ACS Local Section
Cleveland

2020

ACS Cleveland

Meeting in Miniature

Monday, March 9, 2020

Cuyahoga Community College

Western Campus

11000 Pleasant Valley Road

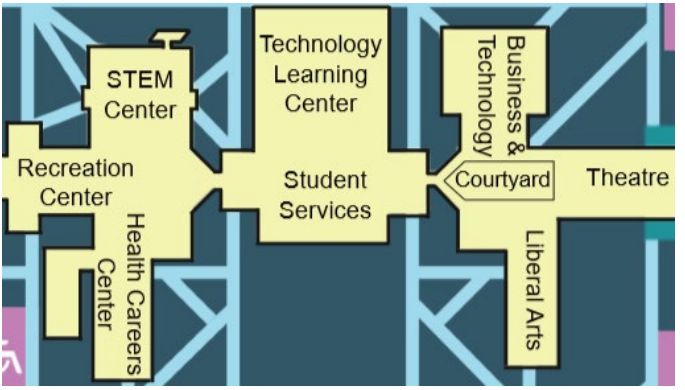
Parma, OH 44130

SCHEDULE

Noon	Registration and Tour of STEM Center
2:00	Welcome and Opening Remarks
2:30	Oral Presentations
4:30	Plenary Presentation
5:30	Dinner
6:30	Awards

Oral Presentations will be held in the Business & Technology Building

All other activities will be in the Student Services Building



Plenary Presentation

Being Purposeful with Your Career; Some Lessons Learned

David A. Schiraldi
Peter A. Asseff Professor of Organic Chemistry
Case School of Engineering, CWRU

You likely will work for about 35-40 years after graduation, consuming 90,000 hours, or ~ two thirds of your waking adult life. Those hours hopefully will engage you, contribute favorably to society, and will be well compensated for. So, do you have a plan? Should you have a plan? How do you go about planning? In school and every year thereafter, you should be learning new things, new facts, new methods, and broadening your portfolio of people with whom you can work. Work is very important, but so is your recreational time. I will provide some examples from my own career. Let's discuss…

On board the USAF B-17 *Aluminum Overcast,* 10,000 feet above Cleveland, 2019

Speaker Schedule

ROOM	236	238	239A	239B
2:30	Pignataro	Keil	Wang	Griffith
2:50	Krul	Ghazala	Y. Zhao	Delgado Rosario
3:10	Weader	Hoehn	Boron	Musaogullari
3:30	Maher	~~Chen~~	M. Zhao	Tomar
3:50	Chan	Lu	Bobba	Jimenez

ROOM	TIME	Presenter	Area	Advisor
239A	4:00	Bobba	Organic	Su
239A	3:00	Boron	Biochemistry	Sun
236	4:00	Chan	Biochemistry	Sun
238	3:30	~~Chen~~	Organic	Doud
239B	2:30	Delgado Rosario	Inorganic/Materials	Protasiewicz
238	2:30	Ghazala	Biochemistry	Belitsky
239B	2:00	Griffith	Physical	Crespo
238	3:00	Hoehn	Physical	Crespo
239B	4:00	Jimenez	Physical	Sauve
238	2:00	Keil	Biochemistry	Sun
236	2:30	Krul	Physical	Crespo
238	4:00	Lu	Inorganic/Materials	Sauvé
236	3:30	Maher	Biochemistry	Bayachou
239B	3:00	Musaogullari	Biochemistry	Chai
236	2:00	Pignataro	Analytical	Bayachou
239B	3:30	Tomar	Biochemistry	Sun
239A	2:00	Wang	Inorganic/Materials	Protasiewicz
236	3:00	Weader	Medicinal Chem	Youngs
239A	3:30	M. Zhao	Physical	Sauve
239A	2:30	Y. Zhao	Biochemistry	Sun

SILENCE ALL CELL PHONES

Bobba, Viharika

Advisor: Su, Bin
Cleveland State University

Synthesis and biological evaluation of selective tubulin inhibitors as anti-trypanosomal agents

Human African trypanosomiasis, also known as African sleeping sickness disease, is a vector-borne parasitic disease in sub-Saharan Africa, is still a considerable burden on rural communities, most notably in central Africa. In the absence of vaccine, disease control relies on case detection followed by treatment, and vector control. Most of the available drugs are suboptimal, but ongoing clinical trials provide hope for safer and simpler treatments. Previously, our lab developed a library of compounds which have exhibited selective inhibition of trypanosome cells, which was based on the tubulin protein structural difference, that showed promise to the treatment of this disease. In this study, we developed a synthetic scheme to derivatize and generate more potent tubulin inhibitors. Cell Proliferative assays were performed using MTS assay for Trypanosoma brucei brucei cells as parasite model, and MTT assay for human normal kidney cells and mouse macrophage cells as 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.

Boron, Mallorie, Xia Liu, Tiffany Hauzer and Xue-Long Sun*

Department of Chemistry, Chemical and Biomedical Engineering and Center for Gene Regulation of Health and Disease (GRHD), Cleveland State University, 2121 Euclid Ave.

Thrombomodulin Expression in Monocytes upon Differentiation to Macrophages

Thrombomodulin (TM) is a transmembrane glycoprotein that is primarily expressed on the surface of endothelial cells, where it serves as a receptor of thrombin for protein C activation, which regulates coagulation and inflammation. Research has revealed that TM is also expressed in immune cells, however its function is still unclear. Profiling the expression of TM in immune cells is the key initial step for clarifying its function in immune cells. The goal of this research is to determine TM expression in THP-1 monocytes upon their differentiation to macrophages. Cell surface levels of TM were evaluated by confocal microscopy and flow cytometry analysis. It was found that THP-1 macrophages express less TM on their surface immediately after differentiation from monocytes. ELISA and Western Blot analysis of cell lysates confirmed that macrophages expressed less TM than monocytes as well. Endothelial TM is known to contain a chondroitin sulfate moiety that serves as a secondary binding site for thrombin to enhance protein C activation. However, glycosylation of TM in immune cells and its influence on TM activity are unknown. We evaluated chrondroitin sulfate level of TM on THP-1 monocytes and macrophages by ELISA and its influence on protein C activation is under investigation.

Withdrawn - Chen, Melanie

Advisor: Doud, Katie
John Carroll University

Toward a Total Synthesis of Pumiliotoxin-(+)-251D

Poison dart frogs are a group of frogs in the family *Dendrobatidae* that are native to tropical Central and South America. Poison frogs have glands on their backs from which they secrete alkaloid toxins as a defense mechanism. The frogs are easy to distinguish due to their vibrant colors, which serve to warn their predators of their toxicity. Poison frogs are thought to derive their defensive molecules from alkaloids found in the arthropods they ingest, but the mechanisms by which those alkaloids are metabolized and modified by the frog are poorly understood. In order to study how poison frogs modify alkaloids biochemically, pure alkaloid is required. To that end, the goal of this research is to complete a total synthesis of one alkaloid of interest, pumiliotoxin-(+)-251D, in eleven steps. Stereochemically pure pumiliotoxin-(+)-251D will be used in future feeding studies to elucidate the metabolic modifications of alkaloids by poison frogs.

Chan, Ka Keung and Xue-Long Sun*

Synthesis of Azide Chain-end Functionalized Glycopolymer for Specific Protein Photo-labeling Applications

Department of Chemistry, Chemical and Biomedical Engineering and Center for Gene Regulation in Health and Disease (GRHD), Cleveland State University, 2121 Euclid Avenue, Cleveland, Ohio 44115, United States.

Carbohydrate-protein interactions are involved in many biological processes. Studying carbohydrate-protein interactions can provide abundant opportunities to discover molecular mechanisms of biological processes, potential therapeutic targets, and diagnostic mechanisms for various diseases. In this presentation, I report a straightforward synthesis of aryl azide chain-end functionalized glycopolymers and their protein photo-labeling application. Briefly, the aryl azide chain-end functionalized *N*-glycan polymers were synthesized from free glycan *via* glycosylamine

intermediates followed by acrylation and polymerization *via* cyanoxyl-mediated free radical polymerization (CMFRP) in one-pot fashion. Aryl azide chain-end functionalized *N*-galactosyl polymers, *N*-glucosyl polymers, and *N*-lactosyl polymers were successfully synthesized and characterized by ^{1}H NMR spectra. Affinity-assisted photo-labeling capability of the aryl azide *N*-glycan polymers was demonstrated with aryl azide *N*-lactosyl polymers for beta-galactose-specific lectin from Arachis hypogaea (PNA) after UV irradiation followed by SDS-PAGE with silver staining. Overall, novel aryl azide chain-end functionalized polymers will be useful multivalent biomimetic probes for specific protein labeling, functionality study, and biomarker identification applications both *in vitro* and *in vivo*.

Delgado Rosario, Emalyn

Advisor: Protasiewicz, John
Case Western Reserve University

Synthesis of New Material For Safer Li-ion Batteries

Lithium-ion batteries (LIBs) are the top choice for a rechargeable battery in electronic devices requiring high energy density. The use of LIBs in these devices has raised concerns regarding safety issues that have arisen and are currently studied to try and mitigate them. These safety issues revolve on the flammability of the organic solvents used in lithium-ion batteries and the high energy density that they require. Due to these safety issues many reports on incidents involving Li-ion battery related fires are widely known. To address these safety issues, a strategically designed lithium borate salt containing flame retardant ions (FRIONS) has been prepared and characterized. This lithium salt is low in molecular weight, displays high air and water stability and exhibits high decomposition temperatures. All of which are desirable properties for possible application in lithium ion batteries.

Ghazala, Maryam

Advisor: Belitsky, Jason
Oberlin College

Small molecule interactions with synthetic melanins: novel modulators and dye capture

Melanins are complex biological pigments that are present in many organisms. Eumelanin, which is the brown-to-black pigment, and its analog, polydopamine, form spontaneously upon oxidation of L-dopa and dopamine, respectively. The polymer formed via this process self-assembles and aggregates, resulting in particles that grow larger over time and form complex, high-mass structures that are visible to the human eye. While synthetic melanins were found to have numerous biomedical, technological, and other applications, the process of their formation remains poorly understood. This research uses the optical properties of melanin to study the aggregation step of its formation by UV-Vis spectroscopy and the addition of small organic molecules. Novel molecules were synthesized and tested and it was found that aggregation of eumelanin can be promoted by small aromatic molecules containing tertiary amines in their structure. The nature of the interactions between melanin and small molecules was investigated using dyes and UV-Vis spectroscopy. Dyes with similar structural properties as aggregation promoters were captured by melanin, suggesting that aggregation promoters become incorporated into the melanin particles as they form, uncovering information on the aggregation process of these biopolymers. Furthermore, these results show the potential use of melanin in capturing organic pollutants for water purification purposes.

Griffith, Cameron

Advisor: Crespo-Hernandez, Carlos
Case Western Reserve University

Photochemical Study of Dibenzothiophene in Different Solvents

The sunlight induced fate of polycyclic aromatic hydrocarbons (PAHs) and their derivatives have been a focus of interest due to their widespread formation from incomplete combustion processes and their varying levels of toxicity and mutagenesis in the environment. Many of the investigations performed to date have centered on PAHs and their derivatives containing nitrogen and oxygen substituents. However, polycyclic aromatic sulfur heterocycles (PASHs) are also found in similar concentrations throughout the environment and exhibit similar toxicity and mutagenic effects than PAHs, but have been studied to a significantly lesser extent. In this study, dibenzothiophene (DBT) was chosen as a model compound of the PASHs. The goal is to investigate the electronic relaxation pathways and the photoreactivity of DBT in solvents that may serve as models of different microenvironments in which PASHs are found in the environment. The relative photodegradation rates of DBT in acetonitrile, ethanol, and cyclohexane were investigated upon excitation with a polychromatic light source (315 ± 20 nm) using steady-state absorption spectroscopy as a function of irradiation time. In addition, transient absorption experiments were performed on DBT in the aforementioned solvents to characterize the transient species populated upon 320 nm excitation. The results from these investigations will be presented and discussed.

Hoehn, Sean, Sarah Krul, and Carlos E. Crespo-Hernández*

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106, United States; * E-mail: cxc302@case.edu

The impact of amino and carbonyl functionalization on the photostability of canonical RNA and DNA pyrimidine nucleobases

The nucleic acid bases that we know today are thought to have originated from simple precursors also referred to as proto-biotic RNA. These molecular ancestors of RNA and DNA may have formed from a vast number of organic compounds found on early Earth and/or delivered by meteorite infall. Understanding the evolution of chemical synthesis ranging from those precursors to today's canonical nucleobases is essential in answering questions to the chemical origins of life. Among other factors, ultraviolet radiation (UVR) from the sun should have played a key role in shaping and selecting the building blocks of life. The biological relevance of the pyrimidine chromophore and its carbonyl- and amino-substituted derivatives make these molecules excellent candidates for investigating how their interaction with UVR may have enabled the selection of the RNA and DNA pyrimidine nucleobases on early Earth. Absorption of UVR by these derivatives may result in the population of long-lived singlet and triplet excited states, which could significantly increase the probability of photochemical damage. Time-resolved spectroscopic results will be presented, which lend support to the idea that functionalization at the C2 and C4 positions of the pyrimidine chromophore has a preponderant role in controlling the inherent electronic relaxation mechanisms and photostability of the DNA and RNA pyrimidine nucleobases and their derivatives.

The authors acknowledge the National Science Foundation (Grant No. CHE-1800052) for financial support.

Jimenez, Jayvic Cristian

Advisor: Geneviève Sauvé
Case Western Reserve University

Further Tuning of Aza-dipyrromethene (ADP) Acceptors for Photovoltaic Applications

Organic photovoltaic or OPV materials offer low-cost production and they are light-weight and can be flexible which enables integration of photovoltaics where rigid silicon-based photovoltaics cannot be integrated, such as building facades, small appliances, or portable devices. OPVs generate electricity within the active layer that is comprised of a donor:acceptor blend for bulk-heterojunction cells. The first organic acceptor materials were fullerenes, but fullerene-based materials have inherent drawbacks such as chemical limitations, poor stability and morphology issues that prevented further efficiency gains; this provided motivation to move towards non-fullerene acceptors. One candidate as a fullerene replacement are aza-dipyrromethenes (ADPs) because of their high absorptivity in the visible to near-infrared (nIR) region of the spectra; they are easy to chemically modify enabling fine-tuning to their processability and physical properties. Our group has successfully developed ADP-based solar cell materials that showed promise as non-fullerene acceptors. In my talk, I will focus on the development of new ADP-based acceptors using a ligand that we developed in our lab called WS3, that have absorption well within the nIR as a platform for this study.

Keil, Joseph, Mallorie Boron, Xia Liu, and Xue-Long Sun*

Department of Chemistry and Chemical & Biomedical Engineering, Center of Gene Regulation of Health and Disease (GRHD), Cleveland State University, Cleveland, Ohio, OH 44115

Chain-end Functionalized Recombinant Thrombomodulin for Site-Specific Modification *via* Bio-orthogonal Chemistry

Thrombomodulin (TM), a membrane glycoprotein predominately expressed on endothelium, plays essential roles in keeping local hemostatic balance. Particularly, TM modulates the activity of thrombin from a procoagulant to an anticoagulant protease. When bound to TM, thrombin activates plasma protein C, which selectively inactivates coagulation factors Va and VIIIa. At the same time, TM-bound thrombin is unable to cleave fibrinogen or to activate platelets diminishing its procoagulant activity. The 4, 5, 6 EGF-like domain of TM (TM_{456}) has cofactor activity for thrombin binding and subsequently protein C activation. Therefore, recombinant TM_{456} is a promising anticoagulant candidate but has a very short half-life. PEGylation and glyco-engieering are practical choices to improve its pharmacokinetics. We report herein a recombinant rTM_{456} with a C-terminal LPETG motif for site-specific modification *via* sortase A-mediated ligation (SML). In addition, an azide functionality was easily introduced at the C-terminus of rTM_{456}-LPETG *via* SML with NH_2-diglycine-PEG_3-azide, which facilitates a site-specific modification of rTM_{456} *via* copper-free click chemistry (CFCC). Both SML and CFCC will facilitate uniform protein PEG- (glyco-)conjugate formation *via* site-specific end-to-end protein conjugation approach. The proposed chain-end functionalized recombinant protein approach can be applied to other protein modification as

well for both tagging or improving its pharmacodynamic and pharmacokinetic properties.

Krul, Sarah[1], Sean Hoehn,[1] Karl Feierabend,[1,2] and Carlos E. Crespo-Hernández*,[1]

[1] Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106, United States; * E-mail: cxc302@case.edu

[2] Present address: Department of Chemistry, College of Wooster, Wooster, Ohio 44691

Generation and dynamics of the guanine radical cation in a guanine quadruplex through the absorption of ultraviolet radiation

Guanine quadruplexes (G-quadruplexes) are four-stranded DNA/RNA structures involved in biological processes such as DNA replication, cell division, aging, and carcinogenesis. These DNA/RNA structures efficiently absorb ultraviolet radiation (UVR), particularly around 260 nm. Whereas monomeric G-nucleobases dissipate the absorbed UVR efficiently, thereby avoiding damage, absorption of a photon at 267 nm is thought to provide enough energy to ionize the guanine nucleobase within G-quadruplexes, forming reactive radicals and oxidatively induced DNA damage. Due to the importance of G-quadruplexes in biological functions, investigation of how the initially formed guanine radical cation can decay to other neutral radical species through events such as deprotonation or electron transfer is important. The proposed reaction path using nanosecond transient absorption spectroscopy (TAS) and computational methods involves deprotonation of the radical cation at the C2 position, $(G)^{+\bullet} \rightarrow (G\text{-}H2)^{\bullet}$, followed by C2 to C1 tautomerization of the deprotonated radicals, $(G\text{-}H2)^{\bullet} \rightarrow$ (G-

H1)•. However, the formation of the radical cation and the rate of its initial deprotonation process have endured elusive, which provides a motivation for the current study using femtosecond broadband transient absorption spectroscopy.

The authors acknowledge the National Science Foundation (Grant No. CHE-1800052) for financial support.

Lu, Chenwei (Charlie) Chunlai Wang, Jayvic C. Jimenez, Muyuan Zhao and Geneviève Sauvé.

Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106, USA.

Synthesis and characterization of Zinc(II) complexes of di(quinolinylethynyl) azadipyrromethene and its fluorinated derivates as electron acceptors for organic photovoltaics

Non-fullerene electron acceptors (NFAs) has achieved high performance in organic photovoltaics. However, most of NFAs have very complex structures. Zinc(II) complexes of azadipyrromethene (ADP) are electron acceptors that have shown good performance and have low synthetic complexity. Also, they are compatible with the industrial scalable electron donor poly(3-hexylthiophene) (P3HT). Previously, our group synthesized zinc complex of di(naphthylethynyl)ADP ($Zn(L2)_2$), resulting a good power conversion efficiency of 5.5%. In this work, we synthesized zinc(II) complex of di(quinolinylethynyl)ADP ($Zn(Q\text{-}L2)_2$) to increase its electron affinity. The identity of $Zn(Q\text{-}L2)_2$ was confirmed by MALDI-TOF, ^{1}H-NMR, ^{13}C-NMR and elemental analysis. The optical property of $Zn(Q\text{-}L2)_2$ was also characterized by Uv-vis. To further increase its electron mobility, we also synthesized its fluorinated derivatives,

Zinc(II)-di(quinolinylethynyl)-distal-trifluoromethyl-ADP (Zn(F1-Q-L2)$_2$) and Zn(II)-di(quinolinylethynyl)-distal-fluoro-ADP (Zn(F2-Q-L2)$_2$). We also characterized the fluorinated derivates by MALDI-TOF, ^{1}H-NMR, and ^{13}C-NMR.

Maher, Shaimaa

Advisor: Bayachou, Mekki
Cleveland state University

Novel Nitric Oxide releasing films based on inducible nitric oxide synthase and their biomedical applications

Although a tremendous number of Biomaterials are recently labelled as biocompatible for blood contacting medical devices, such as vascular grafts, stents, heart valves, and catheters, the thrombogenic nature of these materials can cause serious complications in patients, and eventually functional failure. In this project, we use layer-by-layer thin film building strategy to form layers of polyethyleneimine (PEI) and recombinant NOS enzymes as NO-releasing coatings. Charge-based layer-by-layer electrostatic adsorption allows for assembly of multi-component protein/PEI films with defined thickness and catalytic properties. When surfaces coated with PEI/NOS multilayered films are exposed to substrate arginine, a source of reducing equivalents, and other ingredients of the NOS reaction, nitric oxide is formed and released. In this work, we characterize the PEI/NOS thin films in terms of structure of NOS within the films as well as the amount of active NOS. We used cyclic voltammetry to determine the active enzyme concentration on the modified surfaces. We also examined how this activity relates to enzymatic activity in terms of NO released fluxes from the thin films. Finally, we assessed the functional performance of these films in terms of the extent to which they counteract platelet adhesion on the coated surfaces. To this end, we used platelet adhesion assays to

determine how the number of platelets adsorbed on the PEI/NOS films is affected by the amount of NO released.

Musaogullari, Aysenur[1], Alysia Mandato[2], Yuh-Cherng Chai[1*]

[1]Department of Chemistry, John Carroll University, University Heights, Ohio, USA

[2] Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Role of glutathione and reactive oxygen species on caspase-3 activation: A study with the kinase inhibitor staurosporine

Oxidative stress is known to contribute to the progression of apoptosis. Staurosporine is a broad-spectrum inducer of apoptosis, but its mechanism of action is not well understood. The goal of the present work was to elucidate the role of glutathione and reactive oxygen species in the execution of staurosporine-induced apoptosis. HeLa cells were treated with staurosporine at 1 μM for up to 4 h. The concentration of glutathione, generation of reactive oxygen species, and activation of caspase-3 were measured. The introduction of staurosporine significantly decreased the concentration of cellular glutathione and increased the presence of reactive oxygen species after 3 h. These findings were concurrent with the activation of caspase-3. Interestingly, pre-treatment of cells with N-acetyl cysteine, a precursor of glutathione, and a thiol antioxidant, failed to block the depletion of glutathione, generation of reactive oxygen species, and activation of caspase-3. Collectively, these results suggest that the cellular redox status may be one of the critical factors of the apoptotic pathway leading to caspase-3 activation by staurosporine.

Pignataro, Gina

Advisor: Bayachou, Mekki
Cleveland State University

Melanin-like Polymer Interfaces as Sensors for Electrochemical Determination of Peroxynitrite

Peroxynitrite is a powerful oxidant that has been linked to a host of medical conditions including Parkinson's disease, inflammatory responses, and cardiovascular dysfunction, to cite a few.

Melanin, a biological polymer, has a molecular framework that is capable of quenching free radicals and neutralizing reactive oxygen species.

The chemical or electrochemical oxidation of 5,6-dihydroxyindole (DHI) results in synthetic melanin-like films. The synthetic and natural melanin films share the ability to quench free radicals. Glassy carbon electrodes with electro-polymerized DHI film were examined as possible electrochemical interfaces to detect and quantify peroxynitrite. The reaction of electropolymerized DHI films and peroxynitrite causes changes in electrochemical responses of the synthetic film on the electrode. We can monitor these electrochemical changes using both cyclic voltammetry and differential pulse voltammetry. We show that the addition of micromolar aliquots of PON at physiological pH results in linear current changes both in cyclic voltammetry and in differential pulse voltammetry. Based on the current work, DHI-modified electrodes have the potential to be used as disposable PON sensors, with a sensitivity that is 214x higher than bare glassy carbon electrodes, and a detection limit as low as 18 uM.

Tomar, Sonia and Xue-Long Sun*

Investigation of substrate specificity of sialidases with membrane mimetic glycoconjugates

Department of Chemistry, Chemical and Biomedical Engineering and Center for Gene Regulation in Health and Disease (GRHD), Cleveland State University, Cleveland, OH, 44115

Sialidases or neuraminidases play important roles in various physiological and pathological processes by cleaving terminal sialic acids (Sias) (desialylation) from the glycans of both glycoproteins and glycolipids. To understand the biological significance of desialylation by sialidases, it is important to investigate enzyme specificity with native substrate in biological membrane of cells. Herein, we report a membrane-mimicking system with liposome ganglioside conjugates containing different lipids for evaluating substrate specificity of sialidase and the lipid effect on the enzyme activity. Briefly, liposomes of phosphatidylcholine (PC) and cholesterol with ganglioside (GM3 or GM1) along with different percentage of phosphatidylserine (PS) or phosphatidylethanol- amine (PE) were prepared and characterized. Their desialylation profiles with Arthrobacter ureafaciens (bacterial) sialidase and H1N1 (influenza viral) sialidase were quantified by HPLC method. A diversity of substrate preference was found for both bacterial and viral sialidase to the liposome ganglioside conjugate platform. The apparent K_m and V_{max} were dependent on the type of lipid. These results indicate that the intrinsic characteristics of the membrane-like system affect the sialidase specificity and activity. This biomimetic substrate provides a better tool for unravelling the substrate specificity and the biological function of sialidases and for screening of functional sialidase inhibitors as well.

Wang, Kai

Advisor: Protasiewicz, John
Case Western Reserve University

Modulation of luminescence in 1,3-benzazaphospholes using isolable *N*-heterocyclic carbenes

Fluorescent compounds that display emission changes in response to analytes continue to be of current interest as components in sensory applications. Recently 1,3-benzazaphospholes (BAPs), a type of low valent organophosphorus molecules, have been identified as a fluorescent material. In this study, we investigate the modulation of benzazaphosphole emission in response to the addition of isolable singlet carbenes, specifically 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (**IPr**) and a cyclic (alkyl)(amino)carbene (2,6-diisopropylphenyl)-4,4-diethyl-2,2-dimethyl-pyrrolidin-5-ylidene (**^{Et}CAAC**). In a published report, our group has demonstrated the ability of the aforementioned singlet carbenes to modulate the emission of secondary amine containing fluorophores.[1] Upon addition of **IPr**, luminescence of the primary 2-thiophenyl-1,3-benzazaphosphole (ThBAP) is quenched due to formation of a H-bonded BAP-carbene adduct; addition of ^{Et}CAAC also leads to the formation of an adduct that exhibits a similar reduction in emission. These reactions are reversible: release of carbene from the adducts formed allows restoration of fluorescence. Emission control is accomplished through not only concentration dependent adduct formation, but also through the addition of a Lewis acid, such as borane. Solution-state dynamics, solid-state characterization, and synthetic strategies towards BAP-carbene adducts will be discussed.

Weader, David[1,2], Michael Stromyer[1], Uttam Satyal[2], Philip Abbosh[2], Wiley Youngs[1]

[1] Department of Chemistry, The University of Akron, Akron, OH, 44325
[2] Molecular Therapeutics Program, Fox Chase Cancer Center, Philadelphia, PA, 19111

Synthesis and Biological Activity of Select Imidazolium Salts Against Bladder Cancer Cell Lines

Abstract: Imidazolium salts show tremendous potential as anticancer compounds. Among these salts are TPP1, which contains a triphenylphosphonium cationic substituent; TCK1, a fluorescent cyanine dye; and IS23. These compounds were synthesized, characterized, and evaluated *in vitro* to determine their efficacy against bladder cancer cell lines and primary mechanism of action. Upon a 1-hour exposure to these compounds and allowing 24-hour recovery, TPP1 was determined to have IC_{50} values ranging from 80-240 μM, TCK1 ranging from 1.0-8.0 μM, and IS23 ranging from 30-42 μM, each against at least 6 bladder cancer cell lines. Further *in vitro* assessments revealed that these compounds induce cytochrome c expulsion from isolated mitochondria and promote mitochondrial depolarization evidenced by JC-1 assays. Confocal microscopy experiments also show a subcellular localization of TCK1 to the mitochondria. These findings support the claim that these imidazolium salts proceed through a mechanism of mitochondrial-induced apoptosis and are potential intravesical therapies for nonmuscle invasive bladder cancer.

Zhao, Muyuan[1], Chunlai Wang [1], and Geneviève Sauvé [1]

[1] *Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106, USA.*

Study of Aza-dipyrromethene (ADP)-based Acceptors Zn(L2)2 and Fluorinated Derivatives for Organic Photovoltaics

In organic photovoltaics (OPVs), the traditional fullerene acceptors have limited tunability and stability, and they are very expensive. Non-fullerene acceptors (NFAs) have been developed to overcome these drawbacks. Aza-dipyrromethene (ADP) material $Zn(L2)_2$ has been shown to perform well in OPV using Poly(3-hexylthiophene-2,5-diyl) or P3HT as a donor, with a PCE as high as 5.5%. To further tune the optoelectronic properties of the zinc complex, fluorinated derivatives $Zn(1F\text{-}L2)_2$, $Zn(1F\text{-}L2)_2$, and $Zn(3F\text{-}L2)_2$ were synthesized, characterized and tested in devices. Fluorination had negligible effect on light absorption in both solution and film. Cyclic voltammetry indicates that fluorination decreased the HOMO energy levels slightly while not affecting LUMO energy levels. Results in OPVs show slightly lower PCE compared to $Zn(L2)_2$. These results are partially explained by poor film morphology observed by AFM, which may correlate with more charge recombination. Further testing is required to fully evaluate the effect of fluorination in these systems.

Zhao, Yu, Lei Yuan, Yang Liu, Dan Wang, Xue-Long Sun*

Department of Chemistry, Chemical and Biomedical Engineering and Center for Gene Regulation of Health and Disease (GRHD), Cleveland State University, Cleveland, OH, 44115

Modulating Cell Surface Sialoform of Macrophages with Zwitterionic Sialic Acid Derivatives

Macrophages are versatile cells that take part in many physiological and pathological processes. Macrophage cell surface expresses a dense layer of glycans often terminated with sialic acids (SAs) in different linkages, which is known as sialoform. Due to their terminal position and properties, SAs can mediate many biological processes of macrophages such as host-pathogen recognition, migration, and antigen presentation. SAs are a family of 9-carbon containing acidic monosaccharides. The most abundant SAs are *N*-acetylneuraminic acid (Neu5Ac) and *N*-glycolylneuraminic acid (Neu5Gc). Notably, humans make Neu5Ac but are incapable of synthesizing Neu5Gc. The NeuGc deficiency in humans is attributed to a truncation in the gene encoding cytidine monophosphate sialic acid hydroxylase (CMAH). In this study, we investigated Neu5Gc incorporation of human THP-1 macrophages and to see its impact on macrophage functions. In addition, we designed a Neu5Gly as a Neu5Gc analog and investigated its metabolic inhibition of Neu5Gc incorporation into THP-1 macrophages. As a result, there is no inhibition of the Neu5Gc incorporation, however, Neu5Gly incorporation was found for THP-1 macrophages. Further, the phagocytosis capability of THP-1 macrophages with different SAs were investigated with FITS-labeled *E. coli* bioparticles. The ability to modulate cell surface sialoform will be useful tool to understand the cell surface SA function and the molecular mechanisms of their underline biological processes and even to direct cell activity and elicit desired cellular functions.

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