
20th ANNUAL
CBGRC
Chemistry and Biochemistry
Graduate Research Conference
NOV 10, 2017

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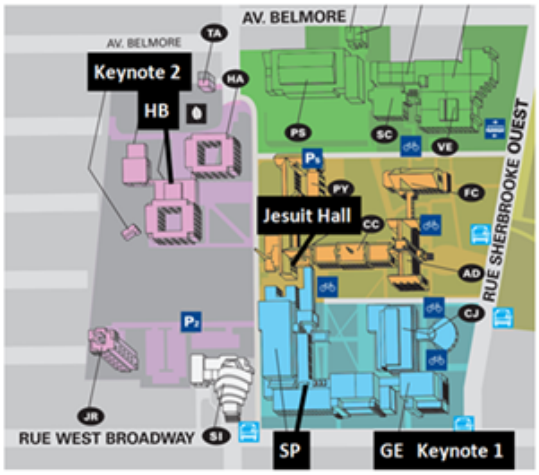

SP: Registration + Student Oral Presentations

GE: Morning Keynote

HC: Afternoon Keynote

Jesuit Hall: Posters and Wine and Cheese

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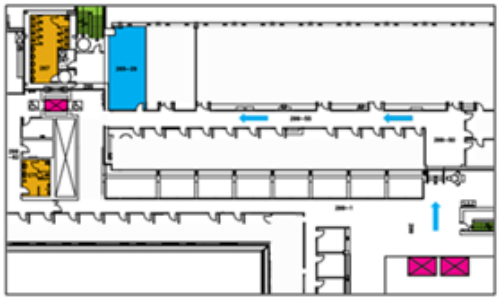

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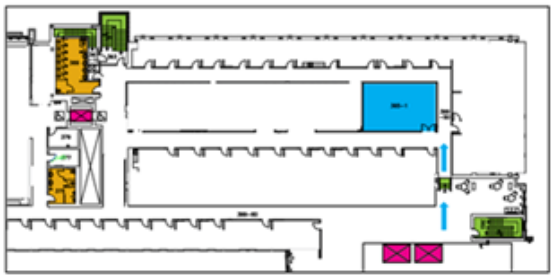

STAIRS

WASHROOMS

ELEVATORS

WELCOME NOTE

LETTRE DE BIENVENUE

Dear friends and colleagues,

It is with great pleasure that we welcome you to the 20th annual Chemistry and Biochemistry Graduate Research Conference. This year, we are especially proud to host such a diverse conference. Covering a wide range of fields, the keynote presentations from Dr. Yudin (University of Toronto) and Dr. Lee (University of Chicago), graduate student presentations and the poster session are sure to be stimulating. The organizing committee hopes to provide you with the best environment to share and discuss your research, build new connections and inspire new thought for your own research. In honor of our 20th anniversary, please join us at the wine and cheese to recognize the invaluable contributions of the past CBGRC organizers.

Once again, we would like to extend our gratitude to you all for being part of the CBGRC this year.

Sincerely,

The CBGRC Orgnaizing Committee

Chers amis et collègues,

C'est avec un immense plaisir que nous vous accueillons à la 20ième Conférence sur la Recherche aux Cycles Supérieurs en Chimie et Biochimie. Cette année, nous sommes particulièrement fiers de vous accueillir à une conférence d'une telle diversité. Couvrant une grande variéter de sujet, les présentations des conférenciers invités de Dr. Yuidin (University of Toronto) et de Dr. Lee (University of Chicago) ainsi que les étudiants aux cycles supérieurs vont vous stimuler en présentant un éventail de sujets abordés; améliorés par l'appui des participants et des juges. Le comité organisateur a fait de son mieux pour fournir aux étudiants, professeurs et représentants de l'industrie le meilleur environnement possible pour partager leur recherche et bâtir de nouvelles collaborations. Nous espérons que cette conférence sera productive et inspirante pour tous. En honeur de notre 20^{ième} anniversaire, joigner vous a nous durant notre vin et fromage pour reconaitre la contribution des organisateurs des années précendent.

De nouveau, nous tenons à exprimer notre gratitude envers vous tous pour votre participation à la CRCSCB cette année.

Sincèrement

Le Comité Organisateur de la CRCSCB

Dr. Andrei K. Yudin

Professor, Department of Chemistry
University of Toronto

Development of bioactive molecules using the tools of chemical synthesis

Production of molecules with desired functional attributes is the enduring objective of chemical synthesis. As structural complexity of therapeutic agents increases, so is the number of interrelated parameters that need to be controlled. Bioactive macrocycles offer a good example underscoring this notion. Their relatively large polar surface area increases the chance to interrogate extended protein binding sites, but also creates an impediment to achieving favorable drug properties. Synthetic tools that allow one not only to cyclize linear precursors but also to exercise control over conformation-driven cellular permeability are in high demand. This part of the lecture will summarize our ongoing efforts in this area and will highlight key experimental findings obtained in the past few months.

Another active area of our research targets biologically active boron-containing molecules. Boron is an abundant element on earth yet, despite its availability, C-B bonds are not present in the structures of natural products. This, however, does not mean that boron has no utility in chemical biology and drug discovery. On the contrary, there are numerous examples of bioactive molecules that bear C-B bonds. Similar to the synthetic utility of organoboron compounds, the biological activity of boron-containing molecules is based on reversible covalent interactions with nucleophiles. I will present the foundational principles of *Boroscan* – an enabling technology to construct boron-containing bioactive molecules using amphoteric molecules.

KEYNOTE SPEAKER
INTERVENANTS PRINCIPAUX

Dr. Ka Yee C. Lee

Professor, Department of Chemistry
University of Chicago

The chemistry of breathing: Wrinkle-to-fold transitions in lung surfactants and other elastic sheet

Lung surfactant is a mixture of lipids and proteins that coats the alveoli, and its main mechanical function is to reduce the work of breathing by reducing the surface tension. Insufficient amount of lung surfactant in premature infants leads to neonatal respiratory distress syndrome, while lung trauma can result in acute respiratory distress syndrome. In order to develop effective treatment for these conditions, a better understanding of the interactions between lung surfactant lipids and proteins is needed. Utilizing optical and atomic force microscopy techniques, we have examined the collapse process in lung surfactant, and have examined how the presence of lung surfactant peptide, SP-B_{1-25}, induces a reversible collapse in lung surfactant monolayers. Our observation indicates that SP-B_{1-25} in simple phospholipid and model lung surfactant monolayers promote the protrusion of folds into the subphase at low surface tensions. The folds remain attached to the monolayer and reversibly reincorporated upon expansion. Without SP-B, an unsaturated lipid-rich phase is irreversibly "squeezed-out" of the monolayer at higher surface tensions. These folded reservoirs reconcile how lung surfactant can achieve both low surface tensions upon compression and rapid respreading upon expansion, and have important implications concerning the design of replacement lung surfactants. The onset of this folding instability can be understood in terms of the mechanical properties of the film. Statistics of the folding events will be presented and the link between folding on monolayers of nm thickness and that on polyester films that are 3 orders of magnitude thicker will be discussed. By studying different types of monolayers, we have shown that this folding transition in monolayers is not limited to lung surfactant films, but rather represents a much more general type of stress relaxation mechanism. Our study indicates that collapse modes are found most closely linked to in-plane rigidity. We characterize the rigidity of the monolayer by analyzing in-plane morphology on numerous length scales. More rigid monolayers collapse out-of-plane via a hard elastic mode similar to an elastic membrane, with the folded state being the final collapse state, while softer monolayers relax in-plane by shearing. For the hard elastic mode of collapse, we have further demonstrated experimentally and theoretically that the folded state is preceded by a wrinkled state.

SCHEDULE
HORAIRE

Time	Activity	Location
08:00	**Registration (All Day)**	SP Atrium
08:00-08:45	**Breakfast**	SP Atrium
08:45-10:00	**Student Presentation A**	**Organic Chemistry (SP 254.01)** **Analytical Chemistry (SP 265.29)** **Biochemistry (SP 365.01)**
10:00-10:30	Sponsors and Coffee Break	SP Atrium
10:30-11:45	Keynote Speaker I	Dr. Andrei K. Yudin (GE 110)
11:45-13:00	Lunch	SP Atrium
13:00-14:15	**Student Presentation B**	**Organic Chemistry and Physical Chemistry (SP 254.01)** **Analytical Chemistry (SP 265.29)** **Biochemistry and Molecular Biology (SP 365.01)**
14:15-14:45	Sponsors and Coffee Break	SP Atrium
14:45-16:00	Keynote Speaker II	Dr. Kai Yee C. Lee (HC 157)
16:00-17:30	**Stundent Presentation C**	**Analytical Chemistry and Environmental (SP 265.29)** **Molecular Biology and Nanochemistry (SP 365.01)**
17:30-19:00	Poster Presentation	Jesuit Hall
18:00-23:00	Wine and Cheese	Jesuit Hall

ORGANIC CHEMISTRY/CHIMIE ORGANIQUE (8:45-10:00)

F. Chacon-Huete (Concordia University): Synthesis of 2,5-diaryl Symmetric and Non-symmetric Furans from Biomass Derived Starting Materials

J.-L. Do (Concordia University): Solvent-free Mechanochemical Approach to the Friedländer Reaction: Implications and Applications in the Synthesis of Small Molecules and Materials

D. Duncan (McGill University): Resensitization of Salmonella enterica to the Antibacterial Metabolite of Macrophages Itaconate

A. Elmehriki (McGill University): Late Stage Introduction of Quaternary Stereocentres: Total Synthesis of Puraquinonic Acid

C. Liczner (Concordia University): Diselenide Cross-linking of Oligonucleotides Between 2'-Deoxy-6-Selenoinosine

ORGANIC CHEMISTRY/CHIMIE ORGANIQUE (13:00-14:15)

J.-C. Grenier-Petel (Université de Montréal): Photochemical Cobalt-catalyzed C-H Functionalization of Heterocycles

J. Guan (McGill University): Stabilized Pantothenamide Analogues as Novel Antimalarial Agents

S. Parisien-Collette (Université de Montréal): Photochemical Intramolecular Amination for the Synthesis of Heterocycles

PHYSICAL CHEMISTRY/PHYSICO-CHIMIE

(13:00-14:15)

R. Miclette Lamarche (Concordia University): Impacts of ω Thiol on Phenolic Surfactant Air-water Behavior: Implications for Deposition onto Gold Surface from the Air-water Interface

H. Youssef (Concordia University): Cholesterol Alters Antimicrobial Peptide GL13K's Organization and Insertion into Model Lipid Monolayers

ANALYTICAL CHEMISTRY/CHIMIE ANALYTIQUE

(8:45-10:00)

J. Asselin (Université Laval): Development and Application of Fluorescent Core-shell Nanoparticles for Ionic Biosensing

A. Bain (McGill University): Designing a Hollow Beam Optical Trap for the Study of Absorbing Atmospheric Aerosol Particles

J. D. Chin (Concordia University): A Novel Interface for Coupling CE to a Capillary Electrophoresis Array for Multidimensional Separations of Complex Biological Samples

B. Desharnais (Concordia University & Laboratoire de sciences judiciaires et de médecine légale): Qualitative Method Validation: A First Approach through Binary Results Applied to a Multi-drug LC-MS/MS Method

E. Eysseric (Université de Sherbrooke): Application of Spectral Accuracy to Assist the Identification of Organic Compounds in Environmental Analysis

ANALYTICAL CHEMISTRY/CHIMIE ANALYTIQUE

(13:00-14:15)

S. Gallant (Université de Montréal): Development and Optimization of Liquid Chromatography-Mass Spectrometry Methods for Characterization of Regenerable Amine Solvents used in CO_2 Capture

A. Gupta (Concordia University): Development of Liquid Chromatography-Mass Spectrometry Assay for Determination of 11β-Prostaglandin F2α and Leukotriene E4 in Human Urine

A. Imfeld (Concordia University): Environmental Forensics: Using Compound-Specific Stable Carbon Isotope Analysis to Track Petroleum Contamination

A. Napylau (Concordia University): Development of Liquid Chromatography-Mass Spectrometry Assay for the Measurement of 28 Eicosanoids

A. Rafferty (McGill University): Investigating Deformed Aerosol Droplets Using A Dual Beam Optical Trap

ANALYTICAL CHEMISTRY/CHIMIE ANALYTIQUE

(16:00-17:30)

I. Slobodchikova (Concordia University): Multi-mycotoxin LC-MS Method for Detection and Quantification of 17 Mycotoxins in Human Plasma

R. Sonnenberg (Concordia University): A Comparison of Two Hydrophilic Interaction Liquid Chromatography Stationary Phases for Global Metabolomics of Human Plasma

X. Yuan (Queen's University): Carbonated Water for the Separation of Carboxylic Compounds: A Green Chromatography Approach

ENVIRONMENTAL CHEMISTRY/CHIMIE ENVIRONEMENTALE

(16:00-17:30)

K. Balind (Concordia University): The role of iron-sulfides on cycling of organic carbon in the St Lawrence River system

A. Kormendi (Concordia University, GEOTOP): Proposed mitigations of challenges faced in aqueous methane stable isotope analysis

BIOCHEMISTRY/BIOCHIMIE (8:45-10:00)

N. Brosseau (Université de Montréal): Human OCT1 Mediates the Uptake of Anticancer Drugs into Cells

M. Chung (Concordia University): Biochemical and Biophysical Characterizations of Mutational Variants of Human tRNA Nucleotidyltransferase

J. Ducharme (McGill University): CYP3A4 Cooperativity Investigation via the Bioconjugation of Natural Ligands

C. Fortinez (McGill University): Structural and Functional Investigations of the Biosynthetic Pathway for Bacillamide, a Thiazole-containing Natural Product

E. Malek-Adamian (McGill University): 4′-***C***-Methoxy-2′-Deoxy-2′-Fluoro Modified Ribonucleotides Improve Metabolic Stability and Elicit Efficient RNAi-Mediated Gene Silencing

BIOCHEMISTRY/BIOCHIMIE (13:00-14:15)

A. Tchoumi Neree (Department of chemistry, Université du Québec à Montréal, Canada): ***In vitro*** Analysis of the Interaction Between Diamine Oxidase and Cholic Acid in Simulated Intestinal Fluid

MOLECULAR BIOLOGY/BIOLOGY MOLÉCULAIRE

(13:00-14:15)

O. Gagnon (Ottawa University): VIPER: A Webserver for ***In Silico*** Simulation of Protein-peptide Interaction Specificity

D. Hossain (McGill University): Vpr Destabilizes Centrosome Homeostasis by Hijacking EDD-DYRK2-DDB1^{VprBP}

V. Lipari (McGill University): Relation Between Dye-filling and Ivermectin Resistance in ***Caenorhabditis Elegans***

S. Logan (Carleton University): Fat but Fit: How Hibernating Ground Squirrel AdiposeTissue Regulates Pro-inflammatory Signaling Pathways

MOLECULAR BIOLOGY/BIOLOGIE MOLÉCULAIRE

(16:00-17:30)

S. Menggad (Université de Montréal): Targeting The Proteasome Associated Deubiquitinase PSMD14 As A Novel Anti-Cancer Therapeutic Strategy

D. Tchelougou (Centre de Recherche de l'Hôpital Maisonneuve - Rosemont, Université de Montréal): A Novel Mechanism of Regulation of the Tumor Suppressor BAP1/ASXL2 Complex by Monoubiquitination

NANOCHEMISTRY/NANOCHIMIE (16:00-17:30)

V. Adibnia (Université de Montréal): Diffusion of Nanoparticles through Engineered Hydrogel Microstructures

W. Copp (Concordia University): Influence of Nucleotide Modifications at the C2' Position on the Hoogsteen Base-Paired Parallel-Stranded Duplex of Poly(A) RNA

V. Marando (NMX Research & Solutions): Revealing and Monitoring Small-molecule Aggregation Properties using T_2-CPMG NMR to Improve Drugs and Drug Discovery Processes

R. Walsh (INRS-IAF): Small Nucleotide Probes For Ligand-Binding Analysis of the Microcystin-LR Aptamer

Poster Session (17:30- 19:00)

ANALYTICAL CHEMISTRY/CHIMIE ANALYTIQUE

A01 - K. Barry (Université de Sherbrooke): Metabolomics Used to Study Sub Lethal Effects of a Mixture of Emerging Organic Contaminants on Model Species Daphnia Magna

INORGANIC CHEMISTRY/CHIMIE INORGANIQUE

I01 - N. Bélanger-Desmarais (Université de Montréal): Variable Temperature Raman Spectroscopy and DFT Frequency Calculations of Coordination Compounds

I02 - Y. Li (Concordia University): Oxygenation of 3,5-di-*tert*-butyl-phenol: reaction, optimization and mechanism

I03 - J. Zsombor-Pindera (Concordia University): Copper Complexes with Novel Chelating Nitroso Ligands

ORGANIC CHEMISTRY/CHIMIE ORGANIQUE

O01 - D. Farajat (Concordia University): Chiral Amplification of Uracil Derivative Conglomerate Crystals via Viedma Ripening

MOLECULAR BIOLOGY/BIOLOGIE MOLÉCULAIRE

M01 - O. Ahmed (Université de Montréal): Ubiquitination of BAP1/ASXL Tumor Suppressor Complex: A Key Mechanism for Gene Regulation and Cell Fate Determination

M02 - A. Boutayeb (Université de Montréal): Role of the Deubiquitinase MYSM1 in the Genotoxic Stress Response Role of the Deubiquitinase MYSM1 in the Genotoxic Stress Response

M03 - A. Caillier (Université Laval): Implication of Sam68 RNA Binding Domains in Migration of Metastatic Cells

M04 - C. DeKraker (McGill University): Examining Repair Kinetics and Cytoskeletal Architecture During Mammalian Somatic Single-cell Wounding

M05 - Z. Lung (Carleton University): DNA Damage and Repair Mechanisms in the Wood Frog, Rana Sylvatica

M06 - J. Mattice (Carleton University): Examining the Regulation of Glutathione Reductase in Response to Ischemic Stress in the Dehydration-tolerant African Clawed Frog, *Xenopus Laevis*

M07 - K. Szereszewski (Carleton University): A Little PARP of DNA Damage During Hibernation in the Hibernating Ground Squirrel

M08 - D. Tchelougou (Centre de Recherche de l'Hôpital Maisonneuve - Rosemont, Université de Montréal): A Novel Mechanism of Regulation of the Tumor Suppressor BAP1/ASXL2 Complex by Monoubiquitination

M09 - D. Zhou (McGill University): Investigating the Balancing Forces of Programmed Cell Death and Survival in Yeast

BIOCHEMISTRY/BIOCHIMIE

B01 - L. T. Canh (Université du Quebec à Montréal): Copper Complexes with Amino Acids as Bioactive Agents for Transdermal Administration in Treatment of Certain Neurodegenerative Diseases

B02 - J. Di Trani (McGill University): Methods for Measuring Enzyme Kinetics Using Isothermal Titration Calorimetry

B03 - C. Fuchs (Université de Montréal ; Centre Hospitalier Universitaire Sainte-Justine, Montreal): Impact of SRP72 on ETV6 Transcription Factor in Acute Lymphoblastic Leukemia

B04 - I. Harb (McGill University): Insight into the Origin of the Formylation Tailoring Domain Found in the Linear Gramicidin Nonribosomal Peptide Synthetase

B05 - M. Jafari (Université du Quebec à Montréal): Nanoscale Size and Morphology Studies of Excipients Made From Complexed Chitosan and Modified Starch

B06 - N. Kuksal (Memorial University): Examination of Importance of ROS Release from Complex I in Ischemia-reperfusion Injury

B07 - L. Masclef (Université de Montréal): Dynamic Regulation of FOXK1 by O-GlcNAcylation During Cell Cycle Progression

B08 - S. Ouellette (Concordia University): Determining Protein-Protein Interactions and Intracellular Organisation of the *E.coli* Enterobactin Metabolon Through *in vivo* Chemical Crosslinking

B09 - N. Reid (Concordia University): Identifying Genes Responsible for tRNA Nucleotidyltransferase Production in the Yeast *Schizosaccharomyces Pombe*

B10 - K. Uggowitzer (McGill University): Perturbing Activity of Class II Lanthipeptide Synthetase Through Mutations of an Overlooked Intrinsically Disordered Loop

B11 - M. Uriarte (University of Montréal): Regulation of the Tumor Suppressor BRCA1 by Ubiquitination and Sumoylation

ENVIRONMENTAL CHEMISTRY/CHIMIE ENVIRONNEMENTALE

E01 - V. Esmaeili (Université du Quebec à Montréal): Toxicity Effect of Cu and Cd on the Cell Physiology of Green Alga *Oocystis Polymorpha*

NANOCHEMISTRY/NANOCHIMIE

N01 - J. Asselin (Université Laval): Metal-enhanced Fluorescence and Energy Transfers in Silver Core@silica Multishell

N02 - J.-R. Macairan (Concordia University): Multimodal Imaging Probes Using Carbon Dots

N03 - G. Mandl (Concordia University): Synthesis of a Near Infrared-Responsive Azobenzene-based Supramolecular Hydrogel using $LiYF_4$:Yb^{3+}/Tm^{3+} Upconverting Nanoparticles

N04 - F. Noun (Concordia University): Metal-induced Fluorescence Quenching in Carbon Dots in Sensing Applications

N05 - J. R. Daniel (Université Laval): Metal Ion Speciation Controls the Morphology of Bimetallic Nanoshells in Galvanic Replacement

N06 - F. Victoria (Concordia University): Synthesis and Design of Chiral Carbon Dots Using Simple Molecular Precurors

CHEMISTRY EDUCATION/ENSEIGNEMENT DE LA CHIMIE

CE01 - K. Lapierre (University of Ottawa): A Large Scale Electronic Card Sort to Investigate Student's Interpretations of Organic Reactions

ABSTRACTS / RÉSUMÉS

ANALYTICAL CHEMISTRY/ CHIMIE ANALYTIQUE

Oral Presentations / Présentations Orales

Development and Application of Fluorescent Core-shell Nanoparticles for Ionic Biosensing

J. Asselin*, D. Boudreau
Université Laval

Biomedical studies of cell metabolism and signaling hinge on quick and precise detection methods for different molecules and ions in physiological conditions. While fluorescence spectroscopy and microscopy apparatus are well implemented for these types of experiments, the intrinsic properties of organic fluorophores with regards to photostability, absorptive cross-section and brightness can be limiting for their long-term observations. Recently, many solutions have been developed to prevent these shortcomings, one of which being plasmonic core@shell particles incorporating fluorescent probes in their architecture. In this study, we have designed and applied such systems to measure variations in extracellular proton (pH), halide and metallic ion concentrations with fluorescence steady-state or time-resolved characterizations. Thorough optimization for the syntheses of metal cores (Ag, Au, In) and the condensation of multiple silica layers have allowed high tunability of analytical properties like sensitivity, ratiometric normalization, bimodal discrimination and response time. The applicability of our nanosensors was demonstrated both on colloidal suspensions and on planar microfluidic substrates, with diversified biological systems of reference such as neurons, cardiac fibroblasts, and *S. salivarius* biofilms.

Designing a Hollow Beam Optical Trap for the Study of Absorbing Atmospheric Aerosol Particles

A. Bain*, T. Preston
McGill University

Several methods exist that allow for the accurate characterization of non-absorbing aerosols on the single particle level, but extending these methods to absorbing particles introduces large uncertainties in retrieved parameters. Conventional aerosol optical tweezers cannot be used to trap strongly absorbing particles as the trapping beam will heat the particle, leading to an unstable trap or particle vaporization. However, hollow beams that utilize the photophoretic force that is caused by this heating have been demonstrated to trap absorbing particles.

We have developed a hollow beam optical trap that can be used to study strongly absorbing aerosol particles. The angular light scattered by aerosol particles with diameters similar to the wavelength of incident light can be described by Mie theory. We collect and fit this angular light scattering. This allows us to retrieve the sizes and refractive indices from trapped particles. Often when collecting scattered light from single particles, intensity is measured without regard for the phase or polarization of the light. Our optics and analysis utilizes this previously disregarded information to improve the accuracy of all fitted parameters. By

pairing the hollow beam trap and fitting algorithm we can determine the complex refractive indices of absorbing aerosol.

A Novel Interface for Coupling CE to a Capillary Electrophoresis Array for Multidimensional Separations of Complex Biological Samples

J. D. Chin*, C. D. Skinner
Concordia University

Analytical separations remain challenging in proteomics due to the sample complexity and large concentration dynamic range. Current online multidimensional separations require compromise; long analysis times if the 2ndD requires regeneration between injections, or reduced separation efficiency if the 2ndD is operated rapidly. Multiplexing the 2ndD with parallel concurrently-operated capillaries achieves fast sampling of the 1stD, while relaxing the constraints on the 2ndD separations, permitting optimal 2ndD separation conditions. We have investigated a novel interface that allows continuous sampling of a 1stD CE separation by a 2ndD CE array for rapid, high peak-capacity separations.

The CE×CE interface performs precision injections across a 2ndD array of 8 capillaries, with separation efficiencies approaching 900,000 plates/m. Utilizing a pH shift (acetate to borate) to approximate orthogonal separation mechanisms, separation performance will be demonstrated using simple peptide mixtures as well as complex model protein digestates. The total analysis time, when sampling 1stD effluent using parallel 2ndD separations, is increased by ***1×2ndD separation window length***, versus ***# of 2ndD injections×2ndD separation window length*** for current multidimensional designs - a significant decrease. This modular interface can accept future addition of more capillaries, leading to higher 1stD sampling rates, and even greater method development flexibility in each dimension.

Qualitative Method Validation: A First Approach through Binary Results Applied to a Multi-drug LC-MS/MS Method

B. Desharnais[1*], J. Laquerre[2], M.-A. Morel[2], C. Côté[2], P. Mireault[2], C. D. Skinner[3]
[1]Concordia University & Laboratoire de sciences judiciaires et de médecine légale, [2]Laboratoire de sciences judiciaires et de médecine légale, [3]Concordia University

The aim of this project is to develop a method validation procedure for qualitative methods that is fully based on their binary output.

Based on the literature discussing the theoretical behaviour of methods with a binary output, and initial experimental results, a validation scheme covering estimation of the standard deviation at the cutoff concentration, preparation of probability curves and calculation of validation parameters (false positives and false negatives rate as well as reliability, selectivity and sensitivity) was outlined.

This validation procedure was applied to a screening method covering 40 drugs and metabolites. Samples were extracted by protein precipitation and analyzed on an LC-MS/MS.

Following analysis of the 10 blood samples spiked at the cutoff, analytes were binned into three groups based on the magnitude of their standard deviation. The final experiment resulted

in 31 out of 40 analytes being validated, with false positive rates oscillating between 0 and 80% and false negative rates oscillating between 0 and 10%. Reliability rate (60% - 100%), selectivity rate (90% - 100%) and sensibility rate (20% - 100%) were also calculated.

Because of the unforeseen problem of daily changing standard deviations, a more developed statistical approach will be necessary and is currently under development.

Application of Spectral Accuracy to Assist the Identification of Organic Compounds in Environmental Analysis

E. Eysseric[1*], K. Barry[1], F. Beaudry[2], M. Houde[3], C. Gagnon[3], P. A. Segura[1]
[1]Université de Sherbrooke, [2]Université de Montréal, [3]Environment and Climate Change Canada (ECCC)

Identifying a substance in environmental samples based only on accurate mass measurements can be difficult especially for medium sized to large molecules. Spectral accuracy (SA) is a powerful a tool for molecular formula generation and helps in the identification process of emerging organic contaminants (EOCs) and their transformation products in surface water for example.

Nine EOCs frequently found in surface water were spiked in methanol and surface water extracts at concentrations ranging from to 0.38 to 12 µg L^{-1}. They were then injected into three different mass analyzers (triple quadrupole, quadrupole-time-of-fight and quadrupole-orbitrap) to study the impact of matrix composition, analyte concentration and mass resolution on the correct identification of molecular formulas using spectral accuracy. SA and ranking of the correct molecular formula were in many cases compound-specific due principally to conditions affecting signal intensity like matrix effects and concentration. Results showed that higher concentrations and higher resolutions favoured the ranking of the correct formula. With SA and mass accuracy, the number of possible molecular formulas for EOCs of molecular masses ranging between 215 to 837 Da to less than 10. In multiple instances, the correct molecular formula could be unambiguously assigned.

Development and Optimization of Liquid Chromatography-Mass Spectrometry Methods for Characterization of Regenerable Amine Solvents used in CO_2 Capture

S. Gallant[*], A. Lapointe, A. Furtos, K. Waldron
Université de Montréal

Post-combustion capture of CO_2 can be achieved using aqueous amine-based solvents. During the solvent regeneration process, many degradation products are formed; primarily amines and nitrosamines. These need to be characterized for both process monitoring and improvement. Our objective is to develop LCMS approaches to identify the unknown products in solvent samples used for CO_2 capture. Being highly polar, separation of these species can only be achieved by HILIC: Hydrophilic Interaction Liquid Chromatography. High-resolution MS and MS/MS provide confident peak identification. Using an 18-compounds standard mixture, five HILIC columns and five mobile phase conditions (i.e., 25 combinations) were screened under the same gradient to find the best efficiency, symmetry and number of peaks. By these performance criteria, 3 stationary phases (Luna-CN, PFP and BEH-Amide) were selected for

optimisation, this time using real samples suspected to have >30 species. Peaks were clustered even for the best conditions (20mM ammonium formate in the aqueous eluent; 5% EtOH in aqueous and acetonitrile eluents), so isocratic separations were studied to evaluate the dead time and k' values of the species as a function of %aqueous eluent. The range of aqueous eluent for HILIC-based retention was quite narrow and guided gradient optimization to improve peak resolution.

Development of Liquid Chromatography-Mass Spectrometry Assay for Determination of 11β-Prostaglandin F2α and Leukotriene E4 in Human Urine

A. Gupta*, A. Napylau, D. Vuckovic
Concordia University

Anaphylaxis is a severe allergic reaction that is rapid in onset and fatal. 11β-Prostaglandin F2α (11β-PGF2α) and Leukotriene E4 (LTE4) have recently been proposed as anaphylaxis biomarkers. The objective of this research is to develop an ultra-performance liquid chromatography-quadrupole time of flight (UPLC-QTOF) method to measure urinary 11β-PGF2α and LTE4. C18 reversed-phase chromatography and water/acetonitrile/acetic acid mobile phase were used to ensure the separation of 11β-PGF2α from other prostaglandin isomers. Negative electrospray ionization (ESI) was selected for both analytes, because it provided better intensity and signal-to-noise ratio. Oasis HLB, Strata reverse phase C18-E, Oasis mixed mode strong anion HLB exchange and weak anion exchange solid phase extraction (SPE) cartridges were tested to develop sample preparation and pre-concentration procedure for this application. Strata C18 (97% for 11β-PGF2α and 95% for LTE) and mixed-mode HLB sorbent gave the best recovery (88% for 11β-PGF2α and 91% for LTE) in standard solution. Additional evaluation of these SPE methods to determine recovery in urine and matrix effects is currently underway.

Environmental Forensics: Using Compound-Specific Stable Carbon Isotope Analysis to Track Petroleum Contamination

A. Imfeld[1*], Y. Gelinas[1], A. Ouellet[2]
[1]*Concordia University,* [2]*Centre d'expertise en analyse environnementale du Québec*

Crude oil and petroleum products are continually being introduced into the environment during transportation, production, consumption and storage. Source identification of these organic contaminants proves challenging due to a variety of factors. Samples are complex, compounds need to be separated from an unresolved complex mixture of highly altered aliphatic and aromatic compounds, and chemical composition and biomarker distributions can be altered by weathering, aging, and degradation processes. The aim of our research is to optimize a molecular and isotopic ($\delta^{13}C$, $\delta^{2}H$) method to fingerprint and identify petroleum contaminants in sediment matrices, and to trace the temporal and spatial extent of the contamination event. This method includes the extraction, separation and analysis of petroleum derived hydrocarbons. Extraction and separation is achieved using sonication, column chromatography and urea adduction. Compound identification and molecular/isotopic fingerprinting is obtained by gas chromatography with flame ionization (GC-FID) and mass spectrometer (GC-MS) detection, as well as gas chromatography coupled to an isotope ratio mass spectrometer (GC-IRMS). This method will be used to assist the Centre d'Expertise en

Analyse Environnementale du Québec to determine the nature, sources and timing of contamination events as well as for investigating the residual contamination involving petroleum products.

Development of Liquid Chromatography-Mass Spectrometry Assay for the Measurement of 28 Eicosanoids

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Eicosanoids are the biological oxidation products of arachidonic acid and related C20 polyene acids and exhibit remarkable physiological activity. It is challenging to develop the assay for the measurement of eicosanoids in brain tissue because of low concentration of eicosanoids (pg/mg of protein), complexity and heterogeneity of brain matrix, instability of some eicosanoids, and the existence of different isomers of many eicosanoids. The main objective of this work was to develop LC-MS method that can be used for reliable determination of prostaglandin, leukotriene, hydroxyeicosatetraenoic acids and epoxyeicosatrienoicacid sub-classes. C18 reversed phase chromatography in combination with acetonitrile/isopropanol mobile phase allowed to separate all isomeric eicosanoids of interest. The effect of mobile phase additives: acetic acid, formic acid and ammonium acetate was evaluated. Acetic acid gave 1.2 and 8-fold improvement, respectively. The stability of eicosanoid standards was evaluated using freeze and thaw and bench-top stability experiments. Finally, the developed method was evaluated using NIST SRM 1950 plasma because standard reference material of brain tissue does not exist. The results show the potential of the developed method for analysis of eicosanoids in complex biological matrixes.

Investigating Deformed Aerosol Droplets Using A Dual Beam Optical Trap

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The effect of aerosols on climate change, both directly and indirectly, represents the "main source of uncertainty" in current climate models according to the Intergovernmental Panel on Climate Change. A large part of this is due to uncertainty in the light scattering properties of aerosols and how this scattering can affect Earth's energy budget. Optical trapping has emerged as a powerful way to investigate aerosols. This technique isolates a single particle from others, thus eliminating ensemble averaging effects and allowing the properties of the particle to be determined with high accuracy. The interpretation of these results, however, relies on the assumption that particles are spherical, which may lead to inaccuracies.

We introduce a dual beam optical trapping setup capable of deforming spherical aerosol droplets. The distortion is observed through changes in the morphology-dependent resonances (MDRs), also called whispering gallery modes, observed in Raman spectra collected perpendicular to one another. Since the deformed sphere no longer has the same cross section when viewed along perpendicular axes, the changes in the MDRs are different when observed in these two directions. Preliminary results are presented and discussed.

Multi-mycotoxin LC-MS Method for Detection and Quantification of 17 Mycotoxins in Human Plasma

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Mycotoxins are natural food contaminants found in worldwide food supply chain. The evaluation of short- and long-term human exposure to mycotoxins is important because of their toxicity and requires cost-effective multi-mycotoxin assay for their measurement in human plasma samples. The optimization of liquid chromatography-mass spectrometry (LC-MS) method for this application focused on chromatographic separation and sample preparation techniques (solvent precipitation, solid-phase extraction, and liquid-liquid extraction). The effective separation of mycotoxins was achieved with pentafluorophenyl column and the mobile phase containing water/methanol with 0.1% acetic acid and water/methanol with 0.02% acetic acid for positive and negative electrospray ionization, respectively. Liquid-liquid extraction provided the best method for extraction of these analytes from human plasma in terms of recovery and absolute matrix effects.

The optimized method was validated according to FDA guidance. LOQs of all mycotoxins ranged from 0.1 to 0.5 ng/ml, except for nivalenol (LOQ 3 ng/ml). Intra-day accuracy ranged from 87.2%-117.3%, and intra-day precision (n=6) ranged from 4% to 16.5% RSD except α-ZOL and ZEN, where poorer accuracy of 146% and 124% respectively was observed for low concentrations of these two analytes. Inter-day accuracy and precision were 84.1%-105.4% and 9.8%-20.6% RSD, showing good analytical performance of the method for this application.

A Comparison of Two Hydrophilic Interaction Liquid Chromatography Stationary Phases for Global Metabolomics of Human Plasma

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In global metabolomics studies, metabolome coverage is affected by two factors; the sample preparation method and the instrumentation used. The most common instrumental analysis technique for global metabolomics is liquid chromatography-mass spectrometry (LC-MS). Typically, both reversed-phase liquid chromatography and hydrophilic interaction liquid chromatography (HILIC) are implemented to achieve coverage of a wide range of metabolites from hydrophobic to hydrophilic. Many stationary phase chemistries are available for HILIC including underivatized silica and zwitterionic stationary phases such as sulfobetaine. In order to determine which stationary phase is better suited to global metabolomics analysis of human plasma, optimized methods for each have been developed and compared using a mix of metabolite standards and methanol-precipitated human plasma samples. A total of 31 standards were chosen to cover a range of logP values (-4.9 to 2.26), molecular weights (103 to 776 Da), and metabolite classes including but not limited to amino acids, hormones, vitamins, and neurotransmitters. The two stationary phases were compared using peak separation, peak shape quality, robustness, and metabolome coverage. The underivatized silica and zwitterionic stationary phases provided quality results for 15 and 17 of 31 standards respectively, and no observable peaks for 10 and 5 of 31 standards respectively.

Carbonated Water for the Separation of Carboxylic Compounds: A Green Chromatography Approach

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Green analytical chemistry seeks to reduce the environmental impact of chemical products and processes through waste reduction and the use of safer solvents / substances. Chromatographic separation in particular generates significant amounts of harmful organic solvents, acids, bases, and salts, as waste by-products. CO_2-modified solvents have been reported as promising routes to the development of greener analytical methodologies, but normally with stationary phases that are inert to the chemical effects of the CO_2 modifier. We now report the impact of pH and dissolved CO_2 mobile phase on separations, by utilizing primary, secondary and tertiary amine functionalized silica particles. Ibuprofen, naproxen and ketoprofen, chosen as examples of pharmaceutical analytes containing carboxylic acid groups, have now been separated with CO_2-modified (carbonated) water. Chromatographic retention, selectivity and zeta potential were utilized to demonstrate a dynamic ion exchange mechanism involving both protonation and deprotonation of stationary phase and analyte functional groups. Primary and secondary amine functionalized columns retain the carboxylic acid compounds more strongly ($t_R \geq 15$ min), suggesting that they are beneficial for separations requiring higher retention. The use of CO_2-modified mobile phases has the potential to significantly reduce both solvent and permanent acid use in chromatographic separations.

ANALYTICAL CHEMISTRY/ CHIMIE ANALYTIQUE

Posters / Affiches

Metabolomics Used to Study Sub Lethal Effects of a Mixture of Emerging Organic Contaminants on Model Species Daphnia Magna

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Traces of emerging organic contaminants have been detected in surface, ground and waste waters. Potential sub lethal effects of mixtures of these compounds on aquatic organisms are unknown. Sensitive evaluation tools are thus necessary to quantify biological changes on aquatic organisms that are exposed to environmental concentrations of these contaminants.

The proposed method aims to use a targeted metabolic approach for the quantification of ecdysteroids, essential metabolites implicated in *Daphnia magna* molting and reproduction. A method based on liquid chromatography coupled to triple quadrupole mass spectrometry has been developed to quantify 3 metabolites of interest (20-hydroxyecdysone, ecdysone and ponasterone A). The average concentration of 20-hydroxyecydone (20-OHE) in non-exposed adults D. magna was 18.3 $pgind^{-1}$. The limit of quantification (LOQ) was 8.5 $pgind^{-1}$. The upper control limit (UCL) was 39.1

pgind^{-1}. Exposition of *D. magna* to a mixture of 19 contaminants (diclofenac, ibuprofen, atrazine, carbamazepine and triphenyl phosphate among others) at a concentration of 1 µgL^{-1} was performed and statistically different concentrations of 20-hydroxyecdysone were observed between control and exposed groups. Next experiments will focus on studying the effect of a lower concentration of contaminants (100 ng L^{-1}) as well as the effect of lipid regulators on *D. magna* 20-OHE levels.

ENVIRONMENTAL CHEMISTRY/ CHIMIE ENVIRONNEMENTALE

Oral Presentations / Présentations Orales

The Role of Iron-sulfides on Cycling of Organic Carbon in the St Lawrence River System

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The biogeochemical cycle of sulfur is intimately linked with that of carbon, as well as with that of iron through the formation of iron-sulfur complexes. Iron-sulfide minerals such as mackinawite (FeS) and greigite (Fe_3S_4) form below the oxic/anoxic redox boundary in marine and lacustrine sediments and soils. Reactive iron species, abundant in surface sediments, can undergo reductive dissolution leading to the formation of soluble Fe(II) which can then precipitate in the form of iron sulfur species. While sedimentary iron-oxides have been thoroughly explored in terms of their ability to sorb and sequester organic carbon (OC), the role of FeS in the long-term preservation of OC remains undefined. In this study, we present depth profiles for carbon, iron, and sulfur in the aqueous-phase along with data from sequential extractions of sulfur speciation in the solid-phase collected from sediment cores from the St Lawrence River and estuarine system, demonstrating the transition from fresh to saltwater sediments. Additionally, we present synthetic iron sulfur sorption experiments using natural organic molecules in order to assess the importance of FeS in sedimentary carbon storage.

Proposed Mitigations of Challenges Faced in Aqueous Methane Stable Isotope Analysis

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Overall project objective is to improve detection limits and sensitivity of methods currently utilized within the lab to both quantify and isotopically characterize methane within water samples. Primary focus is placed on estuarine/marine porewaters of the St. Lawrence Estuary, Gulf, and Saguenay Fjord, though deep seawater and groundwater matrices are also of interest. Static headspace extraction will precede quantification using gas chromatography with flame ionization detection (GC-FID) and isotope characterization using gas chromatography-isotope ratio mass spectrometry (GC-IRMS) to obtain both carbon and hydrogen isotope signatures. This concentration and isotopic data will allow for distinction between biological and thermogenic sources of methane, as well as provide insight into methane removal pathways

(i.e. aerobic and anaerobic oxidation). Cryogenic cooling will be utilized as a preconcentration method, coupled to both GC-FID and GC-IRMS, to improve the high detection limits of current instrumentation.

ENVIRONMENTAL CHEMISTRY/ CHIMIE ENVIRONNEMENTALE

Posters / Affiches

Toxicity Effect of Cu and Cd on the Cell Physiology of Green Alga *Oocystis Polymorpha*

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Copper and Cadmium are essential trace element that can be toxic at high concentrations for living organisms, and their release through wastewater represent a major issue in Canada concerning water quality. For developing bioremediation application of wastewater, microalgae can play key role since they have a high efficiency to bioaccumulate metals. In this study, the objective of this project is to investigate the bioaccumulation and toxicity effects of Cu and Cd in algal biomass of *Oocystis polymorpha* exposed during 72 h to different concentrations of $CuCl_2$ and $CdCl_2$.

The capacity of algal biomass to bioaccumulate Cu and Cd was determined by inductively coupled plasma optical emission spectrometry (ICP-OES). Spectroscopic methods of analysis were used to determine the toxic effects of Cu and Cd on algal cells division, pigments content and photosynthetic activity. Our results showed that both metals induced an inhibition of cells growth, bioaccumulation efficiency and an alteration of total chlorophylls and carotenoids content were observed. The tolerance capacity of *O. polymorpha* for the toxicity effect of these metals is discussed. Therefore, this study contribute to a better understanding of using the green alga *O. polymorpha* for the bioremediation of contaminated water by Cu and Cd.

BIOCHEMISTRY/BIOCHIMIE

Oral Presentations / Présentations Orales

Human OCT1 Mediates the Uptake of Anticancer Drugs into Cells

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The human genome consists of nearly 450 solute carriers or transporters grouped into 52 families. While the functions of many of these transporters remain unknown, mutations

causing defects in at least 145 of the transporters revealed connections to various medical conditions, underscoring the importance of the transporters in maintaining biological functions. The SLC22A family consists of several organic cation transporters that include OCT1, OCT2, OCT3, OCTN1, OCTN2 and OCT6. These transporters perform important roles in the uptake, distribution and excretion of cationic compounds such as nutrients and therapeutic drugs, and they are either ubiquitously or uniquely expressed in defined organs such as the liver, small intestine, kidney and brain. We discovered that OCT1 is responsible for the accumulation of the anticancer drug, anthracyclines including doxorubicin and daunorubicin into cells. Downregulation of OCT1 blocked the uptake of anthracyclines and cells displayed resistance to the drugs. In contrast, overexpression of OCT1 stimulated the uptake of the drugs into cells. Efforts are underway to explore if cancer patients who are resistant to anthracyclines are defective in OCT1 function.

Biochemical and Biophysical Characterizations of Mutational Variants of Human tRNA Nucleotidyltransferase

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Cytidine-cytidine-adenosine (CCA) nucleotide sequence at the 3' end of all tRNAs is required for aminoacylation. In eukaryotes, this nucleotide sequence is added post-transcriptionally by ATP(CTP):tRNA nucleotidyltransferase (tRNA-NT). The importance of this enzyme in humans is highlighted by the diseases that have been linked to mutations in the TRNT1 gene encoding tRNA-NT. For example, SIFD has been linked to a mutation changing a specific arginine residue to tryptophan (R99W), while retinitis pigmentosa has been associated with the deletion of a specific glutamate residue (E43Δ) or two frame shift mutations.

As little research has concentrated on determining how these specific amino acid changes alter the structure, stability and activity of tRNA-NT leading to these disease phenotypes, a combination of biophysical and biochemical approaches is used here to compare the properties of native and variant tRNA-NTs.

Comparing the circular dichroism and fluorescence spectra among the proteins, as well as their thermal stabilities, reveals no changes in secondary or tertiary structure or stability. However, preliminary enzyme kinetics suggest a small increase in ATP binding in the missense mutant and a decrease in turnover number in the frameshift variants, suggesting that changes in enzyme activity, and not stability, may lead to the disease phenotypes.

CYP3A4 Cooperativity Investigation via the Bioconjugation of Natural Ligands

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Cytochrome P450 (CYPs) consists of a large family of hemoproteins catalyzing essential oxidation reactions to the biosynthesis of endogenous substances (steroids, lipids, vitamins). They also include some of the most important enzymes involved in drug and xenobiotic metabolism. As such, CYPs are known to be involved in numerous drug-drug interactions and have also been implicated in drug resistance and xenobiotic toxicity. Human CYP3A4 alone is

involved in the metabolism of ~50% of all drugs in the clinics. Interestingly, this enzyme displays novel cooperative behaviour, attributed in part to its large and flexible active site, which has been shown to simultaneously bind multiple substrate molecules. To get a better understanding of this particularity of CYP3A4, we propose a way to covalently attach various substrate-like molecules in the enzyme binding-site and investigate their impact on catalytic efficiency and cooperativity. This will help isolate the effect of the different substrates bound and give insight on how each of them impacts the overall activity of CYP3A4. Such information will help understand drug metabolism better and contribute to our general knowledge in enzymology.

Structural and Functional Investigations of the Biosynthetic Pathway for Bacillamide, a Thiazole-containing Natural Product

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Nonribosomal peptide synthetases (NRPSs) are large enzymes that produce many important therapeutic compounds including bleomycin (anti-tumour). The architecture and synthetic cycle of NRPSs are modular: repeating sets of domains ("modules") each perform a set of reactions to elongate the peptide. Some modules are basic, containing only the 3 domains needed to add monomer amino acid building blocks, while others have alternative or optional tailoring domains, which also introduce chemical modifications into the peptide co-synthetically. This tailoring helps NRPS products to access a wide range of chemical space, and to possess their important therapeutic activities.

Bacillamide synthase (BS) is a 3-module, 6-domain NRPS which has a tailoring heterocyclization domain, and an in-trans tailoring oxidase protein (Ox). My goal is to elucidate structural and functional details of this bacillamide biosynthesis. I have solved the structure of Ox to a resolution of 2.4Å and performed initial characterization that surprisingly shows that Ox causes BS to dimerize, which is an uncommon characteristic in NRPSs. In addition, our data suggests that Ox works co-synthetically with BmdB and uses FMN as a cofactor for its oxidation. The hope is to further our understanding of NRPSs and potentiate their manipulation for production of novel therapeutic derivatives.

4′-*C*-Methoxy-2′-Deoxy-2′-Fluoro Modified Ribonucleotides Improve Metabolic Stability and Elicit Efficient RNAi-Mediated Gene Silencing

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The pursuit of novel modifications to nucleotides comprising oligonucleotide-based therapeutics such as small interfering RNA and antisense oligonucleotides is currently an area of active research. Our laboratory has focused on 2′- and 4′- modifications to nucleosides and their incorporation into oligonucleotides as they are predicted to bind mRNA targets with high affinity. Towards that end, we designed novel 4′-modified 2′-deoxy-2′-fluorouridine (2′-F U) analogues with the aim to improve nuclease resistance and potency of therapeutic siRNAs by introducing 4′-*C*-methoxy (4′-OMe) as the alpha (C4′α) epimer (4′-*C*-Methoxy-2′-deoxy-2′-fluoro-rU (**1**)). Compound (**1**) was synthesized by a stereoselective route in six steps. ^{1}H-NMR analysis and computational investigation of (**1**) revealed that the 4′-OMe group imparts

a conformational bias towards the *North-East* sugar pucker, due to intramolecular hydrogen bonding and hyperconjugation effects. In addition, while it conceded similar thermal stability as unmodified nucleotides, it conferred increased nuclease resistance. The latter property can be explained by the close proximity between 4′-OMe substituent and the vicinal 5′- and 3′-phosphate group, as seen in the X-ray crystal structure of modified RNA obtained by the Egli laboratory. siRNAs containing (**1**) monomers in the sense or antisense strands triggered RNAi-mediated gene silencing with efficiencies comparable to that of 2′-F U.

In vitro Analysis of the Interaction Between Diamine Oxidase and Cholic Acid in Simulated Intestinal Fluid

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Introduction: Inflammatory bowel diseases (IBD) as ulcerative colitis and Crohn disease are more expand in Canada (15% inhabitants are affected). The usual therapies based on antiflammatory, corticocorticoid and immunosuppressor drugs have many side effects. Instead these synthetic drugs, we propose a plant enzyme, Histaminase, also called diamine oxidase (DAO) able to decompose the histamine which is the main actor involved in allergies and inflammatory reactions. In addition, various digestive agents such as biliary salts are present on the intestinal tract

Objective: To investigate *in vitro* the role of different biliary acids on the DAO activity.

Methodology: Spectrophotometric and fluorimetric techniques were used to study the interaction of the DAO with cholic acid under various forms (free, micelles and liposomes).

Results: DAO activity was dependant of the composition of different simulated intestinal fluid used. The enzyme was inhibited through time and in presence of high osmolarity fluid. Pancreatin (trypsin and chymotrypsin) and sodium bicarbonate have a negative impact on the stability of the enzyme. Biliary acids (as cholic acid) preserve the activity of DAO for minimum 48 hours.

Conclusion: This study brings a novel perspective in the comprehension of different interactions between DAO and biliary acids in the intestine.

BIOCHEMISTRY/BIOCHIMIE

Posters / Affiches

Copper Complexes with Amino Acids as Bioactive Agents for Transdermal Administration in Treatment of Certain Neurodegenerative Diseases

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There are very few treatments for neurodegenerative diseases generated by deficiency of copper (ex Menkes disease). Copper complexes with amino acids have been

proposed as injectable forms for Menkes treatment but, their stability is low in aqueous solution.
Objective: Synthesis and characterization of the copper complex with (L-histidine) and its inclusion in polymeric films for transdermal applications.
Methodology: The structures of chitosan-PVA composite films with loading copper complex were characterized and their application properties, including permeability, water uptake and release characterization were assessed. Evaluation of biocompatibility and cytotoxicity of this films has been tested on P19 cells.
Results: The complex Cu $(His)_2$ was well incorporated in our biocompatible films such as revealed by FTIR and DSC. Composite films could provide suitable adhesive properties for transdermal application and a good capacity for copper complex loading and release (> 50%). The results of the viability of cells showed that films with Cu $(His)_2$ have excellent biocompatibility and no obvious toxicity *in vivo*.
Conclusion: The preliminary results support the use of the copper complex as therapeutic agents for transdermal administration in treatment of some neurodegenerative diseases.

Methods for Measuring Enzyme Kinetics Using Isothermal Titration Calorimetry

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Isothermal titration calorimetry (ITC) is a powerful tool for acquiring both thermodynamic and kinetic data for biological systems. ITC offers several advantages over other experimental kinetics methods as it can be performed entirely in solution under physiological conditions, does not require spectroscopically-active (eg. fluorescent) molecules, it is compatible with spectroscopically opaque solutions, and can be applied to relatively dilute samples. Despite its long history and technical advantages, kinetic applications of ITC remain fairly rare. In order to expand the use of ITC kinetics we have developed several techniques in order to measure physical properties of enzymes and enzyme inhibitors. These techniques allow us to measure both Michaelis-Menten and non-Michaelis-Menten properties of rapidly evolving enzyme reactions, extract the mode and strength of enzyme inhibitors in a single experiment and, lastly, directly measure the association and dissociation rates of enzyme inhibitors. These experiments are simple, allow for rapid and complete characterization of enzymes and enzyme inhibitors, and will broaden the overall applicability of ITC.

Impact of SRP72 on ETV6 Transcription Factor in Acute Lymphoblastic Leukemia

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Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer and is an important cause of death in childhood. ALL is a complex genetic disease whose causes remain unclear. In 25% of ALL patients, the *ETV6* gene is inactivated due to the t(12;21) translocation followed by deletion of the residual allele.

ETV6 is a transcriptional repressor implicated in hematopoiesis and ubiquitously expressed but only a few transcriptional targets of ETV6 are known. We used a high throughput shRNA screen to identify potential ETV6 modulators including SRP72 which plays a role in the translation through the SRP complex and is potentially implicated in the transcription. The aim of this study is to characterise the impact of SRP72 on ETV6 and show his implication in ALL development.

First, we showed that the inhibition of the SRP complex doesn't affect transcriptional repression by ETV6 suggesting that the impact of SRP72 is independent from the translation pathway. We now wish to investigate SRP72 binding with the ETV6 transcriptional complex using co-immunoprecipitation assays. The identification of new transcriptional partners of ETV6 and the characterisation of their functional impact will allow us to learn more about the origin of ALL and its progression.

Insight into the Origin of the Formylation Tailoring Domain Found in the Linear Gramicidin Nonribosomal Peptide Synthetase

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The presence of tailoring domains in nonribosomal peptide synthetases (NRPSs) increases the diversity of nonribosomal peptides. Linear gramicidin synthetase has evolved to include a formylation (F) domain at the start of its initiation module. The formylation of the first residue is crucial for linear gramicidin's bioactivity. Our earlier bioinformatics studies suggest that the F domain originates from a sugar formyltransferase (FT) and was fused to the NRPS through horizontal gene transfer. We have now identified a gene for a sugar FT in *Anoxybacillus kamchatkensis* that is likely to be similar to the pre-transfer gene transfer FT that is the ancestor of the F domain. This FT is located in a gene cluster similar to the CMP-pseudaminic acid pathway. In the latter, UDP-GlcNAc is processed by a series of Pse enzymes; however, in the *A. kamchatkensis* gene cluster, the third enzyme has been substituted with the putative FT (PseFT). Using biophysical techniques and X-ray crystallography, we show that PseFT binds and formylates its sugar-nucleotide substrate, and that exhibits remarkable structural resemblance to the linear gramicidin

F domain. Together, these experiments display compelling evidence that PseFT is representative of the precursor sugar FT prior to incorporation into the NRPS.

Nanoscale Size and Morphology Studies of Excipients Made From Complexed Chitosan and Modified Starch

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Modified starch is an inactive pharmaceutical ingredient of interest in the preparation of tablet formulations due to key physicochemical characteristics such as increased acidic resistance and formation of a protective gel film promoting controlled drug delivery. The matrix of as-synthesized tablet formulations consists of several macromolecular components that can impact drug delivery and release. The stability and morphology of these materials in physiological conditions can be significantly affected by variations in pH, temperature, and gastrointestinal enzymes. The goal of this work was to characterize the size and morphology of modified starch and modified starch chitosan nanoparticles in aqueous solution. A series of modified starch micro- and nanoparticles (chitosan nanoparticles, chitosan modified starch nanoparticles and chitosan modified starch nanoparticles crosslinked with tripolyphosphate) were evaluated in order to better understand how the external environment can influence material morphology. Characterization was done using [J1] dynamic light scattering and atomic force microscopy. Dynamic light scattering measurements demonstrated the existence of several material population sizes (nanometer and micrometer) due to dispersed nanoparticles as well as their aggregates. Atomic force microscopy enabled measurements of individual nanoparticle size as well as the evolution of mesoscale ordering of the nanoparticles as a function of synthesis conditions.

Examination of Importance of ROS Release from Complex I in Ischemia-reperfusion Injury

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Recent work has suggested that complex I of the respiratory chain is the sole source of ROS during ischemia-reperfusion (IR) injury to the myocardium. However, complex III was also found to serve as a major source of ROS in liver and cardiac mitochondria. Krebs cycle enzymes have also been shown to display high rates for ROS release in liver and cardiac mitochondria. Here, we examined the importance of ROS release from complex I during IR injury. Using mice deficient in complex I (NDUFS4+/-), we found that other mitochondrial sources of ROS can contribute to IR injury. We observed that the partial loss of complex I did not alter ROS release from mitochondria. In contrast to liver mitochondria, the respiratory chain served as the main source of ROS in cardiac mitochondria from WT and NDUFS4+/-. IR injury modeling revealed that fully functional complex I is required to curtail IR injury to the

myocardium. Complex I deficient mitochondria produced significantly more ROS following reperfusion injury. This increase correlated strongly with a significant increase in myocardial infarct size and loss of myocardial function. In aggregate, these results refute the recent claim that complex I is the sole source of ROS following IR injury.

Dynamic Regulation of FOXK1 by O-GlcNAcylation During Cell Cycle Progression

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O-GlcNAcylation, catalyzed by OGT, is an extensively studied modification which consists in the addition of an O-GlcNAc moiety to serine and threonine residues of targeted proteins. OGT is known to be a major partner of the deubiquitinase and tumor suppressor, BAP1, a transcription regulator that assemble a mega dalton multi-protein complex and deubiquitinate histone H2A on lysine 119 (H2Aub). H2Aub plays critical roles in DNA-dependent processes and is essential for cell cycle progression. Among the different partners of the BAP1/OGT complex, the transcription factors FOXK1 and FOXK2 have recently emerged as potential regulators of BAP1 transcriptional activity at specific gene promoters. FOXK1 is critical to maintain the cell proliferation state of myoblaste progenitors and thus could mediate BAP1 activity during cell cycle progression. However, how FOXK1 and FOXK2 function within the BAP1 complex is still unclear. In this study, we show that FOXK1 is required for normal cell proliferation and demonstrate that this transcription factor is O-GlcNAcylated. In addition, we found that FOXK1 interaction with BAP1 is greatly compromised in response to stress conditions. Our data support a model whereby BAP1 function, at specific gene promoters, could be modulated though FOXK1 O-GlcNAcylation.

Determining Protein-Protein Interactions and Intracellular Organisation of the *E.coli* Enterobactin Metabolon Through *in vivo* Chemical Crosslinking

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Metals ions such as iron are crucial for bacterial metabolism and growth, and many micro-organisms have evolved mechanisms to scavenge extracellular metals. In low-iron conditions, *E. coli* synthesizes the catecholate siderophore enterobactin, a high-affinity iron chelator that is secreted in order to acquire extracellular iron. Enterobactin is produced through the sequential activities of six biosynthetic enzymes (EntA-F). We hypothesize that some of these enzymes engage in protein-protein interactions to enhance the efficiency of enterobactin biosynthesis *via* substrate channeling. Our lab has previously reported *in vitro* evidence of such interactions (EntB-EntA, EntA-EntE). The *E. coli* membrane protein EntS acts as the inner-membrane channel for

enterobactin export. We additionally hypothesize that the enterobactin biosynthetic machinery is in direct contact with EntS *via* protein-protein interactions. To investigate these hypotheses, we are employing *in vivo* formaldehyde crosslinking to determine the intracellular organisation of the enterobactin biosynthetic enzymes as well as the EntS transporter. Initial *in vivo* crosslinking results indicated that a recombinant H6-tagged EntB forms higher-order complexes with chromosomally-encoded *E. coli* proteins expressed during iron restriction. We are also developing a detergent screen to find conditions to optimally extract H6-tagged EntS in order to identify crosslinked binding partners.

Identifying Genes Responsible for tRNA Nucleotidyltransferase Production in the Yeast *Schizosaccharomyces Pombe*

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Schizosaccharomyces pombe has two genes (*cca*1 and *cca*2) that are thought to encode tRNA nucleotidyltransferase (tRNA-NT). This enzyme catalyzes the addition of cytidine-cytidine-adenosine (CCA) to the 3'-termini of tRNAs and is essential for aminoacylation and protein synthesis. That S. pombe has two genes potentially encoding tRNA-NT is of interest as most eukaryotes have a single gene encoding this enzyme which functions in multiple intracellular destinations (mitochondrion, nucleus, cytosol). Here the function and location(s) of the *S. pombe cca*1 and *cca*2 gene products will be determined. The *cca*1 and *cca*2 open reading frames from an S. pombe cDNA library were amplified and cloned into vectors for expression in yeast and for heterologous protein production and purification from *E. coli*. The data show that neither gene product is sufficient to complement a defect in the gene encoding the single S*accharomyces cerevisiae* tRNA-NT. Moreover, enzyme assays indicate that the *S. pombe cca*1 gene product is able to incorporate CMP but not AMP into a model tRNA template. Taken together these data suggest that *S. pombe* is the first example of a eukaryote with separate genes encoding –CC and –A adding activities as has been seen previously only in a small number of bacteria.

Perturbing Activity of Class II Lanthipeptide Synthetase Through Mutations of an Overlooked Intrinsically Disordered Loop

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Lanthipeptides are a family of peptide natural products that contain characteristic thioether rings within their structure. These rings are post-translationally installed into the C-terminal core region of ribosomally synthesized precursor peptides (LanAs). In class II lanthipeptides, the thioether rings are biosynthesized in a multistep mechanistic pathway catalyzed solely by a single lanthipeptide synthetase (LanM). Due to their antibiotic properties and the growing crisis of antibacterial resistance, lanthipeptides are major targets of drug development; thus, understanding their

biosynthesis is essential. Recently, the first crystal structure of a class II lanthipeptide synthetase (CylM) was solved, providing an opportunity to investigate potentially vital structural characteristics of LanMs. One interesting structural characteristic is an intrinsically disordered loop that appears to be strategically placed between both the dehydratase and cyclase domains of the enzyme. A sequence alignment of hundreds of known LanMs showed that not only does this loop have a conserved length of about 50 amino acid residues, it also contains a conserved S/T-D motif as well as conserved flanking proline residues. Mutating these residues in the class II Lanthipeptide synthetase HalM2 leads to interesting perturbations in enzymatic activity, and implies a functionally critical role for this loop, which has been previously overlooked.

Regulation of the Tumor Suppressor BRCA1 by Ubiquitination and Sumoylation

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Mutations of the tumor suppressor BRCA1 are associated with high risk of breast and ovarian cancers. BRCA1 is involved in DNA double strand break repair and maintenance of genome stability, and recent findings indicated that this function requires a highly coordinated ubiquitin signaling pathway independently of proteasomal degradation. On the other hand, BRCA1 protein levels are also regulated during cell cycle and ubiquitination-mediated proteasomal degradation plays an important role in this process. Moreover, sumoylation has also been involved in coordinating BRCA1 function. However, little is known about how deubiquitinases (DUBs) and SUMO-proteases regulate BRCA1 stability and function under normal conditions and in response to DNA damage.

We conducted DUB RNAi screening in which the 100 DUBs of the human genome were individually depleted to analyse BRCA1 and RAD51 repair foci following ionizing radiations. We identified few DUBs whose depletion increase or decrease BRCA1 and RAD51 foci. Interestingly, we also identified USPL1 that was recently discovered as a SUMO-protease as a candidate for regulating DNA repair.

In the future, we will investigate the mechanisms by which DUBs and SUMO-protease coordinate BRCA1 function in DNA repair. Our findings might help identifying cancer cell weaknesses that can be exploited for novel therapeutic strategies.

MOLECULAR BIOLOGY/ BIOLOGIE MOLÉCULAIRE

Oral Presentations / Présentations Orales

VIPER: A Webserver for *In Silico* Simulation of Protein-peptide Interaction Specificity

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Understanding protein-peptide interaction specificity is of primary importance in systems biology research as it can help identify protein binding pairs involved in the regulation of many cellular signaling pathways. Currently, peptide arrays are used to determine binding specificities *in vitro*. This experimental method has been used extensively throughout the years but remains costly, time-consuming and condition dependent. Here, we developed a platform for simulating peptide arrays based on a structure-based computational approach. Using a single peptide-bound crystal structure from the PDB as input, our platform (VIPER) outputs a virtual peptide array based on predicted stability of every single point mutants as well as a recognition motif for the protein binding domain. We benchmarked the algorithm against various well characterized proteins such as methyltransferases, PDZ and Src Homology 3 domains. The predicted active and inactive peptides were compared to experimental data to assess the quality of predictions. The VIPER procedure is particularly efficient when pruning inactive peptides with an average of 86% being correctly rejected will retaining more than 70% of the active ones. VIPER (available at http://viper.science.uottawa.ca) showed an average accuracy of 82% and therefore, represents a cheap and fast alternative to experimental permutation peptide arrays.

Vpr Destabilizes Centrosome Homeostasis by Hijacking EDD-DYRK2-DDB1^{VprBP}

D. Hossain
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The centrosome is the major microtubule organizing center of cells that plays a crucial function in the cell division process. Furthermore, the centrosome has a role in biogenesis of cilia, hair-like protrusions found on the cell surface important for sensation and locomotion. Understanding how centrosome and cilia are assembled could shed light on the many human diseases caused by mutations of genes that affect protein function in this organelle. Previously we report that centrosomal protein of 78 kDa (Cep78), localizes to mature centrioles and interacts with EDD-DYRK2-DDB1^{VprBP}, an E3 ligase that recognizes, and adds ubiquitin to a substrate CP110. The human immunodeficiency virus viral protein R (Vpr), when bound to the Vpr-binding protein (VprBP) subunit of the host E3 ligase EDD-DYRK2-DDB1^{VprBP} in the nucleus, alters the ubiquitinating activity of the enzyme. In this study we found that Vpr localize to the centrosome and interacts with Cep78 through VprBP. And enhanced CP110 ubiquitination and degradation, thereby affecting centriole length. Vpr does not induce ubiquitination of Cep78 but the effects caused by Vpr can be overcome by expression of

Cep78. Overall our data suggest that Vpr mediated disruption of centrosome homeostatis control by Cep78.

Relation Between Dye-filling and Ivermectin Resistance in *Caenorhabditis Elegans*

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Parasite resistance to commonly used drugs in the livestock industry is a global issue that leads to significant losses in productivity and profit. The study of anthelminthics such as ivermectin is thus detrimental to finding new ways to protect mammals from these parasites and to increase farming income. We are interested in the relationship between genes that confer ivermectin resistance and are defective in dye-filling of the sensory neurons, called *dyf* genes. We study *dyf-7* because it has been shown to directly confer ivermectin resistance, and consequently *dyf-3* because it can be studied independently in the *Caenorhabditis elegans* sensory neurons. In this project, we investigate the mechanism by which the *dyf* genes confer ivermectin resistance: by altering drug entry, communication within the nervous system, and stress response pathways. As the dye-filling mechanism involves dye entering sensory neurons, we suspect that altered drug entry confers ivermectin resistance.

Fat but Fit: How Hibernating Ground Squirrel AdiposeTissue Regulates Pro-inflammatory Signaling Pathways

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Carleton University

In the summer months leading up to hibernation, ground squirrels go through a period of intense eating and increase their body weight by 40-60 %. Fat reserves in the white adipose tissue are essential for these animals to survive months without eating. Brown adipose tissue, the organ necessary for non-shivering heat production, also increases in weight (by 2- to 3-fold in the Arctic ground squirrel) before hibernation. The advanced-glycation end product (AGE) receptor (AGE-RAGE) signaling pathway is emerging as an important signal transduction pathway that influences immune and oxidative stress responses and is often dysregulated in patients with obesity and diabetes. Hibernating ground squirrels are “fat but fit”, providing an excellent model of controlled energy metabolism and regulated inflammatory/immune responses. Thus, it is essential to study the AGE-RAGE pathway (which is overactive in obesity and diabetes) and the pro-inflammatory pathways it regulates (i.e. MAPK, JNK, NF-κB) in fat-storing hibernators, which are capable of reversible insulin resistance and resistant to tissue damage brought on by oxidative stress. This research highlights the regulation of RAGE, its ligands (S100B, HMGB1 and CML-AGE), and transcription factors activated by the MAPK signaling pathway in WAT and BAT from hibernating ground squirrels.

Targeting The Proteasome Associated Deubiquitinase PSMD14 As A Novel Anti-Cancer Therapeutic Strategy

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University of Montréal

Introduction: Multiple Myeloma (MM) is the second most common blood cancer. In 2012, 114 000 people were diagnosed with MM worldwide, unfortunately 80,000 died of this disease. Although survival rates have significantly improved since the introduction of proteasome inhibitors (bortezomib), patients develop resistance and relapse. Therefore this disease remains a major health problem and there is an absolute need for novel therapies.

Methods/ Results: In our study, we generated bortezomib-resistant cancer cell lines and conducted deubiquitinase (DUB: 100 genes) and ubiquitin-conjugating enzyme (E2: 35 genes) RNAi screens to identify which genes of these families affect cell proliferation of sensitive and/or resistant cancer cells following abrogation of their function.

We identified the proteasome-associated DUB PSMD14 as a potential candidate cancer target. Using RNAi or CRISPR/Cas9 approaches applied to sensitive or resistant cancer cells, we found PSMD14 depletion induces dramatic decrease of cell proliferation. This appear to be caspases-dependent, but p53-independent apoptosis. Moreover, we observed the extent of histone H2A ubiquitination and HSP70 expression levels are correlated with sensitivity to proteasome inhibition. Thus, these factors could be potential biomarkers for prognostic.

Conclusion: PSMD14 is required for protein deubiquitination that precedes substrate degradation and its inhibition induces effective killing of bortezomib-resistant cancer cells.

A Novel Mechanism of Regulation of the Tumor Suppressor BAP1/ASXL2 Complex by Monoubiquitination

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Introduction: Histone H2AK119 monoubiquitination is a critical epigenomic modification. We previously reported that the tumor suppressor and mammalian H2A deubiquitinase, BAP1, forms two mutually exclusive complexes with ASXL1 and ASXL2.

Methods and Results: We focused on ASXL2, which used its ASXM domain to interact with the C-terminal domain of BAP1. Significantly, we found that BAP1/ASXL2 complex is regulated by monoubiquitination that occurs on lysine 370 of ASXM. We hypothesized that this monoubiquitination can play a critical role on coordinating BAP1/ASXL2 complex stability and function. Indeed, we found that, when ubiquitinated, ASXL2's stability is significantly decreased compared to a non-ubiquitinated KR mutant. Moreover, we use human siRNA library and CRISPR/Cas9 constructs for ubiquitin conjugating enzymes (E2s), ubiquitin ligases (E3s) and deubiquitinases and we identified UBE2E3, and the E3 ligase TRIM37 as ubiquitin ligases for ASXM. Depletion of the deubiquitinase PSMD14 induced a poly-ubiquitinated ASXM domain on the same K370 residue. Functionally, ASXM mutant K370R rescues the senescence phenotype triggered by ASXL2 WT. Finally, we identified cancer mutations of BAP1 that abolish ASXM monoubiquitination.

Conclusion: Our results indicate that, through monoubiquitination, BAP1 and ASXL2 exert a tightly controlled regulation on cell proliferation, and provide an insight to BAP1 tumor suppressor function.

MOLECULAR BIOLOGY/ BIOLOGIE MOLÉCULAIRE

Posters / Affiches

Ubiquitination of BAP1/ASXL Tumor Suppressor Complex: A Key Mechanism for Gene Regulation and Cell Fate Determination

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Monoubiquitination of histone H2AK119 (H2Aub) is a critical epigenomic modification associated with development, cell proliferation and cancer. In Drosophila, H2Aub is reversed by the deubiquitinase (DUB) Calypso, which associates with ASX forming a transcription regulatory complex.

We previously found that the tumor suppressor and mammalian orthologue of Calypso, BAP1, forms two mutually exclusive complexes with ASXL1 and ASXL2, two orthologues of ASX. ASXL1 and ASXL2 use their highly conserved ASXM domain to interact with BAP1 and stimulate its DUB activity. In further understanding the mechanism involved, we found that ASXL1 and ASXL2 are monoubiquitinated on their ASXM domains in a BAP1-dependent manner. Importantly, we found that the monoubiquitination of ASXL2 is required for BAP1 DUB activity towards H2Aub in vitro and in vivo.

Consistent with these observations, we also showed that the monoubiquitination of ASX is conserved in drosophila and is dependent on Calypso. Using the drosophila model, we found that mutating the monoubiquitination site of ASX induces a halter to wing homeotic transformation due to an alteration in the expression of the Hox gene, ultrabitorax.

Our results indicate that the monoubiquitination of ASXLs coordinates the DUB activity of BAP1 which might be highly relevant to tumor suppression.

Role of the Deubiquitinase MYSM1 in the Genotoxic Stress Response Role of the Deubiquitinase MYSM1 in the Genotoxic Stress Response

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Deubiquitinases (DUBs) catalyze the reverse reaction of ubiquitination. They control cell cycle, gene expression, DNA damage response (DDR) and other cellular processes, deregulation of which play crucial roles in cancer development. MYSM1 is a nuclear DUB that has been described as a major histone H2A DUB, regulating

hematopoietic development, and is also a positive regulator of androgen receptor-induced gene activation in prostate cancer. Recent studies have shown that MYSM1 depletion results in DNA double-strand breaks (DSB) induction, suggesting its involvement in DDR. Indeed, this DUB is phosphorylated by the ATM kinase in response to genotoxic stress. In order to elucidate the function of MYSM1 in DNA repair, we conducted MYSM1 loss of function experiments in vitro followed by treatments with DSB inducing agents. We then analyzed H2A ubiquitination levels and DNA repair phenotypes. Our results confirm that MYSM1 is involved in DNA damage signaling. In addition, using a tandem affinity immunopurification approach, we identified novel MYSM1-interacting partners which might play an important role in mediating MYSM1 function. Further experiments targeting ubiquitination and phosphorylation sites, that are mutated in cancer cells, will be conducted to elucidate the exact role of MYSM1 in DNA repair and carcinogenesis.

Implication of Sam68 RNA Binding Domains in Migration of Metastatic Cells

A. Caillier*, M. Huot

Université Laval

The formation of secondary tumors remains the leading cause of cancer-related deaths and most of the time defines the prognosis. Dissemination of cancer cells is a complex process that requires several interdependent biological mechanisms such as proliferation, adhesion and cell migration. Our laboratory focuses on RNA-binding proteins, including Sam68, which are known to regulate some of these mechanisms in the cell including adhesion and migration.Studies have revealed that over-expression of Sam68 is associated with a poor prognosis in some advanced stage cancers. Our hypothesis is that Sam68 would have an important role in tumor progression through the migration of metastatic cells. Our first objective is to identify protein and RNA targets of Sam68 that are implicated in cancer cells migration. Our second objective is to determine the implication of the two functional domains of Sam68 in migration. To assess our first objective, we are using in vivo proximity labelling that could lead to identify RNA and protein that directly interact with our protein of interest during migration. For the second objective, we established stable cell lines expressing mutations of Sam68 in the two functional domains and characterize their effect on migration by using wound healing assays and eventually Boyden chamber.

Examining Repair Kinetics and Cytoskeletal Architecture During Mammalian Somatic Single-cell Wounding

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Damage to the plasma membrane (PM) and underlying cortical cytoskeleton occurs routinely in multiple cell types. To survive such insults, a cell must both reseal its PM

and restore normal cytoskeletal architecture. In *Xenopus laevis* oocytes, cytoskeletal repair involves the intracellular formation and contraction of an actomyosin ring around the wound. We hypothesize that an actomyosin ring also forms during mammalian somatic single-cell wound repair. We measure the dynamics of PM and actin wound repair and examine the presence of a potential actomyosin ring in mammalian single-cell wound repair. Cells are wounded using a micropoint UV laser and kinetics of PM and cortex repair are tracked using live spinning disk confocal microscopy. We find that mammalian PM and cortical cytoskeleton recover from ablation at different rates, and mammalian single-cell wound repair may sometimes involve the formation of an actin ring-like structure.

DNA Damage and Repair Mechanisms in the Wood Frog, Rana Sylvatica

Z. Lung*, K. B. Storey
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Cell cycle control has been shown to be suppressed in order to regulate metabolic rate depression in response to stresses such as freezing, anoxia, or dehydration . This suppression can affect many cell division and growth processes, including DNA replication and DNA repair mechanisms. Certain proteins and substrates that are involved in Double Stranded Break (DBS) repair also regulate cell cycle control and transcription. The DNA repair mechanisms acting in the wood frogs, Rana sylvatica, in response environmental stresses have not previously been characterized. This study of DNA double stranded break repair provides new information on how the genome is maintained when frogs experience extreme stress conditions. The focus of this project is to analyze proteins involved in DBS repair in R. sylvatica in response to freezing or anoxia, and recovery from these conditions. Using Western Blots, the expression and relative levels of the main proteins involved in DNA repair by non-homologous end joining (NHEJ) and homologous recombination (HR) in double stranded break repair are being analyzed and quantified.

Examining the Regulation of Glutathione Reductase in Response to Ischemic Stress in the Dehydration-tolerant African Clawed Frog, *Xenopus Laevis*

J. Mattice*, K. Storey
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The African clawed frog (*Xenopus laevis*) endures the loss of nearly 40% of its total body water when exposed to prolonged desiccation. One consequence is tissue ischemia due to impaired circulation and increased reactive oxygen species (ROS) generation that can injure cells. Glutathione reductase (GR) regulates the ratio of oxidized (GSSG) and reduced (GSH) glutathione to ensure continuous supply of GSH for ROS detoxification. This study purified and analyzed GR from liver of dehydrated versus control *X. laevis*. Liver GR from dehydrated and control frogs showed a similar substrate affinity for GSSG; however, under physiological conditions (that include 55

mM urea in dehydrated frogs), GR from dehydrated animals had a significantly greater GSSG affinity than control. Activity of the control enzyme was also much more sensitive to high urea than the dehydrated enzyme. Immunoblotting revealed reduced threonine-phosphorylation of the dehydrated GR form compared with control. Incubation studies stimulating endogenous protein kinases produced a more phosphorylated form of GR with decreased GSSG affinity under conditions similar to physiological. Oppositely, stimulation of endogenous protein phosphatases produced a less phosphorylated enzyme with greater GSSG affinity. These results suggest that frog GR is regulated by post-translational modifications in response to dehydration stress.

A Little PARP of DNA Damage During Hibernation in the Hibernating Ground Squirrel

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One of the causal factors of DNA damage is the accumulation of both endogenous and exogenous oxidative agents and result in various pathologies. Through differential gene regulation, many organisms have developed specialized adaptations that have enabled them to survive the prolonged exposures to these oxidative stressors. One such model animal is the thirteen-lined ground squirrel, Ictidomys tridecemlineatus. During winter, the squirrel is capable of surviving months in a hypometabolic state, during which time it undergoes multiple bouts of arousal. While its tissues cycle through periods of ischemia, they have developed protective mechanisms to avoid reperfusion injury and ischemic stress. Indeed, research has shown that the squirrel does not accumulate significant DNA damage during hibernation. Multiple pathways exist and function in concert to modulate the repair mechanisms. Current work focusing base excision repair and non-homologous end joining pathways in the double stranded DNA damage response during torpor-arousal in the hibernating ground squirrel is analyzed. Important mechanisms including Poly ADP-ribosylation of damaged DNA along with the recruitment of repair proteins have been found to be differentially regulated in various tissues. This work will better our understanding of the molecular mechanisms that control the DNA repair and cell fate.

A Novel Mechanism of Regulation of the Tumor Suppressor BAP1/ASXL2 Complex by Monoubiquitination

D. Tchelougou*, O. Ahmed, S. Daou, H. Barbour, L. Masclef, N. S. Nkwe, E. B. Affar
Centre de Recherche de l'Hôpital Maisonneuve - Rosemont, Université de Montréal

Introduction: Histone H2A-K119 monoubiquitination is a critical epigenomic modification. We previously reported that the tumor suppressor and mammalian H2A deubiquitinase, BAP1, forms two mutually exclusive complexes with ASXL1 and ASXL2.

Methods and Results: We focused on ASXL2, which used its ASXM domain to interact with the C-terminal domain of BAP1. Significantly, we found that BAP1/ASXL2 complex is regulated by monoubiquitination that occurs on lysine 370 of ASXM. We hypothesized that this monoubiquitination can play a critical role on coordinating BAP1/ASXL2 complex stability and function. Indeed, we found that, when ubiquitinated, ASXL2's stability is significantly decreased compared to a non-ubiquitinated KR mutant. Moreover, we use human siRNA library and CRISPR/Cas9 constructs for ubiquitin conjugating enzymes (E2s), ubiquitin ligases (E3s) and deubiquitinases and we identified UBE2E3, and the E3 ligase TRIM37 as ubiquitin ligases for ASXM. Depletion of the deubiquitinase PSMD14 induced a poly-ubiquitinated ASXM domain on the same K370 residue. Functionally, ASXM mutant K370R rescues the senescence phenotype triggered by ASXL2 WT. Finally, we identified cancer mutations of BAP1 that abolish ASXM monoubiquitination.

Conclusion: Our results indicate that, through monoubiquitination, BAP1 and ASXL2 exert a tightly controlled regulation on cell proliferation, and provide an insight to BAP1 tumor suppressor function.

Investigating the Balancing Forces of Programmed Cell Death and Survival in Yeast

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Programmed cell death (PCD) plays a central role in many key biological processes that regulate developmental, homeostatic and immune functions in humans. Therefore, dysregulation of PCD can lead to several disease states. Much is known about what drives cells towards PCD; less is known about the regulation of the cellular pro-survival response. We have identified the human LIM-domain-containing cysteine and glycine rich protein 3 (CSRP3) as a pro-survival, Bax-suppressing sequence using a high throughput screen of a human cDNA library in *S. cerevisiae*. We report that overexpression of CSRP3 in yeast protects against Bax and copper-mediated cell death but enhances sensitivity to iron stress. We found no direct orthologues of CSRP3 in yeast, however yeast have four LIM-domain containing proteins: *Rga1, Rga2, Lrg1* and *Pxl1*. LIM domain-containing proteins have been reported to regulate the actin cytoskeleton and transcription, but little has been said regarding its potential as a pro-survival domain. Interestingly, these LIM-containing proteins are known regulators several stress responses in yeast. We hypothesize that like CSRP3, these LIM domain-containing proteins are also involved in the regulation of PCD responses. This work aims to expand our comprehension of these elements and their utility in the cellular pro-survival response.

NANOCHEMISTRY/NANOCHIMIE

Oral Presentations / Présentations Orales

Diffusion of Nanoparticles through Engineered Hydrogel Microstructures

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Hydrogels are crosslinked networks of hydrophilic polymers that have widespread applications in science and technology. Biocompatible hydrogels made of naturally-derived polymers, such as chitosan and collagen, are especially interesting for biomedical research. They are frequently used as drug carriers in drug delivery, and as scaffolds for tissue engineering. Transporting nanoparticles, nutrients, and other chemicals to the polymer network is a key factor to consider when designing hydrogel microstructures, which are composed of micro- or nano-sized pores. In this study, gelation of chitosan is modified to engineer organized microcapillaries within the normal hydrogel pores. These microcapillaries, which compose up to twenty percent of the hydrogel, can significantly affect nanoparticle diffusion in the hydrogel. At the first step, development and shape of these microstructures are characterized quantitatively. Next, diffusion of fluorescently tagged nanoparticles will be studied while the nanoparticles diffuse out of or into the gel. The facilitated diffusion of nanoparticles in the modified chitosan gel makes this material an interesting candidate for a broad range of biomedical applications.

Influence of Nucleotide Modifications at the C2' Position on the Hoogsteen Base-Paired Parallel-Stranded Duplex of Poly(A) RNA

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Polyadenylate (poly(A)) has the ability to form a parallel duplex with Hoogsteen adenine:adenine base pairs at low pH or in the presence of ammonium ions. In order to evaluate the potential of this structural motif for nucleic acid based nanodevices, the effects on duplex stability of substitutions of the ribose sugar with 2'-deoxyribose, 2'-deoxy-2'-fluoro-ribose, arabinose and 2'-deoxy-2'-fluoro-arabinose were characterized. Deoxyribose substitutions destabilized the poly(A) duplex both at low pH and in the presence of ammonium ions: no duplex formation could be detected with poly(A) DNA oligomers. Other sugar C2' modifications gave a variety of effects. Arabinose and 2'-deoxy-2'-fluoro-arabinose nucleotides strongly destabilized poly(A) duplex formation. In contrast, 2'-deoxy-2'-fluoro-ribo modifications were stabilizing either at pH 4 or in the presence of ammonium ions. The differential effect suggests they could be used to design molecules selectively responsive to pH or ammonium ions. To understand the destabilization by deoxyribose, we determined the structures of poly(A) duplexes with a single DNA residue by NMR spectroscopy and X-ray crystallography. The structures revealed minor structural perturbations suggesting that the combination of sugar pucker propensity, hydrogen bonding, pKa shifts determine duplex stability.

Revealing and Monitoring Small-molecule Aggregation Properties using T_2-CPMG NMR to Improve Drugs and Drug Discovery Processes

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All compounds exist in a unique three-phase equilibrium in aqueous solution between single lone-tumbling molecules, self-associated aggregates and a solid precipitate form. The nature of said equilibria profoundly dictates compound properties, yet, characterization of this phenomenon remains relatively unexplored – especially in the field of drug discovery. Dynamic light scattering has demonstrated that some compounds can self-assemble into micelle-like colloids, resulting in false-positive and false-negative results in drug screens. However, the existence of smaller nano-entities has historically been undetectable and thus, their corresponding properties remain uncharacterized. We present a new NMR strategy that employs T_2-CPMG pulses to expose the presence of these smaller nano-entities. This present method was first validated using known aggregators and non-aggregators, followed by cross-validation with our published NMR dilution assay. Using this T_2-CPMG method, comparisons between related compound series clearly revealed structure-nano-entity relationships which begin to expose the intriguing atomic sources of small molecule self-assembly. The advantages of this NMR strategy in drug discovery are demonstrated such as the rapid screening of compound libraries. Ultimately, this new tool has the potential to expose nano-entities of compounds and will enable correlation with their intriguing properties for future design purposes.

Small Nucleotide Probes For Ligand-Binding Analysis of the Microcystin-LR Aptamer

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The production of DNA aptamers for small molecules has the potential to radically change the fields of detection and diagnostic. However, the characterization of small target binding affinity can be a challenging aspect of aptamer-based sensor development. The nucleic acid sequence of aptamers makes them a unique type of receptor that allows for the design of complement binding probes with predictable binding affinities over their full length.

By targeting the full length of the aptamers' structure, these probes may provide a means of detecting portions of the aptamer sequence responsible for ligand binding. Also, these probes may allow for the determination of ligand binding affinities using the competitive binding displacement model. This information would accelerate the characterization and modification of aptamers simplifying their incorporation into biosensor applications.

Here we examine the viability of this approach by incorporating the hybridization sensitive fluorescent nucleotide pyrrolo-dC into short complementary sequences of the microcystin-LR aptamer. This study demonstrates that these probes are useful for the determination of binding affinities providing another avenue for investigating aptamer small ligand interactions.

NANOCHEMISTRY/NANOCHIMIE

Posters / Affiches

Metal-enhanced Fluorescence and Energy Transfers in Silver Core@silica Multishell

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Metal@silica concentric nanoparticles capable of metal-enhanced fluorescence (MEF) represent a powerful means to improve the brightness and stability of encapsulated organic fluorophores. As such, the rational design of MEF-enabled labels and sensors can involve the comparison of fluorescence enhancement factors (EF) between nanostructures having different structural properties (e.g., metal core diameter, silica shell thickness, extent of spectral overlap between plasmon band and fluorophore). In this work, $Ag@SiO_2@SiO_2+x$ (where x is fluorescein, eosin or rhodamine B) nanostructures were synthesized with excellent control of core size, silica spacer shell thickness and fluorophore concentration and the influence of key structural factors on emission intensity were investigated. Our experimental assessments of EFs corroborated well with theoretical simulations and other works in literature. The results were used to develop a generalized methodology for the determination of fluorescence enhancement factors in core-shell nanoparticles. Moreover, energy transfer mechanisms, like Förster Resonant Energy Transfer (FRET) were studied in similar multishell particles. Interestingly, the optimal distance between the core and the fluorophore(s) for MEF and ME-FRET changed with both phenomena. These different architectures should be of general importance to designing MEF-enabled nanostructures, sensors and related analytical techniques.

Biocompatible Dual Emitting Carbon Dots for Bioimaging Applications

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Carbon dots are carbon-based nanoparticles with versatile optical properties and high biocompatibility. These nanoparticles have attracted much attention and have been investigated for various applications such as drug delivery, biosensors and catalysis. The carbon dots' emission can be tailored from the blue to the near infrared regions, with the latter targeting deep tissue imaging. In this project, carbon dots are synthesized as bimodal imaging probes for optical and magnetic resonance imaging applications. To obtain these nanoprobes, we synthesized near infrared emitting carbon dots using a one-step microwave-assisted reaction and integrated gadolinium ions during synthesis to endow magnetic properties to the nanoparticles. Work is also put on investigating the effects of different reaction parameters and gadolinium doping on the optical properties of the carbon dots. We also demonstrate that the

optical properties of these carbon dots can be used to develop optical nanothermometers and pH sensors.

Synthesis of a Near Infrared-Responsive Azobenzene-based Supramolecular Hydrogel using $LiYF_4:Yb^{3+}/Tm^{3+}$ Upconverting Nanoparticles

G. Mandl*, J. Capobianco
Concordia University

Stimuli-responsive hydrogels have found wide attraction in the biomedical community as potentially highly effective drug delivery systems. Light is a particularly attractive stimulus because it is non-invasive and highly specific. Traditional photoresponsive molecules, such as azobenzene, require ultraviolet light to induce a response. UV light is cytotoxic and has low depth penetration in skin, rendering UV-responsive molecules impractical for biological applications. Near-infrared light is nontoxic and can penetrate deeper in tissue, making it an attractive choice for a biological system. Herein, we present the synthesis of a NIR-responsive hydrogel that utilizes UV-responsive azobenzene as the photoresponsive moiety. By utilizing $LiYF_4:Yb^{3+}/Tm^{3+}$ upconverting nanoparticles, a gel-sol transition can be induced by energy transfer from the emissions of the UCNPs to azobenzene. Incorporation of azobenzene in a poly(acrylic acid) backbone renders the polymer photoresponsive, and deoxycholate-B-cyclodextrin is employed as the crosslink. Host-guest interactions of trans-azobenzene with cyclodextrins is widely demosntrated, while cis-azobenzene has low affinity for the CD cavity. Modification of CD with deoxycholic acid results in competitive binding of azobenzene and deoxycholate to the CD cavity. Trans-azobenzene will enter into the CD cavity and force deoxycholate into the aqueous external environment. Hydrophobic interactions of neighboring deoxycholate molecules result in a physical crosslink.

Metal-induced Fluorescence Quenching in Carbon Dots in Sensing Applications

F. Noun*, R. Naccache
Concordia University

Heavy metal contamination from anthropogenic sources is a great environmental concern. This research focuses on the development of a novel, cheap and green method for heavy metal capture using carbon dots, fluorescent nano-spheres composed primarily of carbon and oxygen. In this work, we present the synthesis of excitation wavelength-independent carbon dots, which can emit in the visible region of the electromagnetic spectrum. The photoluminescent properties of both functionalized and un-passivated carbon dots will be exploited to develop quenching assays as both qualitative and quantitative indicators for successful heavy metal capture. The quenching mechanism in both selective and non-selective metal binding will then be determined through ultra-fast spectroscopy techniques.

Metal Ion Speciation Controls the Morphology of Bimetallic Nanoshells in Galvanic Replacement

J. R. Daniel[1*], S. Yazdi[2], E. Ringe[2], D. Boudreau[1]
[1]Université Laval, [2]Rice University

Plasmonic nanomaterials have found applications in multiple fields such as catalysis, molecular sensing, imaging and single molecule spectroscopy, among others. The performance of a given nanomaterial in terms of absorption, scattering or local electric field enhancement can be optimized for a specific application by controlling physical properties such as size, shape and composition. In this context, hollow bimetallic nanostructures provide additional variables, including shell thickness and metallic component ratio, which can be manipulated to finely tune the plasmonic and optical properties of the structures. Galvanic replacement is an efficient and versatile synthesis strategy for the preparation of hollow and semi-hollow nanostructures with enviable plasmonic properties. This presentation will discuss our recent progress on the synthesis of hollow bimetallic nanostructures using silver nanoparticles as sacrificial templates and partial galvanic replacement by more noble metals (Au, Pd, Pt). These structures could find applications in various fields such as reprogrammable sensors, responsive materials, optical memory units, molecular sensing, cellular imaging and *in situ* microscopy of chemical reactions.

Synthesis and Design of Chiral Carbon Dots Using Simple Molecular Precurors

F. Victoria[*], R. Naccache
Concordia University

Carbon dots are one of the new members in the carbon nanoparticle family. Typically, less than 10 nm in size and composed primarily of sp^2 carbons, these nanoparticles have excellent tunable fluorescence, low toxicity, chemical inertness and biocompatibility. Thus, they have applications ranging from drug-delivery, bio-imaging, chemical sensing to catalysis. These properties of the carbon dots are determined by the starting materials and they can be synthesized from various carbon sources and passivated using agents with various functional groups. As such, we are interested in exploring residual chirality in these carbon nanomaterials by starting with chiral precursors. This is due to the fact that chirality has been very important in pharmaceutical research for drug development and design, as well as in applications of organocatalysis, enantioselective recognition and chiral sensing.

ORGANIC CHEMISTRY/CHIMIE ORGANIQUE

Oral Presentations / Présentations Orales

Synthesis of 2,5-diaryl Symmetric and Non-symmetric Furans from Biomass Derived Starting Materials

F. Chacon-Huete*, P. Forgione
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The synthesis of high-value biomass derived 2,5-diaryl furans has been achieved successfully from good to excellent yields with a wide scope of coupling partners of aryl halides and FDCA, and the article has been published already with the results and protocols developed. Keeping in mind that FDCA comes from the direct oxidation of HMF, a route to access 2,5-assymetric furans is proposed utilizing the latter molecules as starting material. Selective oxidation of the aldehyde moiety has not been reported under mild accessible conditions, therefore a solvent-free mechanochemical assisted selective oxidation is proposed to synthesize the required 5-hydroxymethyl-2-furoic acid (HMFA). Subsequent optimization of the decarboxylative cross-coupling of HMFA with an aryl-halide would yield a 5-hydroxymethyl-2-aryl furan, a versatile building block. Second oxidation of the primary alcohol and second cross-coupling would yield the asymmetric useful target.

Solvent-free Mechanochemical Approach to the Friedländer Reaction: Implications and Applications in the Synthesis of Small Molecules and Materials

J.-L. Do[1*], T. Friščićb[2], L. Cuccia[1]
[1]*Concordia University,* [2]*McGill University*

In its initial form, the Friedländer reaction consisted of a double condensation reaction between 2-aminobenzaldehyde with ketones to afford quinoline derivatives.[1] With an extensive history of development and success,[2] the Friedländer reaction remains one of the simplest, accessible, and powerful tools in the synthesis of industrially- and academically-relevant heterocyclic materials.[3] Despite investigations into more effective catalyst systems and reaction conditions, the methodologies surrounding the Friedländer reaction have not deviated much from solution-based routes with comparatively few explorations in the solid state.[4]

Mechanochemistry utilizes mechanical force to affect chemical transformation without the need of bulk liquids and has gained attention in recent years as a means to reach unique, cleaner, and more efficient reactivity.[5] Herein, we present preliminary results in the development of a solvent-free mechanochemical approach to the Friedländer condensation as a versatile alternative to traditional solution-based routes. Utilizing widely available catalysts, we are able to conduct rapid, solvent-free, and room temperature transformations of a variety of classical and specialty liquid and solid 2-aminocarbonyl compounds as precursors to functional materials.

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Resensitization of Salmonella enterica to the Antibacterial Metabolite of Macrophages Itaconate

D. Duncan*, F. Hammerer, J. Chan, K. Auclair
McGill University

Antibiotic resistance is a global health crisis. If current trends in antibiotic resistance continues, these superbugs are expected to kill more people per year than cancer by 2050. Many of the drugs developed are modifications of old drugs, which leads to rapid acquisition of resistance in bacteria. Therefore, it is necessary to develop new targets and new methods of attacking bacterial infections. Additionally, it is essential to find targets that are less prone to developing antibiotic resistance. This work showcases a novel method of targeting bacteria by re-sensitizing them to the human innate immune system. This re-sensitization is only possible under high stress, nutrient poor conditions such as those found in macrophages. Therefore, this method reduces the likelihood of the bacteria developing resistance to these sensitizers.

Late Stage Introduction of Quaternary Stereocentres: Total Synthesis of Puraquinonic Acid

A. Elmehriki*, J. Gleason
McGill University

Quaternary stereocentres are a common, yet challenging feature encountered in the synthesis of natural products and biologically active compounds. This challenge becomes particularly difficult when two or more of the groups at the stereocentre possess similar steric and electronic properties. The natural product puraquinonic acid presents one such challenge, as the stereo-defining elements are far removed from its stereocentre. Our group has previously demonstrated a reliable method for the construction of quaternary stereocentres, via the alkylation of a bicyclic thioglycolate lactam. This allows access to a variety of well-defined stereocentres which can be leveraged for the synthesis of complex targets. To further the synthetic utility of this technique, we herein describe advancements allowing for the rapid late stage introduction of the quaternary stereocentre of puraquinonic acid in the context of its total synthesis.

Photochemical Cobalt-catalyzed C-H Functionalization of Heterocycles

J.-C. Grenier-Petel*, S. Collins
Université de Montréal

C-H Bond functionalization of benzoxazole is made possible via cobalt catalysis employing either a carbazole-based organic photocatalyst, or an iridium-based transition metal photocatalyst. Optimization of the reaction conditions to promote addition to alkynes will be described.

Stabilized Pantothenamide Analogues as Novel Antimalarial Agents

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[1]McGill University, [2]The Australian National University

Nearly half of the world's population was at risk of malaria, reported by World Health Organization. However, parasite resistance to artemisinin, the first-line antimalarial medicine, has been detected in five countries of the Greater Mekong subregion. Therefore, developing novel antimalarial agents is necessary and urgent. Pantothenamides, the amide derivatives of pantothenate (also known as vitamin B5), have been shown to possess antimalarial activity arising from their action as pantothenate antimetabolites. Though being potent and non-cytotoxic, pantothenamides cannot be used in clinic due to their instability in human blood. This presentation will summarize our recent efforts in developing various novel pantothenamide analogues to address the instability problem and to identify new antimalarial agents. In particular, some of our compounds can inhibit growth of the virulent malaria parasite *Plasmodium falciparum* at nanomolar concentrations.

Diselenide Cross-linking of Oligonucleotides Between 2'-Deoxy-6-Selenoinosine

C. Liczner[*], V. Grenier, C. Wilds
Concordia University

The chemical modification of nucleic acids, achieved through organic synthesis, can enhance the properties of these molecules and expand their range of applications. For example, incorporation of selenium in DNA has been shown to be a powerful approach to aid in the X-ray crystallographic determination of nucleic acid structures by assisting with solving the phase problem. Selenium is a heavy atom of choice due to its efficient anomalous scattering, resemblance to oxygen and the many sites available for modification, including the sugar, phosphate backbone and nucleobase. Our lab was initially interested in expanding the incorporation sites of selenium in an oligonucleotide through the synthesis of a nucleobase modified 2'-deoxyinosine (dI). The novel d^{6Se}I phosphoramidite was synthesized and incorporated into an oligonucleotide by solid-phase synthesis. Unexpectedly, after deprotection, spontaneous diselenide cross-linking between two non-complementary DNA strands was observed. This cross-link, which has not been observed before for other selenium nucleobase modified nucleic acids, is readily formed in aerobic conditions. Moreover, it is quickly and quantitatively removed under mild reducing conditions. This opens up a facile synthetic route to site-specific cross-linking of oligonucleotides (or conjugation to other biomacromolecules) while having the added advantage of facilitating the determination of structures by X-ray crystallography.

Photochemical Intramolecular Amination for the Synthesis of Heterocycles

S. Parisien-Collette*, C. Cruché, X. Abel-Snape, S. Collins
Université de Montréal

Previously, our group has reported the photochemical oxidation of diaryl- and triarylamines to form carbazoles, but the existing methods fail to promote heterocycle formation when starting materials possess a free amine. In the current context of sustainable synthesis, the development of practical photochemical amination would be a welcome addition to the toolbox of synthetic chemists.

We have recently developed a photochemical continuous-flow synthesis of heterocycles using UV light. This methodology affords unprotected, free N-H, carbazoles, indoles and pyrroles. The use of low energy UV light, such as purple LED (394 nm), allow the formation of halogen containing carbazole, without deshalogenation of the desired product. In addition, we tested scale up strategies, numbering-out and numbering-up, in continuous-flow to improve the throughput of the reactor. Lastly, investigation of telescope reaction is on going to further functionalize the carbazole core.

ORGANIC CHEMISTRY/CHIMIE ORGANIQUE

Posters / Affiches

Chiral Amplification of Uracil Derivative Conglomerate Crystals via Viedma Ripening

D. Farajat, L. Cuccia
Concordia University

The origin of chirality and its role in biology are of great intrigue within many disciplines of science. In medicine, chirality is crucial for the binding specificity of drugs and aids in understanding biological abnormalities. Understanding and developing methods for chiral amplification have both practical industrial applications as well as fundamental interests. The scope of this study is to explore attrition enhanced deracemization, also known as Viedma Ripening, on conglomerate crystals as a means of chiral amplification and, in doing so, add to the growing library of compounds that can undergo Viedma Ripening. The conglomerates being studied include 1-(p-toluenesulfonyl)uracil and 1-(1-naphthylsulfonyl)uracil. Pyrimidine bases have been shown to have strong antitumor activity, therefore, functionalizing and characterizing these bases may prove beneficial for pharmacological use.

PHYSICAL CHEMISTRY/PHYSICO-CHIMIE

Oral Presentations / Présentations Orales

Impacts of ω Thiol on Phenolic Surfactant Air-water Behavior: Implications for Deposition onto Gold Surface from the Air-water Interface

R. Miclette Lamarche*, C. DeWolf
Concordia University

Thiol containing molecules can chemisorb onto gold surfaces to form a monolayer, this is done by immersion in a solution of the thiol compound, creating a SAM (self-assembled monolayer). An alternative would be to deposit the monolayer after it was formed in a different organisation than the one obtained by SAM. We propose to do this by pre-assembling the monolayer at the air-water interface using surfactants that have been ω-functionalized to have a thiol at the end of their carbon chain. To deposit the monolayer, we first need to study the behavior of surfactants that have been modified. Using a Langmuir trough balance with ellipsometric measurement at the air-water interface revealed that the surfactants first stand upright, the headgroup (phenol) in the water and the thiol point upward toward the air but over time the thiol contact the water. Thiol location dictates the deposition process and possible strategy. Learning more about its location and behavior at the air water interface would make it possible to create monolayer with organisation customized for specific task.

Cholesterol Alters Antimicrobial Peptide GL13K's Organization and Insertion into Model Lipid Monolayers

H. Youssef*, C. DeWolf
Concordia University

GL13K is a thirteen-residue antimicrobial peptide that is effective against Gram-positive and Gram-negative bacteria while exhibiting low hemolytic and cytotoxic effects. We probe the impact of cholesterol incorporation on the behaviour of GL13K with model membranes, as cholesterol content is a fundamental difference between the composition of prokaryotic and eukaryotic cell membranes. In previous studies with bilayer model membranes, GL13K attacked anionic membranes with high specificity, and the presence of cholesterol in the membranes resulted in aggregation.

Monolayer studies coupled with spectroscopic techniques provide insight into the behavior of the peptide at the outer leaflet of the membrane biointerface. The model membrane systems consist of negatively-charged 1,2-dioleoylphosphatidylglycerol (DOPG) and mixed-lipid systems at various DOPG:cholesterol composition ratios. In the absence of cholesterol, GL13K forms an extensive inter-peptide ß-sheet, which is disrupted in the systems containing cholesterol. The increased monolayer packing and rigidity of those systems causes an increased tilt angle of the inserted peptide. The absence of stabilizing peptide-peptide interactions and solvent-accessibility of the hydrophobic residues may be triggering the aggregation observed in the bilayer studies.

INORGANIC CHEMISTRY/ CHIMIE INORGANIQUE

Posters / Affiches

Variable Temperature Raman Spectroscopy and DFT Frequency Calculations of Coordination Compounds

N. Bélanger-Desmarais*, C. Reber
Université de Montréal

Raman spectroscopy is a general, non-destructive characterization technique applicable to a wide range of compounds. This technique has known improvements in terms of sensitivity and resolution over the two past decades that has made it more interesting and accessible. Moreover, it can be used on samples of different states with little to no preparation and can be easily coupled to a variable temperature set-up to monitor different phenomena and to achieve better resolution. Given these advantages and the ease to measure a Raman spectrum, this technique provides valuable experimental results to compare with electronic structure calculations. Indeed, the vibrational frequencies obtained by Raman spectroscopy can be calculated by these methods to assess the performance of the methodology used or to obtain additional informations. However, in order to assess the performance of a computational approach or to assign vibrational frequencies, one must have resolved vibrational spectra to compare with, which are not always available. Therefore, we present variable temperature Raman spectra for different coordination compounds in the solid-state along with DFT-calculated vibrational frequencies to study various effects in coordination compounds of d^6, d^8 and d^{10} configuration.

Oxygenation of 3,5-di-*tert*-butyl-phenol: reaction, optimization and mechanism

Y. Li*, X. Ottenwaelder
Concordia University

The copper-catalyzed aerobic oxygenation of phenols is an attractive green method for the preparation of reactive and synthetically useful *ortho*-quinones. Recently, the Lumb group has developed fully catalytic conditions to perform this reaction with unsurpassed simplicity and efficiency.[1] This reaction employs catalytic amounts of copper(I) and *N,N'*-di-*tert*-butylethylenediamine (DBED) as the supporting ligand. Our group unveiled the mechanism of this reaction with 4-tert-butylphenol, and showed that the oxygenation proceeded via side-on peroxodicopper(II) core (**P**) and copper(II)-semiquinone (**SQ**) intermediates.[2] However, not all substrates behave equivalently under these or similar reaction conditions, with some substrates undergoing oxygenation with subsequent C–O coupling, some undergoing only oxygenation, and some undergoing radical-based C–C coupling. In order to better

understand the selectivity of the reaction, we screened a library of ligands with different nitrogen donors and denticities on two test substrates (4-*tert*-butylphenol and 3,5-di-*tert*-butylphenol). We will present an extensive mechanistic study on the oxygenation reaction, including characterization of intermediates and kinetic studies.

Copper Complexes with Novel Chelating Nitroso Ligands

J. Zsombor-Pindera[1*], L. Escomel, X. O[1]
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Nitrosoarenes (ArNO) have been identified as redox-noninnocent ligands potentially conferring enhanced electronic and oxidative malleability on metal centres, which could be used to improve the catalytic versatility of cheap, safe coinage metals. Several transition metal complexes with monodentate ArNOs have been reported, but these complexes may not be stable under different nitroso oxidation states, so we are interested in synthesizing complexes with a nitroso function integrated into a chelating ligand in order to better study the nitroso group's electronic properties and to discover new catalysts. With this aim in mind, we have synthesized two novel multidentate pyridyl- based nitro (NO_2)-functionalized ligands, which are reduced to amines (NH_2) or hydroxylamines (NHOH). With copper (I) salts, the NHOH function disproproprtionates to NO and NH_2, and with copper (I) halides, the NHOH function is conserved on complexation, and can be chemically oxidized to NO. These results are supported by ESI-MS, UV-Vis, and HNMR experiments. Additionally, we report several new crystal structures, illustrating the structural effects imbued by complexation ligands with the nitrogen functional group in different oxidation states.

CHEMISTRY EDUCATION/ ENSEIGNEMENT DE LA CHIMIE

Posters / Affiches

A Large Scale Electronic Card Sort to Investigate Student's Interpretations of Organic Reactions

K. Lapierre[*], K. Galloway, A. Flynn
University of Ottawa

Expertise in Organic Chemistry relies heavily on interpreting visual representations and applying this knowledge when predicting and justifying reactivity. A newly implemented curriculum at the University of Ottawa directs focus on understanding the patterns of mechanisms governing reactions as opposed to the traditional functional group approach used to teach Organic Chemistry. This shift aims to provide students the tools to predict reactivity and explain mechanisms of unknown reactions. Our research group developed a card sort activity to investigate the organization of students thinking regarding organic chemistry reactions presented within the new

curriculum. Organic Chemistry II students completed an open (*N*=92) and closed (*N*=72) electronic card sort of 25 organic reactions cards at the beginning of their course. Participant's card groupings and explanations were categorized into five levels of interpretation previously observed: identical structural features, similar properties of structure, similar reaction type, similar mechanism, and unknown reactions. We investigated the relationship between card groupings, group names, and explanations, as well as similarities and differences of the open and closed sorting. Methods, findings, and implications for teaching and learning will be presented.

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