Synthesis of a Sialic Acid Derivative for Modifying Cell Surface Sialylation
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The exterior cell surfaces express a dense layer of glycans which are often terminated by sialic acid (SA). SA is an acidic monosaccharide whose presence on the terminal ends of glycans of either glycoproteins or glycolipids. Due to its hydrophilic and electronegative feature, SA is often involved in both physiological and pathological processes, such as in regulating cellular interactions with ligands, microbes and neighboring cells and in controlling cellular activation, differentiation, transformation and migration. Cell surface glyco-metabolic engineering provides a useful tool to remodel cell surface SA. In this study, a 9-amine derivative of SA was designed and synthesized for modulation of cell surface SA application. By treating cells with amine derivative of SA it is possible to modify the native SA expressed on the cell surface, also known as sialylation status. We hope to find information regarding the specific mechanisms that are involved in SA binding events as well as possible cellular consequence due to SA derivation. Eventually, by modifying the cell surface sialylation status it may be possible to modify cellular functions.

Synthesis and Evaluation of N-Glycan Polymers as Biomimetic Macro-Glycoligands
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Carbohydrate recognitions are crucial events in many biological processes where glycoproteins, glycolipids, or proteoglycans exist as cell surface carbohydrates involved in cell–cell signaling, immune recognition events, pathogen/host interactions, tumor metastasis, tissue growth, repair, and many more. Glycoscience research specifically concerning the cell surface carbohydrates can provide an abundant opportunity to discover potential therapeutic targets or diagnostic mechanisms for various diseases. In the past decades, glycopolymer, polymers with glycan pendant groups, have been extensively explored as multivalent carbohydrate ligands for studying carbohydrate - protein interactions and for important biomedical applications because they can act as agonists or antagonists for understanding the molecular mechanisms of many biological processes, and also provide tremendous opportunities for therapeutic applications. Herein, we report a straightforward synthesis of N-glycan polymers from free glycans via glycosylamine intermediates followed by acrylation and polymerization via cyanoxyl-mediated free radical polymerization (CMFRP) in one-pot fashion. No protection and deprotection were used in either glycomonomer or glycopolymer synthesis. In addition, their immunomodulation effects on macrophage regarding their cell viability, inducible cell surface biomarkers and cytokine release profile were investigated.

Characterization of Melanin-based Colorimetric Water Sensors
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Many families across the US have been affected by recent heavy metal water pollution. Currently, field water sensors can only detect dangerously high levels of heavy metal pollutants. The ability to determine concentrations of heavy metals in water could prevent accidental exposures. Serendipitously, the Belitsky lab determined that melanin-like coatings, derived from the oxidative polymerization of catechols, change color in response to binding metal ions. These catechol-based coatings are not yet sensitive nor selective enough to be practical for field use, but understanding how different coatings bring about color change could help the lab develop more powerful melanin-inspired colorimetric sensors for heavy metals in the future. The Belitsky lab has explored various characterization methods to help us understand and improve the sensors. As one such tool, we have modified the Folin-Ciocalteu assay to elucidate the polyphenol content of various coatings. This presentation will describe the development of our modified FC assay and preliminary results it has revealed.
Computational exploration of the interface interaction between S100A8/A9 and GAPDH in the GAIT complex
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Selective nitrosylation of glyceraldehyde 3-phosphate dehydrogenase (GAPDH) at Cys-247 affects gene regulation through the interferon-gamma (IFN-γ) activated inhibitor of translation (GAIT) complex. Oxidized low-density lipoprotein (LDLox) and INF-γ induces assembly of the nitrosylase complex composed of inducible nitric oxide synthase (iNOS), S100A8 and A100A9 proteins. Intracellular GAPDH has been shown to exist as a mixture of monomer, dimer, and tetramer in cell lysate. Our goal is to investigate the interaction interface between GAPDH and S100A8/A9 proteins by using protein-protein docking calculations and molecular simulations program. The candidate molecular models were analyzed by measuring the shortest distance from GAPDH interaction domains (a1 and a3) to each of the three residues of S100A8 (I22, D32, C42, D52), which when used as anchor points for the FeBABE moiety, leads to significant cleavage of GAPDH. Proposed models of the S100A8/A9/GAPDH complex presented herein were selected as the best candidates from each category based on this criteria and overall consistency with the FeBABE cleavage experimental data. Our analysis concludes that molecular models of GAPDH dimer contributes most to the to cleavage patterns that agree with the experimental data.

Elucidating the Mechanism of 6-Hydroxynicotinate 3-Monoxygenase, a Decarboxylative Hydroxylase in Aerobic Nicotinate Degradation
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N-Heterocyclic aromatic compounds (NHACs) are environmental contaminants that cause adverse effects to non-target organisms. Aerobic bacterial catabolism of nicotinic acid serves as a model for understanding the biodegradation of NHACs, and a key enzyme of this pathway is 6-hydroxynicotinate 3-monoxygenase (NicC). NicC is a flavin-enzyme that catalyzes the hydroxylative decarboxylation of 6-hydroxynicotinic acid (6-HNA) to 2,5-dihydroxypyridine (2,5-DHP) with concomitant oxidation of NADH to NAD. This type of hydroxylation is a common chemical strategy that bacteria have evolved to degrade NHACs. Understanding the mechanism of this reaction and the structural determinants of the enzyme’s specificity will provide insight on the conditions NHAC degradation requires to optimize bioremediation efforts. Our research objective is to elucidate the chemical mechanism of the NicC-catalyzed reaction. Based on the crystal structure of this enzyme we offered two mechanistic proposals: Mechanism A, involving the keto tautomer, covalent addition, decarboxylation and then hydroxylation of the substrate, while Mechanism B involves deprotonation, hydroxylation and then decarboxylation of the substrate. In this talk we present the evidence, from additional structural, kinetic and inhibitor binding studies, that the reaction catalyzed by NicC likely follows mechanism B, and that this enzyme may be sufficiently promiscuous to be engineered to degrade other NHACs in novel bioremediation processes.

NMR studies of conformational dynamics of hnRNP H on RNA splicing
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Members of the heterogeneous nuclear ribonucleoprotein (hnRNP) H/F family are multi purpose RNA binding proteins that participate in most stages of RNA metabolism. Despite having similar RNA sequence preferences, hnRNP H/F proteins function in overlapping but distinct cellular processes. The domain organization of hnRNP H/F proteins is modular consisting of N-terminal tandem quasi-RNA Recognition Motifs (H/FqRRM12) and a third C-terminal qRRM3 embedded within glycine-rich repeats. The tandem qRRMs are connected through a 10-residue linker with most of the amino acids strictly conserved between hnRNP H and F. A significant difference occurs at position 105 of the linker where hnRNP H contains a proline and hnRNP F an alanine. To investigate the influence of P105 on the conformational properties of hnRNP H, we probed the structural dynamics of its HqRRM12 domain with x-ray crystallography, NMR spectroscopy, and Small Angle X-ray Scattering (SAXS). We observed in the HqRRM12 domain multiple structures in solution by SAXS. These exchangeable conformations that located on the linker region and RNA recognition sites reach certain equilibrium in different temperature by NMR relaxation dispersion and Fluorine spectrum. The collective results best describe that HqRRM12 exists in a conformational equilibrium between compact and extended structures. The compact structure displays an electropositive surface formed at the qRRM1-qRRM2 interface. Comparison of NMR relaxation parameters between HqRRM12 and FqRRM12 indicate that FqRRM12 primarily adopts an extended conformation. Thus, our work
demonstrates that the linker compositions confer different structural properties between hnRNP H/F family members that might contribute to their functional diversity.

**Modulating the activity of trimethylamine lyase CutC/D, a gut microbial enzyme**

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Recent clinical research points to trimethylamine oxide (TMAO) as a biomarker molecule associated with several homeostasis disruptions, such as myocardial infarction, atherosclerosis, secondary hypertension, irritable bowel syndrome, chronic kidney disease, stroke, and heart failure. Our goal in this project is to alter the biosynthetic pathway of TMAO through the inhibition of the gut microbial trimethylamine (TMA) lyase: the choline utilization cluster enzyme (CutC/D). We are using structure activity relationships (SAR) to predict new classes of chemical structures as potential efficient inhibitors. Thus, we are exploring the synthesis of new chemical compounds, non-lethal to gut microbial community, with high enzymatic efficacy both in vitro and in vivo. We are preparing and assessing inhibitors that can work either through irreversible non-competitive or competitive mechanisms, have minimal side effects, possess appropriate physico-chemical pharmaceutical properties as needed for a drug. Our leading candidates have excellent enzyme blocking efficiency and display good pharmacokinetic/pharmacodynamics properties.
Biochemistry II
Session Abstracts

Role of RNase L in Kidney
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Renal diseases have been continuing to be a prevalent problem. Current data indicate that 1% of patients admitted to the hospital are diagnosed initially with acute kidney injury (AKI), while about 2-5% of hospitalized patients develop AKI secondarily. It has been reported that epidermal growth factors (EGF)/EGFR activation contributes to the development and progression of renal diseases such as obstructive nephropathy, diabetic nephropathy, hypertensive nephropathy, and glomerulonephritis through mechanisms involved in induction of tubular atrophy, overproduction of inflammatory factors, and/or promotion of glomerular and vascular injury. In this study, we showed that Ribonuclease L (RNase L), one of the key enzymes playing an important role in the molecular mechanisms of interferon functions against microbial infection and cell proliferation, mediated EGF/EGFR activation. Interestingly, we found that kidneys from aged RNase L deficient mice were significantly smaller than that from wild type mice under the same condition. Histological staining revealed that there were remarkably a higher number of vacuoles in the kidney of RNase L deficient mice than that in wild type mice although the biological significance of the observation is largely unknown. Proteomic analyses of urine discovered that lack of RNase L exclusively block EGF excretion to urine. In this study, we will determine the role of RNase L in the pathogenesis and elucidate how RNase L regulates the level of EGF in the kidney.

RNase L is Involved in Glucose Homeostasis and Insulin Resistance
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Diabetes is characterized by hyperglycemia mainly due to defect in insulin secretion and/or action. Regulation of glucose transport and use by insulin is central to the maintenance of whole-body glucose homeostasis. One of the potential mechanisms associated with insulin sensitivity is the activation of insulin receptor (IR) and subsequently transduces the signal through phosphorylation of insulin receptor substrate (IRS)1 and activation of the PI-3K/Akt pathway. In contrast, activation of the mechanistic target of rapamycin (mTOR) and ribosomal protein S6 kinase (p70S6K) inactivates the signal cascade. RNase L, an IFN-inducible enzyme, plays an important role in IFN functions against viral infection and cell proliferation. However, a direct link between RNase L and insulin sensitivity has yet to be clearly established. In this study, primary RNase L+/+ and -/- mouse embryonic fibroblasts (MEFs), hepatocytes and adipocytes were used to investigate the role of RNase L in insulin signaling and sensitivity. Cells were treated with insulin at various time points and different concentrations. Activation of the insulin signaling pathway was determined by immunoblot analyses for the protein level and phosphorylation status of these components such as IR/p-IR, IRS1/p-IRS1 and AKT/p-AKT in the presence or absence of chemical inhibitor. We found that RNase L plays an important role in glucose homeostasis through impacting insulin receptor (IR) which is a trans-membrane receptor activated by insulin. The phosphorylation status of IR was significantly reduced in the cells deficient RNase L. As a result, activation of IRS1, the downstream substrate of IR, and the PI3K/AKT pathway was significantly inhibited in RNase L/-/- cells. Further investigation of the molecular mechanism underlying the role of RNase L in mediating the activation of IR revealed that RNase L may regulate the cleavage of the precursor of IR via the ubiquitin/ proteasome system. In addition, the level of activated S6 kinase in the mTOR pathway was also markedly elevated. In summary, the role of RNase L in the insulin signaling pathway suggests that RNase L may be a novel target in the design of therapeutic strategies for diabetes. Treatment of this disease may be achieved through regulating the expression and activation of RNase L. In addition, RNase L may be used as a prognostic marker for diabetes as well.

Characterizing the Effects of the delta32 Mutation on CCR5 Expression and HIV Infectability
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HIV must first bind to a primary receptor on the human T-cell, CD4, and one secondary receptors, CCR5 or CXCR4, to infect a cell. The mutation known to affect HIV infectivity. ccr5 delta32 is a deletion mutation of 32 base pairs of the ccr5 human gene sequence. It is thought this mutation truncates the CCR5 receptor, rendering it incapable of reaching the human T-Cell surface. When an individual is homozygous for delta32, the mutation will confer resistance to HIV infectivity, as well as Yersinia pestis. Twenty percent of European Caucasians are heterozygous for ccr5 whereas, one percent is homozygous for delta32. We identified an individual, subject EN2, a descendant of plague survivors, whom is homozygous for ccr5 delta32 alleles. A PCR was performed using primers that circumscribe the ccr5 gene. We acquired both wild type and delta32 allele from this individual. This product
was cloned into pCR4-TOPO vector. This will be excised and cloned into pLXSN retroviral expression vector. pLXSN will then be transfected into PT67, a retroviral packaging cell line. The retroviral products will then be used to create stable and transient transductants into H9 Lymphoid cells. These will be tested for HIV infectability and CCR5 expression.

HIV Infectivity Counteracted by the CCR5-delta32 Mutation Effect on CXCR4 Gene
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The Human Immunodeficiency Virus (HIV), which can progress to Acquired Immune Deficiency Syndrome, or AIDS, is a virus that targets and weakens the body's immune system. An infection initially occurs when HIV interacts with two receptors on a human T-cell: the primary receptor, CD4, and one co-receptor, either CCR4 or CCR5. According to Agrawal et al, it is hypothesized that the CCR5-Delta32 mutation affects CCR5 expression and, plausibly, CXCR4 as well. This research will determine the effects the CCR5-Delta32 mutation has on CXCR4, and the possible role it has in preventing HIV from infecting the human T-cell. After isolation, the human cxcr4 gene was subcloned into pLXSN, a retroviral shuttle vector. Retroviral particles from the pLXSN-CXCR4 transfected PT67 packaging cell line will be used to transfect both primary and tumor cells. This process will be carried out with cxcr4 and again with ccr5 alleles. The ccr5 alleles will include the delta32 mutation, the wild type allele, and a novel point mutation called TG5. The novel point mutation was isolated from a possibly HIV-resistant subject. This will allow HIV-resistance to be tested by infecting cells expressing various ccr5 alleles and cxcr4.

Biocompatibility improvement of blood-contacting medical devices based on Nitric Oxide (NO) release
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Blood-contacting medical devices, such as vascular grafts, stents, heart valves, and catheters, are often used to treat cardiovascular diseases. These implantable medical devices, even if labeled as bio compatible, can cause serious complications in patients. Thrombus formation and infection are the main causes of failure of these devices. In contrast to the healthy endothelium, which actively resists thrombosis, artificial surfaces promote clotting through a complex series of interconnected processes that include protein adsorption, adhesion of platelet, leukocytes and red blood cells, ending with thrombosis. Nitric oxide is an important intercellular and intracellular signal molecule that regulates the cardiovascular, nervous, and immune systems. It is generated from L-arginine by a family of enzymes, called nitric oxide synthases. Under physiological conditions, a constitutive Ca2+-dependent NOS in endothelial cells (eNOS) is responsible for the continuous release of NO. In addition to its role in vasodilation and regulation of vascular tone, continuous release of NO by the endothelium has also been shown to counteract the adhesion of platelets to the inner walls of blood vessels. From this standpoint, NO is a natural antithrombotic agent in blood vessels. In this regard, NO-releasing films as coatings on blood-contacting devices have shown the potential to be effective in preventing platelet adhesion, activation, and aggregation, therefore reducing the risk of thrombus formation on the treated surfaces. Therefore, NO-releasing coatings have the potential to prolong vascular graft and stent potency. In this project, we use layer-by-layer thin film building strategy to form layers of polyethyleneimine (PEI) and iNOSoxy as NO-releasing coatings. Charge-based Layer-by-layer electrostatic adsorption allows for assembly of multi-component protein/PEI films. Here, the iNOSoxy enzyme protein used is negatively charged and adsorbed onto the positively charged matrix layer, polyethyleneimine. When discs coated with PEI/iNOSoxy films are exposed to substrate arginine, a source of reducing equivalent, and other required ingredients of the NOS reaction, nitric oxide is formed and released. In this work, we characterize the PEI/iNOSoxy thin films in terms of structure of iNOSoxy within the films as well as the amount of active (iNOSoxy) concentration. Fourier transform infrared (FTIR) spectroscopic analysis was used to characterize structure-activity relationships of these NOS-containing thin films. We used cyclic voltammetry to determine the active catalyst (iNOSoxy) concentration on the modified surfaces, and how this relates to enzymatic activity and resulting NO release fluxes from PEI/NOS-containing thin film. Next, we will conduct platelet adhesion assays to determine if the amount of platelets adsorbed on the PEI/iNOSoxy films is inversely proportional to the amounts of NO released from these coatings.
The Role of CphA and CphB With Respect to Nitrogen Availability in Planktothrix Agardhii

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Unlike the phosphorus dependent algal blooms of Western Lake Erie, Sandusky Bay’s Planktothrix agardhii blooms are often dependent on nitrogen inputs. Nitrogen levels of the bay drop significantly by midsummer, but the blooms persist, despite the fact that Pa is a nondiazotrophic organism. (Davis et al. 2015). Certain strains of cyanobacteria house two genes that are responsible for nitrogen storage and utilization. cphA encodes the enzyme cyanophycin synthetase that synthesizes a nitrogen storage polymer of arginine and aspartic acid called cyanophycin. cphB encodes the enzyme cyanophycinase that breaks down cyanophycin. The presence of these two genes in Sandusky Bay Pa strain was demonstrated through PCR. It is expected that cphA should be expressed when nitrogen is replete and that cphB should be expressed during nitrogen depletion. In this experiment, two cultures of Planktothrix agardhii were grown in BG-11 media. The culture was divided, centrifuged, rinsed, and resuspended: one in BG-11 and one in nitrogen free BG-11. Every three days a portion of each culture was filtered for chlorophyll a, phycocyanin, and RNA. Furthermore, the color of the cultures was observed daily for signs of nutrient stress. The experiment continued until the N free culture showed significant signs of chlorosis. The levels of chlorophyll a and phycocyanin were tested using a fluorometer to measure any difference between the two cultures. RNA was extracted and RT-PCR was performed using primers for cphA and cphB to monitor the expression of those genes.

Optimization of magnetic fluidic SELEX to select aptamers for ovarian cancer biomarker HE4

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Ovarian cancer is among the most difficult to detect and deadly cancers, bringing about the need for more sensitive tools in clinical diagnosis. High-affinity nucleic acid aptamers demonstrate many advantages over traditional diagnostic antibodies. In order to select aptamers for the ovarian cancer biomarker HE4, we have optimized magnetic-fluidic SELEX as well as implemented a bioinformatic pipeline to aid in the refinement of the resultant sequence data. As suggested by its name, magnetic-fluidic SELEX makes use of Ni-NTA magnetic agarose beads complexed with the tagged protein of interest, HE4-6-His, aided by a fluidics platform to fix and separate strongly binding potential aptamers from weakly binding potential aptamers. In addition, we improved processing between SELEX rounds by optimizing asymmetric PCR and gel extraction. We used this system for five rounds of SELEX, after which each candidate pool was sequenced on an Illumina HiSeq; resulting sequence data were processed using the Galaxy bioinformatics platform. We found that the population of DNA has been substantially altered during SELEX, with some evidence that select candidates may show affinity for HE4. We expect to continue to use Galaxy alongside capillary electrophoresis and fluorescence anisotropy to analyze the binding capabilities of top aptamer candidates.
Analytical I
Session Abstracts

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Monitoring concentrations of nutrients and chemical substances that would affect plant growth would be a useful tool for precision agriculture. Passive samplers are power-free devices containing specialized adsorbents that measure the bioavailable fraction of compounds via diffusion from an environmental matrix. Many passive sampler designs are available for air and water, but there is a lack of systems that can be used in soil and sediments. Here, we describe work on the development of soil insertion passive samplers that can access a wide range of small molecule compounds. Porous organosilica adsorbents having a mechanically expandable pore architecture were developed to have broad specificity to adsorb different compounds which have a wide range logKow's. In addition, organosilica adsorbents were designed to have high capacity to prevent saturation upon multi-analyte adsorption and fast kinetics. Practical knowledge about the design and use of direct soil insertion passive samplers was achieved through controlled laboratory experiments as well as ad hoc field trials at an Illinois corn and soybean farm and Ohio golf course. The potential of soil passive sampling, in addition to the trials and tribulations of device engineering, will be presented.

In situ Shallow Subsurface Reflectance Spectroscopy for the Geochemical Characterization of Archaeological Features and Anthropogenic Soils
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In situ shallow subsurface soil spectroscopy (S4) is employed to survey three archaeological sites in Kansas. The resulting spectra enable the chemical characterization of the anthropogenic features of these archaeological sites. A reflectance probe attached to the mobile instrument (Veris P4000) recorded near infrared and visible diffuse reflectance spectra of the sites on a grid pattern at a range of the depths from the surface down to 1 meter deep. Spectral data is obtained along with the electrical conductivity of the soil and the insertion force of the probe in the soil. A limited set of core samples were extracted for chemical composition including organic matter, pH, sodium, potassium, calcium, magnesium and phosphorus. A principal component regression involving the limited set of lab analyses enabled the construction of a chemometric model, capable of making the estimation of chemical species concentrations on the three dimensional grids of these sites. Connection between these two data sets (spectral and chemical) is the basis to build a reasonably acceptable model, which is then applied to the rest of the grid. The contour plots of various depths in soil of these sites produced from these estimated analyses values provide a three dimensional visualization with respect of the chemical characteristics of each site. Thus significant archaeological features are observed without excavation of the site. The estimated values are in well accordance with directly measured chemical and physical characteristic values, which denotes the reliability of the chemometric method. Ancient features and activities of these archaeological sites can be predicted with this advanced method in combination with traditional topographic, surface and subsurface geophysical survey methods.

GC-MS Analysis of Unprecedented Whiskey Flavors Created by a Novel Aging Process
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Gas chromatography-mass spectroscopy (GC-MS) can be readily utilized to generate an analytical profile of flavor compounds in whiskey. This method has been successfully applied to bourbon whiskeys produced by a novel accelerated aging process which employs pressure, as opposed to conventional time, to mature the spirit in a few days as opposed to a few years. Using this innovative technology of accelerated pressure aging, spirits have been matured not only with traditional oak but also with other alternative woods. As such, new experimental and completely original flavors of whiskey including black cherry, apple, Hickory, sugar maple and honey locust have been created where the spirits are naturally flavored with these woods. The distinct flavor compounds in each of these unprecedented wood flavored bourbons were identified and profiled using routine straight injection GC-MS. As such, it has been observed that black cherry bourbon contains more ethyl octanoate, a compound known to impart a sweet fruity flavor, than traditional oak flavored bourbon. Further, cherry bourbon contains less phenethyl alcohol, a compound known to impart a
floral and bready flavor, than traditional oak bourbon. Bourbons flavored with apple, hickory, sugar maple and honey locust woods showed analogous results for various flavor compounds.

**GC-MS Analysis of Chinese Baijiu Spirit Flavored as American Whiskey**

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Gas chromatography-mass spectroscopy (GC-MS) is routinely used to profile the flavor compounds in alcoholic beverages. This method has been applied to experimental samples of Chinese baijiu liquor where the flavor has been modified to taste more similar to American bourbon. Chinese baijiu is a clear spirit, usually considered by the Western palate as strong in exotic flavors. In an effort to modify these liquors into something more akin to the routine Western palate, experimental samples of baijiu flavored to taste more similar to American bourbon were produced by aging the spirits with wood. This has been accomplished by processing baijiu spirit via a novel accelerated pressure aging process to mature the spirit within a few days, thereby coloring the spirit with wooden barrel flavors. The distinct flavor compounds in these experimental liquors have been identified and profiled using routine straight injection GC-MS. As such, it has been observed that the flavor of Chinese baijiu aged with American oak is dominated by a series of unbranched ethyl ester compounds. Foremost, oak aged baijiu flavor is characterized by an increase in ethyl hexanoate, which imparts a sweet and fruity nuance to the liquor. Ultimately, analytical profiles of the flavors of these unprecedented spirits were generated, which aids in product development.

**The Salinity Mediated Release of Ammonium from Treated Wastewater**

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The release of nitrogen in effluent from wastewater treatment plants into coastal systems can contribute to eutrophication and coastal degradation, particularly in systems that are nitrogen limited. One model suggests that ammonium can coulombically bind to dissolved organic matter in wastewater treatment plants, which protects it from removal during the treatment process, only to be bumped off by salt cations as the effluent encounters more saline waters. This presentation analyzes the response of effluent from four sequencing batch reactors each running a different treatment processes that varied from minimal, nitrification only, to more advanced, biological nitrogen and phosphorus removal. Each of the four effluents produced was then put through one of three disinfection treatments (no disinfection, germicidal UV, and chlorination) producing twelve treatment disinfection combinations; the combinations were produced twice in the summer and twice in the winter. Each of these combinations was then added to saline solutions producing four salinities (0, 10, 20 and 35). The salinity-mediated release of ammonium was observed in almost all of the effluent from two of the sampling periods (one summer and one winter). Effluent that had been chlorinated or received increased aerobic digestion resulted in lower rates of salinity release. These results indicate that salinity-mediated release of nitrogen should be considered when selecting the most effective treatment method for effluent released to saline waters.

**Metabolomics Analyses of Antiviral and Antibacterial Chinese Herbal Formulations “Shuang Huang Lian (双黄连)” by UPLC-QTOF-MS/MS**

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Shuang Huang Lian (SHL) is a Chinese herbal medicine for treatment of fever, cough, sore throat and upper respiratory tract infection. In vitro cell culture studies showed that SHL inhibits the respiratory syncytial virus (RSV), para-influenza I-IV, and 23 kinds of pathogenic bacteria such as Staphylococcus aureus. SHL is comprised of alcohol-water extracts from three medicinal plants, Lonicerae japonicae flos, Forsythiae fructus, and Radix scutellariae, in the ratio of 1:2:1. The analytical methods currently available for SHL are those of targeted analyses for quantitation of a few marker components which may not even be the effective components of the herbal medicine. Since SHL is a complex herbal mixture containing hundreds of compounds, in order to elucidate antiviral
and antibacterial components of SHL, we have developed an untargeted metabolomics method based on ultra-performance liquid chromatography and quadrupole time-of-flight tandem mass spectrometry (UPLC-QTOF-MS/MS) technology and bioinformatics for profiling and compound identification. In this work, we have studied three SHL formulations (i.e., granule, tablet, and oral liquid) using the metabolomic workflow developed in our laboratory and revealed that each formulation consisted of 178 to 216 entities using METLIN AM database. Among the 95 common entities from the three formulations, 47 of them have been identified with chemical names and formulas, including the 5 marker compounds of SHL specified by Chinese Pharmacopoeia and 8 compounds which were reported to have therapeutic effects. We have also performed principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA) to assess the correlations and differences among the three SHL formulations, and the reproducibility of technical and biological repeats.

**Compositional Changes Associated with the Exfoliation of Lithium Cobalt Oxide into Atomically Thin CoO2 Nanosheets**

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Layered transition metal oxides have a variety of applications due to their intrinsic properties ranging from metallic to wide-gap insulating. When isolating into atomic layers, these expansive properties can be utilized along with quantum confinement of two-dimensional structures for various applications such as energy generation and storage, catalysis, sensing, optoelectronics, and more. Exfoliation of lithium cobalt oxide is realized with a two-step wet-chemical method using a protic acid and a bulky amine and the resulting defect structure is examined. Using X-ray photoelectron spectroscopy, X-ray diffraction, ultraviolet-visible spectroscopy, inductively coupled plasma-optical emission spectroscopy, and scanning electron microscopy, structural and chemical changes associated with each step of this process are studied. During the first step of protonation, expanded interlayer spacing, dissolution, leaching of both lithium and cobalt ions, and an increased oxidation state of some cobalt is observed. The second step of intercalation of bulky amines yielded atomically thin nanosheets as was observed with atomic force microscopy. Additional characterization of solutions and unexfoliated powder was used to develop a better understanding of structural-property-processing relationships.
Investigation of Spontaneous Co-crystal Formation: A Study of Caffeine and Malonic Acid
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Co-crystals are crystalline substances comprised of two or more chemical entities held together non-covalently, wherein both constituents retain their chemical identity. This retention of chemical identity provides a means of tuning the bulk properties of a compound with favorable reactivity without losing functionality, which is appealing for materials and pharmaceutical design. Furthermore, certain co-crystals have been found to form spontaneously upon contact between crystallites of the reactants, although the mechanism of this reaction is elusively. Solid-state NMR (ssNMR) is an ideal method for interrogating co-crystal formation reactions because of its sensitivity to local electronic environments and ability to detect non-diffracting phases. The caffeine and malonic acid co-crystal (CA:MA) is the subject of this work, as it has been shown to form spontaneously. CA:MA co-crystal formation was monitored in situ using ssNMR with isotopically enriched malonic acid, in order to increase sensitivity. With this higher signal to noise ratio, detection of low-abundant intermediates is possible. The goals of this work were threefold: to study the CA:MA co-crystal formation reaction, unmodified, in situ using ssNMR, investigate the effect of temperature on the reaction kinetics, and search for evidence of co-crystal formation through a gas or liquid phase intermediate. Most interestingly, preliminary results from the in situ ssNMR data suggest that an intermediate may form, and liquids spectra confirm this new species is in the solid phase. Additionally, temperature seems to play an important role in the kinetics of co-crystal formation, with elevated temperatures accelerating the rate of co-crystal formation.

Bile acids metabolic profiling in diabetic patients by liquid chromatography tandem mass spectrometry
Ibrahim Choucair, Ina Nemet, Stanley L. Hazen, Valentin Gogonea

Primary bile acids synthesized in the liver are bio-transformed by gut microbial enzymes into secondary bile acids. Bile acids regulate their own synthesis, lipid and glucose metabolism, energy expenditure and inflammation. We investigated the relationship between bile acids and metabolic disease by developing and validating an isotope-labelling liquid chromatography–tandem mass spectrometry (LC-MS/MS) method for the analysis of more than 50 primary and secondary bile acids in human and mouse physiological fluids and tissues. The method was applied to establish the normal ranges of different bile acids in healthy volunteers and to study a cohort of diabetic patients. While higher concentrations of conjugated secondary bile acids showed a lower risk of developing diabetes, increased concentrations of bile acids extensively metabolized by gut bacterial enzymes showed increased risk of developing diabetes. In preliminary studies, concentrations of structurally defined secondary and tertiary bile acids were identified whose levels are associated with the presence of diabetes. Further studies are being performed to validate these findings, and to confirm if they are related to the presence of diabetes, glucose homeostasis measures, and medication use.

Cost-Effective Alternatives to Sampling and Analysis of Book Degradation Emission Products
Abigail Bucher, Jim McCargar

Recent studies have reported on an effective headspace Solid Phase Micro-extraction/Gas Chromatography-Mass Spectrometry (SPME/GC-MS) method utilized to identify volatile organic compound (VOC) emissions from both historic and modern books. While headspace SPME/GC-MS has proven to be superior to previous methods developed for sampling and analysis, it is by no means cost effective, especially for replicate analyses. Reported here are novel and more cost effective alternatives for headspace analysis of VOC emissions from books due to aging and decomposition using GC-MS. One sampling method reported here is the use of a commercial vacuum chamber to directly sample the headspace with subsequent bubbling of the sample through methanol. Captured VOCs are then analyzed using GC-MS. Although the novel approaches reported are more cost effective, further improvements must be realized to match the efficacy of current headspace SPME/GC-MS methods.
Analysis of Pygeum Dietary Supplements Marketed for the Treatment of Enlarged Prostate
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Benign Prostatic Hyperplasia (BPH) or enlarged prostate is a common condition in older men and is often a precursor to prostate cancer. Dietary supplements made from the powdered bark of Prunus africana are marketed as pygeum to treat BPH, but they are only loosely regulated by the U.S. FDA. Commercial pygeum products were tested for N-butylbenzenesulfonamide (NBBSA), ferulic acid, atraric acid, atranorin, and β-sitosterol (BSST), components of pygeum that are thought to be effective in treating BPH. Two parallel liquid-solid extractions were conducted for each product. A direct extraction used acetone:hexane to extract NBBSA, atraric acid, and atranorin. The other extraction followed saponification that released ferulic acid and BSST from their natural esters and used dichloromethane solvent. After evaporation and reconstitution, the extracts were analyzed by liquid chromatography–tandem mass spectrometry (LC–MS/MS). The amount of ferulic acid, atraric acid, atranorin, and BSST varied widely among the products, but no NBBSA was detected in any product. The levels of each active compound found in the products can be used to evaluate their possible effectiveness for the treatment of BPH.

Mass spectrometry as discovery platform for candidate metabolite driving non-alcoholic steatohepatitis (NASH)
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Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver condition in the United States. NAFLD is associated with dyslipidemia, cardiovascular disease, obesity, chronic kidney disease, insulin resistance and type II diabetes mellitus. Nonalcoholic steatohepatitis (NASH) is a serious NAFLD phenotype which is characterized by inflammation, necrosis, and may progress from simple steatosis to hepatic fibrosis, cirrhosis, and hepatocellular carcinoma. Histological data from invasive procedure of liver biopsy remains the clinical standard for diagnosis of NASH and simple steatosis. The present work aims to use non-targeted and targeted mass spectrometry (MS)-isolable internal standard based methods to determine the potential utility of plasma metabolic profiling in defining candidate biomarkers that correlate with liver metabolic pathways and could be useful in differentiation between NASH and simple steatosis. To accomplish this we perform metabolomics analyses for gut microbiota metabolites, bile acids, polyols, carboxylic and amino acids (using ultra-performance liquid chromatography-mass spectrometry, UPLC-MS) on plasma samples from human subjects who underwent a liver biopsy, or from mice (model of NASH that developed fibrosis), and determine which metabolites correlate with the starting of fibrosis and initial stages of chronic hepatic lesion.

Porous Organosilica Adsorbents Tailored for the Extraction and Analysis of Perfluoroalkyl Substances from Water
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Perfluoroalkyl substances (PFAs) are highly fluorinated alkyl chemicals where one or more H substituents have been replaced by F. Surfactants and polymers comprised of PFAs have been used in industrial and commercial applications such as fire fighting foams. Analysis of PFAs is important for environmental monitoring. Microporous organosilica materials have been developed to adsorb a broad range of PFAs including PFOA and PFOS, but also fluorinated substances with cationic and zwitterionic groups. The approach is to use self-assembly of alkoxysilane precursors to create pore structures possessing mixed mode surface chemistry including the addition fluoroalkyl groups to promote adsorption of PFAs. The addition of the fluoroalkyl groups to the adsorbent improves adsorption over standard non-polar adsorbents. Application of these materials for solid-phase extraction and downstream analysis by LC-MS will be discussed.
Quantification of hydrogen sulfide in biological samples by liquid chromatography–tandem mass spectrometry

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Hydrogen sulfide (H2S) is a water soluble and colorless gastro-transmitter with a distinctive rotten egg smell. Most endogenous H2S is produced in mammalian cells through enzymatic pathways using L-cysteine as a substrate. In addition, H2S is generated by the sulfur reducing bacteria present in the intestinal flora. As a gas, H2S serves as a signaling molecule playing several physiological roles in the cardiovascular, gastrointestinal, central nervous, and respiratory systems. Abnormal levels of H2S in plasma and tissue are linked to various pathological conditions in humans. Different methods used to quantify H2S levels give differences of orders of magnitude among tissues tested. The purpose of this project is to develop and validate an isotope-labelling liquid chromatography mass spectrometry (LC-MS/MS) method that can be used to accurately quantify H2S in biological matrices such as blood, plasma, and tissues, and to examine the relationship between H2S levels and incident risks for development of cardiovascular disease and its adverse outcomes (heart attack, stroke and death).
Organic/Materials

Session Abstracts

Synthetic Melanin Films as Potential Interfaces for Peroxynitrite Detection
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Excessive concentrations of peroxynitrite are associated with several human pathologies, such as arthritis, inflammation, and carcinogenesis, as well as aging-associated diseases. Thus, the precise detection of this analyte in biological systems is essential, not only to understand the genesis and causes of ailments at the tissue/cellular level but also to suggest and design potential therapies. Melanin is a natural pigment that has many physiologic functions including neutralizing highly reactive oxidative species. Tyrosine and its derivative 5,6-dihydroxyindole (DHI) are some precursors of eumelanin, a black form of melanin that is also photo-stable. In this project, we examined the chemical interaction between synthesized peroxynitrite and polymerized films of DHI as a model of synthetic melanin. First, we studied the electrochemical characteristics of polymerized 5,6-dihydroxyindole on graphite electrodes, and then monitored the changes after adding aliquots of peroxynitrite. This part of the work reports mainly on chemical changes within the electro-polymerized films of melanin on the electrode. We also studied the rates of chemical decay of peroxynitrite in the presence of the transparent ITO electrodes coated with melanin films using absorbance spectroscopy. Ultraviolet-visible spectroscopy showed a dramatic difference between the decomposition rates of peroxynitrite alone and in the presence of DHI films. Scanning electron microscopy (SEM) has been used to image the change on the synthetic melanin films. We will discuss the implication of the changes of the electrochemical signal of DHI films. We will also compare the reactivity of peroxynitrite in the presence and absence of DHI films. Finally, we will explore the possibility of using DHI films as a platform for the quantitative detection of peroxynitrite in solutions.

Metallophosphaalkene synthesis via insertion chemistry of Na[OCP] with benzyne complexes
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Recently, sodium phosphaethynolate, Na[OCP], has become a useful synthon in main-group chemistry due to its ability to participate in cycloaddition reactions or to act as a [P] or [O=C≡P] transfer reagent. Furthermore, the stability of Na[OCP] against self-oligomerization reactions commonly encountered with multiply-bonded phosphorus species permits easier use and storage. Na[OCP] should thus be an ideal reagent for the development of P=C containing π-conjugated materials. In coordination chemistry, however, reactivity of Na[OCP] has remained limited to salt-metathesis with the potential for additional decarbonylation pathways. Using a zirconium-benzyne complex, CpZrCH(PMe), we have found unique insertion chemistry for Na[OCP] to give a metallophosphaalkene dimer bound within a coordination polymer. The sodium bridged [CpZr(κ-C,κ-P=CHC(OiPr))] units can be disrupted through addition of trimethylsilyl chloride to give a discrete dimer. The chemistry of these materials has been explored through derivatization and rearrangement reactions and we plan to use this knowledge towards the formation of additional main-group and organometallic compounds.

Chemical Reactive Anchoring Lipids with Different Performance for Cell Surface Re-Engineering
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Introduction of chemoselective functional groups at the cell surface enables for rapid and site-selective cell surface labeling and modification opportunity and thus facilitate enormous capability to study the cell surface molecule structure and function and the molecular mechanism it underlines. Further, it offers the opportunity to change or improve the cell functionality for the interest of choice. In this study, two chemical reactive anchor lipids, phosphatidylethanolamine-PEG-dibenzocyclooctyne (DSPE-PEG2000-DBCO) and cholesterol PEG-dibenzocyclooctyne (CHOL-PEG2000-DBCO) were synthesized and their potential applications for cell surface re-engineering via lipid fusion were assessed with RAW 264.7 cells as model cell. Briefly, anchor lipids were incubated with the cells under various concentrations and at different incubation times were investigated. The successful incorporation of anchor lipids was confirmed by biotinylation via copper-free click chemistry followed by confocal microscopy and flow cytometry confirmation of the specific streptavidin-FITC binding onto the cell surface biotin introduced. In comparison, cholesterol-based
anchor lipid afforded higher cell membrane incorporation efficiency with less internalization than phospholipid-based anchor lipid. In addition, lower cytotoxic effect of both anchor lipids upon incorporating onto the RAW 264.7 cells was assessed. Finally, the cell membrane residence time of the cholesterol-based anchor lipid was evaluated with confocal microscopy. This study suggests the potential cell surface re-engineering applications of the reactive anchor lipids.

Accommodating volume change and imparting thermal conductivity by encapsulation of phase change materials in carbon nanoparticles

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A Pickering-type emulsion is used as a template to encapsulate the phase change material stearic acid (SA) using graphene oxide nanosheets stitched together. GO-coated SA particles are solid at room temperature and can be used for latent heat storage during the phase change of the SA core. The carbon shell prevents leakage of SA during phase transition from solid to liquid, and also significantly improves the thermal conductivity. Additionally, integrity of the GO/PCM particles is maintained upon heating and cooling, even when the particles were composed of up to 85% PCM, maximizing the energy storage capabilities of the material. The “stitched” graphene oxide shells encapsulate, contain, and improve thermal conductivity of PCMs, and thus provide a new materials construct for thermal energy management and storage.

One-pot Allylsilane Synthesis from Enolizable Aryl Ketones

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A convenient one-pot synthesis converting methyl aryl ketones to allylsilanes is developed. The protocol is based on the abnormal Peterson Olefination reaction affording products in fair yield.

Isomeric Organic Ligands Demonstrate How Ligand Shape Directs the Symmetry of Lead Oxide Carboxylates

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Lead oxide carboxylates are a family of hybrid inorganic-organic compounds in which edge-sharing PbO tetrahedra form extended inorganic substructures that are further coordinated by carboxylate ligands. Some members of this family have noncentrosymmetric crystal structures, resulting in unusual properties such as second-harmonic generation. Extended inorganic substructures may afford these compounds unique properties unlike those of other hybrid materials, such as high thermal stability and mechanical anisotropy. Our lab has previously shown that the dimensionality of lead oxide carboxylates correlates with noncoordinating to coordinating volume ratio of the organic ligand. We have since synthesized four novel lead oxide carboxylates – two with isomeric naphthoate ligands and two with isomeric biphenylcarboxylate ligands – in order to further address the role of ligand shape in directing the condensation, topology, and symmetry of extended inorganic motifs. Each crystallizes with a unique space group, and analysis of their crystal structures indicates that these differences in symmetry relate to the ligands' abilities to fill space around helical inorganic chains. The structural patterns found may be applicable to other hybrid systems.
Tubulin inhibitors as selective Anti-Trypanosomal agents for treating human african trypanosomiasis - design, synthesis & biological evaluation
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Human African trypanosomiasis, known as African sleeping sickness disease, is a vector-borne parasitic disease in sub-Saharan Africa categorized as Neglected tropical diseases (NTD’s) with limited medical resources. High toxicity and limited efficacy of trypanocidal drugs contributed to an immediate need for novel drug development for human African trypanosomiasis (HAT). We identified sulfonamide derivative as selective tubulin inhibitors that showed the promise to the treatment of this disease, which was based on the tubulin protein structural difference between mammalian and trypanosome cells. In this study, we developed a synthetic scheme to generate these tubulin inhibitors and characterized all the compounds using NMR spectroscopy and HPLC-MS. Further lead optimization was performed to improve the efficiency of the drug candidates. Cell Proliferative assays were performed using MTS assay for Trypanosoma brucei brucei cells as the parasite model, and MTT assay for human normal kidney cells and mouse macrophage cells as the host model to evaluate the compounds. One new analog showed great potency with an IC50 of 70 nM to inhibit the growth of trypanosome cells and did not affect the viability of mammalian cells. Western blot analyses reveal that the compound decreased tubulin polymerization in T. brucei cells. Hence, I hypothesize that, our compounds showed better selectivity to inhibit the parasite cell growth. Currently, further structural modification of these tubulin inhibitors derivatives to enhance the cellular uptake is being performed in our lab.