2024 American Chemical Society Cleveland Local Section Meeting in Miniature

Schedule

2:00 – 2:40	Registration (1st floor, Administration Building)
2:40 – 5:00	Technical presentations (1st floor, Administration Building)
5:15 – 6:15	Plenary Speaker (Performing Arts Center, lowest level in Administration Building)
6:30 – 7:30	Dinner (1st floor atrium, Administration Building)
7:30 – 8:00	Presentation of awards (1st floor atrium, Administration Building)

Thanks to Cleveland Chemical Association (https://www.clevelandchemicalassociation.com/) for their support in sponsoring student awards. Additional support for awards is from generous section members who wish to remain anonymous.

The American Chemical Society Cleveland Local Section Welcomes this Year's Plenary Speaker

Kelly A. Dobos

From Concept to the Consumer: The Transformative Power of Chemistry in Cosmetic Product Development

Kelly A. Dobos is a consultant cosmetic chemist and adjunct professor of cosmetic science at the University of Cincinnati. Kelly has over 20 years of expertise in developing both skin care and color cosmetic formulations working for notable consumer brands like Bonne Bell, Purell, and Jergens. She graduated from Oberlin College with a bachelor's degree in chemistry and obtained a Master of Science in pharmaceutical sciences with an emphasis in cosmetic science from the Winkle College of Pharmacy (WCOP) at the University of Cincinnati. Kelly also holds an MBA from Cleveland State University.

Kelly is an inventor with 4 patents and has written numerous technical and educational articles for cosmetic science publications like Cosmetics and Toiletries. She is also part of the American Chemical Society's expert panel and serves as a subject matter expert for magazines like Allure and New Beauty in addition to news organizations like NPR, the Washington Post, and most recently the Wall Street Journal.

Session A (Room 120, 2:40 to 5:00 – 15 min presentations including questions)

2:40 pm *Mst Ummul Khair* - Elucidating the Influence of Mobile Phase Component Polarity on the Enantiomeric Separation of Muricholic Bile Acids by RPLC-MS

3:00 pm *Weizhuan He* - Rapid Authentication of Star Anise Fruits by Real-time Mass Spectrometry with Machine Learning

3:20 pm *Arvind Singh Heer* - The Electrostatic Stimulation of Adsorbed Carbon Monoxide Oxidation on Pt in Aqueous Acidic Electrolytes

5 min break

3:45 pm *Era Srivastava, Sara Desai* - Optimizing in-vitro Quantum Dot Biosensors to Detect the Presence of Metals

4:05 pm *Weizhuan He* - Development and Validation of a UHPLC-MS/MS Method for Quantifying ISRIB in Human Plasma: Accelerating Clinical Translation of a Promising Therapeutic

Session B (Room 118, 2:40 to 5:00 – 15 min presentations including questions)

2:40 pm *Grace Hamilton* - The Postprandial Levels of the Metabolites in the Metaorganismal Trimethylamine N-Oxide (TMAO) Pathway are Altered in A Diet-, Microbe-, and Sex-Specific Manner.

3:00 pm *Ganesh Subedi* - Combined application of crosslinking mass spectrometry and molecular modeling in deciphering the structure of the mammalian multi-tRNA synthetase complex

3:20 pm *Heather R. Everson* - DNA-Origami Stability and Cellular Uptake: Exchanging the Counter-Ion

5 min break

4:05 pm *David Fan Yan* - Inhibition of HSD17B7 and SC4MOL shifts cellular sterol composition and promotes oligodendrocyte formation

4:25 pm *Ian Zagorac* - Development of Securine-derivitive containing liposomes and inhibition of Thioredoxin Reductase I as a novel treatment for Acute Myeloid Leukemia

4:45 pm *Justin Gray* - The Development and Validation of a GC-MS Method to Quantify Short and Branched Chain Fatty Acids in Human Stool and Applied to Patients with Inflammatory Bowel Disease and Healthy Controls

Session C (Room 122, 2:40 to 5:00 – 15 min presentations including questions)

2:40 pm *Austin M. Williams* - Pharmacological targeting of gut microbial phenylacetylglutamine production in cardiovascular disease

3:00 pm *Akshay Suresh Patil* - Investigating the Therapeutic Potential of Astragalus Radix in Allergic Rhinitis: Insights from Metabolomics

3:20 pm *Erin M Thorpe* - Quercetin sensitizes Burkitt lymphoma to TRAIL-induced apoptosis

5 min break

3:45 pm *Joan Bore* - Synthesis and characterization of isoindoline derivatives

4:05 pm *Aman L. Roy* - Octahedral distortions in hybrid morpholinium metal halide 2D structures, $(C_4H_{10}NO)_2MX_4$ (M = Pb, Sn; X = Cl, Br)

4:25 pm *Konpal Raheja* - Polymer Architecture Control to Tune Thermal Transition and Flow Behavior

ABSTRACTS

Session A

2:40pm **Elucidating the Influence of Mobile Phase Component Polarity on the Enantiomeric Separation of Muricholic Bile Acids by RPLC-MS**

Mst Ummul Khair, David J. Anderson

Cleveland State University

Recognizing the crucial role of drug enantiomers in clinical pharmacology, where typically only one of the enantiomers effectively interacts with the target protein for therapeutic impact, it becomes imperative for analytical methods to distinctly identify the closely related compounds within an enantiomer pair. This study aims to optimize the reversed-phase HPLC technique for separating alpha and beta muricholic bile acid enantiomers and omega and gamma muricholic bile acid enantiomers. The investigation focuses on assessing the impact of three polarity components of the mobile phase - hydrogen bond donor acidity (α), hydrogen bond donor basicity (β), and dipolarity/polarizability (π) - on enantiomer separation (selectivity factor). The experimental setup involves separating steroid isomers on a C18 column at a column oven temperature of 40°C, employing two different organic modifiers in water at a flow rate of 0.2 mL/min. Detection is performed using ESI-LC/MS, and the mobile phase's polarity is adjusted by varying proportions of binary organic modifiers. Plotting the selectivity factor against the mobile phase's polarity component values reveals a notable correlation between the dipolarity/polarizability (π) component for six different organic modifier pair combinations for the two enantiomer pairs separation. The separation of bile acid enantiomers is notably governed by the dipolarity polarity component. This finding holds practical importance, as it suggests the possibility of predicting the separation outcomes by simply examining the dipolarity values, eliminating the necessity for conducting actual experiments.

3:00pm **Rapid Authentication of Star Anise Fruits by Real-time Mass Spectrometry with Machine Learning**

Weizhuan He, Akshay S. Patil, Yan Xu

Cleveland State University

Chinese star anise, the fruit of the medium-sized evergreen Illicium verum tree, is a key ingredient in many culinary traditions worldwide. It's valued in traditional Chinese and Ayurvedic medicine for digestive benefits, anti-inflammatory properties, and as a critical source of shikimic acid for synthesizing the anti-flu medication oseltamivir. However, distinguishing edible Chinese star anise (Illicium verum) from toxic Japanese star anise (Illicium anisatum) presents challenges due to minimal morphological differences, with the latter causing severe neurotoxicity upon ingestion. Ensuring the authenticity and safety of star anise is thus paramount.

We introduce an innovative analytical framework combining a Plasmion SICRIT® ionizer for soft analyte ionization via dielectric barrier discharge (cold plasma), an Agilent high-resolution QTOF-MS analyzer for sample profiling and compound identification, and an Ensemble Bagged Tree (Machine Learning) model for pattern recognition. This approach facilitates direct, preparation-free analysis of dried star anise fruit, significantly improving the efficiency and accuracy of differentiation. We optimized the operating parameters of the SICRIT ionizer and QTOF-MS analyzer to profile star anise varieties comprehensively. The

unique and shared Chinese and Japanese star anise components were annotated using the Agilent METLIN AM database. The data obtained from the instrumental analysis was utilized for training, validating, and testing the ML model. This methodology delivers nuanced chemical profiles that distinguish the Chinese and Japanese star anise with a remarkable accuracy rate of 92.5%, offering a rapid and reliable tool for star anise authentication and safety assurance, demonstrating the potential for broader application in natural product analysis.

3:20pm **The Electrostatic Stimulation of Adsorbed Carbon Monoxide Oxidation on Pt in Aqueous Acidic Electrolytes**

Arvind Singh Heer, Daniel Scherson

Case Western Reserve University

The oxidation of adsorbed carbon monoxide on Pt electrodes, CO(ads)|Pt, in aqueous electrolytes ranks among the most studied reactions in electrocatalysis both from theoretical [Gao et al] and experimental viewpoints [Scott et al]. Much of the interest in this electron transfer process stems from the role CO(ads) plays as an impurity that affects adversely the operation of $H_2|O_2$ fuel cells. Consensus appears to have been reached regarding the role of adsorbed hydroxyl, OH.(ads) in controlling the activation and ultimate oxidation of CO(ads). The present contribution illustrates the use of electrochemical stimulation techniques developed in our laboratory [Qi et al] to explore new aspects of this process not as yet unveiled by the use of more conventional methods. As will be shown, a single stimulation lasting 140 ms can trigger the full oxidation of the entire adsorbed CO layer in CO|Pt over a subsequent period of ca. 4 s. Moreover, a potential step down to 0.4 V following stimulation, can stop the propagation of CO oxidation making it possible to monitor the possible diffusion of adsorbed CO on the surface, experiments are now in progress to image the surface of the CO|Pt electrode during and after the stimulation to monitor in real time the rates of propagation and to provide a more details theoretical model to account for this phenomenon.

3:45pm **Optimizing in-vitro Quantum Dot Biosensors to Detect the Presence of Metals**

Era Srivastava, Sara Desai, Divita Mathur

Case Western Reserve University

Exposure to metal contaminants can have severe effects on human health. Current biosensors that detect the presence of metals in fluids are largely cell-based with inefficient response times, portability issues, and lack multiplexing capabilities. Studies show that bacteria are capable of detecting and responding to metals. Bacterial operons are primarily responsible for such “sensing” mechanisms and can be harnessed and coupled with enzymatic activity to report the presence of metals in cell-free systems. Quantum dots (QDs) are semiconductor fluorescent nanoparticles that have unique and diverse optical properties that allow them to be distinguishable from each other. When excited, QDs transfer energy to other “acceptor” fluorescent molecules in close proximity, which then emit energy in the form of fluorescence. By linking a QD and acceptor molecule through DNA containing an enzyme recognition sequence, we can observe changes in fluorescence over time in the presence of the enzyme. QDs’ unique emission spectra allows for the possibility of creating a multiplexed sensor with the ability to detect multiple analytes. Thus, by coupling bacterial operons with QD-based sensors, we aim to create a multiplexed sensor that is time

efficient and can work in a cell-free environment to detect multiple heavy metals. In this talk, we discuss the optimization of the bacterial operon reporter and repressor construct system, as well as the validation of a QD-acceptor dye sensor that is responsive to enzymatic activity.

4:05pm **Development and Validation of a UHPLC-MS/MS Method for Quantifying ISRIB in Human Plasma: Accelerating Clinical Translation of a Promising Therapeutic**

Weizhuan He, Akshay S. Patil, Yan Xu

Cleveland State University

The Integrated Stress Response (ISR) is a process our cells use to protect themselves under stress. When the ISR is activated, it slows the production of proteins, the building blocks that cells use to function. ISRIB (integrated stress response inhibitor) is a molecule that can allow the cells to regain their normal function even when the ISR has been triggered. Researchers are enthusiastic about ISRIB because precise control over ISR activation could accelerate cellular recovery from stress, potentially benefiting aging-associated diseases. However, understanding ISRIB's effects on the body necessitates a robust quantification method. Currently, no validated approach is publicly available for measuring ISRIB in human plasma samples.

This study describes the development and validation of a UHPLC-MS/MS method for measuring ISRIB in human plasma, adhering to the FDA's guidance for bioanalytical method validation. ISRIB and its analogous internal standard were extracted from human plasma by liquid-liquid extraction, dried under nitrogen gas, and reconstituted in the mobile phase. Reverse-phase chromatographic separation was achieved using isocratic elution with a mobile phase containing methanol: water (v/v, 70/30). Quantification was carried out by tandem mass spectrometry operated in the multiple-reaction-monitoring mode with positive ion-spray ionization. The linear calibration range of the method for ISRIB was 0.500-1.00x10^3 nM with excellent assay accuracy, precision, recovery, and matrix factor. This validated UHPLC-MS/MS method fills a critical methodological gap, enabling precise quantification of ISRIB in human plasma. Its potential impact extends to advancing clinical investigations of ISRIB.

Session B

2:40pm **The Postprandial Levels of the Metabolites in the Metaorganismal Trimethylamine N-Oxide (TMAO) Pathway are Altered in A Diet-, Microbe-, and Sex-Specific Manner.**

Grace Hamilton[1,2,3,5*], Amanda L. Brown[1,2,3*], Jennifer D. Wilcox[2,3*], Valesha M. Province[2], Rakhee Banerjee[1,3], Amy C. Burrows[1,3], Marko Mrdjen[1,3], Nour Mouannes[1,3], Valentin Gogonea[2,3,5], Zeneng Wang[2,3], W.H. Wilson Tang[3,4], J. Mark Brown[1,3]

[1.] Department of Cancer Biology, Lerner Research Institute of the Cleveland Clinic, Cleveland, OH 44195, USA, [2.] Department of Cardiovascular & Metabolic Sciences, Lerner Research Institute of the Cleveland Clinic, Cleveland, OH 44195, USA, [3.] Center for Microbiome & Human Health, Lerner Research Institute of the Cleveland Clinic, Cleveland, OH 44195, USA, [4.] Cleveland Clinic Foundation, Heart, Vascular and Thoracic Institute, Cleveland, OH 44195, USA 5. Department of Chemistry, Cleveland State University, Cleveland, OH 44195, USA

Elevated levels of TMAO, a gut-microbial derived metabolite, have been associated with increased risk of cardiovascular disease. Here, we investigated the potential for a single meal to dynamically alter TMAO and related metabolites based on sex, diet, and microbial influences. We designed a study consisting of 35 healthy human participants assigned to either receive broad spectrum antibiotics or no antibiotics. These groups were further subdivided into diet groups, with one group eating a highly processed meal and the other group eating a whole foods meal. Blood samples were taken prior to the meal and at time points between 15 minutes and 6 hours postprandially. Plasma metabolites were quantified using liquid chromatography tandem mass spectrometry. We found that, although TMAO levels between food groups did not significantly change, separation based on sex showed that TMAO levels were significantly reduced in females at 6 hours but remained steady for males. Particularly in the processed food groups, TMAO levels were significantly lower in females than males at the 6-hour time point. Neither of these observations held true for TMAO precursors choline, carnitine, or betaine. However, plasma levels of γ-butyrobetaine showed clear diet-microbe-host interactions, with plasma levels significantly increased for males in the processed food group on antibiotics. Our results showed the postprandial levels of TMAO and its precursors dynamically change in a diet-, microbe-, and sex-dependent manner. These findings provide new insights into the postprandially levels of TMAO-related metabolites and may inform precision nutritional approaches in those who could benefit from TMAO-lowering strategies.

3:00pm **Combined application of crosslinking mass spectrometry and molecular modeling in deciphering the structure of the mammalian multi-tRNA synthetase complex**

Ganesh Subedi[1,2], Isaac Zin[1,2], Camelia Baleanu Gogonea[2], Belinda Willard[1], Valentin Gogonea[1,2*], Paul L. Fox[1,2*]

[1.] Department of Cardiovascular and Metabolic Sciences, Cleveland Clinic, Cleveland OH [2.] Department of Chemistry, Cleveland State University, Cleveland OH

The mammalian multi-tRNA synthesis complex (MSC) is a large multi-protein complex consisting of eight aminoacyl-tRNA synthetases (AARSs) and three non-synthetase proteins. The MSC has important physiological roles beyond its involvement in decoding the genetic information for protein synthesis. Despite our knowledge of the structure of individual components, the holo-MSC is a very large protein assembly (1.2-2.0 MDa), which has posed a challenge to crystallization and cryo-electron microscopy,

therefore its high-resolution structure remains unknown. To overcome this challenge, we utilized crosslinking mass spectrometry (XL-MS) in combination with molecular docking to predict the structure of the entire MSC complex. Using four different crosslinkers with a range of arm lengths (0-12 Å), we successfully mapped interaction domains of each protein component within the MSC. This information reveals structural details of the MSC and provides insights into its non-canonical physiological functions. The combination of XL-MS and molecular docking can provide a comprehensive structural blueprint of the MSC, giving insights into its intricate arrangement and biological importance.

3:20pm **DNA-Origami Stability and Cellular Uptake: Exchanging the Counter-Ion**

Heather R. Everson, Kayla Neyra, Soumya Chandrasekhar, Thorsten-Lars Schmidt, and Divita Mathur

Case Western Reserve University

Delivery systems are vital for drug facilitating to reach target tissue or cells while limiting any potential off-target interactions. To foster this voyage, the advantageous delivery system would be a biocompatible, biodegradable, programmable, consistent, and modular nanocarrier; DNA origami nanoparticles (DON) encompass the desired characteristics for a drug delivery system. Recently, DONs have shown promise as therapeutic delivery systems. DONs are a 10-100 nm large particle that can be assembled via self-assembly of a long single-stranded DNA, known as a scaffold, and a set of complementary oligonucleotides, called staples. Mammalian cells have been shown to uptake DONs via an endocytic pathway encasing the nanoparticle in an endosome. Once the endosome reaches the late endosomal phase it is merged with lysosomes containing acidic components that will degrade DONs, known as endosomal entrapment. A way to bypass endosomal entrapment is by making the endosome unstable, allowing the contents to reach the cytosol, known as endosomal escape. Studies have shown that using divalent calcium instead of divalent magnesium to accompany nucleic acid cytosolic transport fosters endosomal escape. We hypothesize that endosomal escape will be more prevalent for DONs assembled with calcium compared to magnesium due to endosomal proton influx and calcium efflux causing endosome membrane destabilization. Preliminary results presented here focus on the effect of calcium versus magnesium on DON stability and cellular uptake.

4:05pm **Inhibition of HSD17B7 and SC4MOL shifts cellular sterol composition and promotes oligodendrocyte formation**

David Fan Yan, Mathew Pleshinger, Ryan Friedrich, Zita Hubler, Adrianna Rivera-Leon, Farrah Gao, Joel Sax, Ramya Srinivasan, Ilya Bederman, Elizabeth Shick, Paul Tesar, Drew Adams

Case Western Reserve University

Although the metabolic pathway for cholesterol biosynthesis has been previously investigated, current work has elucidated previously undiscovered links between sterol pathway enzyme inhibition, unique sterol substrates accumulation, and biological areas including neurodegenerative disease, immunology, and cancer. We previously reported that multiple small molecules increase regeneration of oligodendrocytes, a type of neuroglial that is often lost in demyelinating diseases such as multiple sclerosis, via inhibition of EBP, Sterol 14-reductase, or CYP51 and stimulate the retention of their 8,9-unsaturated sterol substrates. Additional adjoining pathway enzymes also possess 8,9-unsaturated sterol substrates but have not

previously been examined as possible targets of oligodendrocyte formation or in other biological contexts, partially because of a lack of relevant chemical probes. Here, the genetic suppression of HSD17B7 or SC4MOL causes enhancement of oligodendrocyte formation. We developed and optimized multiple potent and novel HSD17B7 and SC4MOL inhibitors that enhances oligodendrocyte formation. Chemical probe CW4142, a SC4MOL inhibitor, cause the accumulation of sterol substrates of SC4MOL in mouse brain which represents a SC4MOL in vivo probe. The 8,9-unsatured sterol cellular accumulation represents a major driver of oligodendrocyte generation, since the exogenous adding of purified HSD17B7 and SC4MOL substrates, unlike their 8,9-saturated analogs, promotes oligodendrocyte differentiation. This work validates HSD17B7 and SC4MOL as new targets for oligodendrocyte generation while also creating the novel and superior chemical probes for SC4MOL and HSD17B7 for investigating the diverse areas of this field.

4:25pm **Development of Securine-derivitive containing liposomes and inhibition of Thioredoxin Reductase I as a novel treatment for Acute Myeloid Leukemia**

Ian Zagorac, Preston Willis, Jude Franklin, Greg Tochtrop, David Wald

Case Western Reserve University

Acute Myeloid Leukemia (AML) is a clonal disorder of immature blast cells in the blood and bone marrow and represents approximately 25% of adult leukemia. The five-year survival rate for AML is approximately 18.2% with median survival between 5-10 months. For decades, AML chemotherapy has utilized the 7+3 regimen consisting of continuous infusion of cytarabine and daunorubicin. To improve patient outcomes, a novel drug is needed for AML.

Since 2011, securinine, the major alkaloid product from the plant securinega suffrictosa, has been studied due to its inhibition of Thioredoxin Reductase I (TxrRI) which is an important mediator in leukemic cell metabolism. S250 was reported by the Tochtrop group in 2021 as a novel securinine-derivative which was a highly specific and potent inhibitor of TrxRI. However, due to its lactone moiety and hydrophobicity, the drug suffers from an extremely short half-life. An alternative delivery method is needed to promote the biostability of the drug and lengthen half-life.

Liposomes are a promising platform for drug delivery due to their ability to encapsulate hydrophobic drugs and improve their pharmacokinetics. In 2017, the FDA granted regulatory approval to a liposome formulation called CPX-351. The 5:1 molar ratio of liposomal-encapsulated daunorubicin and cytarabine demonstrated a significant improvement in patient outcomes. Liposomes have been proposed as a delivery vehicle for S250.

The current methods create S250-containing liposomes of approximately 150nm with an encapsulation efficiency of greater than 40% which shows great promise for in-vitro studies. This represents a potential paradigm shift in AML treatment.

4:45pm **The Development and Validation of a GC-MS Method to Quantify Short and Branched Chain Fatty Acids in Human Stool and Applied to Patients with Inflammatory Bowel Disease and Healthy Controls**

Justin Gray

Cleveland State University

The study of short (SCFAs) and branched chain fatty acids (BCFAs) in human stool related to gastrointestinal diseases, gut microbiota, metabolism and diet has dramatically increased. As a result, a fast, reliable method with minimal pretreatment is needed for quantification of these metabolites (acetic, propionic, isobutyric, butyric, isovaleric, valeric and caproic acid) in stool. Therefore, a GC-MS method meeting this criterion was developed. Stool samples were homogenized, diluted with 80:20 water:methanol (v/v) and adjusted to a pH of 1.5 - 2.5. Samples were vortexed, centrifuged and directly injected into the GC-MS using pulsed splitless injection offering two-to-three-fold signal enhancement over a 10:1 split injection. DB-FATWAX Ultra Inert Polyethylene Glycol (PEG) Column showed no peak tailing, reduced responses or retention time shifts after 1476 stool injections while other columns failed before 361 injections. A cohort study was conducted using 53 remnant raw stool samples with a positive diagnosis of either ulcerative colitis (UC) or Crohn's Disease (CD) which comprised the Inflammatory Bowel Disease (IBD) group and were compared to a control group of 21 samples for SCFA and BCFA concentrations. Strong statistical differences were observed between groups whereas the IBD group contained less propionic, butyric and valeric acid ($p < 0.05$). A receiver operator curve was plotted using the sum of significantly different SCFAs normalized against acetic acid resulting in 96% AUC (95% CI: 0.89 – 0.98) demonstrating potential diagnostical application.

Section C

2:40pm **Pharmacological targeting of gut microbial phenylacetylglutamine production in cardiovascular disease**

Austin M. Williams[1,2], Mohammed Dwidar[1,3], Zeneng Wang[1,3], James T. Anderson[1,3], Joseph A. DiDonato[1,3], Valentin Gogonea[1,2,3], Stanley L. Hazen[1,3,4*]*

[1.] Department of Cardiovascular & Metabolic Sciences, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA. [2.] Department of Chemistry, Cleveland State University, Cleveland, OH. [3.] Center for Microbiome and Human Health, Cleveland Clinic, Cleveland, OH, USA. [4.] Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH, USA

Recent studies show the gut microbe-generated metabolite phenylacetate, upon absorption into the host, is transformed into phenylacetylglutamine (PAG), a metabolite both clinically and mechanistically linked to cardiovascular disease. Our long-term goal is to produce gut microbe targeting, small molecule inhibitors that suppress host PAG levels, for the prevention and treatment of diseases linked to PAG. Gut microbial production of phenylacetate begins with dietary phenylalanine, which is readily converted to phenylpyruvate by multiple gut microbes and catalytic strategies. Recent studies show phenylpyruvate is further transformed by gut microbes through both oxidative and non-oxidative enzymatic pathways. In the oxidative pathway phenylpyruvate ferredoxin:oxidoreductase (PPFOR) produces phenylacetyl-CoA; and in the non-oxidative pathway phenylpyruvate decarboxylase (PPDC) produces phenylacetaldehyde, which is further oxidized to phenylacetate. To assay inhibition of microbial phenylacetate production, we developed several assays under different conditions: an assay using lysate of recombinant E. coli expressing PPDC from

P. mirabilis detecting derivatized phenylacetaldehyde via LC-MS/MS, and an assay using lysate of E. coli expressing PPFOR from B. thetaiotaomicron producing phenylacetate detected spectrophotometrically by a coupled reaction. We have synthesized small molecule inhibitors designed to selectively target PPFOR and PPDC as mechanism-based inhibitors: substrate analogues, which upon catalysis, produce reactive electrophilic species capable of reacting with nucleophilic active site residues, irreversibly inactivating the target enzymes. When tested in our assays, these compounds have shown inhibition of both PPFOR and PPDC. These results demonstrate feasibility in the first step of creating a therapeutic that targets the gut-microbiome to attenuate cardiovascular disease risk by reducing PAG production.

3:00pm **Investigating the Therapeutic Potential of Astragalus Radix in Allergic Rhinitis: Insights from Metabolomics**

Akshay Suresh Patil, Yachun Shu, Yan Xu

Cleveland State University

Allergic rhinitis is characterized by nasal inflammation responding to allergens, leading to significant alterations in metabolic pathways. The adverse effects of conventional synthetic medications, such as dizziness, weakness, and increased heart rate, have spurred interest in herbal alternatives. Astragalus radix (AR), a herb widely used in traditional Chinese medicine for its immunomodulatory and anti-inflammatory effects, presents a promising option. However, the specifics of its metabolomic influence and the pathways it affects in allergic rhinitis are not well understood.

This research utilized human mast cells to model allergic rhinitis. The cells were first stimulated with lipopolysaccharide (LPS) to mimic an allergic response, then treated with an aqueous extract of AR, with triprolidine and zileuton serving as positive controls. UHPLC-QTOF/MS-based untargeted metabolomic analysis detected a notable upregulation in metabolomic profiles under LPS-induced conditions compared to untreated controls, whereas the AR extract and positive controls significantly downregulated these profiles compared to the LPS-induced ones. Critical metabolites, including histamine, leukotrienes, prostaglandins, ceramides, and specific amino acids, exhibited significant changes across the experiments. Pathway analysis identified histidine and arachidonic acid metabolism as the pathways most affected by treatment, suggesting a mechanism by which AR extract counters allergic rhinitis. A semi-quantitative approach, using a known internal standard for comparison, further validated the impact of AR on key metabolites under different conditions. This study marks a significant step forward in elucidating the metabolic pathways and mechanisms through which AR may offer a natural alternative for allergic rhinitis management.

3:20pm **Quercetin sensitizes Burkitt lymphoma to TRAIL-induced apoptosis**

Erin M Thorpe, Yan Xu, Michael Kalafatis

Cleveland State University

Burkitt lymphoma (BL) is an extremely aggressive non-Hodgkin's lymphoma that originates in the germinal center of B cells. The standard treatment for BL is intensive high dose chemoimmunotherapy, which often leads to toxic side effects and clinical complications. Therefore, it is important to develop better treatment strategies for BL with greater specificity to improve patient outcomes and quality of life. One promising treatment for BL is the endogenously produced immune surveillance protein, tumor necrosis factor-related apoptosis inducing ligand (TRAIL). TRAIL initiates the extrinsic pathway of apoptosis by binding to death receptors that are more abundantly expressed on the surface of transformed cells. This binding causes the cancer cells to undergo programmed cell death without exhibiting any significant toxicity towards normal cells. Unfortunately, many cancers display resistance to TRAIL treatment but luckily this resistance can be overcome through co-treatment with nature-derived compounds that modulate the underlying factors responsible for the apoptotic resistance. The anticancer effects of the dietary flavonoid quercetin, both alone and in combination with other treatments, as well as the ability of quercetin to safely sensitize various cancer cell lines to TRAIL-induced apoptosis, have been extensively demonstrated. Preliminary data with the moderately TRAIL sensitive BL cell line, Ramos-1, has shown that quercetin alone can induce significant apoptosis through both the extrinsic and intrinsic pathways. Furthermore, the combination treatment of TRAIL and quercetin was considerably more effective than either treatment alone, indicating that this cocktail may be a potent novel treatment strategy for BL.

3:45pm **Synthesis and characterization of isoindoline derivatives**

Joan Bore, Prof Viktor Nemykin, Prof Christopher Ziegler

University of Akron

The chemistry of isoindoline and its derivatives remains vital in the development of phthalocyanines, new chromophores, and chelating ligands such as hemiporphyrazines, bis(alkylamino)isoindolines, and semihemiporphyrazines. In 1953, Linstead and coworkers reported on the preparation of a key isoindoline compound, 1,3-diiminoisondoline (DII), produced by the reaction of phthalonitrile and ammonia. In 1956, Clark and coworkers followed up on Linstead's work by investigating the synthesis of DII derivatives. They observed the formation of a new compound when they used secondary amines instead of primary amines in reaction with phthalonitrile. In this work, we revisited the synthesis and characterization of iminoisoindoline derivatives produced by the addition of secondary amines to phthalonitrile as first reported in Clark's work. The secondary amines we have investigated so far include diethylamine, diisopropylamine, pyrrolidine, piperidine, piperazine, N-ethyl benzylamine and morpholine. X-ray structures of three of the derivatives have been obtained and exhibit double bond character between the secondary nitrogen position and the adjacent carbon atom. This is also observable by NMR spectroscopy, which shows a barrier to rotation observable by variable temperature NMR. The measured energy barrier for rotation of the diethylamine product is 15.6 kcal/mol while the pyrrolidine product is 18.1 kcal/mol. These values are similar to those seen in substituted amides.

4:05pm **Octahedral distortions in hybrid morpholinium metal halide 2D structures, $(C_4H_{10}NO)_2MX_4$ (M = Pb, Sn; X = Cl, Br)**

Aman L. Roy, Matthias Zeller, Douglas Fabini, Catherine M. Oertel
Oberlin College

Organic-inorganic hybrid metal halides are a class of materials of interest for the variety and tunability of their optoelectronic properties. One important driver of these properties is the degree of asymmetry present in the inorganic substructure. Therefore, understanding of the causes of distortions from regular geometry is valuable in guiding the design of functional materials. In this work we report the synthesis and characterization of three new isostructural morpholine-based hybrid metal halide products, each exhibiting differing levels of octahedral distortion within their inorganic substructures. All three structures belong to the centrosymmetric space group P21/m and take the form of alternating organic and inorganic two-dimensional layers. The extended inorganic layered substructure is made up of corner-sharing distorted metal-halide octahedra, separated from the next layer by dimerized organic morpholinium cations. Density functional theory (DFT) computations were performed, allowing for examination of the influences of $5s^2$ or $6s^2$ stereochemically active lone pair (SCALP) cations and morpholinium hydrogen bonding interactions on the resulting octahedral distortions. The powder products were synthesized in bench-top solution conditions, while single-crystal samples were synthesized using solvothermal slow-cooling methods. Characterization methods include powder and single-crystal X-ray diffraction, combustion elemental analysis, thermogravimetric analysis, and diffuse reflectance UV-Vis spectroscopy. This project represents a step forward in the understanding of local asymmetries in functional hybrid metal halides by synthetically demonstrating the distortion impacts of metal-center and halide substitutions.

4:25pm **Polymer Architecture Control to Tune Thermal Transition and Flow Behavior**

Konpal Raheja, Metin Karayilan
Case Western Reserve University

The dramatic change in viscosity of fluids with increasing temperature impacts the overall performance of various applications: lubricants for operations spanning a wide temperature range, paints and personal care items aiming to enhance product performance, 3D printing ink for precise viscosity control ensuring accurate printing outcomes, as well as maintaining the integrity of cell sheets for detachment and ensuring the effectiveness of sealants and adhesives in their adhesion and sealing properties. The goal is to develop a material capable of either maximizing or maintaining viscosity at elevated temperatures. This research study delves into the utilization of "smart" thermoresponsive polymers as alternative additives to enhance the viscosity-temperature behavior. Of particular interest is the ability of these polymers to adjust viscosity by manipulating temperature owing to their lower critical solution temperature (LCST) behavior. We hypothesize that by controlling the polymer architecture and functionality, we can tailor the thermal properties of the polymers, including LCST and thermal transition. Consequently, we aim to optimize the performance of these polymers by developing unique architectures and tuning the architectural parameters. Our investigation will explore the thermal transition and rheological properties of these polymers. Exploring viscosity properties aligns with the broader vision of creating a solution that adapts seamlessly to dynamic temperature conditions. Ultimately, the success of this research hinges on translating these innovative thermoresponsive polymers from laboratory experimentation to practical applications.