Program & Abstracts

January 22, 2021
9:00 am - 5:00 pm

Webinar: https://albany.zoom.us/j/98560406796?pwd=OFpna1dTWVdTVk44d2dSUjJiczl0Zz09

University at Albany
State University of New York
College of Arts & Sciences
9:00 - 9:10 **Opening Remarks**: Dr. Jim Dias, Vice President for Research, SUNY Albany

9:10 - 9:15 **Postdoc Association**: Kate Tubessing

9:15 - 9:20 **Scientista**: Lindsey Tolman

9:20 - 9:40 **Speed Talks I**: Moderator Alex Valm

Pearl De-Veer Biology, Ali Ropri Biomedical Sciences, Emmanuel Adade Biology, Aaron Premo Chemistry, and Ian Rapisarda Biology

9:45 - 10:50 **Keynote Presentation I**: "Science in the Time of COVID and America’s Reckoning with Race."

Dr. Shirley Malcom, Director of Education and Human Resources, American Association for the Advancement of Science.

10:50 - 11:10 **Coffee Break**

11:10 - 12:10 **Selected Student Presentations I**: Moderator: Jeremy Feldblyum

Leonard Breindel Chemistry, Carl Shotwell RNA Institute, Pheonah Badu Biology, Melanie Lolier Psychology, Weilan Zhang Environmental & Sustainable Engineering, and Nicholas Moskwa Biology

12:10 - 12:30 **Speed Talks II**: Moderator Alex Valm

Justin Waldern Biology, Anwesha Sarkar Biology, Jacob Schroader RNA Institute & Biology, Jennifer Cardinal Chemistry, and Mahera Kachwala Chemistry

12:30-1:30 **Lunch Break**

1:30 - 2:00 **Speed Talks III**: Moderator Jeremy Feldblyum

Lorianna Colon Psychology, Raghu Ram Katreddi Biology, Nicholas Sciolino Chemistry, Khalid Al-Lakhen Biology, Haley Caldwell Biomedical Sciences, Kristen Kaytes Biology, and Christopher Smith Chemistry

2:00 - 3:00 **Selected Student Presentations II**: Moderator: Alex Valm

Alex Lemus Biology, Kate Tubbesing Physics, Benjamin Bennink Biology, Ya Ying Zheng Chemistry, Lifeng Zhou RNA Institute, and Tyler Mitchell Biology

3:00 - 3:20 **Tea Time**

3:20 - 4:30 **Keynote Presentation II**: DNA dynamics and mutagenesis: How DNA directs its own copying errors

Dr. Hashim Al-Hashimi, James B. Duke Professor of Biochemistry and Chemistry, Director of the Duke Center for RNA Biology, Duke University

4:30 - 4:50 **Award Ceremony**: Dr. Jeanette Altarriba, Dean, College of Arts & Sciences, SUNY Albany
Program

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9:20 - 9:40 Speed Talks I: Moderator Alex Valm
   9:20 Pearl De-Veer - Biology, pde-veer@albany.edu, 'Effect of NF-kB on ATF3 Activation in ZIKV Infection'
   9:24 Ali Ropri - Biomedical Sciences, aropri@albany.edu, 'Cis-acting Super Enhancer IncRNAs as Diagnostic Markers of Progression to Early Stage Breast Cancer'
   9:28 Emmanuel Adade - Biology, eadade@albany.edu, 'Understanding the Spatial Structure of the Gut Microbiome in Zebrafish (Danio rerio)'
   9:32 Aaron Premo - Chemistry, apremo@albany.edu, 'Function, Inhibition, & Structure of the Formin hDia1 Complexed with ctRAGE'
   9:36 Ian Rapisarda - Biology, irapisarda@albany.edu, 'RNA Modification Landscape and it’s Contribution to Egg Production'

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   'Science in the Time of COVID and America’s Reckoning with Race'

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11:10 - 12:10 Selected Student Presentations I: Moderator Jeremy Feldblyum
   11:10 Leonard Breindel - Chemistry, lbreindel@albany.edu, 'Active Metabolism Unmasks Functional Protein–Protein Interactions in Real Time In-Cell NMR'
   11:20 Carl Shotwell - RNA Institute, cshotwell@albany.edu, 'The Disruption of RNA Modifications in Myotonic Dystrophy'
   11:30 Pheonah Badu - Biology, pbadu@albany.edu, 'ATF3 Regulates Antiviral Response in ZIKVPR Infected Cells'
   11:40 Melanie Lolier - Psychology, mlolier@albany.edu, 'The Effects of Synthetic Progestin Exposure on the Development of the Mesocortical Dopamine Pathway and Subsequent Behaviors'
11:50 Weilan Zhang - Environmental & Sustainable Engineering, wzhang4@albany.edu, ‘Exposure of Juncus Effusus to Seven Perfluoroalkyl Acids: Uptake, Accumulation & Phytotoxicity’

12:00 Nicholas Moskwa—Biology, nmoskwa@albany.edu, ‘FGF2 Stimulated Mesenchyme Controls Salivary Epithelial Differentiation Through BMP7’

12:10 - 12:30 Speed Talks II: Moderator Alex Valm

12:10 Justin Waldern—Biology, jwaldern@albany.edu, ‘Ribosomal RNA Modification Limits Group II Intron Retrotransposition’

12:14 Anwesha Sarkar - Biology, asarkar@albany.edu, ‘Epitranscriptome and tRNA-Writer Mediated Protection of Human Liver Cells From Arsenic Stress’

12:18 Jacob Schroader - RNA & Biology, jschroader@albany.edu, ‘Detection of Inosine Using Direct RNA Nanopore Sequencing’

12:22 Jennifer Cardinal - Chemistry, chuljenn@hotmail.com, ‘Ancient and Unknown’

12:26 Mahera Kachwala - Chemistry, mkachwala@albany.edu, ‘Hybridization Chain Reaction and CRISPR-Cas Systems for Disease Diagnostics’

12:30 - 1:30 Lunch break

1:30 - 2:00 Speed Talks III: Moderator Jeremy Feldblyum

1:30 Lorianna Colon - Psychology, lcolon@albany.edu, ‘Role of Gonadal Hormones in Sexual Differentiation of Context Fear Conditioning’

1:34 Raghu Ram Katreddi - Biology, rkatreddi@albany.edu, ‘Role of Notch Signaling in the Apical vs Basal Neuronal Cell Fate Determination in the Vomeronasal Organ’

1:38 Nicholas Sciolino - Chemistry, nsciolino@albany.edu, ‘Microfluidics Delivery of Target Protein Enhances Cell Viability for In-Cell NMR Spectroscopy’

1:42 Khalid Al-Lakhen - Biology, kallakhen@albany.edu, ‘Culturomics Approach to Identify Spatial Relationships in the Human Oral Microbiome’

1:46 Haley Caldwell - Biomedical Sciences, hcaldwell@albany.edu, ‘Host-biased West Nile Virus Quasispecies Facilitate Host-Specific Adaptation’

1:50 Kristen Kaytes - Biology, khaytes@albany.edu, ‘The role of conserved poly A’ Sequences in the 3'UTR of Zika Virus Translation’

1:54 Christopher Smith - Chemistry, cwsmith@albany.edu, ‘Coupling RT-LAMP with CRISPR-Cas12a for Detection of Lyme Disease’
2:00 - 3:00  Selected Student Presentations II :  Moderator Alex Valm  
2:00  Alex Lemus—Biology, alemus@albany.edu, ‘Multi-Species Bacterial Aggregates Contribute to Spatial Heterogeneity in an Oral Biofilm Model’
2:10  Kate Tubbesing - Physics, ktubbesing@albany.edu, ‘Iron Homeostasis in Breast Cancer Cells—Unique Investigations with Raman Hyperspectral Imaging’
2:20  Benjamin Bennink - Biology, bbennink@albany.edu, ‘Neuronal Glutamate Transporters Control the Temporal Structure of Repetitive, Reward-Based Behaviors’
2:30  Ya Ying Zheng - Chemistry, yzheng21@albany.edu, ‘Mapping and Functional Study of RNA Phosphorothioate Backbone’
2:40  Lifeng Zhou - RNA Institute, lzhou2@albany.edu, ‘Rapid Detection of SARS-Cov-2 RNA by DNA Nanoswitches’
2:50  Tyler Mitchell - Biology, tamitchell@albany.edu, ‘Role of MSL3 in Spermatogenesis’

3:00 - 3:20  Tea time

3:20 - 4:30  Keynote Speaker II :  Dr. Hashim Al-Hashimi, James B. Duke Professor of Biochemistry and Chemistry and Director of the Duke Center for RNA Biology, Duke University ‘DNA Dynamics and Mutagenesis: How DNA Directs Its Own Copying Errors’

4:30 - 4:50  Award Ceremony :  Dr. Jeanette Altarriba, Dean of the College of Arts & Sciences, SUNY Albany
Keynote Speakers

Dr. Shirley Malcom
Director of Education and Human Resources, American Association for the Advancement of Science, smalcom@aaas.org

‘Science in the Time of COVID and America’s Reckoning with Race’

Shirley Malcom, PhD, is the Director of SEA Change and a Senior Advisor for AAAS. In this position she works to improve the quality of and increase access to education and careers in STEMM. Dr. Malcom is a trustee of Caltech, a regent of Morgan State University and a former member of the National Science Board, the policy-making body of the National Science Foundation. Dr. Malcom chaired the NASEM Committee on Barriers and Opportunities to 2-Year and 4-Year STEM Degree Completion. She serves on the boards of the Heinz Endowments, Public Agenda, the National Math-Science Initiative and Digital Promise. In 2003, she received the Public Welfare Medal of the National Academy of Sciences, the highest award given by the Academy.

(SEA—STE MM Equity Achievement)
Dr. Hashim Al-Hashimi
James B. Duke Professor of Biochemistry and Chemistry and Director of the Duke Center for RNA Biology, Duke University, hashim.al.hashimi@duke.edu
DNA dynamics and mutagenesis: How DNA directs its own copying errors

Dr. Hashim M. Al-Hashimi is James B. Duke Professor of Biochemistry and Chemistry at Duke University School of Medicine and is the Director of the Duke Center for RNA Biology. He received his doctorate in Biophysical Chemistry from Yale University in 2000 for research on the development of residual dipolar coupling NMR methods to study the structure and dynamics of proteins. Between 2000-2002, Dr. Al-Hashimi was a Research fellow, Research Associate, and Senior Research Scientist at the Memorial Sloane-Kettering Cancer Center in NYC, where he developed and applied NMR methodology to study the structure and dynamics of nucleic acids. A year after starting his postdoctoral studies, Prof Al-Hashimi accepted an offer to join the Department of Chemistry and Biophysics Research Division at the University of Michigan where he spent 11 years (2002-2013) as Assistant Professor (2002-2008), Associate Professor (2008), Robert L Kuczkowski Professor (2009-2012), and J Lawrence Oncley Collegiate Professor (2012-2013) of Chemistry and Biophysics. In January 2014, Prof. Al-Hashimi moved to the Department of Biochemistry at the Duke University School of Medicine where he also holds a secondary appointment in the Department of Chemistry. He is the recipient of several awards and honors, including the Founder’s Medal in NMR spectroscopy, the Vilcek Prize For Creative Promise in Biomedical Science, and the Agilent Thought Leader Award. Dr. Al-Hashimi’s work on molecular visualization and nucleic acid dynamics was also recognized by Popular Science Magazine, which listed him among the ‘Brilliant 10’ scientists and engineers in USA (2011). In 2009, he co-founded Nymiurm Inc, which is using the methods developed in the Al-Hashimi lab to increase the pace of RNA structure characterization and RNA-targeted drug discovery.
Pearl De-Veer  Biology, pde-veer@albany.edu  
‘Effect of NF-kB on ATF3 Activation in ZIKV Infection’

Nuclear Factor Kappa Light Chain enhancer of activated B cells (NF-kB) is a sequence-specific transcription factor that regulates the expression of many cellular and viral genes including Activating Transcription Factor 3 (ATF3). ATF3 is an adaptive and stress-response gene, whose expression is induced when NF-kB is activated. Previous studies have indicated the role of ATF3 in modulating or regulating viral responses via various methods including inflammation.

A research question my project is focused on answering is “What is the effect of NF-kB on ATF3 activation in a Zika Virus(ZIKV) infection?” One of the ways I have attempted to answer this question is by setting up a ZIKV infection using A549 cells, then proceeding to inhibit the NF-kB pathway using the Bay 11–7082 inhibitor, harvesting of proteins, and finally, observing ATF3 activation via Western Blot Analysis.

For my talk, I will be giving a brief overview of NF-kB, its pathways, ATF3, and my research project.

Ali Ropri  Biomedical Sciences, aropri@albany.edu  
‘Cis-acting Super Enhancer IncRNAs as Diagnostic Markers of Progression to Early Stage Breast Cancer’

An increase in breast cancer screening over the past three decades has led to a consequential rise in the diagnosis of ductal carcinoma in situ (DCIS). Although DCIS lesions precede invasive ductal carcinoma (IDC), they do not always transform into metastatic cancer. The current standard-of-care is an aggressive course of therapy to prevent invasive and metastatic disease. There is a critical need to identify functional determinants of progression of DCIS to IDC to allow discrimination between indolent and aggressive invasive breast cancers. Super enhancers are regulatory regions of DNA that play critical roles in driving expression of genes that define cell fate decisions and importantly, their normal function can become co-opted during tumorigenesis. Recent studies have found that enhancers, in addition to promoting other gene transcription, are themselves transcribed producing enhancer-associated RNAs. Long noncoding RNAs (lncRNAs) are non-protein coding RNAs that can be associated with enhancer regions, and interact with enhancer sequences to influence activities of neighboring genes. Utilizing microarray technology, we have identified differentially expressed super enhancer associated IncRNAs (SE-lncRNAs) in the MCF10A breast cancer progression series which can shed light on how DCIS lesions become cancerous. Furthermore, cross-referencing these SE-lncRNAs with patient samples in the TCGA database, we have highlighted 36 SE-lncRNAs that potentially interact with their enhancer to regulate nearby genes. We seek to validate our findings in-vitro and patient samples, in addition to using the H3K27ac mark to identify super enhancers acquired during progression that may regulate genes important for the transition of DCIS to IDC.
Emmanuel Adade  Biology, eadade@albany.edu
‘Understanding the Spatial Structure of the Gut Microbiome in Zebrafish (Danio rerio)’

The vertebrate gastrointestinal tract comprises a taxonomically diverse and metabolically active ecosystem. As organisms transition from juvenile to adult, sequential development of the microbiota occurs from the proximal to the distal part of the gut. Metagenomics analyses have revealed that dysbiosis, defined as changes in the microbiome community membership that promote a disease state, in the gut is implicated in diseases such as obesity, diabetes and inflammatory bowel disease. While specific microbial taxa have been reported to play protective roles in maintaining gut health, the cellular mechanism behind this protective function is not fully understood. We hypothesize that the spatial organization of community members might mediate their function. To enhance our understanding of the spatial structure of the gut microbiome, especially relating to health and disease states, we are developing systems imaging technology to complement sequencing approaches to visualize the intact gut microbial communities. In this study, we aimed at delineating the spatial structure of a model 10 member community in zebrafish larvae, as this model provides us with the ability to visualize the intact gut and its microbial composition in-vivo. Here, we utilized FISH targeting the 16S rRNA to determine and quantify the specific localization of bacteria in the gut of our zebrafish model. Our preliminary data suggest that bacteria present in the gut may exist as biofilm aggregates or single cells with varying densities along the longitudinal axis of the gut as revealed by 2D and 3D analysis of confocal images. Other evidence shows that bacteria are also present on the skin. Our future directions involve the application of CLASI-FISH to explore the greater array of microbial interactions within the gut as well as to investigate the protective roles of Chryseobacteria massilliae and selected microbiome community members in our zebrafish model against F. columnare, a common fish pathogen.

Aaron Premo  Chemistry, apremo@albany.edu
‘Function, Inhibition, & Structure of the Formin hDia1 Complexed with ctRAGE’

Human Diaphanous homologue 1 (hDia1) is a dimeric regulatory protein that plays a key role in actin polymerization. Its autoregulatory nature provided by the diaphanous autoregulatory domain (DAD) prevents hDia1 from spontaneously polymerizing globular actin in vitro but can be activated by the addition of c-terminal Receptor for Advanced Glycation End-products (ctRAGE). AGEs are produced in abundance because of aging, degenerative diseases, or diabetes mellitus and as a result can overstimulate ctRAGE causing downstream radical production which may be a potential cause of inflammation. The small molecule nicknamed R229 was developed as a method of inhibiting ctRAGE from activating hDia1. As monomeric hDia1 is nearly 150 kDa, its structure cannot be solved using NMR so cryo-EM will be employed once sample prep has been established with preliminary negative staining methods using uranyl acetate and transmission EM.
Ian Rapisarda  Biology, irapisarda@albany.edu
‘RNA Modification Landscape and it’s Contribution to Egg Production’

Germline stem cells differentiate into mature egg and sperm cells that go on to give rise to all sexually reproducing organisms. During this process of differentiation, germ cells undergo a switch from mitosis to meiosis that allows for proper development and specification of the future gamete. The mechanisms that facilitate this shift from mitosis to meiosis, however, are not well understood. To gain insight into this process, we used Drosophila oogenesis as our model. After genetically enriching for each stage of oogenesis from germ cell to mature oocyte, we performed mass spectrometry and obtained a readout of RNA modifications at each stage and their relative abundance at those stages. We identified one modification, inosine, to have a noticeable increase and subsequent decrease around the time of differentiation. Inosine is a modified version of adenosine that acts as an intermediate in the conversion of adenosine into guanosine. The enzyme raspberry (ras) acts as the rate-limiting step of the conversion of inosine into guanosine. Using immunohistochemistry to identify germline cells, somatic cells, and meiotic markers, ras RNAi Drosophila showed cyst accumulation, failure to enter meiosis, and subsequent loss of germline resulting in infertility. Based on these observations, we hypothesize that regulation of the inosine modification by ras is required for proper oogenesis to occur.

Leonard Breindel  Chemistry, lbreindel@albany.edu
‘Active Metabolism Unmasks Functional Protein–Protein Interactions in Real Time In-Cell NMR’

Protein–protein interactions, PPIs, underlie most cellular processes, but many PPIs depend on a particular metabolic state that can only be observed in live, actively metabolizing cells. Real time in-cell NMR spectroscopy, RT-NMR, utilizes a bioreactor to maintain cells in an active metabolic state. Improvement in bioreactor technology maintains ATP levels at >95% for up to 24 hours, enabling protein overexpression and a previously undetected interaction between prokaryotic ubiquitin–like protein, Pup, and mycobacterial proteasomal ATPase, Mpa, to be detected. Singular value decomposition, SVD, of the NMR spectra collected over the course of Mpa overexpression easily identified the PPIs despite the large variation in background signals due to the highly active metabolome.
Carl Shotwell  RNA Institute,  cshotwell@albany.edu
‘The Disruption of RNA Modifications in Myotonic Dystrophy’

In recent years, RNA modifications have emerged as key regulatory elements in a wide array of cellular RNA-related processes. Because of their widespread functionality, RNA modifications are also key sites for potential misregulation in disease. The expression of expanded repeats in DM1 and DM2 causes nuclear sequestration of the MBNL proteins, which disrupts their role as master regulators of RNA processing. We have performed mass spectroscopy on RNA from several DM1 and DM2 patient-derived cell lines, which revealed significant epitranscriptomic changes. Analysis of matching RNAseq data from these cell lines shows significant misregulation of RNA modifying enzymes, including those that catalyze RNA modifications. Lastly, mined RNA-seq data of DM1 patients which showed changes in RNA modification enzymes directly correlates to disease severity indicating the changes observed may have a significant role in the disease. We propose two models that may cause the altered levels of RNA modifications in DM, 1) sequestration of MBNL proteins leading to misregulation of RNA modification writer enzymes and/or 2) the toxic repeats sequester cause mislocalization of RNA modification writer enzymes. This data is the first evidence of global misregulation of RNA modifications in DM and may provide clues to disease pathogenesis and future therapeutic targets.

Pheonah Badu  Biology,  pbadu@albany.edu
‘ATF3 Regulates Antiviral Response in ZIKVPR Infected Cells’

Activating transcription factor 3 (ATF3) is a key transcription factor that belongs to the ATF/CREB family of transcription factors. Expression of ATF3 gene is rapidly induced by different stress signals. As a stress response gene, ATF3 modulates the inflammatory pathway in distinct cell types. Furthermore, ATF3 has been implicated in regulating antiviral response in the cell. In a recent study on the impact of Zika virus infection on differential gene expression and alternative splicing in a neuroblastoma cell line, our RNAseq data showed that ATF3 expression is enhanced during infection with the contemporary Zika virus strain (PRVABC, ZIKVPR). Clearly, this suggests a critical role for ATF3 during ZIKVPR infection. However, the exact function and mechanism of ATF3 during Zika infections in different cell contexts remains unknown. Moreover, ATF3 could potentially have a direct role in the viral life cycle that merits investigation.

Therefore, to examine the importance of ATF3 in ZIKVPR infections, we performed RT-qPCR and immunoblot analysis on RNA and proteins derived from mock and virus-infected human colon carcinoma wild type (WT) and ATF3 knock out (KO) cell lines (HCT-116). Our results showed a significant increase in viral mRNA and proteins in ATF3 KO cells compared to WT cells. This suggests that, the presence of ATF3 in WT cells is necessary for antiviral immune response. In future, we will determine whether Zika-induced ATF3 response is cell-type specific, by examining transcript and protein levels of ATF3 in HCT-116, A549, JEG-3, HUH7 and SHSY5Y cell lines. In subsequent experiments, we will address the mechanism of Zika-induced ATF3 action, by exploring the role of upstream targets like p53 using HCT p53 KO cells. Additionally, using ChIPseq, we will examine promoters that ATF3 interacts with to provide novel mechanisms by which ATF3 regulates antiviral response.
Melanie Lolier  Psychology,  mlolier@albany.edu

The Effects of Synthetic Progestin Exposure on the Development of the Mesocortical Dopamine Pathway

The synthetic progestin 17-α-hydroxyprogesterone caproate (17-OHPC) is commonly prescribed to pregnant women with a history of preterm delivery, despite little evidence of efficacy. The timing of 17-OHPC administration coincides with fetal mesocortical dopamine pathway development, yet the potential effects on cortical development and cognition are virtually unknown. In rodent models, the developing brain is sensitive to progestins, and developmental 17-OHPC exposure increased dopaminergic innervation of the medial prefrontal cortex (mPFC) in adolescence, an aberrant pattern of connectivity that may underlie deficits in cognitive function observed in adulthood. Here, we tested the hypothesis that 17-OHPC exposure during development alters early mPFC innervation and subsequent cognitive behaviors. Indeed, 17-OHPC significantly altered dopaminergic innervation of the mPFC and also altered microglia activity, which is critically involved in sculpting axonal outgrowth in development. A behavioral attention task confirmed that early 17-OHPC exposure caused deficits in decision-making, reminiscent of the attention deficit hyperactivity disorder predominantly inattentive presentation in humans. Finally, data from a large prospective human cohort study allowed us to compare developmental screening data between progestin-exposed and non-exposed children, which revealed persistent developmental domain failures in exposed children. These findings highlight the need for studies on the long-term impact of 17-OHPC exposure in humans.

Weilan Zhang  Environmental & Sustainable Engineering,  wzhang4@albany.edu

Exposure of Juncus Effusus to Seven Perfluoroalkyl Acids: Uptake, Accumulation & Phytotoxicity

Phytoremediation of per- and polyfluoroalkyl substances (PFAS) appears to be a sustainable remediation technique. To remove PFASs from contaminated water, this study investigated plant uptake of PFASs by a native wetland plant species in the USA, Juncus effusus. The results showed that J. effusus translocated selected PFASs, including perfluoropentanoic acid (PFPA), perfluorobutanesulfonic acid (PFBS), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorohexanesulfonic acid (PFHxS), perfluoroctanoic acid (PFOA), and perfluorooctanesulfonic acid (PFOS). During the 21-day experimental period, the uptake of PFASs increased with increasing PFASs exposure concentration and time. PFOS was largely accumulated in the roots with limited upward translocation. PFASs with shorter carbon chain length were taken up by J. effusus roots and tended to accumulate in plant shoots. The highest removal efficiency (11.4%) of spiked PFASs by J. effusus was achieved when it was exposed to PFASs at around 4.6 mg/L for 21 days. The exposure to PFASs stimulated the antioxidative defense system in J. effusus shoots but inhibited the superoxide dismutase (SOD) and catalase (CAT) activities and damaged the antioxidative defense system in J. effusus roots. These results warrant further studies to evaluate J. effusus's long-term performance in a PFASs contaminated environment.
Nicholas Moskwa  
*Biology, nmoskwa@albany.edu*

‘FGF2 Stimulated Mesenchyme Controls Salivary Epithelial Differentiation Through BMP7’

Multicellular life is possible because cells compartmentalize into organs. A key developmental biology question is how cells within these compartments synergize form and function. The neural crest-derived stromal mesenchyme (NCS) supports critical early developmental signaling in salivary gland and analogous organ epithelium. However, specific stromal developmental contributions are incompletely understood. We developed a complex epithelial-stromal salivary organoid for identifying instructional developmental signals. These organoid’s growth and differentiation are dependent on NSC FGF2 signaling. We hypothesized that the NSC FGF2 signaling drives paracrine factor expression that directly controls epithelial morphogenesis and differentiation. We generated a presumptive factors list using organoid stroma whole-transcriptome microarrays. Factors were screened based on biological and chemical characteristics, and then tested as an NCS substitute in simple epithelial organoids. We screened for epithelial differentiation using the water channel protein, Aqp5, and for proliferation using organoid size. The signaling molecule BMP7 substituted for NCS, allowing for epithelial Aqp5 expression but not morphogenesis. However, the epithelium required FGF2 in conjunction with BMP7, indicating that multiple signals specify epithelial development including BMP7. Here, we demonstrate our organoid model’s usefulness as a screening tool capable of dissecting developmentally important cell-cell communication.

Justin Waldern  
*Biology, jwaldern@albany.edu*

‘Ribosomal RNA Modification Limits Group II Intron Retrotransposition’

Group II introns are mobile genetic elements that can invade new locations through RNA-based transposition. So-called retrotransposition can be harmful to the host if uncontrolled and is therefore often limited by the host organism. Using a mutant screen in the native lactococcal host of a group II intron, we identified an rRNA methyltransferase that, in wild-type cells, functions to enhance ribosome binding to group II intron RNA and thereby limit retrotransposition. This work has revealed a novel role for ribosomes as suppressors of retrotransposition, preventing their rampant spread.
Anwesha Sarkar  Biology, asarkar@albany.edu
‘Epitranscriptome and tRNA-Writer Mediated Protection of Human Liver Cells From Arsenic Stress’

Epitranscriptomic marks in the form of RNA modifications are key regulators of translation. tRNA has over 100 known modified residues, and environmental stress has been shown to dynamically regulate the levels of different tRNA modifications. We have used epitranscriptomic analysis to demonstrate that the levels of 5-methoxy carbonyl methyluridine (mcm5U), N6-methyl-N6-threonylcarbamoyladenosine (m6t6A), and queuosine (Q) are increased when liver carcinoma (HepG2) cells were exposed to the iAs (sodium arsenite: a reactive oxygen species inducer). The International Agency for Research on Cancer (ICAR) has classified arsenic as a carcinogen. Hence, defining the cellular epitranscriptomic response to arsenic stress is vital for understanding the iAs mechanism in liver cells. The iAs up-regulated RNA modifications are found in the anticodon loop of specific tRNAs. The modification mcm5U (position 34) is written by alkylation DNA repair alkB homolog 8 (ALKBH8) on tRNAArg and tRNAsec. The m6t6A (position 37) is written by tRNA methyltransferase O (TRMO) on tRNAThr. Q (position 34) is written by queuine-tRNA ribosyl transferase (QTRT) on tRNAasn, tRNAasp, tRNAtyr and tRNAhis. We hypothesized, that elevated levels of m6t6A, Q and mcm5U modifications on tRNA protects cells against ROS induced toxicity, by regulating codon-anticodon interactions to promote the translation of stress response proteins. We used a lentiviral vector-based strategy to knockdown ALKBH8 (mcm5U), TRMO (m6t6A) and QTRT1 & QTRT2 (Q). Initial experiments indicated that the ALKBH8 and TRMO knockdown cells are sensitive to iAs stress, have elevated levels of cellular ROS and exhibit a slower cell growth phenotype, as compared to the control cells. Knock down of QTRT1(catalytic subunit) or QTRT2 (non-catalytic subunit) resulted in elevated levels of cellular ROS and for QTRT2 knockdown increased cellular sensitivity to iAs. Inability of the QTRT1 and QTRT2 knockdown cells to attenuate cellular ROS levels could be linked to translational regulation of the ROS response proteins. Next, we did a polysome fraction analysis and the resulting data provides evidence that the QTRT2 knockdown cells have decreased polysome levels compared to the control cells. We plan on comparing the mRNAs present in the polysome fractions in the epitranscriptomic writer knockdown cells under iAs treated condition by mRNA-seq. To further analyze for translational changes in the QTRT knockdown cells, we have developed a codon specific GFP/mCherry based dual reporter system. We observed that when exposed to iAs, the U-optimized reporters have increased levels of activity in the QTRT1 proficient cells as compared to the QTRT1 knockdown cells. Additionally, we would like to investigate if there is a codon level translational bias in the knockdown cells when treated with iAs by ribosome-sequencing. Our working model is that in response to iAs stress, increased modifications in the tRNA anticodon promote the translation of proteins which play specific roles in the cellular response to iAs.
Jacob Schroader  RNA & Biology, jschroader@albany.edu
‘Detection of Inosine Using Direct RNA Nanopore Sequencing’

Nanopore sequencing can directly sequence RNA or DNA, by distinguishing adenosine (A), thymidine (T), cytidine (C), guanosine (G), and uridine (U) using changes in current. My project involves using nanopore sequencing for the direct detection of inosine (I) in RNA. I can be an enzyme catalyzed base modification in tRNA or mRNA, but it must be restricted from the nucleotide pool to prevent unregulated incorporation. Inosine monophosphate (IMP) has the potential to be phosphorylated into inosine triphosphate (ITP), which can be aberrantly incorporated into RNA. Inosine triphosphate pyrophosphatase (ITPase, coded for by the ITPA gene), catalyzes the hydrolysis of ITP to prevent inosine misincorporation into RNA during transcription. Individuals with ITPA null mutations harbor inosine misincorporation within RNA of their cells and develop a Martsolf-like syndrome with fatal infantile dilated cardiomyopathy and encephalopathy. My project has used the ONT MinION sequencer and Direct RNA Sequencing Protocol to sequence Luciferase RNA generated with increasing concentrations of ITP during in vitro transcription. The I containing library showed a higher number of variants and an overall decrease in the accuracy of the base calls. In the future, we will compare raw current values to visualize changes specific to inosine and to generate a set of training data to create a tool for the direct detection of inosine.

Jennifer Cardinal  Chemistry, chuljenn@hotmail.com
‘Ancient and Unknown’

There are billions of ancient food service artifacts stored in museums, universities, and research institutions around the globe. To date only a tiny portion of these artifacts have been analyzed for their former contents. Destructive analyses are not ideal, expensive, and time consuming. These residue samples are also finite and precious. Raman is an ideal method of analysis as it is non-destructive and rapid. My research is aimed at applying Raman to the identification of ancient residues, mainly those from the ancient Maya and Aztec of Central America.
Hybridization Chain Reaction (HCR) is a DNA-based target-induced cascade reaction. Due to its unique enzyme-free amplification feature, HCR is often employed for sensing applications. Much like DNA nanostructures that have been designed to respond to a specific stimulus, HCR employs nucleic acids that reconfigure and assemble in the presence of a specific trigger. Despite its standalone capabilities, HCR is highly modular, therefore it can be advanced and repurposed when coupled with latest discoveries. To this effect, we have developed a detection approach which combines the signal amplification feature of HCR with the programmability and sensitivity of CRISPR-Cas12a system. By incorporating CRISPR-Cas12a, we have achieved greater sensitivity and the ability to rapidly reprogram the assay for detection of a different target by merely changing a single reaction component in the detection kit. This assay has also enabled the detection of double stranded DNA targets, which is hard to achieve for systems driven by hybridization and strand displacement.

Our previous research demonstrated a developmentally divergent pattern of context mediated freezing, such that context fear expression in male Long Evans rats increases from pre-adolescence into adulthood while context fear in females decreases from pre-adolescence into adulthood (Colon et al, 2018). This unique developmental pattern initiated prior to puberty may suggest that gonadal hormones play a role in organizing the neural systems underlying contextual fear conditioning. The aim of this study is to investigate the potential role of early circulating gonadal hormones in organizing the neural systems underlying contextual fear conditioning. In order to determine whether or not neonatal gonadal hormone exposure and/or pubertal gonadal hormone exposure organizes the neural systems underlying context fear conditioning, we conducted two behavioral experiments. In experiment 1 we removed the testis within 8 hours on the day of birth (P0), and fear conditioned male Long Evans rats either 24 (pre-adolescence) or 60 (adult) days later. In experiment 2, prior to puberty at P28 and fear conditioned male and female Long Evans rats 32 days later at P60. Our preliminary findings indicate that gonadectomy alters the expression of contextual fear compared to control subjects, suggesting that gonadal hormones have an organizational influence on the neural systems underlying contextual fear conditioning.
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‘Role of Notch Signaling in the Apical vs Basal Neuronal Cell Fate Determination in the Vomeronal- sal Organ’

The Vomeronasal organ (VNO) is a part of accessory olfactory system (AOS) that plays a primary role in the detection of pheromones that trigger a spectrum of sexual and social behaviors. The mouse VNO has two main classes of vomeronasal sensory neurons (VSNs) – 1) Apical VSNs that express V1R receptors, Gai2 G-protein subunit and project their axons to the anterior (apical) portion of the accessory olfactory bulb (AOB) and 2) Basal VSNs that contain V2R receptors, Gao subunit and project to the posterior (basal) portion of the AOB. Till now, Bcl11b is the only transcription factor known to play a role in the apical vs basal cell fate determination however, complete mechanisms are not fully understood. We recently obtained VNO single cell RNA sequencing data, using 10x genomics, from adult C57B6 wildtype males. We used Seurat, R package for quality control and analysis of the data. From the initial analysis, we were able to identify apical vs basal neuronal dichotomy from a common pool of stem cell progenitors. Moreover, within the neuronal precursors population, we also identified notch signaling related genes, specifically Notch1 receptor in one specific cluster and Dll4 which is a notch 1 receptor ligand in another cluster at the dichotomy. Preliminary studies also showed the presence of Notch1 and Dll4 positive cells in the VNO. Gain and loss of function studies related to Notch signaling may further help in understanding the mechanisms of apical vs basal cell fate determination.

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‘Microfluidics Delivery of Target Protein Enhances Cell Viability for In-Cell NMR Spectroscopy’

High-resolution structural studies of proteins and protein complexes in a native eukaryotic environment present a challenge to structural biology. In-cell NMR can characterize atomic resolution structures but requires delivering high concentrations of labeled proteins into intact cells. Most delivery techniques are either limited to specific cell types or too destructive to preserve cellular physiology. We demonstrate the feasibility of microfluidics transfection or volume exchange for convective transfer, VECT, as a means to deliver labeled target to HeLa cells. VECT delivery does not impede cell viability thereby providing a route for long term eukaryotic in-cell NMR experiments. Following delivery of the target protein DARPP32, phosphorylation modifications and changes in the interaction surface were easily detected. Rapid usage of target-loaded cells will facilitate detecting changes in metabolic states due to internal and external stimuli and stresses.
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‘Culturomics Approach to Identify Spatial Relationships in the Human Oral Microbiome’

The human oral microbiome is composed of over 700 different species of bacteria as well as viruses and fungi. Human oral microcosm cultures, seeded with dental plaque inocula from human volunteers have proven to be a remarkable tool for cultivating mixed microbial communities with extraordinary diversity. The overall goal of the Valm lab is to culture in vitro biofilms and analyze the systems level spatial structure via CLASI-FISH. A parallel aim is to isolate and culture pure populations of microbial species, retrieved from healthy volunteers for genetic and molecular analysis. This will be done by growing dental plaque on optimized Shi media, then isolating morphologically distinct colonies, darkfield microscope examination and MALDI-TOF mass spectrometry to identify the species, which will then be confirmed with 16s rRNA sequencing. Our overall aim is to understand structure-function relationships in oral biofilms at the individual cell and community levels.

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‘Host-biased West Nile Virus Quasispecies Facilitate Host-Specific Adaptation’

The composition of the West Nile virus (WNV; Flaviviridae; Flavivirus) mutant swarm varied significantly between avian and mosquito hosts, presumably due to unique selective and stochastic pressures. Previous studies identified non-synonymous minority variants in the WNV replicase (NS3/NS5) with host biases and a putative role in host-specific fitness. To characterize the role of NS3 in host-specific fitness, we engineered two non-synonymous NS3 mutations, P1825L (mosquito-biased) and S1852T (avian-biased) into a WNV 02 infectious clone and characterized them. In vitro growth kinetics revealed competent replication of S1852T in avian (DF1), mosquito (C636), or mammalian cell lines (Vero, A549) whereas P1825L was attenuated in vertebrate and avian cell lines, suggesting it may confer host specific advantages. One-step growth kinetics and plaque measurements also supported attenuation of P1825L in vertebrate cells. Both NS3 mutants demonstrated altered susceptibility to the mutagen ribavirin, consistent with differences in replicase fidelity and/or function. While structural modeling of P1825L, located in highly conserved motif of NS3 in the linker region between the N and C core domains, indicated potential for altered enzymatic activity. In vivo studies in Culex pipiens pipiens demonstrated increased infectivity of P1825L exposed mosquitoes relative to the wildtype, indicating a host-specific advantage of increased infection.
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‘The role of conserved poly A’ Sequences in the 3’UTR of Zika Virus Translation’

Zika virus (ZIKV) and Dengue virus (DENV) are flaviviruses within the family of Flaviviridae. These viruses have a single-stranded positive-sense RNA genome that contains a 5’-cap but lack of a polyA tail in the 3’ untranslated region (UTR). This suggests that these viruses likely use a mode of translation distinct from that of cellular mRNAs. Despite the lack of a PolyA tail, DENV is known to interact with polyA binding protein. Bioinformatic analysis of the 3’ UTR of ZIKV and DENV revealed six short stretches (3-6 nucleotides long) of adenosines with unknown roles in flavivirus gene expression. Our overarching goal is to dissect the mechanisms by which ZIKV subverts the host translation machinery. We propose that the multiple short polyA motifs within flavivirus 3’ UTRs mimic the function of the polyA tails in cellular mRNAs. To investigate this we used site directed mutagenesis to mutate three conserved motifs from polyA to polyU within a ZIKV minigenome construct. We next in vitro transcribed and capped the minigenome RNA and performed an in vitro translation activity rabbit reticulocyte lysate and cellular transfection. Specifically, we measured Nano luciferase units as a proxy for examining effects on translation. Our data show that the polyA motif within pseudo dumbbell structure affects ZIKV translation.

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‘Coupling RT-LAMP with CRISPR-Cas12a for Detection of Lyme Disease’

Lyme disease is responsible for ~300,000 new tick-borne infections annually, with infections concentrated in the North Eastern United States. Commonly in the North East, this silent epidemic is caused by the family Borrelia and species B.burgdorferi sensu stricto (B.burgdorferi). Current government-approved methods of diagnosis are by the presence of a “bulls-eye rash”. However, the lack of rash presence requires two-fold diagnostics to detect antibodies in the host. However, sensitive detection requires the infection by B.burgdorferi to be persistent long enough for antibodies to be produced. Therefore, a new technology that is more rapid is required for both specific and sensitive detection of B.bugdorferi. Technologies such as reverse transcription loop-mediated isothermal amplification (RT-LAMP) and clustered regularly interspaced palindromic repeats (CRISPR) have proven to be both sensitive and specific diagnostics tools when coupled together during the current COVID-19 pandemic. Here, a proposal is being described for applying RT-LAMP CRISPR in the detection of the RNA expression of four genes of B.burgdorferi during infection. The proposed idea has the potential for aiding in diagnosis and lifetime exposure of the infection. In a real-world application, the described system could be used both as a diagnostic and biomonitoring tool for Lyme disease.
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‘Multi-Species Bacterial Aggregates Contribute to Spatial Heterogeneity in an Oral Biofilm Model’

The fundamental processes that underlie biofilm structure are not well understood. We hypothesize that early stochastic events mediated by aggregates of interacting microbial cells leads to heterogeneous biofilm development. To test this hypothesis, we modeled oral biofilm development, an in vitro flow-cell culture system, seeded with sonicated or unperturbed dental plaque isolates. Quantitative analysis by confocal microscopy, spectral imaging, and FISH (labeled against seven oral taxa) demonstrated that unperturbed dental plaque derived model biofilms resulted in highly diverse, spatially structured, and heterogeneous microbial communities. In contrast, model biofilms derived from sonicated dental plaque isolates resulted in a more homogeneous community with severely reduced microbial diversity and spatial structure, suggesting that multi-species bacterial aggregates contribute to spatial heterogeneity in the oral microbiome.

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‘Iron Homeostasis in Breast Cancer Cells– Unique Investigations with Raman Hyperspectral Imaging’

Iron homeostasis is critical to cell survival and proliferation, and cancer cells may have adapted iron regulatory processes which require further elucidation. Two critical aspects of cellular iron homeostasis include transferrin (Tf) mediated uptake of iron, and the storage of excess iron in the cytoplasmic protein ferritin (Ft). In addition, the distribution of heme containing proteins throughout the cell may be a significant indicator of cell health. Iron-bound Tf will bind to the Transferrin receptor (TfR) at the cell surface and undergo endocytosis where iron is released into a mildly acidified endosome. Inside the endosome the iron is reduced for transport across the membrane for utilization or into the cytosol for storage in Ft. Understanding the cellular distribution of iron-bound Tf and ferritin in intact, unlabeled cells is essential in the study of heterogenous cancer cell populations. Our understanding or iron homeostasis regulation via IRP1/2 does not always reflect in the expression of iron regulatory proteins in cancer cells. Previously we have demonstrated that Raman hyperspectral imaging could identify cellular regions with increased iron-bound Tf. The amount of iron-bound Tf would decrease efficiently with time in T47D cells but not MDAMB231 cells, suggesting some cells may have dysregulation of intracellular iron transport. It remained unclear if dysregulation of Tf mediated iron would impact Ft expression or cellular distributions. To address this, we are now incorporating the identification of ferritin populations into our Raman hyperspectral analysis. We are collecting data on the unlabeled heterogenous breast cancer cell populations to determine the relationship of iron-bound Tf and Ft in single-cell Raman hyperspectral imaging, which will be able to accelerate our understanding of iron homeostasis in breast cancer cells.
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‘Neuronal Glutamate Transporters Control the Temporal Structure of Repetitive, Reward-Based Behaviors’

Regulating the time course of neurotransmitter release and its clearance from the extracellular space has profound implications to set the activity of neural networks throughout the brain. One of the molecules known to control glutamate clearance from the synaptic cleft is the neuronal glutamate transporter EAAC1, a molecule mostly expressed in regions that control the execution of reward-based behaviors, like the striatum. Here, we show that loss of EAAC1 is associated with increased impulsivity in reward-based behavioral tasks. These findings indicate that small changes in the temporal control of glutamate clearance alter the timing, not the frequency, of reward-based behaviors.

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‘Mapping and Functional Study of RNA Phosphorothioate Backbone’

Post-transcriptional modifications in cellular RNAs play important roles in gene regulation, biological and or physiological processes in both healthy and abnormal cells. To date, scientists have discovered over 170 chemical modifications in rRNA, tRNA and mRNA in all domains of life. We have recently reported the first discovery of phosphorothioate (PS) modification on the RNA backbones in both prokaryotes and eukaryotes with mass spectrometry serving as the main method for both detection and quantification in a series of model cells. UPLC-MS is employed first to identify RNA phosphorothioate modifications. An optimized LC-MS/MS method is then employed to quantify the frequency of PS-RNA in these test samples. Our present method was developed to study GpsG, a specific PS dinucleotide modification, since it occurs at the highest frequency with the most noticeable fold change occurs in HeLa rRNA. We have further demonstrated that HeLa total RNAs with iodine and iodide treatment only cleave at the PS sites. By primer extension of iodine/iodide treated RNA vs untreated control, it is possible to accurately map the PS site to the single nucleotide resolution. Complementary to primer extension, the cleaved fragments can be fluorescently labeled and separated by capillary electrophoresis for accurate size or fragment analysis when compare to the uncleaved control. Finally, deep sequencing by Illumina Hi-seq platform will also be supplemented into our mapping strategy. For the functional study of PS modification in HeLa rRNA, we will focus on translation efficiency by ribosomal profiling, differential gene expression by RNA-Seq and oxidative stress response when compare the normal with the PS-knockout strain.
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‘Rapid Detection of SARS-CoV-2 RNA by DNA Nanoswitches’

Rapid detection is critical to slow down the spread of COVID-19 pandemic caused by SARS-CoV-2. Here, we developed an assay to detect SARS-CoV-2 RNA based on DNA nanoswitches and isothermal nucleic acid amplification. Shown in our preliminary tests, this method can detect as low as 50 copies of targeted SARS-CoV-2 RNA sequence within one hour. In addition, we reprogrammed our DNA nanoswitches so that they can detect the influenza A, influenza B and SARS-CoV-2 in single reaction. The cost of each detection is less than five dollars and the operation is simple, making it practical for point-of-care tests. We are also investigating and optimizing the detection ability of our method by using nasopharyngeal swab samples from collaborators. We envision that this detection assay can be developed into a marketable test kit, assisting the fight of COVID-19 and other emerging pandemics.

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‘Role of MSL3 in Spermatogenesis’

MSL3 is a protein involved in drosophila meiosis and a part of the MSL complex involved in dosage compensation. MSL3 has also been found to be present in mouse testes indicating a potential role in spermatogenesis. MSL3 may act downstream of Stra8 signaling to promote meiotic entry in mammals. We analyze the testes of MSL3 Knock-out mice for recombination and check for an observable phenotype in these Knock-outs.