone), along with the isolation of eight new alkaloids. Interestingly, one alkaloid contains a highly unusual sulfate functionality that has not previously been observed in *I. plicata* secretions. Finally, initial SAR efforts and pharmacokinetic studies confirm that substituting the ester with an ether significantly increases the half-life ($t_{1/2}$ from 20 min to >255 min) without compromising overall potency.

P-106 – Naozumi Kondo

A New Natural Phenazine Antibiotic with Selective Activity Against *Mycobacterium tuberculosis*

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The continuous global health challenge and rise of drug-resistant tuberculosis highlights the need for new anti-TB agents with novel mechanisms of action. Clofazimine is a phenazine-derived drug with demonstrated clinical utility against *Mycobacterium tuberculosis*, but with limited utility due to tissue accumulation. Despite the therapeutic relevance of synthetic phenazines, relatively little is known about the anti-mycobacterial activity of natural analogs. Our in-house bioactivity-guided screening campaign for exploring actinobacterial producers of antimicrobials recently identified a novel phenazine analog, which was purified and characterized by $HRMS^2$ and extensive 1D/2D NMR. The compound exhibited potent and selective activity against *M. tuberculosis*, with no activity against other Gram-positive and Gram-negative bacteria, non-tuberculous mycobacteria, and mammalian cell lines. Feeding experiments with biosynthetic precursors to enhance production are currently ongoing.

P-107 – Seung Hwan Lee

Discovery of Bile Acids-Derived Biotransformation Products from *Mycobacterium* spp.

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Members of the genus *Mycobacterium*, belonging to the Actinomycetes, are known to transform cholesterol and phytosterols into a wide range of derivatives. The steroid metabolism of mycobacteria has been studied in detail, mainly for the large-scale production of precursors for steroid pharmaceuticals. However, the biotransformation of bile acids (BAs), endogenous steroids produced in the human body, by mycobacteria has not been extensively studied. In this study, BA biotransformation was investigated in three *Mycobacterium* species: *M. tuberculosis*, *M. avium*, and *M. conceptionense*. BA derivatives were isolated from large-scale bacterial cultures and characterized by HRMS and NMR analyses. A total of 40 BA derivatives (**1**-**41**), including eighteen new compounds (**1**-**17**) were fully elucidated. The identified BA metabolites revealed that these mycobacteria catalyze diverse enzymatic reactions,

such as methylation, reduction, ring degradation and dehydrogenation. Further biological assays will be conducted to explore their potential for the discovery of novel steroid-based drug candidates.

P-108 – Rocky Lowenthal

Advancements in Cultivation, Extraction, and Separation Methods for the Isolation and Characterization of *Trametes Versicolor* Bioactive Secondary Metabolites

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Turkey tail mushroom (*Trametes versicolor*) is a traditional Chinese medicine that has been demonstrated to have significant anticancer and immunomodulatory properties. *T. versicolor's* ethanolic extract induces PARP cleavage and apoptosis, upregulates LC3-II, increases MHC II and PD-L1, and shows anti-migratory effects when tested against SK-MEL-5 melanoma. While several promising compounds, including β-glucan polysaccharides, have been previously isolated, they do not fully explain the fungi's bioactivity. To effectively extract and characterize the secondary metabolites of *T. versicolor*, improved methods in cultivation, extraction, and bioactivity-guided separation are necessary and have been optimized herein. Liquid-based mycelium cultivation increases raw material yield and avoids the inclusion of substrate in extractions. Simultaneous liquid/liquid partitioning with H2O/EtOAc in conjunction with sonication (ultrasound-assisted extraction) increases extraction efficiency from ~1-3% to up to ~50%, providing sufficient material for further compound isolation. By using bioactivity-guided separation, fractions are prioritized based on their activity in murine bone marrow-derived dendritic cells (BMDCs), which has facilitated the identification of a UV-active portion of the EtOAc fraction of the H2O/EtOAc extract as particularly potent and bioactive. Although further work is needed to improve separation efficiency and to streamline natural product characterization workflows, the methods developed herein are expected to enable the future isolation of novel fungal metabolites.

P-109 – Rachel Mata

Synthesis and Production Enhancement of Gymnoascolide A

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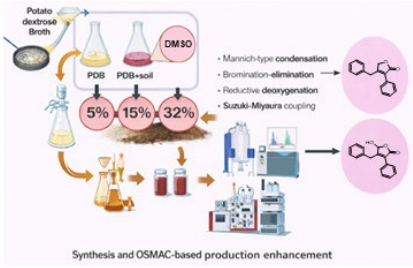

Gymnoascolide A (**1**) and microperfuranone (**2**) are bioactive fungal butenolides produced by *Malbranchea dendritica*. An integrated synthetic and cultivation strategy was used to increase the production of gymnoascolide A (**1**). Optimization of *M. dendritica* cultures increased yields to 15% with a soil-derived decoction and to 32% with 5% DMSO. Parallel total synthesis enabled structural validation by UPLC comparison with fungal extracts.

P-110 – Sahar Mofidi

Discovery of Neuroactive Secondary Metabolites from *Acacia sieberiana* with Potential Analgesic Properties using Multi-Well Electrode Assay (MEA)

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Acacia sieberiana is a medicinal plant used in the African pharmacopeia. In our previous study, its extract demonstrated significant efficacy in a reserpinized mouse model, suggesting potential therapeutic activity against pain-depression. These findings highlight this plant as a potential source for natural product drug discovery for analgesics. We reported secondary metabolites present in the active extract and fraction based on molecular networking analysis and in the present study, we report the isolation, structural elucidation, and total synthesis of two secondary metabolites, piperine and moupinamide. The neuropharmacological activity of these compounds, as well as analogs, was assessed using MEA assays. Screening revealed that both moupinamide and piperine significantly reduced baseline neuronal firing activity. Notably, this inhibitory effect was not pronounced under heat-stress conditions, indicating that the sensory function of the neurons remained intact. These results suggest that the compounds may modulate basal neuronal excitability without impairing sensory function. Overall, this study supports *A. sieberiana* secondary metabolites as promising lead compounds for pain drug discovery.

P-111 – Garrett Potter

Assessing Botanical Extracts for Antibiotic Potential against *Mycobacterium tuberculosis*

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Tuberculosis is the deadliest infectious agent worldwide, with two billion people infected and 1.25 million annual deaths. As resistance to standard-of-care treatments increases, new drugs are urgently needed to improve outcomes and reduce toxicity. Botanical extracts are promising natural sources of novel anti-tubercular compounds. *M. tuberculosis* (Mtb) possesses a complex, plant-like cell envelope that limits drug entry, leading us to hypothesize that botanical extracts may contain compounds better suited to penetrate this barrier. We performed ethanol extractions on plant materials and screened 92 extracts for growth inhibition against a BSL-2 laboratory strain of Mtb (H37Rv mc26030), while concurrently assessing total phenolic content (Folin–Ciocalteu) and antioxidant activity (ABTS, DPPH). Four extracts—frankincense, grains of paradise, witch hazel leaf, and yerba santa—showed significant inhibition (>2σ; <42% growth). These plants all have known antibiotic properties and folklore for use against tuberculosis, but systemic scientific testing is limited and specific active molecules are unknown. Phenolic content and antioxidant activity were strongly correlated (r = 0.86), but only weakly or not associated with antibacterial activity (r = −0.167 and −0.363), suggesting mechanisms beyond general redox or phenolic effects. These findings support botanical extracts as a source of targeted anti-Mtb compounds and motivate further expansion and fractionation to identify active constituents.

P-112 – Diego Rangel Rodríguez

Bioprospecting of Marine Bacteria of Mexico for the Discovery of Novel Antibiotics

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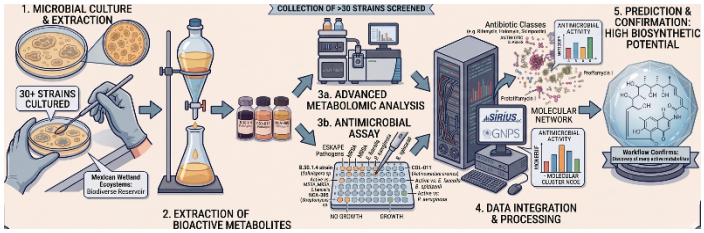
In response to the global challenge of antimicrobial resistance, this study investigated marine microbes from Mexican wetlands to discover novel antibiotics. From a collection of over 30 strains cultured in marine media, the organic extracts from three specific strains displayed significant inhibition of ESKAPE pathogens: *Salinispora* sp. (B.30.1.4) *vs.* MSSA, MRSA, and *E. faecalis*; *Actinomadura cremea* (COL-011) *vs. E. faecalis* and *B. spizizenii*; and *Streptomyces* sp. (NCA-385) *vs. P. aeruginosa.* Bioactivity-guided fractionation and advanced metabolomic analysis using HRMS-MS/MS led to the identification of several metabolites, including rifamycin, halomycin, and salinipostin derivatives. Overall, these findings confirm that Mexican wetland ecosystems are underexplored reservoirs of high-biosynthetic-potential microbes for discovering new leads against multidrug-resistant bacteria.



P-113 – Yulin Ren

Effects of Cryptanoside A on Cytokine Production from Human Prostate Cancer Cells

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The cardiac glycoside, cryptanoside A, has been reported for its potent growth inhibitory activities against different human cancer cells, including LNCaP human prostate cancer cells, and several Gram-positive and -negative bacteria, for which cytokines are critical components. Thus, the effect of this cardiac glycoside on the production or release of 12 cytokines and the related components from LNCaP cells over 24 or 48 h has been investigated in the present investigation. The cytokines comprised B-cell activating factor (BAFF), interferon (IFN)-α, IFN-γ, interleukin (IL)-6Rα, IL-8, IL-10, IL-11, IL-19, IL-27, IL-28A, IL-34, and tumor necrosis factor (TNF)-α, while cytokine-related components include proteins, aggrecan (ACAN), cluster of differentiation 163 (CD163), and pentraxin 3 (PTX3), proteinases, matrix metalloproteinases (MMP)-1 and -3, and an IL-6-shared transmembrane signal-transducing receptor subunit, glycoprotein 130 (gp130). Treatment with cryptanoside A decreased the production of Baff, GP130, IL-6Rα, IL-11, IL-28A, and PTX3 but increased that of CD163, IL-8, and IFN-α, indicating that exhibition of this compound could regulate cytokine secretion by LNCaP cells.

P-114 – Yulin Ren

Rotation Conformational Effects of Selected Cytotoxic Cardiac Glycosides on Their Interactions with Na^+/K^+-ATPase

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Cardenolides have been used successfully for the treatment of cardiovascular diseases by targeting Na^+/K^+-ATPase (NKA) and were found more recently to show potential anticancer activity. Biological investigations indicate that both the C-17 lactone unit and the C-3 saccharide moiety of these compounds play an important role in their interaction with NKA and in manifesting the resultant bioactivities. Interestingly, the crystal structures of several cardenolides show various conformations, due to a rotation of the C-3 saccharide moiety or the C-17 lactone unit. These rotation conformations could affect their binding to NKA and the resultant bioactivities, and thus docking profiles for several cardenolides, including cryptanoside A, digoxin and its aglycone, digoxigenin, and gitoxin, and NKA have been investigated in the present investigation. The results indicate that the binding poses of the rotation conformations of the compounds selected are different when they bind to NKA, as indicated by their docking scores calculated. For each compound, the rotation conformations observed could be in a dynamic equilibrium, of which each conformer may interact with NKA differentially, and these rotation conformers could act on NKA cooperatively to lead to a specific bioactivity.

P-115 – Vivian Rivera

Phytochemical Antiproliferative Evaluations of the Endemic Malagasy Plant *Phyllarthron articulatum*

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The ecosystem of Madagascar is characterized by high biodiversity and endemism where it is estimated that up to 80% of the vascular plant species are endemic.[1] These ecological characteristics provide avenues for the discovery of novel and bioactive secondary metabolites. Members of the endemic genus *Phyllarthron* (Bignoniaceae) are traditionally used to treat asthma, stomach pain, and many others. Species of this genus are rich in secondary metabolites known to exhibit anti-inflammatory properties. To characterize the chemical landscape of the unexplored species, *P. articulatum,* classical molecular networking was performed and confirmed the presence of triterpenoids, phenolic glycosides, flavonoids, and iridoids. Cytotoxic evaluations showed that the hexanes partition exhibits moderate antiproliferative activity. Bioassay-guided fractionation led to the isolation of a bioactive pentacyclic triterpene. Preliminary assays found it to be active against MDA-231, A549, PC-3, and for the first time MDA-435 and OVCAR3 cells. It exhibited a micromolar IC_{50} against MDA-435 and OVCAR3. Isolation of structurally related triterpenes is being performed to characterize the structure-activity relationship. Further exploration of the bioactive fraction and the structure elucidation of the isolated compounds will be discussed. [1]Razafindraibe et al. J Ethnobiology Ethnomedicine, 9, 73, 2013.

P-116 – Christine Salomon

Antiparasitic Norditerpenes from Podocarpus Plants

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The genus *Podocarpus* (Podocarpaceae) encompasses approximately 100 species of evergreen conifers characterized by significant ecological diversity and a broad distribution across the Southern Hemisphere. The genus has an extensive ethnobotanical history, with uses as traditional medicines to treat respiratory and gastrointestinal ailments, and several species are a prolific source of bioactive secondary metabolites which exhibit potent antimicrobial, antioxidant, and cytotoxic properties. Our anti-parasitic drug discovery program is focused on developing and characterizing new compounds to treat Cryptosporidiosis, a globally distributed water-borne gastrointestinal disease caused by protozoan parasites in the genus *Cryptosporidium*. We are especially interested in norditerpene dilactone metabolites that are uniquely produced by *Podocarpus* sp. due to their close structural similarity to potent antiparasitic compounds isolated from several species of fungi. To further expand the diversity of bioactive norditerpene compounds for structure activity relationship studies, we obtained 26 Podocarp species and conducted preliminary in vitro testing of crude extracts against *C. parvum*. Bioassay guided fractionation was used to identify the antiparasitic components of two of the most active species, *P. gracilior* and *Nageia nagi,* resulting in the isolation of twelve and seventeen pure norditerpenes, respectively. The potency, selectivity and SAR of the active compounds will be presented.

P-117 – Anand Swaroop

Mechanistic Convergence of a Standardized Triple-Botanical Combination on Cholinergic, Neurotrophic, and Anti-Neuroinflammatory Pathways In Vitro

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Cognitive decline involves concurrent dysregulation of cholinergic signaling, neurotrophic support, neuroinflammation, and oxidative stress; single-target interventions address these domains in isolation. We evaluated a standardized triple-botanical combination — Scopoletin (*Convolvulus pluricaulis*), Celastrol (*Celastrus paniculatus*), and Huperzine A (*Huperzia serrata*) — for convergent multi-pathway activity in vitro. Eleven mechanistic endpoints were assessed across four cell models (SH-SY5Y, BV2, HT22, U-373 MG) with compounds tested individually and in combination at four concentration levels. Primary readouts included Chou–Talalay combination index (CI) for acetylcholinesterase (AChE) inhibition, ARE-luciferase Nrf2 reporter activity, LPS-induced cytokine suppression, IL-1β/TNF-α-induced GFAP secretion, p-CREB/BDNF signaling, mitochondrial bioenergetics, autophagic flux, synaptic plasticity protein panel, and neurogranin release under injury. At the mid-dose, Scopoletin and Huperzine A produced synergistic AChE inhibition (CI = 0.71; 91.4% inhibition). The combination induced 4.82-fold Nrf2 activation — exceeding the strongest single compound by 51.6% — and suppressed LPS-induced TNF-α and IL-6 by 77–78% in microglia with concurrent 54.2% GFAP reduction in activated astrocytes. p-CREB/CREB increased 1.68-fold and secreted BDNF 2.14-fold; no single compound independently met these neurotrophic criteria. Autophagic flux rose 1.87-fold with 39% p62 reduction, four of five synaptic plasticity markers increased ≥1.3-fold, and neurogranin release was reduced 33–38% across three injury models. Ten of eleven endpoints met predefined criteria at mid-dose; all eleven at high-dose. The combination exhibits mechanistically necessary — not merely additive — multi-pathway cognitive neuroprotection, supporting advancement to animal bridging studies and clinical evaluation.

P-118 – Kevin Tidgewell

Applications of Calcium Imaging in Natural Product Drug Discovery

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As a fundamental regulator of intracellular signaling and stress responses, calcium provides a functionally relevant readout of molecular activity. Store-operated calcium entry (SOCE) is a specific calcium signaling pathway activated in times of cellular stress that is key in maintaining calcium homeostasis and downstream responses within the cell, making it an excellent target for drug discovery, but this process has been under-investigated within the early hit identification phase. We have We have optimized a calcium re-addition protocol for use as a SOCE screening method. We can detect SOCE activation and inhibition by delivering the extract or compound through a perfusion system to a stage containing HEK293 cells on an inverted microscope. This assay has been validated using known SOCE modulators and has since been applied to screening natural product extracts, fractions, and synthetic analogs from natural product scaffolds. This work highlights SOCE and calcium signaling as a functional, phenotypic readout, enabling the discovery and prioritization of novel calcium modulators across both natural product and synthetic chemical spaces. In the future, we aim to continue adapting this assay to screen natural product extracts and synthetic compounds for other cationic channel modulations.

P-119 – Alexandria Evans

Complementary Dual Mode of Action of the Marine Natural Product Barettin and Analogues Thereof

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Natural products are invaluable starting points for the discovery of new therapeutics, but those originating from marine sources have been underexplored. Barettin is an indole-containing diketopiperazine isolated from the marine sponge *Geodia barretti* that was initially reported for its antifouling activity and low cytotoxicity. Here, we demonstrate here this compound also exhibits complementary modes of action through the targeting of topoisomerase IIα, while simultaneously alleviating chemotherapy-induced peripheral neuropathy *in vivo* through inverse agonism of the serotonin 5-HT2A identified through a PRESTO-Tango assay. Despite modulating 5-HT2A, an *in vivo* head-twitch assay ruled out hallucinogenic liability often associated with the 5-HT2A receptor. Medicinal chemistry optimization coupled with *in vitro* growth inhibition assays to improve topoisomerase IIα potency ten-fold, from 1 μM to 100 nM, with other analogues also enhancing 5-HT2A inverse agonism four-fold. Our findings demonstrate the promising potential of this marine-derived small molecule with dual therapeutic potential: functioning as a chemotherapeutic agent while simultaneously addressing the common and dose-limiting side effect of peripheral neuropathy in cancer treatment.

P-120 – Eun Jin Heo

Antimicrobial Constituents of *Sphaerophorus globosus* against *Staphylococcus aureus*

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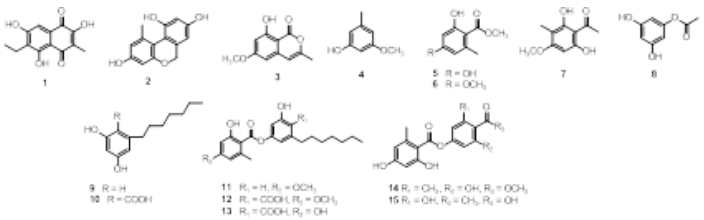
Sphaerophorus globosus, a polar lichen with scarcely studied chemical constituents, produces unique secondary metabolites. Bioactive fractions of its methanolic extract against *Staphylococcus aureus* yielded 15 compounds (**1-15**), including a novel naphthoquinone (**1**) and a novel dibenzofuran (**2**), their structures elucidated by 1D/2D NMR and HRMS. Compound **12** was identified as the primary active constituent with significant antimicrobial activity against *S. aureus*, and its antibiofilm activity is further being assessed via qRT-PCR and 3D-ODT.



P-121 – Jiyan Ni

UPLC-qToF-MSE Metabolomics to Investigate Century-old Botanicals: Medicinal Aconite

Ella T. Vardeman[1,2,3], Jiyan Ni[1,2], Matthew Pace[4], and Edward J. Kennelly.[1,2] [1]PhD Program in Biology, The Graduate Center, City University of New York, NY 10016, USA; [2]Department of Biological Sciences, Lehman College, City University of New York, Bronx, NY 10468; [3]The Center for Plants, People and Culture, New York Botanical Garden, Bronx, NY 10458; [4]The William and Lynda Steere Herbarium, New York Botanical Garden, Bronx, NY 10458

Despite their importance in botanical research, many herbaria worldwide have closed due to high maintenance costs and limited funding. These collections are especially valuable today, in the era of plant metabolomics, as they allow access to species that are typically inaccessible or otherwise difficult to re-collect, enabling analysis through both untargeted and supervised methods. This study highlights this potential by analyzing historic samples of medicinal Aconitum from the New York Botanical Garden Rusby Collection. Untargeted analysis facilitated chemotaxonomic identification of unidentified Aconitum samples in the collection. Three diester diterpenoid alkaloids, along with their derivatives, were identified and compared across specimens. Even after more than a century, several of these compounds were detectable, although detection varied among samples. Supervised analysis was used to identify additional chemical features useful as Aconitum marker compounds at the species level. By curating and prioritizing historic collections, future researchers can better understand the phytochemical profiles of key medicinal plants and how these profiles change over time.

P-122 – Jiyan Ni

LC–MS/MS Metabolomic Analysis of Diterpenoid Alkaloids from *Aconitum columbianum*

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Plant-derived natural products are valuable sources of analgesics, the clinical use of *Aconitum* roots in traditional Chinese medicine is restricted by the high toxicity of diterpenoid alkaloid diesters. The diterpenoid alkaloid composition and bioactivity of North American *Aconitum* species remain largely underexplored. We hypothesized that *Aconitum columbianum*, found in western North America, contains less toxic analgesic diterpenoid alkaloids based on our initial zebrafish assays. In this study, LC–MS/MS–based metabolomic profiling was used to analyze the aerial tissues of *A. columbianum* and compare them with selected Asian *Aconitum* species. Multivariate analyses were applied to evaluate chemical profile differences. Based on variable importance in projection scores, 21 marker compounds were identified, among which talatisamine has been demonstrated to possess analgesic potential. Notably, the highly toxic diterpenoid alkaloid aconitine was not detected in the aerial tissues of *A. columbianum*. Orthogonal partial least squares discriminant analysis further revealed that many significant marker compounds are unique to *A. columbianum*, suggesting that this species possesses a distinct alkaloid profile and may represent a promising source of safer analgesic candidate compounds.

P-123 - Rubyat Sara

Biocatalytic Labeling of Small Molecules via Laccase-Mediated Tyrosine Modification

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Site-selective bioconjugation is a powerful tool for advancing applications in drug discovery, chemical biology, and biomaterials. In particular, selective modification of small molecules is increasingly important for developing probes to study permeability, cellular uptake, and molecular interactions. However, achieving efficient and selective labeling under mild, aqueous conditions remains a significant challenge. Tyrosine-targeting strategies are attractive due to the distinct reactivity of phenolic groups, but existing approaches often suffer from instability and undesired side reactions in water. In this study, we report a biocatalytic strategy using a *Bacillus licheniformis* laccase (Blich-CotA) variant to oxidize commercially available 4-phenylurazole, enabling controlled *in situ* generation of reactive intermediates. Under mild conditions (pH 8, 37 °C), this system enables rapid and selective labeling of tyrosine residues in structurally diverse small molecules, including vancomycin, eupenifeldin, and vasopressin, demonstrating broad substrate scope. The method is also applicable to peptides and proteins,

while minimizing undesired side reactions. Importantly, reaction selectivity can be tuned by pH- at pH 8, selective tyrosine labeling is observed, whereas lowering the pH to 5 enables preferential tryptophan modification using the same enzymatic system. The resulting conjugates are compatible with downstream click chemistries (SPAAC/CuAAC) for installation of fluorophores or affinity tags. This work provides a versatile and environmentally friendly platform for selective small molecule tagging with tunable amino acid specificity.

P-124 – Jared Seale

Neuropathic Pain Modulated by Halogenated Tunicate Metabolite Derivatives

Jared T. Seale[1], Kevin Chase[2], Manju Karthikeyan[2], Meah Phan[1], Shrinivasan Raghuraman[2], Eric W. Schmidt[1]. [1]Department of Medicinal Chemistry, College of Pharmacy, University of Utah, Salt Lake City, Utah 81112, United States, [2]Department of Biology, University of Utah, Salt Lake City, Utah 81112, United States

Tunicates have long been a source of chemically diverse and bioactive compounds with therapeutic applications. Although primarily recognized for their role in defense, iodinated tyramine derivatives are common metabolites in the *Didemnum* genus of tunicates, whose neuroactive effects remain largely unexplored. Our group has identified 2-(3,5-diiodo-4-methoxyphenyl)ethan-1-amine (DIMTA) as a potent modulator of the mouse dorsal root ganglion (DRG), with preferential activity on low-threshold cold thermosensors, physiologically represented by a decreased sensitivity to cold pain in vivo. Electrophysiological and calcium imaging data suggest a bifunctional mode of action, inhibiting both voltage-gated potassium and calcium channels. To gain a deeper understanding of how this compound exhibits its neuroactive effects, a structure-activity relationship study was conducted. A library of DIMTA analogs containing modifications to the halogen, ether, and amine modalities was synthesized and assessed. Remarkably, modest changes to the DIMTA skeleton produced profound differences in DRG cell type and ion channel selectivity. This work highlights not only the challenges of developing selective ion channel inhibitors but also the complexity of neuronal signaling underlying peripheral sensation.

P-125 – Nigel Yeboah

Antimicrobial Evaluation and Chemical Profiling of the Leaves of *Liriodendron tulipifera* Against MRSA

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Antimicrobial resistant bacteria have been associated with 1.27 million annual deaths globally, a number that's risen to nearly 5 million in 2019. Natural products serve as a historically proven source of diverse chemical scaffolds with potent antimicrobial properties, many of which have been successfully developed into clinical antibiotics. The objective of this study is to use bioassay-guided fractionation and liquid chromatography-mass spectrometry (LC-MS) to identify antimicrobial compounds in *L. tulipifera* leaves active against methicillin-resistant *Staphylococcus aureus* (MRSA). Dried *L. tulipifera* leaves were subjected to methanolic extraction followed by liquid-liquid extraction. The semipolar partition was fractionated using normal phase flash column chromatography, where fraction 3 (tested at 200 μg/mL) inhibited the growth of MRSA by 61%. Another chromatographic separation employed on fraction 3 afforded 15 subfractions, where fractions 4 and 6 (both tested at 200 μg/mL) displayed mild antimicrobial activities (25% and 57% respectively). These active fractions were analyzed using LC-MS to facilitate dereplication, allowing for the putative identification of known compounds previously reported within the genus *Liriodendron* based on high-resolution mass spectrometry data. Ongoing research aims to isolate and purify these target molecules to facilitate full structural elucidation using NMR spectroscopy.

P-126 – Elhadj Saidou Balde

Pharmacological Evaluation of Guinean Medicinal Plants Used in Male Reproductive Disorders and Prostate Cancer

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Male reproductive disorders are a major public health concern in Guinea, where access to conventional therapies remains limited. As a result, populations widely rely on traditional medicinal plants. We conducted an ethnobotanical survey to identify species commonly used to treat male reproductive disorders. Extracts from these species were evaluated for their antioxidant, anti-inflammatory properties, as well as for their in vitro anticancer activity against DU-145, PC3, MCF-7, A549, and DLD-1cell lines. Several plant extracts exhibit significant antioxidant and anti-inflammatory activities. *Annona senegalensis* and *Croton hirtus* showed moderate antiproliferative effects on prostate cancer cells. These effects were associated with phenolic content, modulation of reactive oxygen species, cell cycle arrest, and induction of apoptosis. Overall, these findings support the traditional use of these plant and highlight their potential as sources of bioactive compounds for the management of prostate-related disorders and male infertility.

P-127 – Hyeon-Mi Kim

Multi-Bioactive Effects of *Tetraselmis* sp. Extract: Antioxidant, Antiviral, and Anti-Inflammatory Properties

Hyeon-Mi Kim[1], Eun-A Kim[1], Nalae Kang[1,2], Areumi Park[1] , Jun-Ho Heo[1] and Soo-Jin Heo [1,2,], [1]Jeju Bio Research Center, Korea Institute of Ocean Science and Technology (KIOST) Jeju 63349, Republic of Korea, [2]Department of Biology, University of Science and Technology (UST), Daejeon 34113, Republic of Korea*

Tetraselmis species (sp.), which are green microalga, were considered a promising source of bioactive compounds for pharmaceutical and food applications. This study evaluated the antioxidant, antiviral, and anti-inflammatory activities of *Tetraselmis species* (sp.) extract (TEE). TEE exhibited strong 2,2-diphenyl-1-picryl-hydrazyl-hydrate radical and hydrogen peroxide scavenging activities and significantly reduced plaque formation in vaccinia virus-infected Vero E6 cells. In LPS-stimulated RAW 264.7 cells, TEE inhibited nitric oxide (NO) production, enhanced cell viability, and downregulated the expression of iNOS and pro-inflammatory cytokines (TNF-α, IL-6, and IL-1β) via MAPK and NF-κB signaling pathways. In a zebrafish model, TEE increased survival rates and decreased cell death and NO production. High-performance liquid chromatography analysis confirmed the presence of lutein in TEE. These findings suggest that lutein-enriched TEE is a potent antioxidant, antiviral, and anti-inflammatory agent with potential for sustainable industrial applications.

P-128 – Areumi Park

Marine Microalgae-Derived Bioactive Extracts for the Development of Serum-Free Media in MDCK and Vero Cell Cultures

Areumi Park [1], Seong-Yeong Heo [1,2], Jun-Ho Heo[1], Hyeon-Mi Kim[1] and Soo-Jin Heo [1,2]. [1] Jeju Bio Research Center, Korea Institute of Ocean Science and Technology (KIOST), Jeju 63349, Republic of Korea [2] Department of Marine Technology & Convergence Engineering (Marine Biotechnology), University of Science and Technology (UST), Daejeon 34113, Republic of Korea*

The development of serum-free media is critical to advance cell culture techniques used in viral vaccine production and address the ethical concerns and contamination risks associated with fetal bovine serum. This study evaluated the effects of marine microalgae-derived bioactive extracts and growth factor cocktails on the activity of MDCK and Vero cells. Five marine microalgal species were used: *Spirulina platensis* (SP), *Dunaliella salina* (DS), *Haematococcus pluvialis* (HP), *Nannochloropsis salina* (NS), and *Tetraselmis* sp. (TS). DS had a proliferation rate of 149.56% and 195.50% in MDCK and Vero cells, respectively, compared with that in serum-free medium. Notably, DS and SP extracts significantly increased superoxide dismutase activity, which was 118.61% in MDCK cells and 125.63% in Vero cells for SP, indicating a reduction in intracellular oxidative stress. Marine microalgal extracts, especially DS and SP, are feasible alternatives to FBS in cell culture as they promote cell proliferation, ensure safety, and supply essential nutrients while reducing oxidative stress.

P-129 – Emma Swystun

Accelerating Natural Product Discovery from Coral-Associated Bacteria Using Integrated HP-TLC Bioautography and LC-MS/MS Metabolomics

Emma Swystun[1], Wilmer Perera[3], Blake Ushijima[2], Wendy Strangman[1]; UNCW Department of Chemistry and Biochemistry[1], UNCW Department of Biology[2], CAMAG scientific[3]

Traditional bioassay-guided fractionation is central to natural product discovery but can be time- and resource-intensive when applied to complex extracts. This research presents an integrated workflow combining high-performance thin layer chromatography HPTLC-based bioautography with LC–MS/MS metabolomics to accelerate metabolite identification. Chemical extracts from coral-associated bacterial strains were screened for antibacterial activity against the coral pathogen *Vibrio coralliilyticus* OCN008 using HPTLC, enabling direct visualization of bioactive zones. In parallel, extracts were evaluated for metal-chelating activity using an HPTLC adaptation of the Chrome Azurol-S (CAS) assay. Active extracts were further separated chromatographically and re-screened for bioactivity, and individual bands were extracted and analyzed via LC–MS/MS for rapid chemical characterization without extensive purification. Mass spectrometry-based dereplication enabled identification of known compounds, while untargeted metabolomics facilitated the discovery of unknown compounds. This streamlined platform improves prioritization of bioactive compounds, reduces analysis of inactive material, and links biological activity to molecular identity early in the discovery process. Multiple known compounds, including isatin and nocardamine, were rapidly dereplicated, minimizing time spent on re-isolation. Bands not dereplicated by LC–MS library searches were prioritized for purification and structural elucidation. Overall, this approach enables more efficient discovery of biologically relevant natural products by focusing efforts on novel and bioactive metabolites.

P-130 – Jun-Ho Heo

Zika Virus NS3/RdRp Proteins Targeted by Gallic Acid In Silico Analysis and Confirmation of Antiviral Activity via In Vitro

Jun-Ho Heo[1], Nalae Kang[1,2], Areumi Park[1], Hyeon-Mi Kim[1], Soo-Jin Heo[1,2]. [1]Jeju Bio Research Center, Korea Institute of Ocean Science and Technology (KIOST), Jeju 63349, Republic of Korea [2]Department of Marine Technology & Convergence Engineering, University of Science and Technology (UST), Daejeon 34113, Republic of Korea*

Zika virus (ZIKV) is a major global health concern with no clinically approved antiviral therapy, prompting evaluation of gallic acid (GA), a naturally occurring phenolic compound, using integrated in silico and in vitro approaches. Molecular docking and dynamics simulations showed stable binding of GA to the catalytic domains of ZIKV NS3 and RNA-dependent RNA polymerase (RdRp), while in vitro assays demonstrated dose-dependent suppression of viral replication in Vero E6 cells, with more than 98% reduction in plaque-forming units and NS1 mRNA expression at 100–200 μM and modulation of host antiviral responses including TNF-α, IFIT, IFITM, OAS, and PKR, indicating potent anti-ZIKV activity through both direct inhibition of viral non-structural proteins and regulation of host antiviral pathways.

P-131 – Soo-Jin Heo

RNA-Seq-Based Investigation of the Antiviral Activity of Chlorophyll A derived from *Tetraselmis* sp.

Soo-Jin Heo[1,2], Jun-Ho Heo[1], Areumi Park[1], Hyeon-Mi Kim[1], Nalae Kang[1,2]. [1]Jeju Bio Research Center, Korea Institute of Ocean Science and Technology (KIOST), Jeju 63349, Republic of Korea, [2]Department of Marine Technology & Convergence Engineering, University of Science and Technology (UST), Daejeon 34113, Republic of Korea*

Tetraselmis sp., a marine microalga amenable to mass cultivation, exhibited antiviral properties partly attributed to chlorophyll a, although the underlying mechanisms remain unclear. To investigate the molecular basis of this activity, transcriptomic analysis was conducted using untreated uninfected cells, ZIKV-infected cells, and chlorophyll a-treated ZIKV-infected cells. The results showed that 5 μM chlorophyll a altered genes associated with interferon-inducible antiviral responses and significantly enriched biological processes related to responses to external and biotic stimuli. In particular, chlorophyll a restored key interferon-stimulated genes, including IFIT1, IFIT2, IFIT3, and IFIT5, consistent with quantitative PCR results, suggesting that its antiviral activity is primarily mediated through modulation of interferon pathways.

P-132 – Hyeon Du Jang

Anti-Inflammatory Effects of *Alnus incana* subsp. *hirsuta* and *Ulmus macrocarpa* Extracts in Periodontal *in vitro* Inflammation Models

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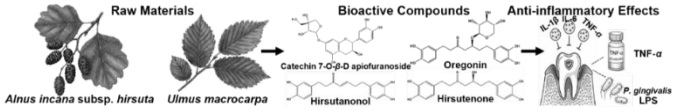
In this study, extracts derived from *Alnus incana* subsp. *hirsuta* (AH) and *Ulmus macrocarpa* (UM) were evaluated for anti-inflammatory effects using *in vitro* human gingival fibroblast-based inflammation models. Two inflammatory models were established by stimulation with TNF-α and LPS. Distinct anti-inflammatory activity was observed in both AH and UM extracts, which may be attributed to major bioactive compounds such as oregonin, hirsutanonol, hirsutenone, and catechin-7-O-β-D-apiofuranoside. These findings suggest that both extracts possess anti-inflammatory potential against periodontal disease, indicating their potential for the development of natural medicines for periodontal disease. Acknowledgements: This study was conducted with the support of the R&D program for Forest Science Technology (RS-2026-25501499, RS-2026-25506646).



P-133 – Alan López Martínez

Dual Vasorelaxant Mechanism of Gymnoascolide A in Rat Aorta

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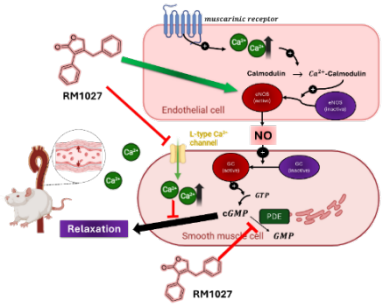
Gymnoascolide A (RM1027), a fungal butenolide, exhibits vasodilatory activity. Its mechanism was evaluated in isolated rat aortic rings. RM1027 induced concentration-dependent relaxation, with higher efficacy in endothelium-intact vs. denuded rings, indicating partial endothelial involvement. Inhibition with L-NAME and ODQ reduced the response, supporting participation of the NO–sGC–cGMP pathway. Greater relaxation in KCl- vs. noradrenaline-induced contractions, along with inhibition of FPL-64176 responses, suggests modulation of Ca^{2+} influx through L-type channels. These results indicate a dual mechanism involving endothelial signaling and direct inhibition of Ca^{2+} entry in vascular smooth muscle.



P-134 – Sung Chul Park

Expanded Substrate Scope of Fungal Isocyanide Synthase Reveals l-DOPA–Derived Isocyanide in *Trichoderma asperellum*

Sung Chul Park[1], Grant R. Nickles[1], and Nancy P. Keller[1,2,*] . [1]Department of Medical Microbiology and Immunology, University of Wisconsin-Madison, WI. [2]Department of Plant Pathology, University of Wisconsin-Madison, WI

Isocyanide synthases (ICSs) are key enzymes in the biosynthesis of isocyanide-derived natural products; however, their substrate scope and broader metabolic roles in fungi remain poorly understood. In this study, we investigated the function of an ICS in *Trichoderma asperellum* with a focus on aromatic amino acid–derived isocyanides. Using targeted metabologenomics and gene deletion, we identified an ICS responsible for isonitrin biosynthesis. Beyond this, untargeted metabolomics revealed that the same ICS also generates previously uncharacterized aromatic isocyanides, including an isocyanide l-DOPA. The structure was validated through chemical synthesis of *N*-formyl-l-DOPA and comparative analysis, providing the first experimental evidence of l-DOPA–derived isocyanide formation in microbe. Our findings expand the known substrate scope of fungal ICS and establish a direct connection between aromatic amino acid metabolism and isocyanide biosynthesis. The discovery of l-DOPA–derived isocyanide highlights new opportunities for exploring its applications in fungal biology and chemical biology.

P-135 – Rachel Washburn

Microbes, Minerals, and Metabolites: Uncovering Bioactive Potential in Kentucky Cave Systems

Rachel L. Washburn[1,2], Jason Backus[1], Andrea Conner[1], Sahar Mofidi Tabatabaei[2], Michael M. McGlue[1], Kevin Tidgewell[2]. [1]Kentucky Geological Survey, University of Kentucky, Lexington, KY 40508, USA. [2]College of Pharmacy, University of Kentucky, Lexington, KY 40508, USA.

Subsurface environments such as oligotrophic cave systems are underexplored reservoirs of microbial and chemical diversity. These environments are hypothesized to host distinct geochemical conditions associated with unique microbial communities and metabolomic profiles. Relationships among geochemistry, microbial diversity, and metabolite production were evaluated across cave systems in Kentucky, USA. Sediment and rock samples were characterized for bulk mineralogy, elemental composition, and carbon and sulfur content, and water samples for major ion chemistry. Microbial communities were profiled using 16S and 18S rRNA gene sequencing to assess alpha and beta diversity, and extracted metabolites were analyzed using untargeted mass spectrometry with molecular networking to identify structurally related molecular families. Sites with similar bulk mineralogy host distinct microbial communities, indicating that mineral composition alone does not explain community structure. Instead, geochemical context, particularly ion composition and carbon sulfur pools, appears to play a stronger role in shaping microbial assembly. Metabolomic patterns reflect this, with differences in molecular network complexity and connectivity aligning with shifts in microbial composition. The long-term goal is to build a predictive framework integrating microbiological and geochemical context to identify high-potential environments for novel bioactive compound discovery.

P-136 – Paige Banks

Heterologous Expression Enables the Discovery and Diversification of New Lantibiotics

Paige Banks[1], Abigail Alford[1], David A. Widdick[1], Eleni Vikeli[1], Sibyl F. D. Batey[1], Martin Rejzek[1], Edward Hems[1], Carlo de Oliveira Martins[1], Stefano Donadio[2], Margherita Sosio[2], Matthew I. Hutchings[1] & Barrie Wilkinson[1]. [1]John Innes Centre, Norwich Research Park, Norwich NR4 7UH, UK, [2]NAICONS Srl, 20139, Milan, Italy

There is an urgent need to develop new antibiotics as resistance to existing classes continues to increase. Lanthipeptides, also known as lantibiotics, are a promising group of ribosomally synthesised and post-translationally modified peptides (RiPPs) with potent antibacterial activity. Their development has been limited by low natural production levels and the difficulty of isolating and genetically manipulating native producers. However, their biosynthetic pathways are well suited to engineering, enabling structural diversification. In this work, we describe a heterologous expression system for the production and diversification of cinnamycin-like lantibiotics in the genetically tractable host *Streptomyces coelicolor*. Biosynthetic gene clusters were identified through genome mining, and core peptide sequences were introduced into the expression platform for production. This approach enabled the discovery of several new cinnamycin-like lantibiotics. One example was produced at scale, isolated, and structurally characterised using HPLC, LC-MS, and NMR, showing promising antibacterial activity against MRSA and high production yield.

P-137 – Ezequiel Cruz Rosa

Into The Abyss: Bio-Prospecting Marine Fungi of the Deep Sea

Ezequiel Cruz Rosa[1], Paola Herrera Figueira[1], Sophia Guillisano[1],Sofia Ruz Padilla[1] , Nhu Vu Lan Nguyen[1], Priscila Halicki[2], Kyle Rhode[2], Bill Baker[1]. [1]Department of Chemistry University of South Florida, USF Cherry Dr, Tampa, FL 33620, USA, [2]Division of Immunity and Pathogenesis, Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, Florida 32827, USA

Since the discovery and widespread implementation of antibiotics in the 20th century, many bacterial diseases, including tuberculosis, have been effectively controlled in affluent countries; however, tuberculosis remains among the top 15 causes of death worldwide. The emergence of drug-resistant strains, particularly against frontline therapeutics such as rifampicin, highlights the urgent need for new antibiotics. Deep-sea fungi represent a promising and underexplored source of novel bioactive compounds, having evolved over millions of years under extreme conditions and constant microbial competition. This research

aims to investigate bioactive secondary metabolites from a library of 256 deep-sea fungal extracts and evaluate their antibacterial activity against *Mycobacterium tuberculosis*, while assessing selectivity using A549 human lung epithelial cells. Active compounds will be isolated through bioassay-guided fractionation, and dereplication of known metabolites will be facilitated using molecular networking and AI-driven tools, accelerating the identification of novel chemical entities.

P-138 – Kirk Maxey

Exploring Microbial Dark Matter: Isolation of a Novel Streptomyces Strain Exhibiting Potent Antibacterial Activity Against Multidrug-Resistant Staphylococcus Species

Donnie Alverson[1], Aaron Koch[2], Ranga Rao Ravu[2], Kirk Maxey[2], and Lia Danelishvili[11]Department of Biomedical Sciences, Gary R. Carlson, MD, College of Veterinary Medicine, Oregon State University, Corvallis, OR. [2]Cayman Chemical Company, Ann Arbor, MI

Widespread antibiotic resistance is outpacing the discovery of new antibiotics, creating a public health emergency. Since the golden age of antibiotics discovery of the mid-20th century, the discovery and clinical development of new antibiotics have relied heavily upon the screening of bioactive secondary metabolites produced by soil microorganisms. However, these discovery efforts focused predominantly on screening of metabolites from culturable soil bacteria which represent a minor component of the total environmental microbial diversity. Overreliance on this limited pool of biological and chemical diversity has resulted in a sharp decrease in the number of new antimicrobial natural products being discovered and prompted new methods for investigating the underexplored natural product chemical space possessed by previously uncultured soil microorganisms. Herein, we report the use of the Isolation Chip (iChip) cultivation method for the discovery of a novel environmental Streptomyces strain possessing putatively novel antimicrobial metabolites with strong inhibitory activity against multidrug-resistant strains of Staphylococcus spp.

P-139 – Albebson Lim

Differential Mechanism of Gram-negative Bacterial Membrane Lipid Disruption by Lipopeptide Antibiotics, Colistin and Turnercyclamycin

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Lipopeptide antibiotics have been used for decades to combat drug-resistant bacteria, though toxicity and resistance remain significant hurdles. In this study, we compared the mechanisms of two seemingly related lipopeptides: the last-resort drug colistin, and shipworm symbiont-derived antibiotic turnercyclamycins. Colistin kills rapidly by binding directly to LPS and destroying both the outer and cytoplasmic membranes. However, turnercyclamycins exhibit no measurable direct binding to LPS, and cause delayed outer membrane disruption. Phospholipidomic analysis reveals that turnercyclamycins are instead modulated by specific phospholipids, altering membrane lipid homeostasis. This structurally driven, fundamentally distinct mode of action provides insight into the unique therapeutic profile of turnercyclamycins and offers a valuable blueprint for designing safer, more targeted lipopeptide antibiotics.

P-140 – Lewis Marquez

MicroED-Enabled Discovery of Small Molecule Antifungals

Lewis Marquez[1], Ella Vardeman[1], Cassandra L. Quave[1], Emory University School of Medicine, Atlanta, GA 30322, USA

Natural products are characterized by a great diversity of scaffolds and high structural complexity and constitute an important source for the inspiration and development of new drug candidates. The isolation of natural products often involves bioassay-guided fraction, which is tedious with many reiterative steps that slows the drug discovery process. We aim to accelerate the natural product antifungal drug discovery process by coupling Microcrystal electron diffraction (MicroED) and MS2 (tandem mass spectrometry) to resolve the structure of novel small molecules from chemically complex crude extracts. To achieve this, we have developed a new workflow that works in tandem with MS2 and MicroED to quickly identify samples from microscale (5 mg) fractionations of plant extracts. We have modified our workflow to produce fractionated extracts collected over two 96-well plates to produce 188 time-selected fractions – with the goal of increasing the resolution and purity within individual wells. These plates are then resuspended and aliquoted into antifungal assay plates for testing against *Candida albicans* to identify wells of interest. Positive hits are then subjected to MS2 for dereplication and duplicate plates are screened for the presence of microcrystalline solids and/or subjected to various conditions to induce crystallization. These microcrystals (~500 nm) are then examined via MicroED using an XtaLAB Synergy-ED electron diffractometer to solve their structure without the need for iterative rounds of purification and isolation.

P-141 - Daniel May

Bee Environment-Isolated Novobiocin Inhibits Honey Bee Pathogen *Paenibacillus larvae*

Akshara Oruganti[1], Andrea McKim[1], Rachel J. Ende[1], Daniel S. May[1]. [1]Washington College, Chestertown, MD 21620

Honey bees (*Apis mellifera*) are among the most critical pollinators, pollinating approximately $15 billion worth of crops each year. Many factors have led to fluctuating bee populations in recent years, including increased pathogen loads. One of the most damaging bee hive pathogens is *Paenibacillus larvae*, the causative agent of American Foulbrood. The *Streptomyces*-produced natural product oxytetracycline is one of the only treatment options for American Foulbrood; however, resistance to this antibiotic is increasing in *P. larvae*. In our search for new antibiotics to treat this bee disease, we isolated an inhibitory *Streptomyces niveus* WCID1014 from the foraged pollen of an American bumble bee (*Bombus pensylvanicus*). Genomic analysis of WCID1014 by AntiSMASH identified a biosynthetic gene cluster for the antibiotic novobiocin. Production of novobiocin by WCID1014 was confirmed by LC-MS/MS and molecular networking analysis with GNPS 2.0. Purchased novobiocin was used to validate the anti-*P. larvae* activity and was found to have a similar IC_{50} to the currently used antibiotic oxytetracycline. Novobiocin and oxytetracycline have been shown to act synergistically against certain pathogens, so we used a DiaMOND assay to test whether these antibiotics could be used synergistically to inhibit *P. larvae*. We found that novobiocin and oxytetracycline do not show a synergistic effect against *P. larvae* and appear to act additively. Novobiocin may represent a promising new treatment for American Foulbrood, especially in the face of growing oxytetracycline resistance in *P. larvae*.

P-142 – Bill Nguyen

Unlocking the Potential of Marine Fungi for the Discovery of Anti-Tuberculosis Compounds

Bill Nguyen[1], Ezequiel Cruz Rosa[1], Priscila Halicki[2], Kyle Rhode[2], Bill Baker[1]. [1]Department of Chemistry University of South Florida, USF Cherry Dr, Tampa, FL 33620, USA, [2]Division of Immunity and Pathogenesis, Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, Florida 32827, USA

Antimicrobial resistance is a growing global health threat, with tuberculosis (TB), caused by *Mycobacterium tuberculosis*, posing a major challenge due to rising drug resistance and prolonged, toxic treatments. Marine-derived fungi are a promising source of novel anti-TB compounds due to extreme environmental conditions. To enhance chemical diversity, the fungi were cultured under epigenetic modification conditions (DNMT and HDAC inhibition). Extracts were purified using chromatography, evaluated for bioactivity, and structurally characterized using mass spectrometry and NMR, alongside dereplication tools such as SMARTNMR, DeepSAT, and SPECTRE.

P-143 – Sofia Avelina Pelera

Understanding the Antibiotic Activity Contained in the Carlson Lab Natural Products Library

Sofia Avelina Pelera, Skylar Carlson. Department of Chemistry, University of the Pacific, Stockton, CA 95211

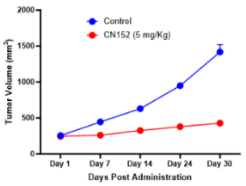
Antimicrobial resistance (AMR) is an issue of global concern where microorganisms that cause infections in humans become resistant to available antimicrobial drugs. This issue is further exacerbated because bacteria develop resistance faster than new drugs are being discovered and approved. Natural products serve as "scaffolds" for a majority of synthetic drugs, and are the origin of numerous approved antibiotics by the United States Food and Drug Administration (FDA). Currently, the Carlson Natural Products Library contains approximately 650 fractions and extracts from bacteria, fungi, algae, and cyanobacteria, which were fractionated and tested for antimicrobial activity against *E. coli, Salmonella* sp., *Bacillus subtilis, and Staphylococcus aureus*. Seven fractions displayed antibiotic activity against either gram-positive or gram-negative bacteria. These were then tested against a larger panel of ESKAPE pathogens, which included *Staphylococcus epidermidis, Enterobacter aerogenes,* and *Acinetobacter baylyi* to determine the specificity of the antibacterial activity against either Gram-negative or Gram-positive bacteria. Actinomycete strain C003 inhibited gram-positive bacteria selectively at a minimum inhibitory concentration or MIC of 2.0μg/mL. This strain was then grown on a large-scale (6 L) for further analysis. The resultant extract was fractionated and tested again for biological activity. Fraction 2 from a silica column had the most significant activity. This fraction was then further separated using reversed-phase high-pressure liquid chromatography (HPLC) to isolate UV-active metabolites. This poster will present my work toward identifying the antibiotic activity in the Carlson Lab Natural Products Library and discuss the isolation and activity of compounds produced by this strain.

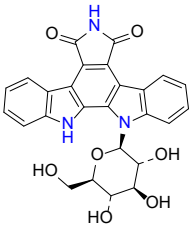
P-144 – John Beutler

A Rebeccamycin Analogue is Active in Mouse Mesothelioma Models

Vivek Singh[1], Khaled A. Shaaban[2], Aarajana Shrestha[2], Md. Rokon Ul Karim[2], Anand Singh[1], Shivani Dixit[1], Nathanael D. Pruett[1], Brice A. P. Wilson[3], Chuong D. Hoang[1], Jon Thorson[2], and John A. Beutler[3]. [1]Thoracic Surgery Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD 20892, [2]College of Pharmacy, University of Kentucky, Lexington, KY 40506, [3]Molecular Targets Program, Center for Cancer Research, National Cancer Institute, Frederick, MD 21702

A high throughput screen for inhibitors of mesothelioma cell growth, but not normal pleural cell growth, identified a known indolocarbazole, BMY 41219 (CN152), isolated from *Actinomadura melliaura* as active. Sarcomatoid, epithelioid and mixed cell types were sensitive in the mid-nanomolar range, whereas normal pleural cells were unaffected at 10 μM. The well-known indolocarbazoles rebeccamycin and becatecarin were equally cytotoxic in both normal pleural and mesothelioma cell lines. The compound was synthesized at 100 mg scale, a formulation was developed for parenteral use, and two mouse xenografts were performed with excellent results.





P-145 – Sang Kook Lee

Antitumor Activity of α-Terthienylmethanol via Suppression of Wnt/β-catenin Signaling Pathway and Galectin-3 in Human Colorectal Cancer Cells

Chaewon Ock[1], So-Ri Son[2], Dae Sik Jang[2], and Sang Kook Lee[1]. [1] College of Pharmacy, Natural Products Research Institute, Seoul National University, Seoul 08826, Republic of Korea, [2] College of Pharmacy, Kyung Hee University, Seoul 02447, Republic of Korea

Colorectal cancer (CRC) is the second leading cause of cancer death globally with early metastatic progression. Aberrant Wnt/β-catenin signaling plays a central role in CRC progression, and galectin-3 promotes metastasis by facilitating β-catenin nuclear translocation. Although several Wnt/β-catenin targeting agents are under development, effective therapeutic candidates are limited. α-Terthienylmethanol (**1**), a terthiophene isolated from *Eclipta prostrata* (False Daisy), has been reported as anti-cancer effects in gynecologic malignancies, but its molecular mechanism against CRC remains to be explored. **1** inhibited CRC cell proliferation, particularly in β-catenin mutant HCT116 and LS174T cells, and suppressed β-catenin signaling by modulating the destruction complex, especially Axin2 and active β-catenin, and galectin-3 expression. Immunofluorescence and reporter gene assays confirmed that **1** inhibited Wnt3a-induced nuclear translocation and transcriptional activity of β-catenin. In addition, **1** suppressed invasion and metastasis-associated EMT biomarker expression, induced apoptosis, and exhibited antitumor activity in vivo xenograft model. These findings suggest that **1** exerts antitumor and antimetastatic effects through inhibition of Wnt/β-catenin signaling in CRC cells.

P-146 – Young-Won Chin

Betulinic Acid Regulates PCSK9 and LDLR through an FXR-Related Mechanism with Functional SHP Dependence in Hepatocytes and HFD Mice

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Proprotein convertase subtilisin/kexin type 9 (PCSK9) promotes lysosomal degradation of the low-density lipoprotein receptor (LDLR) and is a key regulator of hepatic cholesterol homeostasis. Betulinic acid (BA) reduced PCSK9 expression and secretion while increasing LDLR expression, and attenuated atorvastatin-induced PCSK9 upregulation. Transcriptomic analysis suggested an farnesoid X receptor (FXR)-associated transcriptional signature in BA-treated cells, including decrease of CYP7A1, CYP8B1, and PCSK9 and increase of SLC51B expression. Pharmacological modulation of FXR influenced the BA response: the FXR agonist GW4064 reduced PCSK9 secretion, whereas the FXR antagonist Z-guggulsterone increased it and partially blunted the effect of BA. Small heterodimer partner (SHP) knockdown attenuated BA-mediated PCSK9 suppression and LDLR induction. In HFD mice, BA reduced hepatic PCSK9 expression and restored LDLR expression along with SHP dependence. These findings indicate that BA suppresses PCSK9 through an SHP-linked mechanism associated with FXR signaling.

P-147 – Jason Clement

Improved Production and In Vivo Anti-apicomplexan Activity of Tartrolon E from *Teredinibacter turnerae* T7901

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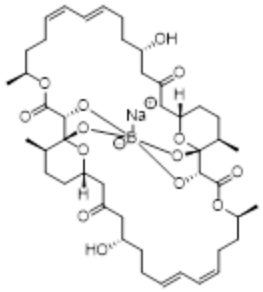
Apicomplexan parasites of genus *Cryptosporidium* are a leading cause of water-borne diarrhea and are a threat to immunocompromised humans. Tartrolon E (TrtE, **1**) is a boronated polyketide produced by the marine bacterium *Teredinibacter turnerae*. TrtE has nanomolar anti-apicomplexan potency against several parasites of interest for human and animal health. In bioreactors, the production of TrtE by *T. turnerae* T7901 reaches about 80 mg/L. In neonatal mice infected with *Cryptosporidium parvum*, oral administration of 4 or 40 mg/kg gave 95% or more reduction in parasite burden. NSG mice infected with *C. parvum* were dosed twice a day for two days at 25 mg/kg, which gave about 50% reduction in parasite burden. These results

suggest that further investigation of the mechanism of action of TrtE is warranted for the development of anti-apicomplexan therapeutics.



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P-148 – Ademola Ayeleso

Attenuation of Scopolamine-Induced Oxidative Stress in *Drosophila melanogaster* by *Thaumatococcus daniellii* Leaf Extract: Relevance to Neuroprotection

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Oxidative stress is a pathological imbalance between reactive oxygen species (ROS) production and antioxidant defense in the body. Furthermore, oxidative stress is one of the mechanisms involved in scopolamine-induced neurotoxicity. This study investigated the potential of *Thaumatococcus daniellii* leaf extract in attenuating oxidative stress in *Drosophila melanogaster* exposed to scopolamine-induced neurotoxicity. Phytochemical analysis of *T. daniellii* leaf extract was done using High Performance Liquid Chromatography (HPLC). The activities of the antioxidant enzymes and levels of oxidative stress biomarkers were investigated using standard procedures. The phytochemical screening revealed diverse bioactive compounds, with quercetin (49.54% peak area) as the most abundant. Furthermore, our results revealed that scopolamine exposure significantly reduced the activities of antioxidant enzymes (catalase, superoxide dismutase, and glutathione peroxidase), glutathione and thiol levels as well as increasing lipid peroxidation. Treatment with the *T. daniellii* leaf extract restored the activities of the antioxidant enzymes; enhanced glutathione and thiol levels; and reduced lipid peroxidation. Conclusively, our study supports that *T. daniellii* leaf extract could have the potential to ameliorate for oxidative stress-related neurodegeneration.

P-149 – Rasha Bashatwah

Characterizing Progesterone Receptor Modulators from *Paeonia lactiflora* Roots

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Botanical preparations are increasingly studied as modulators of progesterone receptor (PR) function may have therapeutic value in conditions such as dysmenorrhea. *Paeonia lactiflora* Pall. (white peony) A traditional Chinese medicinal widely used for dysmenorrhea was investigated to identify bioactive small molecules that modulate PR and glucocorticoid receptor (GR) signaling. Extracts were screened using a luciferase reporter assay in a bioassay-guided fractionation workflow. The parent extract reduced progesterone-induced activity, consistent with PR antagonism. Paeoniflorin inhibited GR in Ishikawa PR-B and OVCAR5 cells and PR in T47D A1-2 (GR^+) but not in parental T47D (GR^-), indicating receptor crosstalk. From aqueous fractions, paeoniflorin sulfite (fraction 5) was inactive but identified as a new compound. Bis-2(ethylheptyl) phthalate was identified in fraction 7 and its presence was reconfirmed in an independently prepared extract batch suggesting it is from the botanical itself. Bis-2(ethylheptyl) phthalate in the fraction suppressed more than 65% of progesterone-induced signaling. This finding is notable because plasticizers and their metabolites are well-characterized endocrine disruptors that can dysregulate PR-driven proliferation. Further studies are planned to identify the PR regulation from Bis-2(ethylheptyl) phthalate exposure in multiple cell types including endometrial and breast cancer cells.

P-150 Alyssa Hardy

Toward a More Comprehensive Understanding of Flavonoids as Progesterone Receptor Agonists

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Botanical supplements are consumed by women across the globe to treat symptoms of gynecological disorders such as hot flashes, menstrual pain/irregularity, or infertility. The constituents responsible for these observed endocrine modulating effects are known as phytosteroids, a diverse class of plant metabolites that bind to endogenous steroid receptors (i.e., estrogen (ER) and progesterone (PR) receptors) and trigger downstream signaling events. Thus far, phytoestrogens have been extensively characterized, while their progestogenic counterparts remain largely understudied. Progestins have widespread implications in women's health, including use in contraceptives, hormone replacement therapy, and prevention of preterm birth and uterine hyperplasia. Our team previously identified the progestogenic activity of six flavonoids across several botanical sources. Given this trend, we screened a commercial library of 536 flavonoids for PR agonist activity. Preliminary evidence from this screen suggests correlations between PR agonist activity and flavonoid sub-class. Future analyses will investigate mechanisms of action using *in silico* molecular docking and *in vitro* metabolism studies. As a whole, this analysis will provide a more comprehensive understanding of the potential PR activity of flavonoid-containing botanicals.

P-151 – Axel Lozano-Ortiz

3*R*-Viscosalactone B is Detected in Human Plasma and Urine Following Ingestion of an Ashwagandha Supplement

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Withanolides are an important group of bioactive phytochemicals found in ashwagandha (*Withania somnifera* (L.) Dunal; WS), a best-selling dietary supplement in the USA. However, data on the oral absorption, metabolism and urinary excretion of withanolides in humans remains limited. Healthy older adults were administered capsules of 240 or 480 mg of Shoden®, a commercial extract of WS roots and leaves. Using liquid chromatography coupled to multiple reaction monitoring mass spectrometry (LC-MRM-MS), we examined participant plasma and urine samples for the presence of several withanolides, including 2,3-didehydrosomnifericin (2,3-DHS), the expected product of epoxide hydrolysis of withaferin A (WFNA), a major withanolide in Shoden®. While 2,3-DHS was not detected in plasma or urine, an abundant peak with slightly shorter retention time (Rt) was detected using MRM transitions for 2,3-DHS. LC-high resolution mass spectrometry confirmed that the unknown compound had the same accurate mass as both 2,3-DHS and its isomer 3*R*-viscosalactone B (3RVB), and the same Rt as 3RVB, the major product of WFNA acid hydrolysis *in vitro*. The (previously unreported) presence of 3RVB in human plasma and urine may indicate its involvement in the biological activity of Shoden® and WS.

P-152 – Alana Ponte

Gut Microbiome-Mediated Transformation of Mangosteen Xanthones and its Impact on Breast Cancer Bioactivity

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Garcinia mangostana (mangosteen) is a widely used botanical supplement known for its anti-inflammatory and anticancer properties. These benefits have been attributed to bioactive polyphenolic compounds called xanthones, located within the pericarp of the fruit. Despite their potent bioactivity, the therapeutic efficacy of xanthones is hindered by low systemic bioavailability. This poor absorption is likely driven by extensive gut microbial metabolism prior to systemic circulation. However, the specific mechanisms that mediate xanthone bioavailability and bioactivity remain poorly understood. To investigate microbiome-mediated transformation of mangosteen, in vitro metabolism assays utilizing commensal human gut bacterial isolates were analyzed via liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based metabolomics. Select strains exhibited distinct metabolomic shifts following incubation with mangosteen, including marked depletion of several xanthones in post-metabolized extracts. Cytological profiling using MDA-MB-134 breast cancer cells confirmed the anticancer bioactivity of unmetabolized mangosteen, establishing a baseline to evaluate the efficacy of post-metabolized extracts across a panel of breast cancer cell lines. Ongoing studies will expand this approach to include pathogenic isolates, mixed microbial communities, and human fecal samples to better capture gut microbiome complexity. Results from this work will establish how gut microbial metabolism influences mangosteen bioavailability and bioactivity, providing broader insight into microbiome-phytochemical interactions relevant to botanical therapeutics.

P-153 – Nandakumara Sarma

Cannabinoids Content of Cannabis Flower on "Dry Weight Basis": Method-Related Variability

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The widespread use of cannabis and its constituents highlight the need to conduct research to obtain data on the safe and effective use of these products. The recent FDA Guidance "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research" provides the current Agency thinking about characterization of cannabis quality to help ensure reproducibility of research. USP proposed a General Chapter <1568> *Cannabis Inflorescence Quality Attributes for Clinical Investigations* to provide complementary and supplementary information to the information already included in the FDA Guidance with specific analytical methods and acceptance criteria to support reproducible research. Section C "Considerations of Control Status Under the CSA" of the FDA Guidance presents the Controlled Substances Act and Drug Enforcement Agency considerations for expression of D9-THC and THCA content in a sample of material "relative to the dry weight with the amount of water removed." In this regard, the FDA Guidance refers to the USP General Chapter <731> *Loss on Drying* (LOD), as well as USP General Chapter <921> *Water Determination*. The methods in these chapters can produce different results. The LOD procedure expresses the results on "dried" basis and involves drying a material at 105° C to constant weight; this is a measure of estimating loss of water as well as the volatile components such as terpenes and the loss from decarboxylation due to high temperatures. USP General Chapter <921> *Water Determination* includes Karl Fischer (KF) method that expresses results on

"anhydrous" basis. KF direct titration for water determination is typically not suitable for botanical materials because water is tightly trapped in plant cells. European Pharmacopoeia employs drying cannabis flower at 40° C under vacuum for 24 hours, to remove water without decarboxylation or loss of volatile principles. Considering the impact of various conditions on expressing the cannabinoid content in a sample of material "relative to the dry weight with the amount of water removed," a data-based guideline about what is meant by "dry weight basis" will help ensure reproducibility of the research by defining the investigational product in a consistent and accurate manner. This presentation will share results from a collaborative study on the impact of assessing moisture content under different conditions. Drying at 105° C until constant weight gave a higher estimate of loss on weight from combined loss of water and terpenes, and from decarboxylation. Drying at 40° C under vacuum for 24 hrs yielded lower estimates of moisture content when compared to KF titration in cannabis and hemp materials that are pre-dried and reconstituted to water activity of approximately 0.60. These findings support efforts to harmonize cannabinoid analysis and improve the accuracy of cannabinoid content labeling for investigational materials.

P-154 – Wendy Strangman

Integrated Approaches for Characterizing Botanicals

Sarah Barr - UNC Wilmington, Wilmer Perera – Camag Scientific, Thomas Williamson - UNC Wilmington Amala Soumyanath – OHSU, Wendy Strangman - UNC Wilmington

Botanicals and related dietary supplements are widely consumed and often contain potently bioactive compounds; however, in contrast to pharmaceuticals, they are subject to limited regulation, standardization, and fundamental evaluation of bioavailability and digestive transformation, processes that represent critical early steps in drug development. To address these gaps, we are developing complementary analytical strategies for a more rigorous and comprehensive assessment of botanical extracts and products. Our first approach developed a versatile in vitro digestion and passive permeability assay using synthetic gastrointestinal fluids under physiologically relevant fasted and fed conditions, coupled with LC–MS/MS-based workflows and molecular networking, to evaluate stability, digestive transformation, and passive permeability of botanical marker compounds and complex extracts. This platform has been applied to extracts and marker compounds of *Withania somnifera* (ashwagandha), *Rubus idaeus* (red raspberry leaf) and *Hericium erinaceus* (lion's mane) to highlight the versatility, detail, and speed in which extracts can be assessed. In a related effort, we integrated high-performance thin-layer chromatography (HPTLC), LCMS/MS, and NMR spectroscopy in a workflow to enable robust chemical characterization, particularly for complex samples lacking verified reference standards or detailed compositional information. This approach was applied to profile extracts commercial products of *Chamaelirium luteum*, also known as false unicorn. The low sample requirements of both approaches, combined with advances in chemoinformatics for molecular networking and annotation of unknown features, enable more high-throughput, high replication studies, improved statistical power, and reduction in overall time and cost.

P-155 – Anand Swaroop

Synergistic White Adipose Tissue Beiging by Four Ayurvedic Phytochemicals via Multi-Node PGC-1α Cascade Activation: An In Vitro Study

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White adipose tissue (WAT) beiging via UCP1 induction is a thermogenic strategy with metabolic potential, yet safe pharmacological inducers remain limited. The PGC-1α cascade governing UCP1 expression is regulated at four non-redundant nodes: cAMP-PKA-CREB induction, AMPK Thr172 phosphorylation, SIRT1-mediated deacetylation, and NF-κB derepression of the UCP1 enhancer. Galangin, 6-gingerol, 6-shogaol, and 5,7-dimethoxyflavone (5,7-DMF), from Ayurvedic botanicals, each engage one node. We investigated whether their combination produces synergistic UCP1 induction via coordinated multi-node activation. A full 2^4 factorial design (25 conditions) was implemented in differentiated 3T3-L1 adipocytes (n = 3 experiments) and primary human adipose stromal cells (hASCs; 3 donors). UCP1 protein and proton leak oxygen consumption rate (OCR) were primary endpoints, analysed by linear mixed models (LMM) with experiment as random intercept. Pairwise synergy was quantified by Bliss Independence, Loewe Additivity, and highest single agent models. Individual agents induced 1.6- to 2.9-fold UCP1 increases. The galangin + 6-gingerol binary achieved >3-fold induction (Bliss $\delta = 0.14$; 95 % CI [0.08, 0.21]), with stronger synergistic amplification at the p-AMPK mechanism node ($\delta = 0.18$), confirming the predicted SIRT1–LKB1–AMPK feedback loop. The quadruplet combination achieved ≥5-fold UCP1 induction, matching rosiglitazone 1 μM. Proton leak OCR increased proportionally ($r = 0.93$) and was attenuated ≥89 % in UCP1 siRNA-knockdown controls. Temporal LMM confirmed sequential cascade activation: p-AMPK, SIRT1, PGC-1α deacetylation, then UCP1. Findings were reproduced in hASCs. Multi-node PGC-1α co-targeting by this Ayurvedic phytochemical combination is a synergistic, mechanistically validated strategy for beige adipogenesis induction, supporting in vivo evaluation.

P-156 – Jianping Zhao

NMR-based Chemometrics for Characterization and Identification of Frankincense Essential Oils

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Frankincense is the common name for the aromatic resin obtained from trees of the genus *Boswellia* (family Burseraceae). Frankincense essential oil (FEO), a high-value product in the global essential oil market, is typically produced by steam distillation of frankincense gum resin. It is characterized by a warm, woody, spicy, and slightly sweet aroma and is widely used in aromatherapy, cosmetic formulations, and incense, in addition to its numerous reported pharmacological properties. Commercial FEOs are derived from various *Boswellia* species, including *B. sacra* (syn. *B. carteri*), *B. frereana*, *B. serrata*, and *B. papyrifera*, yet they are often marketed under the generic label "frankincense oil," which may lead to ambiguity and misinterpretation. The chemical composition of FEO varies substantially depending on species origin, as well as environmental and harvesting conditions. In this study, NMR spectroscopy was employed to systematically characterize the chemical profiles of FEOs derived from different *Boswellia* species, with the aim of evaluating compositional variability and distribution patterns. Comparative NMR spectral fingerprinting revealed pronounced differences among samples, including the presence of species-specific signals. Furthermore, integration of NMR data with principal component analysis (PCA) enabled effective classification of FEO samples according to botanical origin. Characteristic NMR signals corresponding to β-thujene, α-pinene, *p*-cymene, and octyl acetate were identified as key markers for distinguishing FEOs from different *Boswellia* species.