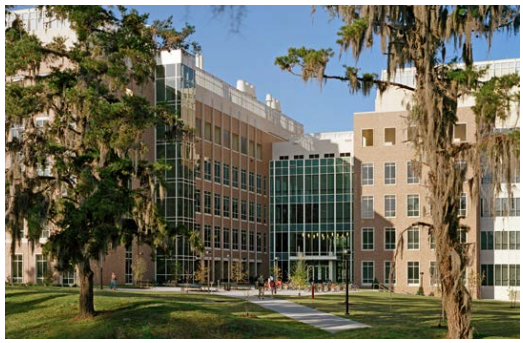
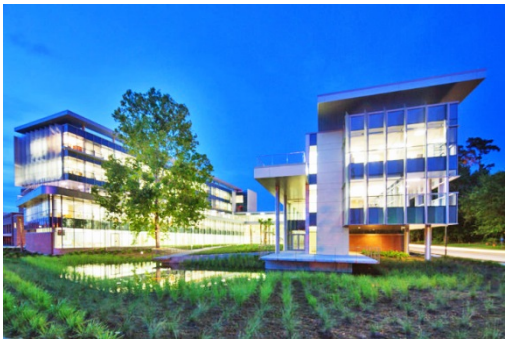
2014 UF Metabolomics Workshop & Symposium

May 20-23, 2014 ● University of Florida ● Gainesville, Florida





Workshop

CTRB – 3rd Floor – Room 3161

Tuesday & Wednesday, May 20th-21st

8:00 a.m.—5:00 p.m.

Symposium

CGRC – 1st Floor – Auditorium 101

Thursday & Friday, May 22nd-23rd

8:00 a.m.—5:00 p.m.

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SECIM; NIH Grant: #U24DK097209.

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UF Metabolomics Workshop & Symposium

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Overview

Welcome to the 2014 Southeast Center for Integrated Metabolomics Workshop and Symposium! We have worked hard to put together a program that provides an introduction to metabolomics and to the capabilities at SECIM while highlighting the state of the art applications from leading experts around the world.

During the first 2 days, workshop participants will get lectures and demonstrations of the basics of metabolomics, starting from sample preparation to basics of data analysis. The workshop presentations are focused around the comprehensive SECIM cores that are available to users. Slides and extra reading material will be available to students, and we will present an overview of several on-line tools available for any metabolomics researchers. The symposium during the last two days features speakers with applications in metabolomics in all areas, including plants, animals, model systems, and cutting edge technologies.

We want to encourage active dialogue and questions and hope that everyone can find some new scientific connections during the week. The poster session, mixer, and BBQ dinner on Wed night will be a perfect time to meet each other and informally further discuss the exciting opportunities in metabolomics.

The organizing committee,

Art Edison, SECIM Director

Sally Assmann, Pennsylvania State University

Sixue Chen, ICBR Proteomics Director

Mike Conlon, SECIM Promotion & Outreach

Glenn Walter, SECIM NMR Core

Tim (TJ) Janicki, SECIM Project Manager

Itinerary, 2014 UF Metabolomics Workshop

Tuesday, May 20, 2014

Introduction to Metabolomics

8:00	Light Breakfast	CTRB 3rd Floor Cafe
8:30	Welcome, organization, and brief intro to SECIM (Art Edison)	CTRB Room 3162
8:45	Introduction to Metabolomics (Jean-Luc Wolfender)	CTRB Room 3162
10:00	Break	CTRB 3rd Floor Cafe
10:15	Basics of Study Design (Lauren McIntyre)	CTRB Room 3162

SECIM Core 1

10:30	Sample Preparation (Alisha Mitchell-Roberts & Tim Garrett)	CTRB Room 3162
11:00	LC-MS for Global and Targeted Analysis (Tim Garrett)	CTRB Room 3162
12:00	Lunch	CTRB 3rd Floor Cafe

SECIM Cores 2, 3, and 4

1:00	Solution NMR for Global Metabolomics (Art Edison)	CTRB Room 3162
2:00	Hyphenated Methods (Jean-Luc Wolfender)	CTRB Room 3162
3:00	Break	CTRB 3rd Floor Cafe
3:15	IROA (Chris Beecher)	CTRB Room 3162
4:15	Introduction to Galaxy (Matt Gitzendanner)	CTRB Room 3162
4:45	Introduction to Quality Control concepts (Peihua Qiu)	CTRB Room 3162

Itinerary, 2014 UF Metabolomics Workshop

Wednesday, May 21, 2014

Biostatistics		
8:00	Light Breakfast	CTRB 3rd Floor Cafe
8:30	Intro to Multivariate Approaches (Peihua Qiu)	CTRB Room 3162
9:00	Galaxy Demonstrations (Sergio Tafur)	CTRB Room 3162
10:00	Break	CTRB 3rd Floor Cafe
Advanced Methods - Tissues		
10:15	MALDI Imaging (Rick Yost)	CTRB Room 3162
11:00	Introduction to *in vivo* NMR/MRI (Glenn Walter)	CTRB Room 3162
11:45	Introduction to DNP (Jim Prestegard)	CTRB Room 3162
12:30	Lunch	CTRB 3rd Floor Cafe
Demonstrations – 2 rotating groups		
2:00	**Group 1:** DNP and HRMAS (Joanna Long, Glenn Walter, Art Edison) **Group 2:** Biorepository and LC-MS (Tim Garrett)	AMRIS Facility Garrett Lab
3:45	**Group 1:** Biorepository and LC-MS (Tim Garrett) **Group 2:** DNP and HRMAS (Joanna Long, Glenn Walter, Art Edison)	Garrett Lab AMRIS Facility
Evening Event		
5:30	Poster session and cocktail reception	CTRB Lobby
6:00	BBQ Dinner	CTRB Lobby

Itinerary, 2014 UF Metabolomics Symposium

Thursday, May 22, 2014

8:00 a.m.	Light Breakfast	CGRC Lobby
Session 1: New Technologies in Metabolomics (Chair: Sixue Chen)		
8:30 a.m.	Yuji Sawada, RIKEN Center for Sustainable Resource Science, Japan: "Integrated LC-MS/MS platforms for Plant Metabolomics"	CGRC Auditorium 101
9:15 a.m.	Xianlin Han, Sanford-Burnham Medical Research Institute, USA: "What We Have Learned from Shotgun Lipidomics-Altered Lipid Metabolism in ob/ob Mice and Its Implication in Obesity"	CGRC Auditorium 101
10:00 a.m.	Break	CGRC Lobby
10:15 a.m.	Lloyd Sumner, The Noble Foundation, USA: "Large-scale Computational and Empirical Annotation of the Medicago Metabolome using UHPLC-MS-SPE-NMR"	CGRC Auditorium 101
Session 2: Metabolomics of Signaling and Trait Association (Chair: Sally Assmann)		
11:00 a.m.	Oliver Fiehn, West Coast Metabolomics Center, UC Davis Genome Center, USA: "Metabolomics for Epidemiological Studies: Large-Scale Metabolomics at High Quality Control"	CGRC Auditorium 101
12:00 p.m.	Lunch	CGRC Lobby
1:00 p.m.	Sarah M. Assmann, Pennsylvania State University, USA: "Metabolomics of Hormone Response in Arabidopsis Guard Cells"	CGRC Auditorium 101
1:45 p.m.	Masami Hirai, RIKEN Center for Sustainable Resource Science, Japan: "Development of Metabolomics Technology for Further Understanding of Plant Metabolism"	CGRC Auditorium 101
2:30 p.m.	Break	CGRC Lobby
2:45 p.m.	Tom Niehaus, University of Florida, USA "Metabolite Damage and its Repair or Pre-emption"	CGRC Auditorium 101
3:30 p.m.	Biswapriya B. Misra, University of Florida, USA "Comparative Metabolomics of Bacterial Flagellin 22 Responses in Plant Single Cell-Types"	CGRC Auditorium 101

Itinerary, 2014 UF Metabolomics Symposium

Friday, May 23, 2014

8:00 a.m.	Light Breakfast	CGRC Lobby
Session 3: Metabolomics of Disease and Defense (Chair: Glenn Walter)		
8:30 a.m.	Eric Schmelz, USDA-ARS CMAVE, USA: "Elucidating Induced Plant Defenses: the Use of Targeted Metabolomics as a Bridge from Elicitation to Response"	CGRC Auditorium 101
9:15 a.m.	Steven Smith, Translational Research Institute for Metabolism and Diabetes, USA: "Metabolomics markers of decreased fat oxidation during weight loss"	CGRC Auditorium 101
10:00 a.m.	Break	CGRC Lobby
10:15 a.m.	Kari Basso, Department of Chemistry, University of Florida, USA: "Quantitative Lipidomics and Proteomics – a Systems Biology Approach to Understanding the Human Tear Film"	CGRC Auditorium 101
11:00 a.m.	Yetrib Hathout, Dept. of Integrative Systems Biology, Biochemistry & Molecular Biology, Center for Genetic Medicine, Children's National Medical Center, USA: "Mass spectrometry methods for serum biomarkers discovery in Duchenne muscular dystrophy"	CGRC Auditorium 101
12:00 p.m.	Lunch	CGRC Lobby
Session 4: Imaging and NMR Metabolomics (Chair: Art Edison)		
1:00 p.m.	Art Edison, Department of Biochemistry, University of Florida, USA: "The pros and cons of ^{13}C NMR for metabolomics"	CGRC Auditorium 101
1:45 p.m.	Jim Prestegard, Complex Carbohydrate Research Center, University of Georgia, USA: "Following metabolic pathways with H-D exchange and DNP NMR"	CGRC Auditorium 101
2:30 p.m.	Rick Yost, Department of Chemistry, University of Florida, USA: "Integrating Imaging Mass Spectrometry with Metabolomics"	CGRC Auditorium 101
3:15 p.m.	Gary Patti, Departments of Chemistry, Genetics and Medicine, Washington University, USA: "Mass Spectrometry and NMR-Based Metabolomics: The Whole is Greater than the Sum of the Parts"	CGRC Auditorium 101
4:00 p.m.	Conclusion of Symposium	CGRC Auditorium 101

List of Speakers

Workshop

Tuesday, Wednesday May 20th & 21st

Chris Beecher, Ph.D.	IROA
Art Edison, Ph.D.	Intro to SECIM DNP and HRMAS Solution NMR for Global and Targeted Analysis
Tim Garrett, Ph.D.	Sample Preparation LC-MS for Global and Targeted Analysis Biorepository and LC-MS
Matt Gitzendanner, Ph.D.	Introduction to Galaxy
Joanna Long, Ph.D.	DNP and HRMAS
Lauren McIntyre, Ph.D.	Basics of Study Design
Alisha Mitchell Roberts, Ph.D.	Sample Preparation
Jim Prestegard, Ph.D.	Introduction to DNP
Peihua Qiu, Ph.D.	Introduction to Quality Control concepts Introduction to Multivariate Approaches
Sergio Tafur, Ph.D.	Galaxy Demonstrations
Glenn Walter, Ph.D.	Introduction to in vivo NMR/MRI DNP and HRMAS
Jean-Luc Wolfender, Ph.D.	Hyphenated Methods Introduction to Metabolomics
Rick Yost, Ph.D.	MALDI Imaging

Symposium

Thursday, Friday May 22nd & 23rd

Sarah M. Assmann, Ph.D.	“Metabolomics of Hormone Response in Arabidopsis Guard Cells”
Kari Basso, Ph.D.	“Quantitative Lipidomics and Proteomics – a Systems Biology Approach to Understanding the Human Tear Film”
Art Edison, Ph.D.	“The Pros and Cons of 13C NMR for Metabolomics”
Oliver Fiehn, Ph.D.	“Metabolomics for Epidemiological Studies: Large-Scale Metabolomics at High Quality Control”
Xianlin Han, Ph.D.	"What We Have Learned from Shotgun Lipidomics-Altered Lipid Metabolism in ob/ob Mice and Its Implication in Obesity"
Yetrib Hathout, Ph.D.	“Mass Spectrometry Methods for Serum Biomarkers Discovery in Duchenne Muscular Dystrophy”
Masami Hirai, Ph.D.	“Development of Metabolomics Technology for Further Understanding of Plant Metabolism”
Biswapriya B. Misra, Ph.D.	“Comparative Metabolomics of Bacterial Flagellin 22 Responses in Plant Single Cell-Types”
Tom Niehaus, Ph.D.	“Metabolite Damage and its Repair or Pre-emption”
Gary Patti, Ph.D.	“Mass Spectrometry and NMR-Based Metabolomics: The Whole is Greater than the Sum of the Parts”
Jim Prestegard, Ph.D.	“Following Metabolic Pathways with H-D Exchange and DNP NMR”
Yuji Sawada, Ph.D.	“Integrated LC-MS/MS Platforms for Plant Metabolomics”
Eric Schmelz, Ph.D.	“Elucidating Induced Plant Defenses: the Use of Targeted Metabolomics as a Bridge from Elicitation to Response”
Steven Smith, M.D.	“Metabolomics Markers of Decreased Fat Oxidation during Weight Loss”
Lloyd Sumner, Ph.D.	“Large-scale Computational and Empirical Annotation of the Medicago Metabolome using UHPLC-MS-SPE-NMR”
Rick Yost, Ph.D.	“Integrating Imaging Mass Spectrometry with Metabolomics”

Development of a Dissolution DNP System for *in vivo* Spectroscopy.

Daniel Downes[1*], James Collins[1], Bimala Lama[1], Glenn Walter[2], Adam N. Smith[1,3], and Joanna Long[1].

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[2]Department of Physiology and Functional Genomics, University of Florida, Gainesville, FL 32610, USA.
[3]Department Chemistry, University of Florida, Gainesville, FL 32610, USA.
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In vivo magnetic resonance spectroscopy (MRS) is a powerful method for measuring carbon metabolism in live animals, but is limited because of a poor signal-to-noise ratio (SNR). Dynamic nuclear polarization (DNP) is a rapidly developing technique in the field of MRS, offering a highly sensitive alternative to traditional MRS. Hyperpolarization of isotopically labeled samples prior to MR spectroscopy allows for a substantial increase in the signal-to-noise ratio *in vivo* (>10,000x). This gain in SNR allows the local cellular metabolism to be monitored in real time. Dissolution DNP has a wide range of applications including metabolic tracking and molecular diagnostic imaging. We are implementing a new École polytechnique fédérale de Lausanne designed dissolution DNP cryostat within a 5T wide-bore magnet with a 140 GHz VDI microwave source. Experimental arrays have been performed to optimize microwave frequency and power and will be presented along with enhancement values for various substrates. Phantom and animal studies have been performed with the use of an automated injection system coupled to a 4.7T and 11T imager. Through utilization of this technique, a variety of *in vivo* applications are evident.

High CO2 response of Brassica napus guard cells - a metabolomics view

Sisi Geng[1, 2], Biswapriya Biswavas Misra[2], Ning Zhu[2], Sarah M. Assmann[3], Sixue Chen[1, 2, 4]

[1]Plant Molecular and Cellular Biology Program, University of Florida, Gainesville, FL 32610
[2]Department of Biology, Genetics Institute, University of Florida, Gainesville, FL 32610
[3]Department of Biology, Pennsylvania State University, State College, PA 16803
[4] Proteomics and Mass Spectrometry, Interdisciplinary Center for Biotechnology Research, University of Florida, Gainesville, FL 32610

Guard cells play a key role in plant response to many biotic and abiotic stimuli. The dynamic molecular networks in the guard cells integrate these signals with stomatal output, e.g., stomatal movement. Stomatal movement plays an important role in regulating CO_2 intake, water transpiration and pathogen infection. Under high carbon dioxide concentrations, stomata will close in order to reduce water loss. However, the global metabolic changes in the course of the CO_2 response are not known. Here we report the responses of stomata to high concentration CO_2 at the morphological, biochemical and metabolic levels. Our data showed that there are significant differences in stomatal aperture as well as reactive oxygen species (ROS) levels between atmospheric CO_2 control (400 ppm) and high CO_2 treatment (800 ppm) after ten minutes bubbling treatment. Metabolomics data have been collected during the stomatal closure process using HPLC-MS/MS on a 4000QTRAP system. We have established a targeted metabolite library containing 287 metabolites which are mapped to the KEGG pathways. Our aim is to correlate the metabolomic changes with physiological and biochemistry changes. By integrating the transcriptomics and proteomics data collected in previous studies, we could further confirm and validate our data, and generate a holistic view of the molecular networks in guard cells in response to high CO_2 levels.

Directed Evolution of β-glucosidase

Madan Godar, Saraswathi Ramachandran, Nicholas Panasik Jr.

Department of Biology and Chemistry, Claflin University, Orangeburg, SC 29115, USA

*E-mail: mgodar@claflin.edu

β-glucosidase is an enzyme that breaks down cellulose by cutting off sugars in this complicated polysaccharide. This plays an important role in metabolism of cellulose and is used in a variety of biofuel production applications. In traditional applications, however, a great deal of heat is often generated in the process which either denatures the protein or requires the additional expense of refrigeration – often making the process too expensive to be competitive as an alternative energy source. While some scientists take the approach of using a thermostable enzyme isolated from an extant thermophile, our approach is to evolve thermo stability in a pre-existing psychrophilic β-glucosidase. It is hypothesized that if the temperature range of the enzyme can be increased, the usual doubling of reaction rates that occur with every 10^0C rise in temperature can be harnessed to create a more highly efficient enzyme at these greater temperatures. Our first step is to increase the temperature range from 37^0C to 41^0C.

pΔαNH/BglA is a pUC18 derived plasmid with the alpha fragment of β-galactosidase deleted. (to avoid any interference with our proposed blue/white screening). We ligated the gene coding for β-glucosidase into pΔαNH at the Nde1 and Sal1 restriction enzyme sites and expressed in E.coli on plates containing the chromogenic substrate X-gal. If the enzyme is active then our substrate will be cleaved yielding a blue precipitate. Error Prone PCR was performed to create mutations in the β-glucosidase gene, using manganese concentration to induce and control the error rate. Similarly, Titanium Taq polymerase, which has its proof reading domain deleted, induces and allows these mutations to accrue. Target mutation rates of 2.7 and 3.5 mutations per 1000 bp were used for Error Prone PCR. PCR purification was done to remove dNTP, manganese, and primers and sticky ends were produced for ligation with the help of double digest (Nde1/Sal1). Finally, ligation was done by inserting bglA into the vector which was followed by Transformation into E.coli JM109 cells.

Metabolomic Analysis for Duchenne Muscular Dystrophy

Brittany Lee-McMullen[1], Chaevien Clendinen[3], Stephen Chrzanowski[1], Ravneet Vohra[1], Rebecca Willcocks[2], Hilary Cunkle[2], Catherine Powers[2], William Triplett[1], Sean Forbes[2], Donovan Lott[2], Claudia Senesac[2], Arthur S. Edison[3], Krista Vandenborne[2], Glenn Walter[1]

[1]Department of Physiology and Functional Genomics, [2]Department of Physical Therapy, [3]Department of Biochemistry and Molecular Biology, University of Florida, Gainesville, FL 32610, USA
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Duchenne Muscular Dystrophy (DMD) is an X-linked genetic disorder in which the absence of dystrophin protein causes sarcolemma fragility resulting in incorrect muscle cell physiology and function. Eventually failed muscle regeneration leads to the progressive loss of ambulation in early teens, and the boys succumb to the disease in third decade of life. Despite the rapid rate of disease progression, there are few accepted surrogate endpoints and the FDA approved clinical outcome measure lacks sensitivity. As a result, there is a dire need for a biomarker to track disease progression in DMD. Our approach for biomarker discovery in DMD has been two-fold: 1) analysis of tissues and serum from a mouse model with a single, conserved mutation leading to the lack of dystrophin; and 2) correlating the phenotypical differences observed with DMD subjects to metabolomics measures of urine and serum. In preclinical studies, we compare differences in the muscle (in vivo/ex vivo) and serum metabolomes of dystrophic mice (mdx) at two stages of the disease. Preliminary analysis has revealed metabolomic differences between the two ages at different stages of the disease. For the clinical study, we determine the urine and serum metabolome from a cohort of 125 DMD boys where their phenotype and rate of disease progression has been determined. Metabolomic screens of both urine and serum are being correlated with biochemical markers of inflammation and the rate of disease progression.

Comparative Metabolomics of Bacterial Flagellin 22 Responses in Plant Single Cell-Types

Biswapriya B. Misra[1], Sixue Chen[1,2*]

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[2] Proteomics and Mass Spectrometry, Interdisciplinary Center for Biotechnology Research, University of Florida, Gainesville, FL 32610, USA
* E-mail: schen@ufl.edu

Bacterial flagellin 22 (flg22), a principal peptidial component of flagella, is a virulence factor that is recognized by the innate immune system of plant cells. However, little is known about the responsiveness of plant single cell-types or the metabolomic perturbations induced by flg22. Using stomatal guard cells (GCs) and mesophyll cells (MCs) of Brassica napus, we compared the metabolic effects of flg22-treatment on the two different single cell-types. The metabolomic changes were monitored for 0, 5, 15, 30, 60 and 120 minutes using a targeted HPLC-MRM-MS/MS approach. Out of the 287 metabolites mapped to the KEGG pathways, the MCs and GCs were characterized by 242 and 207 metabolites, respectively, indicating a differentially operative metabolism in both these cell-types. Both the cell types responded to flg22 at a differential magnitude, with MCs showing more radical changes as demonstrated using orthogonal-partial least square-discriminant analyses (PLS), whereas about 70% of the flg22 treatment-induced changes could be explained by just one principal component (PC). Furthermore, flg22 induced rapid metabolomics changes in GCs as early as at 5 min, while the metabolic changes in MCs peaked at 15 min. In GCs, flg22 elicitated global changes and shifts in sugar, phenolics, flavonoid, amino acid, phytohormone metabolisms. These metabolomic time-course results indicated that GCs, which are the first line of defense in plant leaves are metabolically well-equipped to re-program the chemical warfare with invading phytopathogens, as indicated by the rapid stomatal closure phenotypes. This study is a starting point for further investigations on plant defense responses at cellular levels of metabolic resolution in order to gain meaningful insights towards crop genetic engineering for elevated resistance against existent and emergent pathogens.

Unravelling the impact of glycolytic mutants in metabolome of *Bacillus subtilis*

Joana Sousa[1], Hanna Meyer[1], Michael Lalk[1]
[1]Institute of Biochemistry, Ernst-Moritz-Arndt-University of Greifswald, Germany
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One of the most well-known biological processes is the Central Carbon Metabolism (CCM). It is increasingly apparent that CCM is not an isolated entity in the cell, and for example in the bacterium *Bacillus subtilis* it has been shown that mutations in pathways of the CCM influence cell wall synthesis, DNA replication, cell division, RNA processing, or secondary metabolite biosynthesis. This is maybe not surprising considering the conserved nature of the CCM pathways, but what is remarkable is that little is known about the mechanisms that link carbon metabolism to these other fundamental processes.

My 3-year PhD project will be focused in investigating metabolic pathways variations, mainly in CCM and cell wall synthesis, in *B. subtilis* by comparing BSB1 wild-type strain and selected mutants, *ΔpgcA*, *ΔgtaB* and *ΔugtP* – glycolytic involved in the synthesis of cell wall components. The measurement of metabolites profiles in *B. subtilis* will help to elucidate the metabolic interactions and will provide new insights into the characterization of dynamic pathways in the cell.

Metabolomics studies using microorganisms has been among the fastest areas of systems biology to be develop since they are relatively simple models, easy to grow and genetically tractable. This makes them a promising probe in pathways studies.

The metabolomic analyzes of my work will lie in determine extracellular and intracellular compounds of the cell. The extracellular metabolome – that consists of medium constituents and derivatives secreted during the cell growth – will be analyzed by 1H-NMR spectroscopy (AVANCE-II 600 NMR spectrometer) since the metabolites are present in high concentrations (>1mmol.L^{-1}). For complementary investigation of intracellular metabolome, HPLC-MS (Agilent HPLC 1100 system 1100 coupled to a Bruker micrOTOF mass spectrometer) and GC-MS (Agilent GC 6890N system coupled to a Bruker quadrupole mass spectrometer) techniques are the methods of choice.

Moreover, I hope to incorporate the metabolic data sets into a comprehensive metabolomics model.

Investigation of bioactive metabolites present in marine fungi

Nithyakalyani Srirangan, Stefanie Schneider, Martina Wurster, Ulrike Lindequist, Michael Lalk
Department of Biochemistry, Department of Pharmaceutical Biology,
Ernst Moritz Arndt University, Greifswald, Germany
Email: Srirangan.nithya@gmail.com

Three marine fungi isolates collected from Greifswald Bay (Baltic Sea; Germany) and the Red Sea (Egypt) are the candidates considered for this study. In particularly the marine fungi from Baltic coastal region is known as Pseudohalonectria lignicola a wood decaying fungi taxonomy belongs to ascomycetes family and the other two strain are not described so far. Since they all are facultative marine fungal strains cultivation was performed using Hagem medium with optimized lab conditions. Ethyl acetate extract of lignicolous fungi P.lignicola showed interesting antimicrobial activity on Gram-positive bacteria and cytotoxic activity against urinary bladder carcinoma cell lines and the compounds responsible for such bioactivity was examined. As a result, it was found that P. lignicola posses clusters of pyron derivatives and one compound responsible for antimicrobial activity was found to be Nectriapyrone which is also a phytotoxic compound. Ergosterol peroxide a another metabolite from P. lignicola was found to be responsible for the cytotoxic activity.

Global Metabolomics of Complications in Pregnancy

Jacquelyn Walejko[1,2*], Maureen Keller-Wood[3], Charles Wood[4], Josef Neu[5], Arthur Edison[1,2]

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[3] Department of Pharmacodynamics, University of Florida, Gainesville, FL 32610, USA
[4] Department of Physiology and Pharmacology, University of Florida, Gainesville, FL 32610, USA
[5] Department of Pediatrics, College of Medicine, University of Florida, Gainesville, FL 32610, USA
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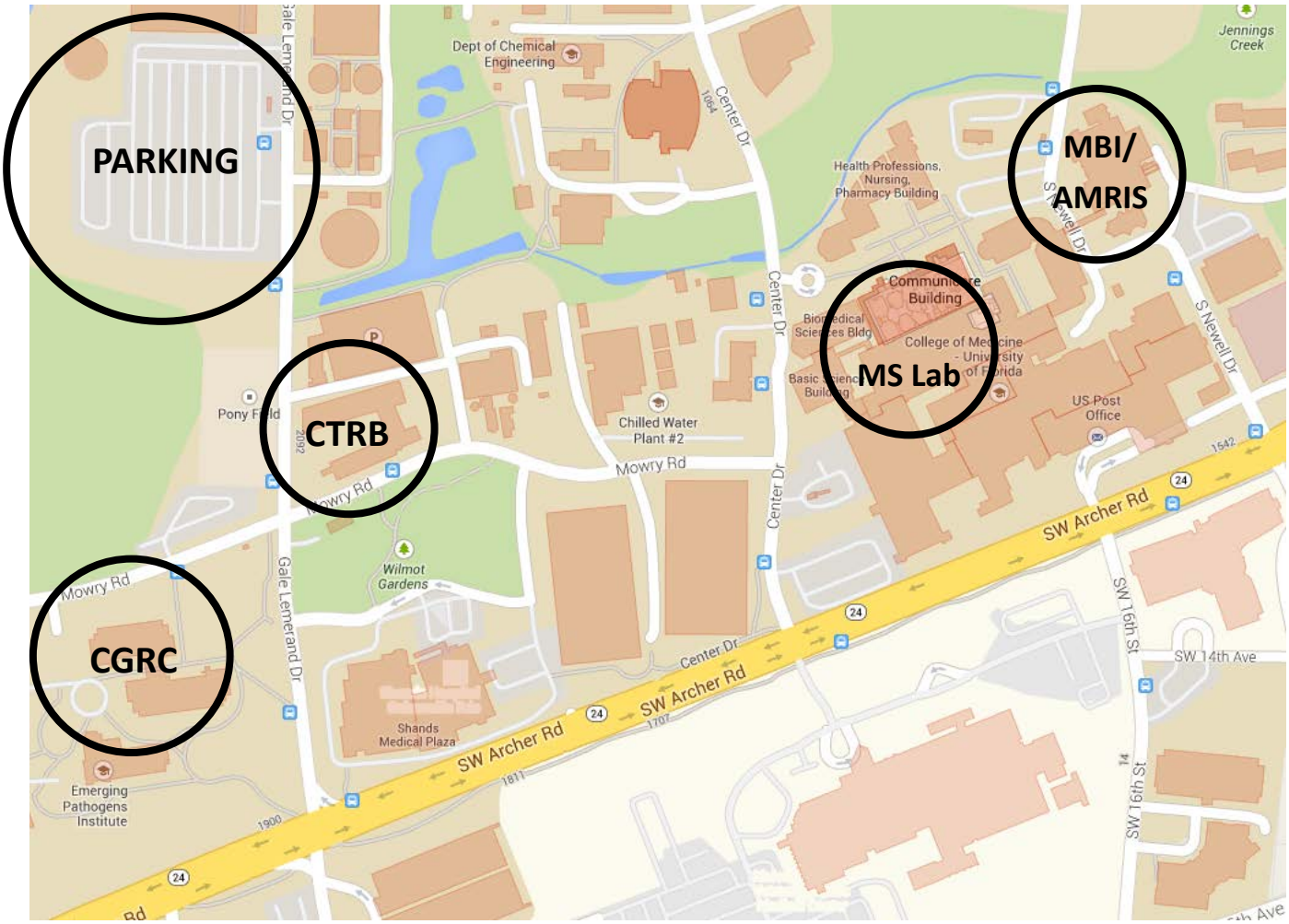
In 2011, the fourth leading cause of infant mortality was maternal complications during pregnancy.[1] Babies born to mothers with gestational diabetes have an increased risk of developing diabetes, obesity, or metabolic syndrome, and women with gestational diabetes are more likely to experience a stillbirth compared to women without.[2] A common cause of birth asphyxia is umbilical cord thrombosis, which is associated with perinatal morbidity and mortality.[3] Previous work from the Keller-Wood lab has shown that maternal increases in cortisol can cause fetal mortality at term, delivery, or immediately after birth in a pre-clinical model of human pregnancy in ewes. Transcriptomic analysis revealed changes in heart metabolism, and these changes along with observed heart failure, bradycardia, lactic acidosis, and premature fetal mortality mimic human babies born to diabetic mothers.[4]

^{1}H-NMR was used to investigate plasma samples from cortisol infused ewes and their fetuses, as well as samples from a control fetus and from the same fetus following umbilical cord occlusion. Fetal plasma spectra revealed a decrease in several amino acids in fetuses from the cortisol infused ewes compared to control fetal plasma. These changes in amino acid levels may be indicative of changes in TCA cycle intermediates. Plasma collected from the same fetus before and after cord occlusion revealed a large increase in peaks corresponding to aspartate that were not present in the plasma before hypoxia. This increase in plasma aspartate seen after birth asphyxia may cause or exacerbate brain damage. Metabolomics findings will be integrated with phenotypic and genomic data to create a systems biology perspective of pregnancy with the ultimate goal being the identification of possible therapeutic targets that will ameliorate harm to the fetus.

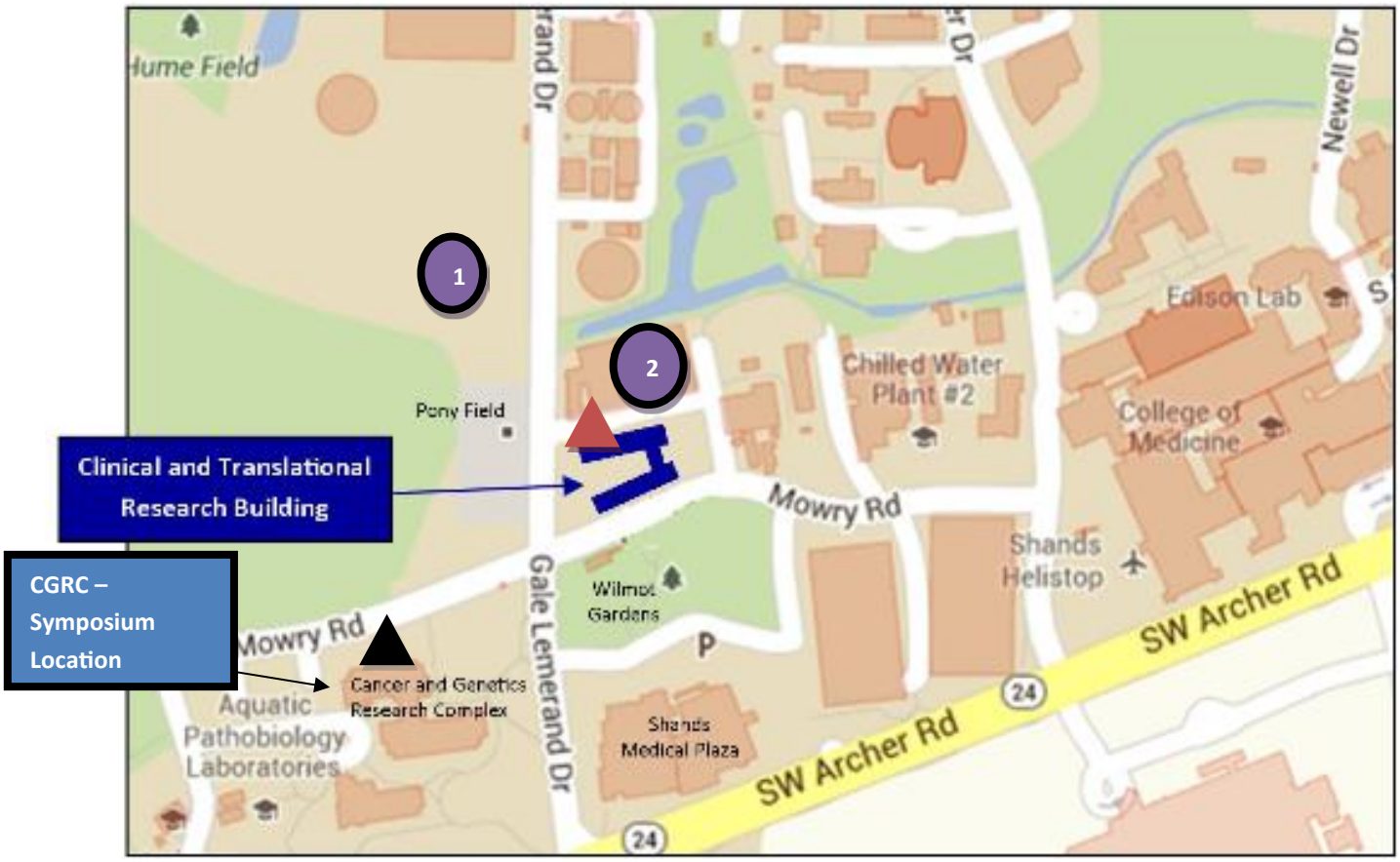
1. **Hoyert DL, Xu JQ.** Deaths: Preliminary data for 2011. National vital statistics reports; vol 61 no 6. Hyattsville, MD: National Center for Health Statistics. 2012.
2. **Malcolm, J**. Through the looking glass: gestational diabetes as a predictor of maternal and offspring long-term health. *Diabetes/Metabolism Research and Reviews* 28: 307–311, 2012.
3. **Heifetz, SA.** Thrombosis of the umbilical cord: analysis of 52 cases and literature review. *Pediatr Pathol* 8: 37-54, 1988.
4. **Bradley RJ, Brudenell JM and Nicolaides KH**. Fetal acidosis and hyperlacticaemia diagnosed by cordocentesis in pregnancies complicated by maternal diabetes mellitus. *Diabet Med* 8: 464-468, 1991.

Campus Event Map



Driving & Parking Directions

2004 Mowry Road, Gainesville, FL 32610



Visiting us at the UF Health Science Center

SECIM is located on the UF Health Science Center campus. If you have not visited us previously and/or are unfamiliar with the UF Health Science Center, leave some extra time to find your way. The UF Health Science Center is very large.

SECIM Campus Location

Southeast Center for Integrated Metabolomics
3rd Floor, North Wing, Clinical and Translational Research Building
2004 Mowry Road (northeast corner of Mowry Road and Gale Lemerand Drive)
University of Florida
Gainesville, FL 32610

Parking Options for the 2014 UF Metabolomics Workshop & Symposium

- Upon arrival for the workshop (May 20-21), please pick up your temporary parking permit at the North entrance of the CTRB (indicated on the map above by the red triangle).
- Upon arrival for the symposium (May 22-23), please pick up your parking permit at the North entrance of the CGRC (indicated on the map above by the black triangle).
- Your "Blue" temporary parking permit will allow you to park in "green" or "blue" designated parking spaces at the following locations:
  - Lot 1: Any space in the commuter lot
  - Lot 2: Any "Blue" space in the parking garage adjacent to the CTRB (Parking is very limited)

Driving Directions to the UF Clinical and Translational Research Building (CTRB)

2004 Mowry Road, Gainesville, FL 32610

From I-75, Exit #384 (State Road 24/Archer Road)

1. East on Archer Road for approximately 2 miles to Gale Lemerand Drive.
2. Left onto Gale Lemerand Drive for one block to Mowry Road.
3. Right on Mowry Road and take the next left into the CTRB circle drive.

From US 441 (13th Street)

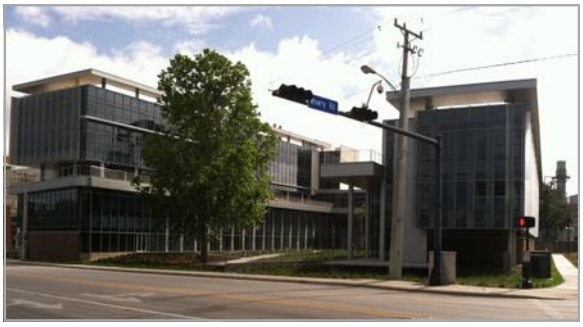
1. West on Archer Road for approximately 1 mile to Gale Lemerand Drive.
2. Right onto Gale Lemerand Drive for one block to Mowry Road.
3. Right on Mowry Road and take the next left into the CTRB circle drive.

From State Road 24 (Waldo Road)

1. South on SR 24 to University Ave. (SR 26).
2. Right on University Avenue for 1.7 miles to US 441 (13th Street).
3. Left on US 441 for 3/4 mile to Archer Road
4. Right on Archer Road for approximately 1 mile to Gale Lemerand Drive.
5. Right onto Gale Lemerand Drive for one block to Mowry Road.
6. Right on Mowry Road and take the next left into the CTRB circle drive.

From the Gainesville Regional Airport

1. Exit the airport and turn right on SR 222 (39th Ave.) for 4 miles to US 441 (13th St.).
2. Left on US 441 for 3 1/2 miles to Archer Road.
3. Right on Archer Road for approximately 1 mile to Gale Lemerand Drive.
4. Right onto Gale Lemerand Drive for one block to Mowry Road.
5. Right on Mowry Road and take the next left into the CTRB circle drive



View of the CTRB from Gale Lemerand Drive.

View of the CTRB main entrance off Mowry Road.

Local Restaurants

The Swamp Restaurant	1642 W University Ave Gainesville, FL 32603
The Top	30 N Main St Gainesville, FL 32601
Satchel's Pizza	1800 NE 23rd Ave Gainesville, FL 32609
Civilization	1511 NW 2nd St Gainesville, FL 32601
Boca Fiesta	232 SE 1 St. Gainesville, FL 32601
Dragonfly Modern Izakaya & Sushi	201 SE 2nd Ave Gainesville, FL 32601
Stonewood Grill and Tavern	3812 W Newberry Rd Gainesville, FL 32607
Leonardo's 706	706 W University Ave Gainesville, FL 32601
Ichiban Sushi	4401 NW 25th Pl Gainesville, FL 32606
BJ's Restaurant and Brewhouse	6611 Newberry Road Gainesville, FL 32605
Amelia's Italian Restaurant	235 S Main St Ste 107 Gainesville, FL 32601
Bonefish Grill	3237 SW 35th Blvd Gainesville, FL 32608
Miller's Ale House	3950 SW Archer Rd Gainesville, FL 32608

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