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BIOMEDICAL RESEARCH SYMPOSIUM
FOR UNDERREPRESENTED SCHOLARS

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Thank you to our sponsors:
5-6 AGENDA

7-12 SCHOLAR PRESENTATIONS

7 Tanisha Maitre and Chloe Smith
8 Zarek Burton and Clairete Jean-Pierre
9 Christian Jenkins and Elizabeth Bardwil-Lugones
10 Emmanuella Kyllians and Hector Romero
11 Omina Nazarzoda and Sabrina Zequeira
12 Ephraim A. Oyetunji

13 ABSTRACTS (by slack channel number)

2 Kera Mansfield
3 Nickol Parkinson
4 Sriya Sanaya
5 Shamin Sultana
6 Yodahe Gebrergababher
7 Angel Garcia
8 Lindsay Days
9 Debby Park
10 Unos Ansari
11 Anthony Jimenez Hernandez
12 Anjita
13 Gregory Francis Jr.
14 Aaron RAMBU
15 Nabeel Anigat
16 Elainora Achmak
17 Paula Garavito
18 Sierra Cotton
19 Shuborno Islam
20 Zama Marie Balde
21 Woesiek Kwon
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23 William Kyayo
24 Daniel Cambron
25 Naomi Cockingston
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27 Katherine Hao
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31 Victoria Gonzalez-Calleja
32 Sierra Williams-McLeod
33 Gcinokuhle Mkhwanazi
34 Sasha DeMeulemaire
35 Jonathan Do
36 Tasneem Ikram
37 Brinnie Philippe
38 Kanze Maurice Hooker Mendoza
39 Mark Youssef
40 Karon Rose
41 Kelly Beharry
42 Aishesha Lawal
43 Hezkiiah Williams
44 Antony Irene
45 Randy Williams
46 Alexandra Boozin
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52 Layam Ibrahim
54 Sidra Jabaen
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57 Gaiana Locker
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65 Amanda Aniqueira-Gonzalez
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73 Kendra Parker
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81 Katherine Park
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AGENDA

9:00 am - 9:45 am
Opening Remarks and Announcements

9:45 am – 10:15 am
Mount Sinai Trainee speakers
- 15 Minute Break -

10:30 am – 12:00 pm
Morning Session presenters

12:00 pm – 1:00 pm
Poster Session/Lunch

1:00 pm - 1:50 pm
Keynote Speaker
- 10 Minute Break -

2:00 pm – 4:00 pm
Afternoon Sessions
Breaks Will Be Incorporated

4:00 pm – 5:00 pm
Networking

5:00 pm - 5:30 pm
Announcement of awards and closing remarks

MODERATORS

Roland Pinzon
Program Manager, Graduate School of Biomedical Sciences

Aya Osman
Postdoctoral Researcher, Seaver Fellow

Sope Oguntuyo
MD/PhD Candidate
Title: Developing a standardized, scalable SARS-CoV-2 neutralization assay

Rachel-Ann Garibsingh
PhD Candidate
Title: Rational drug design for the glutamine transporter, ASCT2

KEYNOTE SPEAKER

Yasmin Hurd, PhD
Warren-Coleman Chair of Translational Neuroscience
Director of the Addiction Institute at Mount Sinai
Title: Diversity: The Path to Scientific Discoveries
E-Cadherin Loss Associated with Triple Negative Breast Cancer in African American Women

CDH1 is a ubiquitously expressed tumor suppressor gene more frequently mutated in invasive lobular carcinoma (IC) compared to invasive ductal carcinoma (IDC). IDC is often found as part of an inherited cancer syndrome with CDH1 also displaying hereditary diffuse gastric carcinomas. While loss of CDH1 expression is well documented in IDC, the relationship between CDH1 expression and IDC remains unknown. Furthermore, the relationship of the CDH1 gene expression with molecular breast cancer predisposition and to the triple negative phenotype, is also unknown. The goals of this project were two-fold: 1) to identify CDH1 mutations associated with breast cancer predisposition and 2) to determine the association between CDH1 expression and tumor clinicopathological features. We display that protein expression (Alm 2), potentially resulting from CDH1 mutations (Alm 1), contributes to breast cancer predisposition and to the triple negative phenotype. Exome sequencing of 80 African American women with and without breast cancer from high risk families were performed. We identified a high frequency of genetic variants in CDH1. A missense variant of unknown significance, rs60331154, will be further functionalized using CRISPR-Cas 9 to knock in the variant in vitro. Cell migration will also be measured and compared to wild-type and siRNA knockouts. To determine the association between CDH1 protein, potentially resulting from mutations, immunohisto-chemical identification of CDH1 was also performed on a separate cohort of breast tumors from 202 African American women. The association between CDH1 protein expression and clinicopathological characteristics such as age at diagnosis, stage, grade, tumor size, hormone expression, molecular breast cancer subtype, recurrence-free and overall survival were performed. Our results demonstrated that loss of CDH1 was associated with ER negative (0.008), PR negative (0.05) and triple negative (0.02) breast cancer subtype, recurrence-free and overall grade, tumor size, hormone expression, molecular breast cancer predisposition and to the triple negative phenotype. The objective of this study is to identify agents more effective than TA to use in combination treatments. The hypothesis is as follows: two derivatives of TA will have more efficient anti-proliferative effects on HRNB cells. Anti-proliferative activity of the two derivatives of TA on HRNB cell lines (LA-155n and SMS-KCNR) was evaluated in combination treatments using less toxic agents to induce sensitization to chemotherapy in HRNB. Non-Stenodi Anti-Inflammatory Drug, tolenuic acid (TA) inhibits Specificity protein 1 (Sp1) and survivin, markers associated with aggressive cancer cell growth and resistance to chemo/radiation therapies.

The dose required to inhibit 50% of cell growth (IC50 value) was also determined by SigmaPlot software. The results showed that when compared to TA (IC50 = 75 µM), TA-D1/TA (IC50 = 29 µM) and FTA-D2 (IC50 = 4 µM) had much lower IC50 values. TA and its derivatives had no effect on cell viability of cardiomyocytes at those doses.

Western blot results showed a decrease in the expression of Sp1 and survivin in HRNB cells treated with CTA-D1. In conclusion, TA derivatives may effectively sensitize certain HRNB cells and induce the response of chemotherapy or radiation. Further studies to understand the mechanisms of action of these derivatives and safety against non-malignant cells are underway.

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Background: Improving cellular integration with biomaterial scaffolds is the primary goal to achieving a successful regenerative outcome. Microporous annealed particle (MAP) scaffolds have been shown to promote enhanced healing outcomes due to the interconnected cell-scale porosity in healthy wound settings, however, lack additional bioactivity to promote healing in chronic wounds. Heparin, the most negatively charged glycosaminoglycan is known for its ability to sequester growth factors important in wound healing. Here we investigated the benefit of including heparin in a MAP scaffold and the influence of heparin molecular weight on cell migration.

Methods: Three different molecular weight (MW) heparin molecules (3000 Da, 6117 Da, and 15000 Da) were thiolated with PDPH. Thiolation extent was determined via a deprotection assay and all resulted in modifications of 2E-04mmol SH/mg GAG. Each molecular weight heparin was immobilized into a pre-gel solution consisting of PEG-maleimide, RGD, and a MMP-2 cleavable crosslinker. Mechanical properties were measured using a MTS instrumentation and hydrogel formation was visualized with a confocal microscope. Heparin conjugation levels were determined via an ELISA assay.

Results: All gel conditions were matched to a similar mechanical modulus of 20kPa and heparin content of 0.41 mg/mL to isolate molecular weight as the only changing variable between gel conditions. The addition of heparin to the MAP scaffolds significantly increased cell migration compared to MAP without heparin. Interestingly, the 3000 Da and high molecular weight heparin groups resulted in more cells migrated compared to the mid molecular weight group, however further studies are necessary to elucidate the differences between molecular weights.

Conclusions: We confirmed our hypothesis that the incorporation of heparin at all MWs in MAP gel promotes enhanced cell migration. Heparin's ability to sequester growth factors presents a novel method to incorporate bioactivity in MAP scaffolds without the addition of external growth factors. A six-week in vivo subcutaneous implant study will be used to assess bulk tissue regeneration and any observed immune response.

Background: In late 2019, a novel betacoronavirus was reported in Wuhan, China. It was identified as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which is responsible for the ongoing COVID-19 pandemic. Since its identification, thousands of SARS-CoV-2 genomes have been sequenced and have revealed the emergence of different viral lineages. In this study, we aimed to characterize genomic diversity among isolates collected throughout the pandemic. To this end, we developed a Python-based command-line application called GeneNovelty Unit-based Virus Identification (GNUVID) that is designed to type SARS-CoV-2 genomes. As of August 17th, GNUVID typed 32,719 complete and high coverage SARS-CoV-2 genomes from the Global Initiative on Sharing All Influenza Data (GISAID) database and compressed 327,190 open reading frames (ORFs) into 19,224 unique alleles in under two minutes on a standard desktop computer.

Analysis of the compressed data showed that most complexies have strong associations with specific geographic locations. We observed strong nucleotide conservation in ORF3a-10. We also measured allelic diversity by generating a collector's curve expressing the number of distinct alleles as a function of different time periods during the pandemic. GNUVID has effectively added in identifying new introductions, hotspots, and rapidly expanding clones of SARS-CoV-2 and, since it can be updated rapidly to track emerging lineages, it can also inform future introductions, hotspots, and rapidly expanding clones of SARS-CoV-2 and, since it can be updated rapidly to track emerging lineages, it can also inform future

Background: Inflammatory bowel disease (IBD) is a chronic inflammation of the gastrointestinal tract affecting over 7 million people worldwide. Types of IBD include Crohn’s disease and ulcerative colitis based on the intestinal area affected. It is unclear what causes IBD, but increased risk has been tied to diet, host genetics, immune response, and an imbalance (or dysbio-sis) of the gut microbiome. The microbiome provides protection from pathogens and chemicals, breaks down parts of our diet, and produces essential nutrients. Disturbances in the microbiome are often associated with diseases, including IBD. Recent studies highlighted a potential link between IBD related microbial dysbiosis and reduced uptake of essential B vitamins: nicotinate (vitamin B3) and pantothenate (vitamin B5), important cofactors in key metabolic pathways that we get from our diets or microbes. Thus, inflammation of the intestine disrupts its ability to take up key nutrients – similar to malnutri-tion from the host perspective, but overnutrition from a microbiome perspective. I hypothesized that malabsorption of vitamins and other nutrients in IBD selectively alters the composition and function of gut microbiota.

To test how nutrient malabsorption affects the microbiome, we created virtual simulations of microbiome metabolic networks. We used a metabolit-ic modeling pipeline that predicts growth and interactions of microbes within a community. We also selected a well-characterized synthetic microbi-ome community of humans (SHU-M) with pre-com-puted metabolic models. Next, we chose a recent iHMP2 study that profiled stool metabolite levels in healthy, Crohn’s, and Ulcerative colitis patients to create virtual metabolic environments. We then ran simulations exposing our SHU-M community to each of these virtual environments. Overall, composition of the virtual communities within each of the simulations predicted less Bacteroides thetaotaomicron and more Escherichia coli, a lower production of nicoti-nate, and differences in vitamin producers and consumers in IBD environments.

Taken together, these results suggest that changes in the intestinal nutrient environment due to IBD can lead to changes in microbiome composition and function. Further studies are needed to see whether these predictions could increase the incidence or severity of IBD in animal models, and exhibit biomarker- or targeted therapies for the treatment of IBD.
Oligodendrogenesis Is Required for Long-term Memory Formation

Learning and memory are essential for all living organisms. Research investigating the underlying mechanisms of learning and memory have mainly focused on neurons, however the involvement of glial cells, specifically oligodendrocytes, have received limited attention. Studies have shown the requirement of newly generated oligodendrocytes in motor learning, fear memory, and spatial memory consolidation. However, whether episodic memories require de novo myelination and whether cortical regions of the brain are implicated, have not been explored. We hypothesize that during long-term memory formation oligodendrogenesis is induced in the anterior cingulate cortex (ACC) of mice, and that oligodendrogenesis is required for memory formation. To understand if memory formation induces oligodendrogenesis, mice were injected with 5-ethynyl-2’-deoxyuridine (EdU) – a cell proliferation marker – 1 hour before inhibitory avoidance (IA) training. We found an increase in oligodendrocyte precursor cell (OPC) proliferation and differentiation in the ACC 1 day after training compared to the untrained control. Next, to determine the requirement of oligodendrogenesis for long-term memory formation, we conditionally knocked out the myelin regulatory factor gene (Myrf). MyRF controls OPC proliferation and differentiation. The Myrf-knockout mice and the control group were trained in IA and object location to assess their memory. The inhibitory avoidance and object location task results showed memory deficiency in Myrf-knockout mice compared to those with an intact Myrf gene. From the initial experiment, we conclude that long-term memory formation induces oligodendrogenesis in the ACC. The deletion of Myrf shows that oligodendrogenesis is required for long-term memory formation. Since OPC proliferation and differentiation are prerequisites for new myelin, the research may have long-term potential to explain and treat cognition and myelin-related disorders such as multiple sclerosis.

Funding: R01-MH086635 to C.M.A.; HHMI Gilliam Fellowship to L.P.; MARC grant 5T34GM008078-31 to O.N.

Omina Nazarzoda  
CUNY Brooklyn College, Brooklyn, NY 11210, USA

Sabrina Zequeira  
University of Florida

Effects of cannabis smoke exposure on working memory performance in aged rats

Cannabis is the most widely used illicit drug in the United States, and individuals over the age of 65 are the fastest growing demographic of cannabis users. Cannabis can provide a number of benefits such as pain management and promotion of appetite and sleep, making it a potential therapeutic intervention for older adults. Across species, aged individuals exhibit deficits in cognitive functions supported by both the prefrontal cortex (PFC) and the hippocampus. These same cognitive functions are impaired by acute administration of cannabis or THC in young subjects; however, effects in aged subjects have been less well evaluated. The goal was to use a rat model to determine whether the effects on cognition of acute exposure to cannabis smoke differ between young and aged subjects. Male, young adult (6 months) and aged (24 months) Fischer 344xBrown Norway F1 hybrid rats were tested on both a PFC-dependent delayed response working memory task and a hippocampal-dependent trial unique non-match to location (TUNL) task in touchscreen operant chambers. The delayed response task required rats to remember the location of a visual stimulus over variable delay periods ranging from 0-24 s. The TUNL task required rats to remember the location of a visual stimulus with varying degrees of discriminability from other, distractor stimuli. A semi-randomized, within-subjects experimental design was used such that each rat was exposed to smoking from burning 0, 3, 5 and 10 Cannabis cigarettes immediately prior to test sessions in each task. As expected, aged rats performed less accurately than young in both tasks. In the delayed response task, acute exposure to cannabis smoke impaired accuracy in young rats but enhanced accuracy in aged rats. In contrast, in the TUNL task, cannabis smoke had no effects on performance in either age group. Considered together, this pattern of results suggests that in aged rats, which exhibit impaired cognitive performance, cannabis smoke can enhance PFC-dependent cognition, but has no effect on hippocampus-dependent cognition.

Ephraim A. Oyetunji  
Washington University in St. Louis

Investigating TREM2’s Role in Tau Accumulation using Antisense Oligonucleotides in a Mouse Tauopathy Model

Neuroinflammation, particularly involving microglia, contributes to the characteristic pathological hallmarks of Alzheimer’s disease (AD) and facilitates hippocampal damage. Partial loss-of-function variants of the gene TREM2, encoding a microglial receptor, increase risk for AD. Though TREM2 knockout models have shed light on TREM2’s role in AD, it is unclear what short-term reductions in TREM2 expression reveal about TREM2’s role in tau pathology.

Since the TREM2 partial loss-of-function variant increases AD risk, I hypothesized that TREM2 reduction would increase phosphorylated tau in the hippocampus. Using antisense oligonucleotides (ASOs) that acutely reduce gene expression, we lowered TREM2 levels in a mouse model of tauopathy at seven months of age, when neurofibrillary tangles composed of phosphorylated tau are apparent. One month later, the brains were stained for phosphorylated tau.

Although TREM2-lowering ASOs appeared to reduce tau phosphorylation within the dentate gyrus and CA3 subregions, there was no statistically significant differences in the proportion of hyperphosphorylated tau found in the overall hippocampus or its subregions (dentate gyrus, mossy fibers, CA3, and CA1). TREM2 reduction in potentially vulnerable subregions may have limited tau spread leading to regional differences in tau pathology. Additionally, these results may be stage-dependent so other intervention times may affect tau pathology differently.
Histamine Receptors Genomic Study in the Bivalve Crassostrea virginica
Kera Mansfield1, Martha Larios1, Mohamed Eid2, Craig Hinkley1, Margaret A. Carroll2 and Edward J. Catapano2
1) Kingsborough Community College, 2) Medgar Evers College, Brooklyn, NY

Histamine is involved in local immune responses and regulating physiological functions. Histamine also is a neurotransmitter for sensory systems. Previous work of our lab found histamine activates the sensory system of Crassostrea virginica, eliciting motor responses in gill. Our immunofluorescence work showed histamine receptors in ganglia and mantle of C. virginica. Recently C. virginica’s genome is being mapped. We hypothesize C. virginica contains genes for histamine receptors similar to those in other animals, including mammals. To study this we did BLAST searches of the NCBI (National Center for Biotechnology Information) database using DNA and protein sequences of C. virginica histamine 1, 2 and 3 receptor (H1R, H2R, H3R) genes. We found matches. H1R genes were found on chromosome 8; H2R on 1, 2, 5 and 10; and H3R on 3. Receptor BLASTS found matches with low Expect Values and moderately high Percent Identity (PI), signifying similarities of H1R, H2R and H3R of C. virginica to those of other bivalves, gastropods, insects and mammals. For H1R, various bivalves had PI above 60%, but poor matches for gastropods and insects. For H2R, C. gigas had a high match of 82%, but other invertebrates, mice, rats and humans had low matches. For H3R, C. gigas had a high match of about 75%; some other bivalves, mice, rats and humans had matches of about 40%. Gastropods and insects did not show good matches as other bivalves and other invertebrates. This study complements our studies demonstrating the presence and function for histamine in C. virginica. It shows the C. virginica genome contains genes to produce histamine receptors similar to those in other animals. This information is valuable in showing the simple nervous system of C. virginica can be used to expand studies on histamine neurotransmission. This work was supported by grants 2R25GM06003 of the Bridge Program of NIGMS, NIH-K12GM093854-07A1 IRACDA Program of Rutgers University and PSC-CUNY 63434-00 50 and 63434-00 51.

Elevated CO2 Effects on Arabidopsis thaliana’s Innate Immune System Constituents & Subsequent Pathogen Interaction
Nickoli Parkinson, SUNY Purchase College

Introduction: Established by previous research such as in “Maternal Effects of Elevated CO2 on Arabidopsis thaliana” by SUNY Purchase’s undergraduate student Allison Wong, sponsored by Dr. Mark Jonas, is the fact that climate change, or the fact that a change in the equilibrium of the constituents of the atmosphere, this case being CO2, will have significant effects on plant growth and integrity. Least studied of all, in this literature and others, is the effects climate change may have on a plant’s immune response to common pathogens. The purpose of this experiment is to study the change in interactions between pathogens and plants that has been grown elevated CO2 levels.

Methods: A sample size of 50 Seeds from highly inbred lines of Arabidopsis thaliana will be selected. 25 will be grown in normal atmospheric conditions and 25 will be grown in elevated CO2 conditions. Two-three generations of each will be grown in the original environmental conditions of their P1 counterparts, then a significant test samples will be selected for HPLC analysis. In doing the HPLC analysis, the levels of pre-formed structures and chemicals that constitute the first line defense against pathogens will be measured. Next in the remaining populations of samples, populations of pathogens will be introduced to document physical observations of the differences between the interactions of Arabidopsis and pathogens in the elevated CO2 levels and Arabidopsis and pathogens in normal atmospheric conditions.

Conclusion: At the end of the experiment, I am expecting to see differences in the interaction of pathogens in Arabidopsis thaliana that were grown in elevated CO2 levels and ones that were grown in normal atmospheric conditions. Though, I am not too sure if these differences will be negative or positive. This remains yet to be seen. Also, in measuring the concentrations of pre-formed structure and chemicals that constitute the first line of defense against pathogens, sufficient data and correlation with findings can be expected.
Abstracts

4

Opsonization of COVID-19 through Self-Assembling Peptide Hydrogel
Sreyan Sanyal, Abhishek Roy, Zain Siddiqui, Vivek Kumar
Department of Biomedical Engineering, New Jersey Institute of Technology, Newark, NJ 07102
Background: COVID-19 is a respiratory virus whose 3D structure shows a conserved receptor binding domain (RBD) from SARS-CoV-2. After binding to the ACE-2 receptor, the virus enters the cell through a complex, multistep process involving several viral proteins and cellular pathways. Our goal is to develop a hydrogel-based therapeutic that can effectively opsonize COVID-19, enabling the virus to be engulfed by phagocytes and cleared from the body.
Methods: We have developed a hydrogel that is composed of self-assembling peptides, which can bind to the RBD of SARS-CoV-2. These peptides form aggregates that can recognition the virus and facilitate its uptake by immune cells. We have tested the opsonization ability of our hydrogel against a range of COVID-19 strains and conditions.

5

Application of VenomSeq Technology to Decipher the Putative Mechanism of Action or Molecular Targets of Venom Peptides
Sharmin Sultana1, Tanya Napolitano2-3; Mandel Holofcener4
1Yale Honors Scholar, Hunter College of the City University of New York; 2Department of Chemistry, Hunter College of the City University of New York; 3Ph.D. Program in Biochemistry, The Graduate Center of the City University of New York; 4Director, M_projected Genetics, Invertebrate Zoology, American Museum of Natural History
Recently, venom peptides have become attractive candidates for the development of therapeutics to benefit human health. For example, the drug ziconotide (Prialt®), derived from the venom of the cone snail Conus magus, is the first non-addictive, non-opioid peptide analgesic approved by the FDA to treat chronic pain. Despite their pharmaceutical potential, characterizing bioactive venom peptides poses several challenges due to the scarcity of reference databases to identify novel venom peptides and the lack of high-throughput assays to identify molecular targets. A collaboration laboratory developed a new project called VenomSeq that is being used to generate putative associations between venom peptides and known drugs via perturbational differential gene expression analysis. VenomSeq exposes various human cell lines to purified venom peptides and produces peptide specific differential gene expression profiles via RNA sequencing (RNA-Seq) to determine which genes and transcriptional regulatory modules are being modified in human cells by the pure venom peptides. The novel expression profiles are compared to open-source databases of known drug expression profiles in order to detect putative conformed molecular targets and mechanisms of action. Using this approach, we tested 11 pure venom peptides (2 control and 9 experimental) on IMR-32 cells, a human neuroblastoma cell line. We found that the venom peptides induced significant differential gene expression profiles, with 25 statistically significant gene perturbations. The other experimental peptides had few or no significant gene perturbations. Interestingly, Mki 8.7 showed similar activity to thapsigargin, a molecule known to be an inhibitor of the sarco/endoplasmic reticulum Ca2+ ATPase (SERCA) pump and a tumor promoter in mammalian cells. With these results, we can hypothesize how Mki 8.7 affects IMR-32 cells. The next step is to test Mki 8.7 in various cell-based assays to confirm our computational predictions. Currently, there will be three cell-based assays that will be done commercially to confirm the predicted activity of Mki 8.7.

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The effects of ATRXLoss and IDH1R132H when combining radiotherapy with the IDH1R132H inhibitor ivosidenib (M-120) in glioma stem cells
Garces AA1,2, Bronik B1,3, Kiyoshi H12,13
1. Dept. of Radiation Oncology, MD Anderson Cancer Center, Houston, TX, 2. Therapeutics and Pharmacology, MD Anderson UTHealth Graduate School of Biomedical Sciences, Houston, TX, 3. Dept. of Translational Molecular Pathology, MD Anderson Cancer Center, Houston, TX.
Co-author: Angel A. Garces, Dept. of Radiation Oncology, MD Anderson Cancer Center, Houston, TX. E-mail: aagarces@mdanderson.org.
Background: Glioma Stem Cells (GSCs), a recently discovered subpopulation of undifferentiated, self-renewable, tumor initiating cells known to promote chemoresistance and metastases, present a novel target for cancer therapy. Importantly, 70-80% of grade-ii glioma (LG2) and secondary Glioblastoma Multiforme (GBM) patients harbor IDH1 R132H, which results in the elevated production of 2-Hydroxyglutarate (2-HG), a metabolite that promotes intratumoral acidosis and impairs post-replication DNA repair (DDR) via the histone deacetylase (HDAC) inhibition. HDAC inhibitors have been tested in clinical trials with improved survival and clinical responses to chemotherapy and/or radiotherapy (RT). However, the mechanisms by which IDH1R132H impacts the efficacy of RT combined with ivosidenib in GSCs are not well understood. We hypothesize that ATRXLoss and IDH1R132H impact the efficacy of RT combined with ivosidenib in GSCs.
Methods: Isogenic MG181-SHMT-IV, MG181-IDH1R132H, TS543-ATRX-IV, TS543-ATRX-IV, and GB185-IDH1R132H(ATRXLoss) GSC neurospheres were treated with 3-6 Gy of RT with the NRK 520 irradiation platform and/or 5 nM Ivosidenib, at 24 hours prior to irradiation. Methods: The other experimental peptides had few or no significant gene perturbations. Interestingly, Mki 8.7 showed similar activity to thapsigargin, a molecule known to be an inhibitor of the sarco/endoplasmic reticulum Ca2+ ATPase (SERCA) pump and a tumor promoter in mammalian cells. With these results, we can hypothesize how Mki 8.7 affects IMR-32 cells. The next step is to test Mki 8.7 in various cell-based assays to confirm our computational predictions. Currently, there will be three cell-based assays that will be done commercially to confirm the predicted activity of Mki 8.7.

7

Yodhae Gebregziabher
Rabinowit Lab, Sunyer Undergraduate Research Fellows in Chemistry (SURF-C), Charles A. Leach, II Summer Scholars Program, Department of Chemistry, Princeton University, Program Manager: Dr. Susan VanderKam PI: Professor Joshua Rabinowitz, Mentor: Xincheng Xu
Metabolism is a very important aspect of the biology of life and genes for enzymes involved in metabolism account for ~10% of the human genome and ~25% of microbial genome. The basic pathways of metabolism have been known for quite some time. However, a quantitative and integrated understanding of the metabolites in these metabolic pathways remains to be explored.
In this proposal, SHMT inhibition – a field within one-carbon metabolism – is investigated. At the heart of one carbon metabolism are folate molecules which function as one carbon carriers – receiving and supplying one-carbon molecules widely used in essential metabolic reactions. These include biosynthesis of purines and thymine, biosynthesis of amino acids (glutamate, serine, and methionine), epigenetic maintenance, and redox defense. SHMT, which stands for Serine hydroxymethyl transferase, is an enzyme that catalyzes the transformation of serine to glycine - one of the many reactions of one carbon metabolism that take place in the cytoplasm and mitochondria.
The regulation or dysregulation of one carbon metabolism has been shown to impact outcomes in health and disease. Inhibiting folate metabolism in particular has been an ideal target in combating dysregulated cell division and proliferation in diseased conditions such as cancer. Consequently, SHMT inhibition, which disrupts folate metabolism, has been shown to reduce tumor growth in many cancer cell lines. This proposal is meant to build upon these findings and more particularly a previous paper that showed SHMT inhibition in B-cell lymphomas affected glycine uptake and retention in addition to folate metabolism. The results from this in vitro study showed that B-cell lymphomas have defective glycine import that can be enhanced by SHMT inhibitors. The aim here is to extend their result by preventing the clearance of effective SHMT inhibitors in-vivo and examining their effect on tumor growth.
Evaluating anticancer activity of a cobalt(III) with a thiosemicarbazone ligand against triple negative breast cancer cells

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Cancer is one of the major causes of death in the world. Breast cancer is an uncontrolled growth of epithelial cells of the breast. Triple negative breast cancer (TNBC), a subtype of breast cancer, lacks estrogen, progesterone, and HER2 receptors. Chemotherapeutic options for TNBC which involves cisplatin have severe side effects, e.g., cytotoxicity of normal breast tissue, drug resistance, and breast cancer recurrence. The objective of this study was to determine less toxic treatment options for TNBC by using a cobalt(III) complex, which like most conventional anticancer drugs was designed to disrupt DNA synthesis as a chemotherapeutic agent. Previously, [Co(phen) 2(H2O)2](NO3)3 1 (where phen = 1,10-phenanthroline) was reacted with 9-anthraldehyde-N(4)-methylthiosemicarbazone (MeATSC) to produce [Co(phen)2(MeATSC)(NO3)] 1.5H2O∙C2H5OH 2. The hypothesis is as follows: complex 2 will have a higher anticancer effect on TNBC cell line MDA-MB-231-VIM-RFP than cisplatin. In vitro cytotoxicity studies involving complex 2 with MDA-MB-231-VIM-RFP were carried out by using Cell Counting Kit-8 (CCK-8) assay. The pro-apoptotic activity of complex 2 was evaluated after incubating the drug with MDA-MB-231-VIM-RFP cells in increasing concentrations (0, 0.125, 0.25, 50, and 100 μM) for 24 hours, then cell viability was measured by CCK-8 assay. Dose curves and doses required to inhibit 50% of cell growth (IC50 values) were obtained by using Origin Pro software, which revealed that MDA-MB-231-VIM-RFP cell viability was negatively impacted by complex 2 with an IC50 value of ~26 μM.

The Jak/Stat Signaling Pathway's Potential Piwi-Dependent Role in Drosophila Oogenesis

Debby Park

Abstract

Piwi has an indispensable role in the Drosophila germline stem cell (GSC) niche and in somatic cells that induce differentiation. It is especially essential in escort cells to repress dpp, an activating gene of BMP signaling. In the absence of these signals, the barn gene is active in GSCs to promote differentiation, though it is unclear how Piwi regulates BMP signaling. Aim 1 reveals whether glucosamine leads to differentiation of self-renewal cells in the absence of somatic Piwi through single germline cell detection. Aim 2 verifies if and how Piwi regulates the Jak/Stat pathway and its target gene expression. Finally, aim 3 tests the hypothesis that glucosamine results in GSC arrest in somatic piwiKD flies through immunofluorescence. Taken altogether, these aims will provide insight into Piwi's function in cell fate decisions.
Background: Ricin is a well-known, acutely toxic protein produced by castor bean plants. The Centers for Disease Control and Prevention (CDC) classifies ricin as a Category B biological agent. Ricin is a member of the type 2 class of ribosome-inactivating protein (RIP) produced by many plants to protect themselves from pathogens. Type 2 RIP is a heterodimer with B-chain (RTB) and A-chain (RTA), a catalytic RNA N-glycosylase domain that targets and deaminates a specific universally conserved sarnic/ricin loop (SRL) of the large RNA, and thus, inhibits protein synthesis. Since their discovery, RIPs have been of great scientific interest due to their importance in human health (as both pathogenic agents and therapeutic agents), and their potential uses in biological warfare and bioterrorism. Currently, there is neither an effective vaccine nor an antidote to protect people from ricin poisoning.

Previous research revealed that the viral protein (VPg) from the lumpy mosaic virus (TuMV) binds to and inhibits RIP activity in vitro and in the cell-free translational system. The long-term goal of this proposed research is to develop a novel peptide inhibitor of RIP toxicity that will serve as a milestone in the development of more effective treatments against RIP.

Methodology: We propose a study using site-directed mutagenesis to create mutant VPg and investigate the interactions between RTA and our mutant VPg. Specifically, we will use Stratagene’s QuickChange® Site-Directed Mutagenesis Kit to substitute the VPg residues consistently predicted in interacting with RTA for similar amino acids (e.g., substituting glutamate with aspartate and vice versa). We will then employ fluorescence titration and high-performance liquid chromatography (HPLC) to quantitatively analyze and identify whether the binding is entropically favored or enthalpically driven, and examine these mutant VPg inhibitory effects on RTA activity.

Expected Outcomes: We will successfully create a series of VPg constructs that have a stronger binding affinity for RTA and a more pronounced inhibitory effect on its RIP activity. This study will lead to the development of optimal treatment against ricin and other RIPs.
VenomFlow: Transcrimptive bioinformatics pipeline for identifying secreted toxins in a venom arsenal
Eleonora Achrak1, Jennifer Ferrd,2 Jessica Schuiman,2,3 Mandé Hofeld, 2,4, Traci Dang4
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More than one and a half billion people worldwide suffer from moderate to severe chronic pain. Existing drugs for the treatment of pain are often associated with serious side effects and rapid development of tolerance, thus, there is a need for new, more selective molecules. Venoms are complex biochemical mixtures designed to address biological interactions such as bacterial infection, pathogen evasion, or defend from predator threats. The latter is often observed in snakes, which are attractive candidates for the development of therapeutics. With the rise of omic technologies, e.g transcriptomics, proteomics, bioinformatics is now possible to obtain in-depth sequence information about venom arsenals from more than a single species. However, identification and characterization of bioactive venom peptides remains a significant challenge due to the enormous number of peptides found in each venom arsenal (upwards of 200) and the unique chemical structures of each peptide. Here, we introduce a rapid and user-friendly in silico bioinformatics pipeline to examine de novo non-modal transcriptomic data from venomous organisms to identify and chemically characterize raw RNAseq reads from venom. This project develops a user-friendly automated bioinformatics pipeline via a Galaxy workflow to identify novel venom peptides from the raw reads of terebrid snakes. While designed for venomous terebrid snakes, with minor adjustments this pipeline can be made universal to secreted toxins from any venomous organism.

De novo design of disulfide-rich mini-proteins to inhibit bacterial biofilm formation
Paula Garavito, Frank D. Teets PhD, Christopher D. Bahl PhD
Institute for Protein Innovation

Biofilms are a prominent health and economical threat to society because microbes can be found in almost every environment, including water supplies, air condition vents, oil pipelines, or even medical devices such as a prosthetic heart valve. The formation of the biofilms in many Gram-negative bacteria is mediated by the Lap system and the intracellular second messenger cyclic-di-guanosine monophosphate (c-di-GMP). High cytoplasmic concentrations of c-di-GMP cause the LapD-LapG complex to sequester the LapG protease to the inner membrane. Once the LapD-LapG complex is formed, LapG can no longer access the LapA adhesin, and thus the bacteria are able to form a biofilm. The binding of the complex relies on the presence of a tryptophan residue in the strictly conserved loop connecting the strands β3 and β4 formed by the GWxQ motif of LapG receptor. Previous studies have shown that the LapG-LapG interaction can be inhibited in vitro by short linear peptides that contain the conserved loop in the GWxQ motif. However, in vivo studies were not possible due to poor solubility of these peptides. I hypothesize that blocking the interaction between LapD and LapG will inhibit biofilm formation, and this proposal will be a critical demonstration of the hypothesis that the Lap system is a viable target for biofilm inhibition.

Identification and Differentiation of Acinetobacter calcoaceticus-Acinetobacter baumannii Complex: Common Nosocomial Pathogens among Children
Shuborno Islam1, 2, Mohdulidin Kabir 1, Md. Hasanuzzaman 2,3, Md. Salitul Islam Sajib 2, 3, Samir K. Baha 2, 3
1Department of Genetic Engineering and Biotechnology, East West University, Dhaka-1212, Bangladesh; 2Nich Health Research Foundation, Dhaka 1207, Bangladesh; 3Department of Microbiology, Dhaka Shishu Hospital, Dhaka 1207, Bangladesh.

Background: Acinetobacter baumannii is one of the most common pathogens causing nosocomial infections worldwide involving a range of infections such as surgical site infections to pneumonia and others. Due to multiresistant worldwide, their identification and effective treatment, Acinetobacter is a complex genus containing multiple species, most of which have similar morphological characteristics and biochemical properties leading to a complicated analysis procedure in a routine laboratory facility. Objective: This study was based on clinical isolate where Acinetobacter baumannii and other closely related pathogenic species of Acinetobacter, commonly called Acinetobacter calcoaceticus-Acinetobacter baumannii (ACB) Complex were observed. They were originally recognized as a single species and later divided into different species using conventional biochemical methods. The ACB Complex is currently divided into three species: Acinetobacter baumannii, A. baylyi and A. calcoaceticus. Previously, two methods have been used to identify these species: 16S rRNA gene sequencing and MALDI-TOF-MS. The latter is the most reliable and can identify almost 99% of the species of the ACB complex. The objective was to develop a technique which would be applicable in routine laboratory diagnostic methods. Conclusively, Burkholderia species was found among these isolates which showed a significant biovar heterogeneity with Acinetobacter baumannii.

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Characterization of Novel Antimalarials from Compounds Inspired by Natural Products Using Principal Component Analysis (PCA)
Zara Baide, Dr. Debopam Chakrabarti, University of Central Florida

Malaria still causes 300 million clinical cases and about 400,000 deaths each year but the drugs that are available for treatment are rapidly losing their efficacy because of widespread prevalence of drug-resistant parasites. Malaria is caused by a protozoan parasite, Plasmodium falciparum, which is responsible for over 400,000 deaths per year worldwide. Although malaria medicines are working well in many parts of the world, antimalarial drug resistance has emerged as one of the greatest challenges facing malaria control today. A previous screen in our lab for novel antimalarials identified several natural products (NPs) with antimalarial activities. The focus of this study is to characterize the hit compounds using Principal Component Analysis (PCA) to determine structural uniqueness compared to known antimalarial drugs. Prioritizing the hit compounds by their chemical uniqueness will decrease the probability of the malaria parasite to form resistance to these drugs. Principal component analysis from this study revealed physicochemical parameters that are most influential in distinguishing our library compounds from natural products. Malaria parasites have well-adapted resistance to drug like compounds such as chloroquine, which is why it is necessary to characterize and prioritize compounds that are more like natural products. Knowing what descriptors have the greatest impact can allow us to modify and create more natural-product-inspired synthetic compounds that have structural uniqueness. Prioritizing a collection of biodesign libraries using PCA can help lessen the probability of future resistance. This study has shown that kinase inhibitors are more drug-like while macrocycles are more natural-product-like and have a trend going from the upper left side of the plot to the lower right side of the 3D chemical space. This means that there are more structural uniqueness and has more potential to be a novel antimalarial with macrocycles. Leveraging this information will enable us to discover potent, selective, and novel antimalarial scaffolds that are unique in the 3-dimensional chemical space and will provide critical information that will serve as advanced starting points for the antimalarial drug discovery pipeline.

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Biophysical Properties and Energetics of NMDA Receptor Gating
William Khayyo, Noelle Certain, Jøhanssen Amin, Lonnie Wollmuth, State University of New York at Stony Brook

Ionotropic glutamate receptors (iGluRs) are a class of ligand-gated ion channels responsible for the vast majority of fast signal transmission in the brain. NMDA receptors (NMDARs) are a unique class of iGluRs that are responsible for the gating of calcium ions in neural communication. They play a major role in brain function including learning, memory, and development of the nervous system. Over 200 variants in NMDARs have been associated with learning deficiencies, neurodevelopmental disorders, epilepsy, and schizophrenia. Common to all iGluRs are four distinct levels of structure: the amino-terminal domain (ATD), ligand binding domain (LB), the transmembrane domain (TMD), and the carboxyl-terminal domain (CTD). NMDARs also contain features that distinguish NMDARs from other GluRs. NMDARs form obligatory heterotetramers, composed of two GluN1 and two GluN2 subunits that bind to glycine and glutamate, respectively. All four LBDs must be occupied, in order for the channel to open and allow calcium to influx into the cell. The LBD consists of a clamshell structure and is the site for agonist (glutamate or glycine) binding to initiate the conformational changes from the closed to opened of the receptor channel. The TMD consists of 3 ĉ-helices (M1, M3, and M4) as well as an M2 pore loop to enable flux of calcium through the aqueous pore. The upper M4 segment contains disease-associated variants (DAVs) associated with learning disabilities and intellectual disabilities within a highly conserved NKGV motif. The M4 subunit of the TMD interacts with the M3 helix in order to open the channel once an agonist is bound. The M4-lineries in association with the pre-M1 and M3 helix is a pivotal opening mechanism for the channel pore. This series of DAVs has been associad with aforementioned disorders in patients, yet less is known on its role in altering NMDARs gating. This work studying NMDAR DAVs will provide insight into how missense mutations at the NKGV motif affects important signal transmission through NMDARs. The identification of target polypeptide will be conducted in order to insert alanine substituted mutant constructs and on cell recordings will be done on transfected HEK 293 cells.

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Modeling PTSD-like Phenotypes in Mice and Reversal of Symptoms by Pharmacotherapy
James Lawrence

Post-Traumatic Stress Disorder affects roughly 3.5% of individuals in the United States who have been exposed to emotional or physical distress. While the symptoms of the disorder have been documented extensively, the neurophysiological mechanisms that result in the onset of symptoms, including anxiety, mood disorders, and various other forms of cognitive decline, remain uncertain. Our examination of the cholinergic neurochemical systems in stress induced laboratory mice aims to derive the mechanism of physiological decline that leads to the onset of the aforementioned symptoms. Modulation of nicotinic acetylcholine receptors, or nAChRs, may provide the possibility of reversing some of the symptoms that accompany this disorder. In analyzing the changes in differential gene expression in response to stress, it is postulated that changes in the genetic sequence of these regions located in the hippocampus, may result in increased mitochondrial substrate production and the aforementioned symptoms. Identifying the factors responsible for behavioral phenotype alterations may allow for the exploration of chemical or behavioral treatment to alleviate these symptoms. By utilizing a targeted examination of these regions with stress variables applied to laboratory mice, a protocol of pharmacological treatment targeted alleviation of the severity of symptoms.

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24 Higher Resolution Investigation of Ovarian Cancer Xenografts

Daniel Cambron, Musheer Aalam, Nagarajan Kannan
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DNA barcoding is an innovative technique that enables scientists to individually label any cell for future identification. One application for DNA barcoding is in cancer research where identifying tumor clone initiating cells (T-CIC) frequency is important for developing targeted treatments. This study focused on the analysis of barcoded cancer cells following next generation sequencing (NGS) of the dissected mouse tumors that formed. T-CIC frequency was calculated for each cell type injected into the mouse and organized by tumor site. Then the clone size of each barcoded cell was calculated within every tumor sample. The T-CIC for mouse 49 showed greatest frequency in the lungs, followed by the primary tumor and right kidney. The T-CIC for mouse 49 showed greatest frequency in the liver, followed by the lungs and spleen. Overall clone size diversity was greater for cells isolated from mouse 49 with index 1.2 cell clone sizes being greatest for both mice. These results demonstrated which cancer cells from the primary tumor were most aggressively replicating and helped predict which organs these cells will metastasize to.

25 Luteolin Induces Cytotoxicity via Caspase Activated-cell Death in Mix Cellularity Classical Hodgkin’s Lymphoma, in vivo

Naomi Codrington, Stephen Redenti, Ph.D., Rajendra Gharbaran, Ph.D.

Although chemotherapy and radiation resulted in a high cure rate in classical Hodgkin’s lymphoma (cHL), the treatment is associated with long-term side effects including cardiopulmonary toxicities and development of secondary neoplasms. To mitigate these concerns, one line of research is focused on the development and discovery of new therapeutic approaches. Luteolin (LUT), a flavonoid that naturally occurs in several plants including fruits, vegetables, and medicinal herbs, and has attracted much attention for its role in the treatment of human ailments and its anticancer activities. To date however, there is no study on the effect of LUT on malignant lymphomas. Therefore, the goal of this study was to investigate the potential anti-cancer effects of LUT on cHL.

In this study, we investigated the effect of LUT on cHL. Cell growth was assessed with water-soluble tetrazolium 1 (WST-1) cell proliferation assay and automated hemocytometry on trypan blue-exclusion assay. Cell death was investigated with acridine orange/ethidium bromide (AO/EtBr) live-dead assay, propidium iodide (PI) flow cytometry, and Annexin-V-PI microscopy. Caspase activation was studied using CellEvent Caspase-3/7 Green detection reagent. High resolution immunofluorescence microscopy was used to detect cleaved-PARP-1.

The cell growth assays showed dose-dependent suppression growth of cHL cell lines KM-H2 and L428, cellular models of mix cellularity (MC) and nodular sclerosis (NS) cHL subtypes, respectively, 48 hours after treatment. However, LUT, at higher doses [40 µM and higher], induced cell death only in KM-H2, as revealed by AO/EtBr assay and Annexin-V-PI microscopy and PI flow cytometry. Caspases3/7 detection dye revealed significantly higher levels of caspases3/7-positive cells in LUT [40 µM]-treated KM-H2 cells. In addition, high-resolution immunofluorescent imaging of LUT [40 µM]-treated KM-H2-revealed nuclear cleaved-PARP-1, in regions presumed to be where PARP-1 interact with DNA. PARP-1 is a DNA repair enzyme and cellular substrate of caspases 3 and 7.

These results suggest caspase-activated cell death is a putative mechanisms by which LUT reduces growth of MC-cHL.

26 The Role of Genetic Factors in Endometrial Cancer Disparities

Leya Groysman, Taylor N. Wallace, Dr. Wen H. Shen
Affiliations: Macaulay Honors College at Hunter, Weill Cornell Medicine, Southern Methodist University

In 2020, about 65,000 new cases of endometrial cancer will be diagnosed. This is the most common cancer of the female reproductive organs. Even though there are more incidences of endometrial cancer in Caucasian women it has been evidenced that more African American women die from it. This disparity in mortality rates is due to not only social factors, like access to healthcare, but can also be caused by genetic factors such as mutation frequency and type. Using databases such as SEER Incidence and the Genomic Data Commons Portal, we explored the most commonly mutated genes in Caucasian and African American populations, treatment outcomes, as well as the impact of age at diagnosis on these mutations. African American endometrial cancer patients have more genes displaying statistically significant mutation frequencies in comparison to their Caucasian counterparts. This data was specifically gathered for Endometrial Adenocarcinoma, since it is the most common subtype. These data can be used to promote bench studies of endometrial cancer disparities with the aim of developing more effective treatments, especially for the African American community.

27 Determining How MSI Impacts Progression And Invasiveness Of BRAF-Driven Serrated Colon Cancer

Katherine Haro1, Kevin Tong1,2, Michael Verzi1,2
1 Rutgers University-Department of Genetics 2Human Genetics Institute of New Jersey (HGINJ)

Colorectal cancer is the third most common cancer in the United States and is the second leading cause of cancer-related deaths. While the most common type of colon cancer is the WNT-driven adenoma, ~20% of colon cancers follow the more lethal “serrated” pathway –which is commonly driven by the oncogene BRAF (Pati, Molnár, Tulassay, & Sipos, 2013). Furthermore, serrated colon cancers can also be classified by Microsatellite Instability (MSI) status, which is characterized by the impaired function of DNA Mismatch Repair (MMR). It is suggested that BRAF-driven serrated cancers are driven by MSI status and are required for the hyperplasia- to- dysplasia transition (Rad et al, 2013). The Verzi lab previously reported that the oncogenic allele BRAFV600E/+ alone is inefficient at tumorigenesis (Hong et al, 2017). However, the loss of tumor suppressor SMAD4 greatly accelerates BRAF-driven tumorigenesis and significantly upregulates WNT signaling. Interestingly, tumors that arose from these mice were primarily Microsatellite Stable (MSS). Thus, we wanted to determine whether MSI or MSI has a substantial difference in dictating how BRAF-driven serrated tumors form. We generated a mouse model in which the oncogenic BRAF mutation was combined with a knockout of both tumor suppressor SMAD4 and DNA mismatch repair protein MSH2 in a Villin-Cre system. Strikingly, SMAD4KO BRAFV600E/+ MSH2KO mice develop multiple macroscopic tumors and serrated invasive tumors within three months. In contrast, SMAD4KO BRAFV600E/+ mice developed fewer serrated tumors within the same time frame, suggesting that MSH2KO accelerates serrated tumorigenesis and progression. Furthermore, the SMAD4KO BRAFV600E/+ MSH2KO tumors show elevated levels of WNT signaling, supporting the notion that elevated WNT signaling is required for serrated tumorigenesis. Whole Exome Sequencing (WES) analysis revealed that WNT-effector β-catenin (Ctnnb1) is commonly mutated in tumor contexts derived from both SMAD4KO BRAFV600E/+ MSH2KO and SMAD4KO BRAFV600E/+ mouse models. To determine whether elevated WNT is critical for serrated tumorigenesis, the Verzi Lab generated a mouse model in which β-catenin was added into a SMAD4KO BRAFV600E/+ mouse model. By doing this, WNT had become significantly upregulated and caused tumors to produce as soon as 7 days while in the SMAD4KO BRAFV600E/+ it took at least 1 month for tumors to be seen. This suggested that a high WNT environment is needed to produce tumors in a shorter amount of time. This supports the initial claim that WNT is needed to progress tumorigenesis and inducing MSI can accelerate it.
Genomic Analysis of Prostate Cancer in Men of African ancestry

Isra Elhussein1,2, Jason white1,2, Tamaro S. Hudson3, Moray J. Campbell4, Clayton Yates2

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Background: African American (AA) men have 2 to 3 times higher prostate cancer mortality rates than European American (EA) men. AA prostate tumors were observed to undergo an earlier transformation from latent into the clinical disease, to be more aggressive at diagnosis. Prostate cancer (PCa) outcome disparity remains even when controlled for access to care and stage at presentation and allocated to differences in tumor subtypes or gene expression profiles. Additionally, tumor microenvironment plays an essential role in tumor progression, aggressiveness, therapeutic response, and patient outcomes. Furthermore, men of African ancestry from the Caribbean and South America demonstrate incidence and mortality rates similar to AA men, suggesting a possible ancestral basis for some of these expected outcomes.

Methodology: RNA sequencing analysis was performed for RNA isolated from macro-dissected FFPE (n=28). The raw reads were aligned to the GRCh38 genome, then gene-level expression was measured from STAR counts using Ensembl gene annotation. Differential gene expression analysis was performed using DESeq2/EdgeR packages based on the race. GSEA analysis was conducted to identify specific gene sets that are enriched in AA men. ADMIXTURE was used to generate a quantitative estimate of each individual ancestral composition.

Results: Descriptive statistical analysis of the study population were conducted and stratified by race and pathology stage. Our results showed that AA men are diagnosed with PCa at a younger age and higher pathology stage (p < T2), contributing to a lower survival rate in AA. Our analyses revealed that intergenomic-inducible gene sets (RS115, IFT1, ST11) were positively enriched (p-value < 0.05), while neutrophil degranulation and interleukins gene sets (IL6, CXCL3, KRT5, IL6, CXCL6) were negatively enriched (p-value > 0.05) in AA men. These enriched gene sets may indicate that immune inflammation signatures play an important role in driving aggressive prostate cancer in AA. Our results were validated using two other data sets. We postulate that African ancestry can drive aggressive prostate cancer in AA men.

Conclusion: Our study would provide new insight to understand how genetic ancestry, transcriptomic alterations, specifically immune-inflammatory signature, and tumor microenvironment may contribute to PCa racial disparities in AA men cohort from African ancestry.

Keywords: Prostate cancer, African American, Disparities, Ancestry

Isolation and Characterization of Anti-cancerous Agents from Bangladeshi Wild Date Fruits (Phoenix sylvestris) for Hepatocellular Cancer Treatment

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Background: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer associated deaths. Therefore, safe, effective and affordable approaches are needed to control cancer development and progression. Potential anticancer agents can be isolated from the extract of Bangladeshi wild date palm fruit (Phoenix sylvestris), as different studies have suggested that it contains apigenin, quercetin, glucans, luteolin, iron and vitamin complex.

Objective: Isolation and characterization of anticancer agents from Bangladeshi wild date extract (WDE) for HCC treatment.

Methodology: HCC inhibitory effects of the aqueous extract of wild dates, collected from different regions of Bangladesh, would be evaluated in rat model having diethylnitrosamine (DEN) induced liver cancer through studying the histological, biochemical and anti-oxidant enzyme status, as well as the related cytokines and gene expression profiles.

Results: High concentration of WDE treated group might show mostly normal hepatocytes than other groups and DEN control group should have abnormal cell morphology. The activity of the anti-oxidant enzymes and anti-tumor cytokines might be increased; liver enzymes and proinflammatory cytokines might be decreased in WDE treated groups compared to untreated control.

Conclusion: Wild date palm fruits from Bangladesh can be promising as an indigenous low cost substance to treat HCC in our country compared to different expensive chemotherapeutic agents.

Key words: Anticancer agent, Bangladesh, hepatocellular carcinoma, Phoenix sylvestris.

Tethered Capsule Endomicroscopy For Identifying the Ampulla of Vater

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Pancreatic Cancer (PC) is one of the deadliest cancers as it is often detected late after it has invaded and metastasized. Finding a solution for early PC detection could significantly reduce mortality, motivating the development of a screening method that is inexpensive and minimally invasive. Pancreatic fluid (PF) is a promising carrier of PC biomarkers, as it is secreted directly by the pancreas into the duodenum through the Ampulla of Vater (AoV). Isolating the AoV for targeted PF sample collection would therefore be ideal for yielding higher concentrations of PC biomarkers. We have developed a technique called tethered capsule endomicroscopy (TCE) that may be configured to accomplish this task. With TCE, patients swallow a tethered capsule that acquires cross-sectional, microscopic optical coherence tomography (OCT) images of their GI tract, including the duodenum where the AoV resides. To determine whether the TCE device can identify the AoV so that it can be subsequently used to sample PF directly, we performed TCE on 27 subjects (male: 19, female: 8; age range: 20 - 53 yrs.) as the capsule traversed up and down the duodenum. A total of 353 videos comprising an average of 10852 OCT frames were recorded. Videos were analyzed by expert OCT readers. Presence of the major and minor ampullae was determined using the following criteria: 1) occurrence of bile expulsions, 2) duodenal folds, 3) relative position of ampullary protrusions, and 4) presence of elongated villi. The major and minor ampulla were discriminated by the knowledge that 1) the minor ampulla is proximal to the major and 2) the minor ampulla is not associated with bile expulsions. Using these criteria, either the major or minor ampulla were retrospectively identified in 78% (95% CI 74%-82%) of all videos and 100% (95% CI 87%-100%) of subjects. We identified the major ampulla in 85% of subjects (85% CI 72%-99%) and the minor in 67% (85% CI 49%-84%). The major ampulla’s mean diameter was 6.49 +/- 2.23 mm (stdev), and the minor ampulla’s was 6.09 +/- 2.05 mm (stdev). The capability of TCE to successfully identify the major and minor ampullae paves the way to create an inexpensive and minimally invasive early PC screening tool that isolates and samples PF from the AoV.
Optimization of Computed Tomography-Based Fat Quantification to Predict Sex-Specific Outcomes in Patients with Kidney Cancer and Glioblastoma

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Visceral obesity is a risk factor for many diseases, including cancer. However, the impact of visceral obesity on sex differences in survival outcomes in cancer patients is not well understood. Here, we show that visceral fat serves as an imaging biomarker for stratifying male/female survival differences. We demonstrated that the relative visceral fat area was significantly higher in males compared to females. However, female overall survival was uniquely stratified by visceral fat and poorer prognosis. We anticipate that this sex-based stratification may potentially identify survival outcomes in other forms of tumorigenesis. These results show visceral fat as an imaging biomarker that was more robust in stratifying overall survival in female patients with kidney cancer and glioblastoma.

Prevalence of colorectal cancer among African Americans adults under 45 years old with no genetic predisposition: Changing the guidelines.

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Background: Based on statistics by the American Cancer Society (ACS) and the National Cancer Institute’s SEER, colorectal cancer is the third most common cancer diagnosed in the United States. In 2020, the American Cancer Society’s estimates for the number of colorectal cancer cases in the United States to be 104,810 new cases of colon cancer and 43,340 new cases of rectal cancer.

Abstract: The ACS 2018 guideline for colorectal cancer recommends that average-risk adults start regular screening with either a high-sensitivity stool-based test or a structural visual exam at the age of 45 years or older. Those with positive results should then follow-up with timely colonoscopy. However, recent studies suggest a steady increase in colorectal cancer diagnosis and mortality in people under the age of 45. Among those diagnosed, African Americans present with more advanced stages and have a disproportionately higher rate of non-hereditary occurrence of colorectal cancer and lowest survival rate of any racial or ethnic group.

Methods: Data was obtained from National Cancer Institute’s SEER program, American Cancer Society, and SurveyMonkey. Previous research from the National Center for Biotechnology Information (NCBI) and PubMed will also be referenced.

Results and conclusions: Results and conclusions will be added once the data has been organized. Charts and graphs will be included.

Mussel-inspired Injectable Hydrogel Adhesive with Regenerative Properties using HIF-1α for Fetal Surgery

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Significance: Fetal surgery has drastically improved outcomes for fetuses with severe conditions like spina bifida, myelomeningocele, and diphtheritic hemias. Fetal surgery has the potential to significantly improve the health of many fetuses, but the surgical fetal membrane puncture remains risky, due to the potential of rupture leading to preterm birth. Here we investigate a new surgical adhesive: a mussel-inspired injectable sealant that is placed between the uterus and fetal membranes, stabilizing them prior to and following surgical membrane puncture. This adhesive has the potential to make fetal surgery safer and a much more routine procedure.

Innovation: In pursuit of achieving a surgical adhesive that maintains its efficacy in aqueous environments, we turn to the liquid protein adhesives secreted by mussels as inspiration. Mussels secrete protein adhesives for stabilization in turbulent environments, and the adhesion of these proteins is extremely robust and largely unaffected by the presence of an aqueous environment.

Research Proposal: In previous experiments, a mussel-inspired adhesive hydrogel was developed, formed upon mixing of an aqueous solution of multi-arm PEG end-functionalized with cysteine and with n-hydroxysuccinimide esters. This material has been shown to have suitable gelation kinetics, exhibit adhesion to wet tissue, and manifest cytoocompatibility with mammalian cells in-vitro and in in-vivo mouse drug delivery models. In-vivo fetoscopy studies were recently performed on rabbits, which gave encouraging insight into the potential of the surgical adhesive. Moving forwards, we are interested in incorporating HIF-1α, an oxygen-regulated protein involved in the transcription of many gene products including those responsible for regenerative processes, to induce angiogenesis, regeneration of the fetal membrane, and accordingly, increase the adhesive stability and efficacy in preventing rupture. HIF-1α has previously been shown to promote spontaneous regenerative healing in MRL mice. The goal is to embed our hydrogel adhesive with the HIF-1α in a structured manner so that it may be released into its local physiological environment upon swelling. In-vitro studies will be performed on the fetal membrane tissue and cells to characterize the response to the modified adhesive. Once evidence of angiogenesis and biocompatibility is confirmed, the in-vitro fetoscopy experiments will be repeated with the modified adhesive.

Pathways that Induce Replication Stress Induced Nucleophagy (ReSIN)

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Background: Tangled sister chromatids arise from replication stressors that result in the formation of micronuclei, a biomarker of genomic instability. It is documented that hydroxyurea, a ribonucleotide deoxyribonucleotide inhibitor, can induce micronuclei formation by depleting nucleotide pools which stall replication forks and tangle sister chromatids. The literature has shown autophagy markers a localize with these structures, suggesting autophagy could play a role in suppressing micronuclei formation. However, it is unclear whether this autophagy pathway is a metabolic response driven by depleted nucleotide pools or by stalled replication forks which activate the intra-S-phase checkpoint. To distinguish, we sought to induce replication stress by depleting proteins required for genome replication instead of depleting nucleotides.

Methods: In order to stall replication forks in nucleotide rich conditions, we introduced a galactose inducible promoter consistent with changes in cell proliferation rather than depleting nucleotides. The literature has shown replication stressors that result in the formation of micronuclei, a biomarker of genomic instability. It is documented that hydroxyurea, a ribonucleotide deoxyribonucleotide inhibitor, can induce micronuclei formation by depleting nucleotide pools which stall replication forks and tangle sister chromatids. The literature has shown autophagy markers a localize with these structures, suggesting autophagy could play a role in suppressing micronuclei formation. However, it is unclear whether this autophagy pathway is a metabolic response driven by depleted nucleotide pools or by stalled replication forks which activate the intra-S-phase checkpoint. To distinguish, we sought to induce replication stress by depleting proteins required for genome replication instead of depleting nucleotides.

Results: GalP-POL1 cells cultured in repressive conditions were arrested after 14hrs consistent with depletion of polymerase. The arrest was similar to treatment with hydroxyurea demonstrating that GalP-POL1 cells are able to engage the intra-S-phase checkpoint. Additionally, at 18hrs, phosphorylation assembly sites (PAS) marked by GFP-Atg8 increased while Atg39 and Atg40, two receptors involved in nucleophagy, showed an enrichment at the nuclear envelope. These changes are consistent with the changes observed in cells treated to deplete micronuclei.

Conclusions: These results are consistent with the replication stress induced by a reduction in polymerase or nucleotide pools, can activate an autophagy pathway. This finding further supports the hypothesis that intra-S-phase signaling is involved in replication stress induced nucleophagy.
Cardiac fibroblasts gene expression and their roles in reverse modeling
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Cardiac fibroblasts is a consequence of almost all myocardial injuries. In myocardial infarction (MI), what starts as protective scarring to prevent ventricular wall rupture becomes pathological remodeling with the accumulation of excess extracellular matrix (ECM) proteins. Previously, cardiac fibrosis was assumed irreversible; however, new evidence shows signs of “reverse” remodeling resulting in improved cardiac function. Recently, cardiac fibroblasts (CFs) and myofibroblasts (MFs) have emerged as potential therapeutic targets in preventing both acute and chronic cardiac fibrotic disease states. However, the mechanisms defining the role of MFs in longstanding fibrosis and reverse remodeling are still unknown. Through analysis of RNA sequencing data of various genes, we have identified several key genes that could potentially be unique cell types in fibroblasts or could possibly be a state of fibroblast.

Mechanism of YAP-dependent podocyte survival
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Within the kidneys, podocytes function to maintain the integrity of glomerular filtration by preventing proteins from entering the urine. Podocytes are terminally differentiated, have a limited capacity to regenerate and are the key target cells for injury across the spectrum of progressive proteinuric kidney disease including diabetic nephropathy and focal segmental glomerulosclerosis (FSGS). While the mechanism of podocyte injury and loss remains unclear, we have identified the Hippo pathway target Yes-associated protein (YAP), a potent oncogene, as a pro-survival mediator of podocyte homeostasis. Moreover, podocyte specific deletion of Yap promotes podocyte injury and death in mice and Yap expression is decreased in glomeruli of patients with FSGS. When Yap is silenced in cultured podocytes, they undergo morphological changes related to cell size and disrupted actin cytoskeletal integrity. RNA sequencing analysis and qPCR validation of Yap knockdown podocytes has identified Kcnn4, encoding the calcium-gated potassium channel KCa3.1, to be upregulated. KCa3.1 overexpression in podocytes replicated injury as seen with Yap silencing. Conversely, KCa3.1 inhibition with the use of TRAM-34 rescued the cytoskeletal changes in Yap silenced podocytes. IF staining has confirmed a decrease in focal adhesion of Yap knockdown podocytes and this phenotype is rescued with the use of TRAM-34. These findings along with using complementary molecular and in vivo studies have the potential to advance the quest for badly needed therapeutic options for glomerular disease patients.

Impact of Low-Level Laser Therapy (LLLT) on the biological behavior of human ligament fibroblasts
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Background: The anterior cruciate ligament injury is one of the most prevalent incidences of osteoarticular issues around in the world. Low-Level Laser Therapy (LLLT) was proposed as a promising therapeutic approach that accelerates the tissue reparative process mediated by biostimulation effects. Fibroblasts are responsible for the healing process. LLLT enhances reparative capacity in these cells. Nevertheless, in clinical practice there is a lack of evidence that supports its use, this limits its application in rehabilitation treatments.
Methods: The units of analysis were the human isolated fibroblasts of the anterior cruciate ligament, obtained from a primary explant to carry out the experimental model. We used a therapeutic laser Chattanooga Intelect® Mobile (850 nm) to irradiate cells for three days each 24 hours. We designed two treatment groups at 1.0 and 5.0 J/cm², and a control group (0 J/cm²). To determine cell proliferation after treatment, we performed a colorimetric analysis. We used the abcam® MTS Assay Kit to detect viable cells 24 hours after exposition to LLLT. We measured the absorbance at 490 nm by the Cytation 3® Cell Imaging Multi-Mode Reader by BioTek instruments, Inc.
Results: In the non-parametric analysis using the Kruskal-Wallis test of proliferation data, we obtained a p-value of 0.089. We concluded that there were no significant differences between the groups in terms of the cell number. Moreover, we compared the mean proliferation between groups. The treated Group at 1.0 J/cm² had a 23% higher cell proliferation than the Control Group, 41% higher compared to treated Group 5.0 J/cm², and the Control Group had a 19% higher cell proliferation than the treated Group 5.0 J/cm².
Conclusions: The findings of this study demonstrated that the LLLT at 1.0 and 5.0 J/cm² on ligament fibroblasts generates no significant differences in cell proliferation. However, it is essential to carry out more experiments about cell metabolism and explain the outcomes of metabolic vies to obtain plausible data regarding this variable. We also suggest future work to evaluate other biological functions like migration and expression of extracellular proteins related to the ligament healing process.

Alzheimer’s Disease Effect on Human Neuron Axon Initial Segment
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Axonal death has been reported in Alzheimer’s Disease (AD) mouse models, yet there has been very little data on AD human neurons. One of the major hypotheses in AD research is that the accumulation of an insoluble neurotoxin, amyloid β-protein (Aβ), in the brain is the main influencer for AD. The Axon Initial Segment (AIS), is a compartment near the base of the axon, which generates and shapes the action potential using the voltage-gated potassium channels (Kv) and voltage-gated sodium channels (Na+) which are concentrated at the AIS by anchoring to the microtubules using a protein called Ankyrin G (Pan et al., 2006; Cooper, 2011; Xu and Cooper, 2015; Meza et al., 2017). Previous studies suggested that the Ankyrin G levels are downregulated in AD transgenic mice models (Sun et al., 2014). Therefore, we hypothesized that human neurons treated with oligomeric Aβ would cause a downregulation in Ankyrin G which would cause the AIS to be smaller, farther from the soma, and after neuronal responsiveness. One of the models used in AD research is the Swedish mutation of APP (APPsw), which has been known to increase cleavage of the amyloid precursor protein (APP) to increase secretion of Aβ. We have constructed a lentiviral vector expressing human APPsw for the secretion of oligomeric Aβ by Human Embryonic Kidney (HEK) cells. Once we have mature human induced pluripotent stem cell (iPSC) neurons, we use conditioned medium from the HEK cells to treat the neurons for 2 days. This is followed by immunofluorescence staining to tag the AIS and the neuron processes using the Ankyrin G and the Beta-III Tubulin antibodies. After the neurons are stained, imaging is done by confocal microscope. These images are then analyzed using image analysis software (Fiji) for axonal morphology and the distance from the soma. The results show significant differences in the AIS between the APPsw treatment and Wild Type. These results are significant as this is the first observed effect of Aβ on human neurons. This information suggests that AD utilizes Aβ to decrease neuronal survivability.
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**Elucidation of ADAMTS10 in Skeletal Muscle Differentiation in C2C12 Myoblast Cells**

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Several connective tissue disorders (CTDs) are caused by mutations in genes that encode extracellular matrix (ECM) proteins. Arometic disopasins represent a group of rare CTDs that share musculoskeletal symptoms, i.e. short stature, short limbs & digits, pseudosyndactylia, and thick skin and derf in the involvement of other organ systems. Arometic disopasins can be caused by mutations in FBN1, ADAMTS10, ADAMTS17, ADAMTS18, LTBP2, LBTP3, SMAD.

The ECM protein under investigation is ADAMTS10, a protease that cleaves fibrillin 1 and 2 and promotes the deposition of fibrillin-1 into the ECM. Mutations in ADAMTS10 have been found to cause an arometic disopasins, Wiskott-Aldrich syndrome (WAS). In addition to the characteristic skeletal muscle presentations, WASMs individuals develop dislocation of the eye lens, cataract formation, and various cardiac abnormalities.

Skeletal muscle cell differentiation proceeds embryonically from myoblasts to myotubes to myofibres formation. In a pilot study, the differentiation of C2C12 myoblasts cells into myotubes was used to determine if ADAMTS10 played a role in myogenesis in vitro and if it could explain the phamorphic assembly observed in WAMS. The inhibition of IFP-C concluded that ADAMTS10 was induced during myofibres formation. Additionally, the overexpression of recombinant ADAMTS10 produced increased myofibres formation and growth, while ADAMTS10 knockdown prevented myofibres formation.

Now knowing that ADAMTS10 is expressed in C2C12-derived myotubes, we will first confirm the results from the pilot study by carefully analyzing the ADAMTS10 overexpression and knockdown C2C12 cell phenotype. We will then identify the signaling pathways and ECM alterations that are dysregulated upon knockdown of ADAMTS10 focusing on Wnt and TGFbeta signaling, based on literature and related published data. However, we will also perform an unbiased RNAseq approach to identify other genes that are dysregulated in the absence of ADAMTS10. The characterization of these pathways will help us understand the role of ADAMTS10 in myogenesis and identify potential therapies for CTDs.

With these proposed experiments, we anticipate to define the role of ADAMTS10 in the formation of skeletal muscle and identify molecular ECM pathways that are dysregulated in the absence of ADAMTS10.

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**The Role of Protein in Shunt Flow and Obstruction**

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Background: Shunts are neurosurgical devices used in the treatment of hydrocephalus, but 85% of shunts fail within 10 years after implantation. Our benchtop gravity-flow system used commonly implanted valves, each equipped with antisiphon devices (ASDs).

Methods: Within an incubator set to 37°C, saline with or without protein was filled in a reservoir of a gravity-driven apparatus that drove flow continuously via 6 catheters through valves and into their respective collecting flasks. The collecting flask heights were alternated between 28.5 cm and 2 cm below the valves for 14 and 8 hours in upright and supine trials, respectively, to mimic a patient’s daily positional changes. Valves were tested in 3 saline studies: protein-free, 1 g/L protein, and 5 g/L protein for up to 30 days.

Results: When comparing the averages of all the trials of protein-free saline and low-protein saline, valve type A increased its supine position flow rates from 0.06 to 3.24 mL/hr (p = 0.03 E-8) and in the upright position increased their flow rates from 21.23 to 21.62 mL/hr (p = 0.34). Similarly, in valve type B, protein increased its supine flow rates from 0.06 mL/hr to 0.23 mL/hr (p = 0.04) and in the upright position the flow rates went from 20.25 mL/hr to 20.13 mL/hr (p = 0.86). When tested with high-protein saline, both valve types became fully obstructed after 12 days, with flow rates at 0 mL/hr for the rest of the trial.

Conclusions: The role of protein on flow rate throughout the system could be due to the protein acting like a detergent, possibly by decreasing surface tension and resistance, therefore increasing flow rates. We hypothesize the decrease in flow rates to 0 mL/hr in the high protein trials may be due to the protein concentration being too high, causing the protein to precipitate out of solution and aggregate in the system. The properties of protein through this system have a potential impact both in understanding the molecular fluid dynamics of CSF and in clinical testing of shunt valves and systems.
Abstracts

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Applying biomedical informatics to establish the relationship between obesity and liver ischemia/reperfusion injury
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Liver ischemia/reperfusion injury (IRI) occurs in clinical situations like transplantation. Obesity with hepatic fat accumula-
tion (steatosis) exaggerates risk for liver IRI via inflammatory mediators, like tumor necrosis factor-alpha (TNF-a). Although
steatotic males have exaggerated liver IRI, it is not as well known whether this also occurs in females. Obese melanocor-
tin-4 receptor (MCR4)-deficient or lean wild-type (WT) male and female rats were subjected to 45° of 70% warm liver
ischemia with plasma and liver tissue harvested at 24 hours of reperfusion or Sham surgeries. EchocMRI revealed that liver
fat was greater (P<0.05) in obese (7 ± 1%) versus lean rats (2 ± 1%) in primarily the female models. After receiving and
analyzing data on both males and females regarding liver IRI, the hypothesis that biomedical informatics and mission
learning techniques can be used to establish the relationship between obesity and liver IRI in obese male and female rats was
developed. This mission learning technique was used to classify, analyze, and identify the phases of liver IRI.
Additionally, this process was executed to create a model which implemented algorithms to facilitate input, middle, and
outer software. This software was integrated with tools on a website to both manually and automatically determine the
severity of liver IRI (early or late onset) based on the data inputted by any stakeholder. The results are then sent to his/her
preferred email and/or physical addresses. In conclusion, a link was created which takes a user to which website
establishes the relationship between the stages of liver ischemia/reperfusion injury and the origin of obesity.

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Irene Antony

Background: Autism spectrum disorder (ASD) impacts 1:40 American children and 1:160 children worldwide. Due to its high
societal and individual costs, autism research must be prioritized in the global health sphere. A largely unexplored area
how mutations in regions of the genome that do not encode proteins play a role in disease pathology. Although
gene-wide association studies have identified hundreds of single nucleotide polymorphisms (SNPs) associated with
ASD, it is difficult to identify which SNPs functionally contribute to disease. We hypothesize that many non-coding ASD risk
variants are in enhancer elements and after expression of genes under their control by disrupting transcription factor binding.

Methods: To test this model, we analyzed de novo SNPs in 2,671 individuals with autism and their unaffected siblings. We
prioritized putative causal mutations by integrating ASD-specific SNPs with functional genomic data from fetal brain tissue
and induced pluripotent stem cell (iPSC)-derived neurons. These datasets included chromatin enrichment for the histone
modification H3K27ac, which marks active enhancers, and accessible chromatin, as defined by ATAC-seq.

Results and Conclusions: When compared to sibling controls, autistic probands had more SNPs in regions with H3K27 acetylation and for SNPs found in known enhancers. Critically, the greatest over-representation of
SNPs in ASD probands occurs in syndromic ASD genes, hinting that many of these SNPs contribute directly to ASD. Our
preliminary data thus supports a model in which functional de novo noncoding variants perturbs enhancer activity and thereby
after transcriptional regulation of ASD liability-linked genes. To test this model, we will next use a Massively Parallel Reporter Profiling (MPRP) to define quantitative effects of these putative ASD risk alleles on enhancer activity and down-
stream gene expression. This high-throughput approach will identify non-coding SNPs that lead to autism, advancing our
understanding of how altered gene regulation disrupts neurodevelopmental gene regulatory networks in ASD. We also
expect our experimental approach to be applicable to identifying and characterizing noncoding mutations that contribute
to other human diseases and disorders.

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Meta-analyses of sex differences in the human placenta transcriptome
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Introduction: The placenta is a crucial organ involved in fetal growth and development that can ultimately program adult life
disease risk. The sex of the fetus has been associated with fetal growth, responses to adverse intrauterine environments and
placental gene expression. Nevertheless, there is still limited information on the association of fetal sex on the transcriptome
in the human placenta.

Methods: We performed a meta-analyses of sex differences in the placenta transcriptome including 594 normal term
placentas from 10 microarray and 2 RNA-seq studies. To test for differential gene expression by sex, we used moderated
1-tests (limma R package) for the microarray studies and negative binomial generalized linear models and Wald tests on the
RNA-seq counts (DESeq2 R package). For the meta-analyses, we used the weighted Stouffer’s method to combine per gene
p-values across results from each study.

Results: Of a total of 7861 genes that were meta-analyzed across all the studies, 127 genes were significant at a false
discovery rate (FDR) of 5%. Amongst these, 54 genes were differentially expressed in consistent in direction between male
and female placentas across platforms. Out of these 54 sex-biased genes, 33 (61 %) located in autosomes and 21 were in
the X chromosome. 48% of X-linked sex-biased genes showed higher expression in females and have been previously
shown to escape X inactivation in other tissues. Of these, the top differentially expressed gene was KDM6A an important
epigenetic regulator that acts as histone demethylase.

Conclusion: Sex-biased gene expression patterns are common across multiple genomic regions in the human placenta.
Identifying these genes in normal term placentas is important to understand sexual dimorphism in placental and fetal
development and could help explain sex-differences described in adverse pregnancy outcomes.

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Generating a double knockout mouse model for Lesch-Nyhan Disease
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Lesch-Nyhan Disease (LND) is a rare X-linked disorder caused by mutations in the HPRT1 gene. The HPRT1 gene produc-
es hypoxanthine phosphoribosyltransferase 1, an enzyme that allows cells to recycle purines, within the purine salvage
pathway. Lesch-Nyhan Disease (LND) has been studied via the use of tissue culture and animal models. However, results obtained
in vitro are not representative of what may occur within the same cells in vivo. Although some animal models displayed similar
metabolic deficits, they failed to display any neurobehavioral phenotype. Other animal models were incapable of displaying
self-injury, without the administration of amphetamine or a dopamine precursor. There does not exist, to date, a model that
displays all the clinical features observed in LND; this leads to the belief that the animal models fail to duplicate the
complete biochemical environment within the human brain. Indeed, mice have an extra enzyme that helps with uric acid
degradation, downstream of HPRT: Urate oxidase (UOX). This enzyme is not functional in humans. We hypothesized that
creating a double knockout mouse, for both the HPRT1 and UOX gene, would generate a biochemically–relevant mouse
model for LND. To achieve this, a breeding scheme was implemented, which included HPRT1 and UOX deficient mice and wild
type mice. The phenotype characterization of mice was based on neurobehavioral testing. Genotyping, data, biochem-
ical and neurochemical analyses were also performed. Should the double knockout mouse prove a success, the lab will
continue with their research and apply for a Research Project Grant (R01) application.
A Pathway-based Genetic Analysis of iPSC-derived Cardiomyocytes following Anthracycline Exposure

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Doxorubicin is an anticancer drug with known cardotoxic effects that can occur several weeks to several years after exposure. Previous studies have been conducted primarily in non-human model systems, therefore with the availability of human induced pluripotent stem cell (iPSC) derived cardiomyocytes the mechanisms of anthracycline induced cardotoxicity can be further explored. iPSC-derived cardiomyocytes from three individual donors were cultured and treated with various doses of doxorubicin. Total RNA was isolated and transcriptome sequencing was performed. From 41,588 transcripts, a list of 105 genes were selected based on their function in cardiac muscle contraction, cardiomyopathy and doxorubicin function and metabolism pathways. Selected genes were further analyzed using bioinformatics software packages: Broad Institute Morpheus, DAVID functional annotation and ConsensusPathDB. In response to doxorubicin, there was a significant fold change in the expression of 43 genes, 14 of which were upregulated and 29 that were downregulated. Doxorubicin was found to upregulate genes critical to cardiac cellular stress response while downregulating genes having cardiac function and aiding in cellular toxic response. Similar studies further support these results. In response to high stress the cardiac system will overexert itself through muscle contraction and mitochondrial respiration in order to quickly metabolize doxorubicin. A variety of genes having cardiac function will be lost due to the toxicity of increasing doxorubicin dosage.

Dielectric characterization of permittivity, conductivity and dielectric loss factors of fetal porcine tissues by impedance spectroscopy

Wilfredo Farfanis Coronado*, Emi J. Fernandez Lozada*

“The Polytechnic University of Puerto Rico, Biomedical Engineering Department, San Juan Puerto Rico Abstract- This investigation was performed to determine whether the mean of fetal porcine tissues analyzed by impedance spectroscopy for their permittivity, conductivity, and dielectric loss properties adhered to the idealized plots. The statistical process was with the purpose of finding a correlation that established the values as normal and true. For this study 2 samples of 3 types of tissues were obtained, a bone, muscle, and skin sample. Both samples belonged to a pig fetus, preserved in formaldehyde an unknown number of days. They were all taken from the ‘leg’ by using a sterilized dissection kit, samples were cleaned and placed in individual containers with a 0.9% NaCl saline solution. The parameters were measured with Impedance Analyzer (U4980A) with a Dielectric Test Fixture (16419B). This equipment works at a frequency range of 20 Hz to 20 MHz; allowing to study how the chemical properties of porcine tissues interact with voltages and currents. In total, 5 tests were performed per sample per tissue. To comply with the statistical approach taken for this investigation, the standard of these 5 tests was calculated for each of them. Higher beta elevations were observed in all conductivity plots along with a sharp decrease affecting Beta in all the permittivities. It’s proposed that this is just the normal electrical behavior of fetus samples. In the end, it was observed that though similar, these fetus tissue samples did not adhere to the idealized plots they were meant to follow, which meant the hypothesis was not supported.

A systematic review of the management of pediatric refractory immune thrombocytopenia (ITP)

Layan Ibrahim

Immune thrombocytopenia (ITP) is a rare cause of thrombocytopenia in children where the immune system destroys platelets which are essential for normal blood clotting. Treatment of pediatric ITP focuses on the termination and/or prevention of bleeding, irrespective of platelet count. Refractory ITP is a condition that is rarely seen in the pediatric population because of the relative avoidance of splenectomy by pediatric practitioners due to this procedure’s potential long-term complications. Defining refractory ITP and identifying optimal management of pediatric patients with refractory ITP is important to understand as this subset of patients may be at increased risk for complications, increased bleeding, and requiring additional first and second line treatments. Due to the gap in knowledge of treatment options for pediatric refractory ITP, we aim to conduct a systematic review of refractory pediatric ITP definitions and management. Three different databases were searched using the Ovid interface. Searches were limited to English, French, German, Polish, or Spanish languages and to the publication year 2000 or more recent. Editorials, letters, and review articles were excluded. Searches were designed and conducted by librarian experienced in systematic reviews using a method designed to optimize term selection. After duplicate records were removed online, records retrieved by the electronic search were downloaded and imported into a Reference Manager database, and uploaded to InsightScope. Records were appraised against the inclusion criteria using a three step method (initial review for inclusion based on defined criteria, abstract review with arbitration, final inclusion and review).

2148 records were identified through the initial database search, resulting in 1471 records for screening. Abstracts were screened by two reviewers and disagreements were adjudicated by three reviewers. The final list of articles was reviewed and summarized for key findings including the definition of refractory pediatric ITP recommended workup, and treatment. Preliminary analysis suggests that <20% of the original articles will be included in the final analysis and data abstraction. Our systematic review demonstrated that there is a paucity of data to guide treatment in children with refractory ITP, highlighting the need for well-designed studies to answer these important questions for this vulnerable patient population.
Abstracts

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Probing the role of apoptosis in zika infection to find points to block replication of virus
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Although the flavivirus Zika (ZIKV) causes microcephaly and Guillain-Barré syndrome, unlike other flaviviruses it is not particularly lethal to cultured cells. We investigated the role of proapoptotic genes during early zika infection. Reproduction of ZIKV was measured by three criteria: PCR of viral RNA, plaque assay for viable virus, and production of virus envelope protein (E) using Mouse Embryonic Fibroblasts (MEFs) knockout for the proapoptotic genes Sept4, ART5, Bax, Bak and Bok. All the knockouts translated more than E as determined by immunofluorescence. Bok-/ cells could not release mature viruses, indicating the requirement of BOK for maturation of the virus. Bok promotes apoptosis in response to ER stress. We therefore addressed role of PERK in zika infection using PERK KO MEFs. PERK proved necessary for zika production, suggesting that zika induces ER stress, which also leads to increase in lipid droplets, necessary for formation of viral envelope. Accordingly, we found that ZIKV-infected MDCK cells produce more lipid droplets. Atorvastatin, an HMG-CoA reductase inhibitor, blocks the synthesis of cholesterol; we found that atorvastatin downregulates Zika viral transcription, translation, and formation of mature progeny. We therefore suggest that host lipids may be a good potential target for therapeutic use against ZIKV. In our future experiments, we will study the connection between PERK pathway and lipid homeostasis. We plan to further explore lipophagy and beta-oxidation of free fatty acids, as are seen in Dengue. Our hypothesis as to the mechanism will be presented in our poster. Our research will help elucidate the mechanism of ZIKV replication and pathogenesis, which we can then use to limit viral replication and cell lethality. These studies should reveal possible targets for therapeutic agents. Supported by NIH grant NIH # 2T34GM070387 to Dr. Zahra Zakeri.

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Gene Transfer Agent Presence in Diverse Orders of α-proteobacteria
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Gene transfer agents (GTAs) are particles that resemble viruses that only carry small pieces of the producing cell's genome. Contrary to a typical virus, GTAs function only in genomic DNA transfer between cells, allowing another method of horizontal gene transfer within bacteria to surge. Moreover, the most studied GTA is that of Rhodobacter capsulatus, and it is also thought that these particles may carry the elements of the α-proteobacterial class when their genomes are highly conserved. Rhodobacter capsulatus GTA-like particles (RcGTA). Analysis of the RcGTA "genome" reveals that the GafA protein is crucial for gene expression, as it can be the specific initiator of RcGTA production. Also, endolysin and holin have been found to be crucial for RcGTA release. Here we show a comparison of the genomes of bacteria from α-proteobacterial orders, determine which of these contained RcGTA-like homologs, and fully understand what elements are necessary for optimal GTA activity. We hypothesized that GTA clusters from these orders contain the previously mentioned elements that regulate GTA activity. Analysis of the various genomes was realized using the Integrated Microbial Genomes and Microbiomes database and BLAST searches. We found that many of the genomes ranging from different orders within α-proteobacteria contained RcGTA homologs, although their function was not clearly stated. Also, endolysin/holin homologs were found to be absent on bacteria outside Rhodobacteriales, suggesting an alternate mechanism for release which could be evaluated in future research. Our findings contribute to the fact that GTA clusters from α-proteobacterial orders contain elements that facilitate horizontal gene transfer in bacteria.

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Comparing the Presence of Mycobacteriophage in the Soil and Sediment From the Eastern Branch of the Elizabeth River
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The aim of the current study is to isolate bacteriophage from the riverbank of the Elizabeth River and compare it to sediment collected from the bottom of the riverbed. A bacteriophage is a virus that infects bacteria. Mycobacteriophage, which are specific viruses that infect the Mycobacterium genus, will be the focus of this work. The specific bacterial host used in this study is Mycobacterium smegmatis mc2155. The exponential exacerbation of antibiotic resistance globally, has increased the urgency for alternative treatments of bacterial infections due to drug resistance. Bacteriophage can be used as an alternative to antibiotics to treat bacterial infections and is known as phage therapy. In this study, phage presence is used to link the phage diversity to the health of the Elizabeth River. Preliminary studies of soil samples collected from the bank of the river produced more phage compared to sediment samples collected at different depths along the riverbed indicating that there may be different environmental microcosms in the intertidal region. The study investigates the phage presence and diversity of samples taken from the bank of the Eastern Branch of the Elizabeth River, Norfolk, VA. Analyzing the tidal flow when samples were collected, will unveil the effects of phage presence in the soil and the sediment. In an initial experiment, the Mycobacteriophage were isolated using a direct isolation method. However, this direct method did not yield any bacteriophage. The same samples were then used in a different method to isolate phage. This alternative method known as the enrichment protocol requires the addition of the host bacteria M. smegmatis to the sample to encourage specific Mycobacteriophage to be propagated. The enrichment method yielded phage specific to M. smegmatis from soil and sediment. Then, the following methods were implemented: pick-a-plaque, serial dilutions, and spot-testing to isolate and purify individual plaques. This study revealed that dilutions could also alleviate contaminants from the phage lysate. Future work is planned to isolate the DNA of the purified phage. Then, the phage genome will be sequenced and analyzed to determine if these phage are novel or similar to other phage genomes.

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Neuropeptidergic regulation of PTSD-like traumatic stress and metabolism via the locus coeruleus
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Clinical observations have shown that patients with psychiatric disorders, like post-traumatic stress disorder (PTSD), may develop metabolic syndromes such as Type II Diabetes and a high body fat index in their lifetime. Empirical evidence from both systems neuroscience and endocrinology have suggested a mechanistic link between psychological stress and metabolism. Our laboratory seeks to further characterize the relationship between traumatic stress and metabolism by investigating Pituitary Adenylate Cyclase-Activating Peptide (PACAP) and its receptor PAC1 using a transgenic mouse line with floxed PAC1 receptors and employing a range of techniques, including viral-mediated knockdown, the stress-enhanced fear learning (SEFL) behavioral model of traumatic stress, immunohistochemistry, in situ hybridization, and qRT-PCR. The neuropeptide PACAP and its receptor PAC1 have been identified to play a critical role in metabolism and stress regulation. Previous findings in the laboratory have shown that PACAP innervates the brown adipose tissue (BAT), a metabolically active type of fat tissue that converts food substrates into heat energy. PACAP receptor PAC1 is also abundant in BAT. These two findings suggest a role for PACAP and PAC1 in BAT thermogenic regulation, a key aspect of energy metabolism. Upon knockdown of PAC1 receptors in BAT, expression of UCP1 (uncoupling protein 1), a critical BAT-specific mitochondrial protein involved in cellular respiration, was increased. We also found that the locus coeruleus (LC), a major source of noradrenaline (NE) in the forebrain, is rich in PAC1 expression. Thus, we investigated the role of PAC1 in the LC in traumatic stress modulation and metabolism via the sympathetic pathway, which innervates the BAT and various brain areas. We have observed that viral-mediated knockdown of PAC1 receptors in the LC led to enhanced fear expression in SEFL, decreased fat mass and enhanced expression of UCP1 acutely. After a chronic time-point, fear expression in SEFL was still enhanced, but fat mass increased. Taken together, our results indicate that PACAP/PAC1 is an important neuropeptidergic system in the sympathetic node that links the brain and the body to regulate traumatic stress and associated metabolic changes.
Synchronized Calcium Oscillations among Astrocytes

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Deep brain stimulation (DBS) is a therapy where regions of the brain are hit with high-frequency electrical stimulation (HFS). This therapy can treat various diseases ranging from epilepsy to Parkinson’s disease. How DBS works is still unclear. In the past, it has been studied that neurons are stimulated under HFS. Astrocytes, support cells in the brain, are not electrically stimulated like neurons but might be excited by voltage-gated calcium channels (VGCC) which could be activated during HFS. In this study, a protocol will be improved where astrocytic calcium oscillations will be measured from ex vivo acute cortical mouse brain slices. HFS was delivered at 125 Hz, with asymmetric biphasic waveform using the Rhode &amp; Schwarz Tidal Bipolar Electrode for acute applications. Calcium imaging would come from a confocal microscope while fluorescent traces of calcium oscillations can be analyzed in MATLAB to look for synchronized elevations during the stimulation. We hypothesize that if there are synchronized calcium elevations in astrocytes when HFS is injected then astrocytes are important to the mechanism of DBS.
Effect of NMDAR Knockout on Developmental Neurogenesis in Zebrafish

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N-methyl-D-aspartate receptors (NMDARs) are a sub-group of ionotropic glutamate receptors (iGLuRs), responsible for most of the calcium-based excitatory signaling in the brain. NMDARs are widely distributed throughout the CNS and play pivotal roles in both development and adult neurological functioning. During development, NMDARs are ascribed essential roles in depolarization of progenitor cells and neuroblasts, cellular migration, neuronal differentiation and maturation, axonal pathfinding, synaptogenesis, synapse maintenance, programmed cell death, and circuit development. Nevertheless, little work has been done on the specific role of NMDARs in developmental neurogenesis. In our work, we have demonstrated that NMDAR knockout causes dysregulation of developmental neurogenesis resulting in an overpopulation of neurons in the forebrain of zebrafish larvae. Many neurodevelopmental diseases, such as autism spectrum disorder and epilepsy, and neuropsychiatric diseases, such as schizophrenia, have been associated with NMDAR mutations and dysfunction and have their roots in neurodevelopment. Therefore, elucidating the roles of NMDARs in developmental neurogenesis may lead to novel therapeutics to prevent or mitigate these disorders.

Our aim was to assess the initial proliferation of neurons in the developing NMDAR mutant zebrafish. First, the zebrafish were crossed in order to retrieve wildtype, and grin1 mutant clutches. Embryos were harvested at the desired timepoints, preserved in neutral buffered formalin, mounted in agarose blocks, and processed for paraffin sectioning. The embryos were sliced at a depth of 5 microns, slide mounted and then Nissl stained to label neurons. This allowed for quantification of the number of neurons in each brain region.

We used Fiji software to measure cell density in coronal sections from 5 dpf larvae and observed an overpopulation of neurons, in all regions of the forebrain, in grin1 double mutants as compared to wildtypes, despite the same overall distribution of cells. This overpopulation is seen in proliferative zones as well as all other regions and cell types examined thus far. These data suggest that NMDA transmission is required for proper neurogenesis and NMDAR dysfunction may produce alterations in neuronal populations in patients with NMDAR mutations.
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In loving memory of Corin Humphrey

Investigating the effects of estrogen and progesterone on hyperexcitability of medial entorhinal cortex layer II stellate cells in a mouse model of temporal lobe epilepsy

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Often in epilepsy seizure frequency and susceptibility fluctuate alongside hormonal state. Previous research has suggested that estrogen is proconvulsive while progesterone is anticonvulsive. We propose to examine the effect of hormones on seizure generation in light of the dentate gate theory of temporal lobe epilepsy which posits that, in healthy mice, the dentate gyrus plays a key protective role in filtering excitatory signals from the entorhinal cortex before they reach the hippocampus. In temporal lobe epilepsy, medial entorhinal cortex layer II stellate cells become hyperexcitable and, as they are the primary excitatory inputs to the dentate gyrus, are thought to be particularly important in seizure generation. Utilizing whole cell slice electrophysiology, we recapitulated the general finding that medial entorhinal cortex layer II stellate cells are hyperexcitable in epilepsy. Next we propose to investigate the effect of acute bath application of estrogen and progesterone on excitability of medial entorhinal cortex layer II stellate cells and the dentate gyrus. Examining the effect of hormones on the dentate gate circuit will help reveal how hormonal state may impact seizure susceptibility in all people with epilepsy, especially people who are postmenopausal, trans, entering puberty, or on birth control.

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Brain-Wide Projection Analysis to Dissect Circuitry Mechanism Underlying DDX3X-Mediated Intellectual Disability and Autism Spectrum Disorder

Natalya Krutovska

DDX3X is an X-linked, high-confidence risk gene accounting for up to 2% of unexplained intellectual disability (ID) cases, predominantly affecting females. Affected individuals can also present with autism spectrum disorder (ASD), hypotonia, movement disorders, and brain anomalies. Understanding how DDX3X mutations impact brain development and circuitry formation, and thus postnatal behaviors, offers new opportunities for uncovering the roots of ID and the ASD gender bias. Previous studies indicate Ddx3x controls the development of cortical projection neurons (PN), whose associated circuitries subserve diverse brain functions. This study aims to investigate cortical projection neuron morphologies and their development in a Ddx3x-deficient mouse model. So far, we have validated a pAAV-CAG-GFP construct to retrogradely label distinct PN populations and titrated a proper dosage for individual neuron morphology analysis. With whole-mount clearing and imaging techniques, we will map GFP+ PN distributions and profile their detailed somatodendritic morphologies, spine density, as well as brain-wide axonal projection patterns in both Ddx3x mutant and control mice. Immunostaining with additional neuronal markers will further aid in understanding overall brain cytoarchitectural differences. Our research seeks to elucidate the molecular, cellular, and developmental functions of Ddx3x to help understand the neurodevelopmental trajectory in DDX3X syndrome goes awry to help develop novel therapeutics.

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BRAIN AMINO ACID METABOLISM IS ALTERED UNDER GLYPHOSATE-BASED HERBICIDE EXPOSURE

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Background: Glyphosate-based herbicides (GBHs) are the most widely used pesticides. Studies have shown that glyphosate exposure may cause immediate and late risks to the brain. GBH-induced neurotoxic effects are potential risk factors for developing neurodegenerative diseases, including Alzheimer’s disease (AD). Whether or not they contribute to pathogenesis and/or progression of AD needs to be better characterized. Here, we aimed at evaluating central and peripheral effects of GBH acute exposure.

Methods: GBH was administered orally (400 mg/kg) to male Wistar rats (90 day-old). Amino acid (AA) and albumin levels in cerebrospinal fluid (CSF) were assessed by High-Performance Liquid Chromatography at 3, 24, and 48 h after administration, as well as in rats that did not receive GBH (control). Serum urea was evaluated by colorimetric assay. L-[3H]Glutamate uptake and AA release were measured in slices of parietal cortex, hippocampus, and striatum tissue of rats 3 h after GBH exposure.

Results: CSF levels of excitatory AA aspartate and glutamate, as well as ornithine, were elevated 3 h after GBH exposure (ornithine levels were 28.2-fold higher than the control condition). Accordingly, high levels of ornithine were released from slices of all brain regions at 3 h (4.6-fold change). We did not observe changes in CSF albumin levels, serum urea, and L-[3H]Glutamate uptake.

Conclusions: We hypothesize that GBH affects brain AA metabolism regardless of its effects in the periphery since we observed changes in CSF AA levels independently of BBB disruption. No changes in serum urea were observed, which points to a normal function of the urea cycle and a higher production of ornithine from brain cells. This suggests a potential unbalance in excitatory AA and arginine downstream metabolism, which also seems to be altered in AD patients’ brains. We intend to further characterize GBH exposure effects to elucidate whether these mechanisms may contribute to neurodegeneration.
NMDAR mutant zebrats as a model for neuronal proliferation in the neuregeneurogenic brain

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Neurogenesis is characterized by the death of neurons. Humans have a limited capacity for adult neurogenesis and brain repair. Other vertebrates, including zebrats, exhibit pervasive adult neurogenesis and the ability to renew and repair the brain. This process of complementary neurogenesis recapitulates the molecular mechanisms of developmental neurogenesis. Therefore, elucidating mechanisms of developmental neurogenesis is critical to uncovering new therapeutic approaches for neurodevelopmental diseases.

Excitotoxicity due to overreactivity of N-methyl-D-aspartate receptors (NMDARs) has been implicated in neurodevelopment. Nevertheless, NMDARs play pivotal roles in the initial architecture of the brain, promote cell survival, facilitate synapse modification and excitatory brain function, and are central to memory and neuroplasticity. Understanding the underlying mechanisms of NMDA transmission in the brain during neurodevelopment and aging, and how their perturbation contributes to diseases, is crucial when studying neurodevelopmental diseases such as Alzheimer’s. In order to study NMDARs, we created loss-of-function mutations in the zebrats grin1a and grin1b genes, which code for the obligate subunit of the receptor, using CRISPR-Cas9 genome editing technique. We cross adult zebrats harboring mutations in grin1a and grin1b to generate clutches containing double mutant embryos. At 5 days post fertilization (dpf), embryos are harvested and fixed in formalin. They are stabilized in agarose molds and paraffin infused. They are coronally sectioned into 5 micron slices, placed on a slides, and Nissl stained, which allows for neuronal quantification and brain morphometric analysis. We quantify neurons at representative forebrain levels and calculate the length, width, and total area of the brain, which may potentially uncover a mechanism whereby neurogenesis is promoted.

Screening for Neurodevelopmental and Behavioral Concerns in Infants and Toddlers with Tuberous Sclerosis Complex (TSC)

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Tuberous Sclerosis Complex (TSC) is a multi-system autosomal dominant genetic disorder characterized by mutations to the TSC1 and TSC2 genes. Those with TSC are affected by a range of behavioral, psychiatric, intellectual, academic, neurophysiological, and psychosocial difficulties. Up to 60% of children with TSC will be diagnosed with Autism Spectrum Disorder (ASD), and up to 90% will experience Global Developmental Delay. Due to a significant treatment gap for those affected a TSC-Associated Neuropsychiatric Disorders (TAND), the TAND Checklist was developed to screen individuals with TSC for neuropsychiatric disorders and provide a tool that describes and evaluates the different levels of TAND. While the TAND checklist has been used in many studies for children and adults, there are limited data on TAND in infants and toddlers with TSC. Within the context of an early intervention trial in infants with TSC called JASPER Early Intervention for TSC (JETS), we evaluated neurodevelopmental and neuropsychiatric symptoms using the TAND checklist, focusing on infants ages 12-42 months. TAND checklist responses were collected from the parents of 39 infants and toddlers aged 13 - 41 months (m = 23.4 months), that were recruited at the UCLA Center for Autism Research and Treatment or the Boston Children’s Hospital Laboratories of Cognitive Neuroscience. Participants included 21 females and 18 males, with 26 participants in between 12-24 months, and 13 participants 25 months or older. Responses to the TAND-Checklist were populated into an Excel spreadsheet to allow for analysis. Response options were primarily ‘yes’ or ‘no’ and open-ended questions. Across all surveys, a running count was performed for each item, and absolute and percentage frequencies were used for qualitative variables. We concluded that the TAND Checklist can be a useful screening tool for infants and toddlers with TSC by assessing and reporting TAND-related concerns, with the nature of the concerns evolving with age.

Effect of Chemogenetic Inhibition of the medial Preoptic area on Maternal Sensitivity

Keishley M. Pizarro-Cotón and Mariana Pereira

Maternal behavior that is sensitive to the needs of the young is essential for the healthy development and wellbeing of all mammals. Our prior research suggests that the medial preoptic area (mPOA), a critical node of the circuitry regulating maternal behavior, plays a significant role in coupling appropriate caregiving with the needs of the young. The present study aimed to investigate the role of the mPOA in maternal sensitivity. To this aim, we used Gi-coupled Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to selectively inhibit the mPOA of mother rats during maternal interaction with pups with varying needs. In order to examine the role of the mPOA in maternal sensitivity (versus maternal behavior), we used multiparous mothers and a within-subject design, with half of the female rats first injected with the DREADD agonist clozapine-N-oxide (CNO) and the other half with vehicle. The treatment conditions were reversed the next day in a counterbalanced design. As expected, vehicle-treated mothers interacting with demanding pups adjusted their caregiving behavior to match their increased needs. However, following CNO treatment, mothers exhibited a similar expression of maternal behavior regardless of the offspring’s needs, indicative of disrupted maternal sensitivity. Together, results from this study demonstrates that the mPOA orchestrates appropriate maternal caregiving with the acute physiological needs of the pups.

Interactions between ceftriaxone and voluntary abstinence on relapse to cocaine seeking

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Cocaine use disorder is characterized by high rates of relapse even after long periods of abstinence and poses significant threats to personal and societal well-being. Contingency management is currently the most effective behavioral treatment for most addicts, offering non-drug rewards to maintain abstinence; however, most addicts relapse once treatment is discontinued. While choice-based voluntary abstinence provides a translationally relevant rodent model of recovery from addiction, it hasn’t been utilized in a cocaine self-administration model yet. Here, we trained male Sprague-Dawley rats to self-administer sucrose pellets (6-10 days, 2 hr per day). Once acquisition criteria were met, rats self-administered intravenous cocaine (5-10 days of 10 or more infusions, 2 hr/day). Rats were then assigned to undergo either voluntary or forced abstinence for 14 days. Voluntary abstinence entailed operant sessions with both sucrose- and drug-associated cues and the opportunity to choose between the two rewards. Rats assigned to forced abstinence were handled daily but did not go back to the operant environment. On Day 15, a relapse test was conducted; only the drug-paired lever and inactive lever were available. To test the additive efficacy of behavioral and pharmacological treatments in relapse prevention, rats received either ceftriaxone (200 mg/kg) or vehicle (saline) injections during the last seven days of abstinence. Ceftriaxone is a beta-lactam antibiotic that has previously been shown to attenuate relapse to drug-seeking behaviors in rodents. Rats were perfused immediately after the relapse test for the quantification of Fos protein expression. We found that the majority of rats preferred the sucrose lever during voluntary abstinence; however, some rats continued to prefer cocaine. Both voluntary abstinence and ceftriaxone attenuated relapse (seeking on the cocaine-paired lever) relative to forced abstinencevehicle treatment. However, the circuitry underlying relapse has been shown to be altered when voluntary abstinence is used and thus, we will compare Fos expression between groups to assess activity in several brain regions involved in addiction-related behaviors.
Uncovering Mechanisms of Rec-8 Cohesin Regulating Chromosome and Centriole Separation In The Germ-line Of Caenorhabditis elegans

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Errors in chromosome segregation can lead to an irregular number of chromosomes (aneuploidy), which is a major contributor to miscarriages and congenital birth abnormalities like down syndrome and is a driving cause for cancer. Our research focuses on the mechanism by which the Rec-8 cohesin protein regulates chromosome and centrosome inheritance during cell division. REC-8 cohesin maintains sister chromatids and centrioles together during the spermatocyte divisions that give rise to sperm. Despite its importance for reproduction and human health, little is known about the mechanism by which Rec-8 maintains both chromosomes and centrioles together. To answer this question we are testing the effect on keeping centrioles together of an inducible Rec-8 mutant that can not be removed from chromosomes by the protease Separase. Rec-8 maintains both chromosomes and centrioles together via similar mechanisms. By visualizing centrioles by immunofluorescence staining we found that in the mitotic germline the Separase resistant mutation in the REC-8 prevents chromosome segregation, but does not appear to affect centriole separation, suggesting that REC-8 may function by different mechanisms in chromosomes and centrosomes. We will further test the effect of this REC-8 mutant in the centrosomes of dividing spermatocytes during meiosis.

PVT to NAc Projecting Neurons Role in Opioid Use Disorder

Preston Siegler, Kelsey Vollmer, MUSC, NIH P50 funding, PREP R25

Opioid use disorder (OUD) is a serious issue plaguing the United States, as data from the CDC shows that approximately 128 people die from opioid overdose each day. When exposed to drug-associated cues, such as the environment or tools used to consume drugs, people with OUD are more likely to relapse despite knowing there may be negative consequences associated with consuming these substances. The mechanism in which drug-associated cues engage reward circuits in the brain to control maladaptive reward-seeking is still largely unknown. More studies are needed to explore how these circuits are involved so that new treatments can be developed to aid health care professionals in treating OUD.

One brain region of interest for understanding this maladaptive reward seeking is the paraventricular nucleus of the thalamus (PVT). Located between other brain regions linked to conditioned reward-seeking behavior, the PVT is known to be involved in natural reward and maladaptive drug-seeking behaviors. While other have shown that PVT is inhibited by natural (sucrose) reward-associated cues, it is unclear how PVT is engaged by opioid-associated cues for the control of maladaptive drug-seeking. This is relevant because previous studies have shown a dense network of opioid receptors (OR) in this brain region, and activation of these receptors reduce excitability within the PVT. However, whether OR activation affects PVT projection neurons for the control of downstream targets is yet to be understood. Here, we aim to target PVT neurons which project to the nucleus accumbens (NAc), a major component of the brain’s reward system. Previous studies done in our laboratory reveal that PVTINAc neurons express µ-OPs, suggesting that µ-OR signaling contributes to changes in this circuit. Using optogenetic viral techniques, we have manipulated PVTINAc neurons during sucrose or heroin self-administration to evaluate this circuit’s role in adaptive and maladaptive reward-seeking, respectively. Mice were virally infused with either a cre-driven halorhodopsin (inhibitory), channelredopsin (excitatory), or YFP (control) in PVT, and a retro-cre in NAc. Animals were equipped with an IV catheter, and once recovered from surgery, underwent heroin or sucrose self-administration. Our viral strategy allowed us to manipulate the PVTINAc pathway after animals had extinguished sucrose or drug-seeking behaviors. We find that, when the PVTINAc circuit is activated or inhibited, heroin mice will re-instate to heroin-seeking behaviors. However, we find that sucrose mice will not re-instate to sucrose-seeking behaviors if PVTINAc is activated, whereas inhibition encourages reward-seeking. Through this study, we hypothesize that heroin prompts changes in PVTINAc neurons that causes an increase in maladaptive drug seeking behaviors.

Collectively, these experiments will bring better clarity as to how these brain circuits are affected by chronic opioid use and exposure to drug-associated cues. Determining how drug-associated cues can engage brain circuits for the control of drug-seeking behaviors is paramount to developing novel therapeutics to treat OUD.
Prefrontal MRS Metabolites in Mild Cognitive Impairment

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Abstract: Mild Cognitive Impairment (MCI) is a transient state operationalized for earlier detection of Alzheimer’s Disease (AD), established to fill the gap between the cognitive changes seen in normal aging and those of AD and other dementias. Individuals with MCI do not fit the diagnostic criteria for AD, though up to 65% of individuals with MCI progress to AD within 6 years.

Having a biomarker for MCI would allow for easier identification of individuals who may progress to AD. One such potential biomarker is the relative concentrations of neurometabolites in the brains of MCI patients. Previous studies have identified a number of metabolites which may be related to cognitive function in MCI and AD patients, including: N-acetyl aspartate, myo-Inositol, GABA, glycerophosphocholine, creatine/phosphocreatine, glutamine, glutamate, and glucose. This project uses Magnetic Resonance Spectroscopy (MRS) to examine the local concentrations of the aforementioned brain metabolites in the prefrontal cortex, which may help to identify and track specific etiologies that characterize MCI in older adults. We also analyzed the MRS data and their association with the data collected from the cognitive assessments to determine the relationship between metabolic changes and cognitive functioning in response to cognitive training.

Methods: This project is part of a larger clinical trial study funded by the National Institute on Aging (NIA) that examines the effect of long-term cognitive training on neurocognitive functioning in patients with MCI and healthy older adults. After 42 MCI and 33 control participants were determined to meet trial inclusion criteria, they completed a neuropsychiatric battery to determine their group placement, NIH Toolbox cognitive battery, and underwent an MRI scan, at which time the MRS data was collected.

Results: The statistical analysis revealed nine statistically significant interactions between a metabolite and cognitive assessment measure. All of the relationships present in the expected direction based on previous studies. These results support that the 20-HETE-GPR75 pairing leads to activation of a downstream signaling cascade contributing to obesity and altered glucose homeostasis.

Deletion of the 20-HETE receptor GPR75 prevents diet-induced obesity and hyperglycemia

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A key contributor to the onset of metabolic disorders like obesity, diabetes and hyperglycemia is 20-hydroxyeicosatetraenoic acid (20-HETE), the product of ω-hydroxylation of arachidonic acid by cytochrome P450 (CYP) 4A and 4F isozymes. At a molecular level, 20-HETE binds to GPR75, an orphan G-protein (Gq/11) coupled receptor (GPRR), through which it activates a signaling cascade that culminates in adipogenesis in vitro and the impaired cellular actions of insulin. This study aims to investigate the role of GPR75 as the 20-HETE target for its bioactions by assessing the genotype and the effects of high-fat diet (HFD) feeding on body-weight gain and glucose homeostasis in generated GPR75−/+ (WT), GPR75+/− (HET) and global GPR75−/− (KO) mice. Real-Time PCR was conducted on tissues (brain, liver, heart, aorta, and kidney) from all three groups. For 12 weeks, food and water intake were measured weekly and fasting blood sugar was collected at the end. Male and female KO and HET mice displayed significantly lower body weight gains compared to WT mice from week 4 to week 12 (19.3±2.2 vs 10.2±2.7 g, p<0.05 and 17.8±2.8 vs 10.2±2.7 g, p<0.05). HFD feeding resulted in hyperglycemia in the WT (170.8±9.3 mg/dL) and the HET (172.5±12.9 mg/dL) mice. These findings indicate that the deletion of the GPR75 gene protects the mice from diet-induced obesity and hyperglycemia because 20-HETE is lacking its cellular target. It also supports that the 20-HETE-GPR75 pairing leads to activation of a downstream signaling cascade contributing to obesity and altered glucose homeostasis.
Manganese Toxicity, Mitochondrial Dysfunction, and Potential Therapeutic Value of p-Aminosalicilic Acid, Taurine and Carnosine
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Manganese is an essential metal. Elevated exposure causes accumulation in human brain causing Manganism, which is similar to Parkinson’s disease. Manganese disrupts dopamine neurotransmission; however, the neurotoxic mechanism is not fully understood. There are no effective treatments. Proposed toxic mechanisms include elevated oxidative stress and mitochondrial dysfunction. Using the Eastern Oyster, Crassostrea virginica, we showed manganese interferes with dopamine’s cilia-inhibitory effect in gill, and reduces mitochondrial oxygen consumption and membrane potential. These toxicities were reduced by p-aminosalicylic acid (PAS), taurine and carnosine. We hypothesize PAS, taurine and carnosine protect against manganese induced mitochondrial dysfunction in other animals including mammals. We analyzed published data about mitochondrial dysfunction in animals exposed to toxic manganese levels and if PAS, taurine and carnosine alleviated manganese toxicity in animals. Manganese also caused mitochondrial dysfunction. The damage included: interference of electron transport chain, decreased oxygen consumption, oxidative phosphorylation interference of ATP synthase, decreased mitochondrial membrane potential, altered mitochondrial permeability and disruption of Ca2+ homeostasis. Meta-analyses to determine prevalence estimates for each infection are in progress.

Results: We identified 4,459 abstracts, of which 547 studies were included in the full-text review. Overall, 66 studies met inclusion criteria: 31 from East Africa, 12 from West/Central Africa, 21 from Southern Africa, and 2 reporting data from multiple African regions. 44 studies including 18,319 women with HIV reported results for gonorrhea, 45 studies evaluated 17,646 women with HIV for chlamydia, 53 studies evaluated 24,079 women with HIV for trichomoniasis, and 13 studies evaluated 3,685 women with HIV for Mycoplasma genitalium. Meta-analyses to determine prevalence estimates for each STI and subgroup of women are in progress. The full text of each study that met inclusion criteria was then assessed by two independent reviewers for conflicts during regular meetings. The findings concur with our work on oyster mitochondria, and support our hypothesis. They support our use of C. virginica as a model animal to study the mechanisms underlying manganese toxicity and generate new information which should be of interest to those exploring possible agents in the prevention or therapeutic treatment of Manganism. This work was supported by grant R25GM06003 of the Bridge Program of NIGMS, NIH grant K12GM038545-01A1 IRACDA Program of Rutgers University and PSC-CUNY grants 62344-0050 and 63434-0051.

What is the Prevalence of Sexually Transmitted Infection (STIs) among Women Living with HIV in Sub-Saharan Africa
Khalela Barracks

Background: Women living in sub-Saharan Africa (SSA) have a high prevalence of HIV and other sexually transmitted infections (STIs). Untreated STIs can lead to complications such as infertility and increased rates of HIV transmission. Screening programs for STIs are not currently widespread in SSA, and the burden of women living with HIV is not well-defined. We are conducting a systematic review and meta-analysis to estimate the prevalence of four curable STIs among women living with HIV in SSA: gonorrhea, chlamydia, trichomoniasis, and Mycoplasma genitalium.

Methods: We searched PubMed, EMBASE, African Index Medicus, Africa Wide Information, and Web of Science for studies published up to December 20th, 2019 that report prevalence of gonorrhea, chlamydia, trichomoniasis, or Mycoplasma genitalium among women with HIV over age 13 in any SSA country. Abstracts were reviewed for inclusion by two independent reviewers. The full text of each study that met inclusion criteria was then assessed by two independent reviewers for inclusion and if included, for data extraction. All included studies were assessed with a validated risk of bias tool, evaluating how well the study population represents the target population and the reliability of study measures. We adjudicated conflicts during regular meetings.

Results: We identified 4,459 abstracts, of which 547 studies were included in the full-text review. Overall, 66 studies met inclusion criteria: 31 from East Africa, 12 from West/Central Africa, 21 from Southern Africa, and 2 reporting data from multiple African regions. 44 studies including 18,319 women with HIV reported results for gonorrhea, 45 studies evaluated 17,646 women with HIV for chlamydia, 53 studies evaluated 24,079 women with HIV for trichomoniasis, and 13 studies evaluated 3,685 women with HIV for Mycoplasma genitalium. Meta-analyses to determine prevalence estimates for each STI and subgroup of women by region, testing location, pregnancy status, and presenting symptoms are in progress.

Conclusions: Numerious studies have assessed the prevalence of curable STIs among women living with HIV worldwide. Results from this meta-analysis will provide important data that can inform STI screening interventions among women with HIV in sub-Saharan Africa and can be applied to different clinical settings and subpopulations.
Examining Cognitive Deficits in Non-Clinical Population
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Schizophrenia is well known to be marked by cognitive deficits, though findings are often obscured by factors such as medication effects, hospitalization, and symptom severity. To circumvent these challenges, one alternative approach is to study cognitive functioning in relation to schizotypy or schizotypal traits in non-clinical samples, though evidence to date is limited. Schizotypy is a multidimensional personality construct encompassing a continuum of experiences and traits ranging from normative to subclinical and clinical psychotic states. Moreover, individuals with high schizotypy are at a greater risk of developing schizophrenia Thus, the schizotypy framework also holds predictive value. In order to expand existing literature, the current study examines the relationship of cognitive functioning (specifically, working memory and processing speed) with (positive, negative, and total) schizotypal traits using a diverse, urban sample of University students. Participants include 34 college students recruited from subject pools across several campuses at a large, diverse, urban University. Data collection was conducted in two sequential parts. Part I consisted of self-report questionnaires administered remotely via the Internet. Measures included a demographic questionnaire, the Multidimensional Schizotypy Scale-Brief (MSS-B), the Schizotypal Personality Questionnaire-Brief (SPQ-B), and the Chapman Infrequency Scale (INFS). Part II consisted of in-person administration of cognitive tasks including the Digit Span, Symbol Search, and Coding subtests of the Wechsler Adult Intelligence Scales – Fourth Edition (WAIS-IV). Based on previous research, it is expected that performance on working memory and processing speed tasks will be significantly, negatively correlated with positive and negative (but not total) schizotypal traits. Likewise, using a dichotomous approach, individuals with high schizotypy will score lower on both cognitive domains (working memory and processing speed) compared to individuals with low schizotypy. Findings from this study are expected to help further our understanding of how cognitive functioning is associated with schizotypal traits, with implications for better understanding risk for psychosis. Future research steps include collecting additional data (to expand the sample size) and considering possible sex differences in processing speed and working memory performance in relation to schizotypy.

"COVID-Toes: A Review of the Clinical Correlation between Chilblains and SARS-CoV-2"
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The novel Coronavirus Disease 2019 (COVID-19) presents with a wide range of symptoms. These may include fever, pneumonia, headaches, sore throat, diarrhea, stroke, liver and kidney damage, and loss of taste. Yet, the most bizarre documented presenting symptoms has been “COVID toes.” Overall, the fifteen studies conducted found that patients with dermatologic symptoms often displayed chilblain-like skin lesions, pernio-like, urticarial, macular erythema, vesicular, purpuric, and reform purpura. Patients presenting with COVID toes, regardless of confirmatory COVID-19 laboratory results, demonstrated epidermal necrotic keratinocytes, dermal edema, perivascular and pericorneal sweat gland lymcytic (CD3/4+) inflammation, vascular changes with endothelialitis, microthrombosis, fibrin deposition, and immune reactant deposits on vessels. Histopathological immunohistochemical and direct immunofluorescence from biopsy showed IgM deposits in most of the cases. Patient symptoms varied in severity from milder pernio-like lesions to progressive reform purpura. These findings could aid in triaging patients COVID-19. To prevent the progression to the known neurologic and destabilizing thrombotic events seen in many COVID-19. In patients with lesions, early identification and intervention with antivirals, antplatelets, and anticoagulants to prevent hypoxia and reperfusion injuries may be avoided. Dermatological features are often overlooked; distinct clinical signs of COVID-19 and further awareness and research are indicated.

Key search words: Coronavirus, COVID-19, SARS-CoV2, toes, thrombotic events, global health

Landscaping the Curricular Frameworks of U.S. Rural Family Medicine Residency Programs
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Background: Rural family medicine residency programs (RFMRPs) encounter unique hardships that threaten their sustainability and efficacy despite their recent success at addressing the rural physician shortage. The aim of this study was to draw from experienced Program Directors (PDs) on how to best structure a developing RFMRP and to better understand the current strategies being employed by RFMRPs to overcome barriers encountered in rural family medicine graduate medical education (GME).

Methods: The authors conducted an in-depth semi-structured telephone interview with 19 PDs of RFMRPs in June and July of 2020. The interviews consisted of open-ended questions aimed at exploring how RFMRPs structure their curriculum. Interviews were audio-recorded, transcribed verbatim, and analyzed using qualitative thematic analysis based on a descriptive phenomenology.

Results: Three main themes emerged from our participating PD’s: engage and utilize your community’s strengths; evolve to meet demands; and focus on building and nurturing relationships. Regarding strategies to overcome barriers in rural family medicine GME, seven themes emerged: revisit mission and program goals annually; forge and strengthen relationships with nearby clinical partners; structure in high volume at the urban location; create opportunities for more exposure in weak areas; recruit strong physician candidates or grow your own; seek out resources and help; and play an active role in undergraduate and GME.

Conclusions: A myriad of factors were identified, such as an institution’s geographical location, a collaborative network of clinical and community partners, and the historical and political atmosphere contribute to the successful establishment and maintenance of a RFMRP. Our findings help identify best practices for developing RFMRPs and highlight strategies utilized by current RFMRPs to help meet the needs of the changing landscape of rural family medicine GME.

Re-Examination of Health Disparities in the United States: A 3-Pronged Health Intervention Proposal
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Decades of research have revealed immense disparities in health in the United States, but scholars are still working to pinpoint the causes of these disparities and find solutions. In this review, new ideas and current findings on the SES-health gradient and the effects of racism on health are analyzed in order to understand the current state of health disparities in the U.S. In addition to this new information, lessons learned from an analysis of the Affordable Care Act, were taken into consideration to develop a 3-pronged health intervention plan to tackle health disparities. The plan prioritizes a “Health in All Policies” approach that emphasizes the importance of understanding the effects of any policy on health and health disparities, ensuring that everyone is actively working towards undoing health disparities in the work they do. Additionally, the plan includes a shift in focus from healthcare expansion to the social determinants of health in order to ensure that the root causes of health care disparities are being addressed rather than a temporary fix, highlighting that health can be addressed through a variety of policies. The third part of the intervention plan focuses on dismantling racism, ensuring that people are held accountable for their implicit biases in order to address systemic racism. This 3-pronged approach will not be enough to completely undo health disparities, but it is a step in the right direction.
Community Mobility Reduction and COVID-19 Growth. [Status: revision requested at May clinic journal]

Citation: Ossimetha, Ashley; Ossimetha, Angelina; Kosar, Cyrus; Rahman, Momotazur. (2020), Socioeconomic Disparities in were also significantly higher for high-SDI counties.

more coronavirus cases/100,000 on May 15 compared with low-SDI counties, respectively. Adjusted deaths per capita

prevalence on April 1, medium- and high-SDI counties had 0.8 (CI, 0.4 to 1.1; p<0.001) and 1.4 (CI, 0.9 to 1.9; p<0.001)

lower for medium- and high-SDI counties relative to low-SDI counties, respectively. Mobility reductions in the

in coronavirus prevalence, coronavirus deaths per capita, and reduction in mobility across three settings: retail/recreation,

Introduction: Recent evidence suggests that economically disadvantaged communities have been disproportionately

Results: Workplace mobility reduction was 1.7 (95% CI, -2.5 to -1.3; p<0.001) and 3.7 percentage points (CI, -4.4 to 3.0; 
p<0.001) lower for medium- and high-SDI counties (defined by tertile) were calculated with linear regression models including state fixed effects.

Methods: US counties with at least one coronavirus case by May 15, 2020 were analyzed. Outcomes were growth in coronavirus prevalence, coronavirus deaths per capita, and reduction in mobility across three settings: retail/recreation, grocery/pharmacy, and workplace. The main explanatory variable was the Social Deprivation Index (SDI), a composite measure of socioeconomic advantage. Adjusted differences in outcomes between low-, average-, and high-SDI counties

Conclusion: It is hoped that our findings will provide biological evidence for the physiological dissimilarity among Black populations and the impact of such differences on disease risk.

Conclusions: US counties with higher SDI scores experienced greater growth in the number of coronavirus cases and related deaths, but reduced mobility at lower rates.

Citation: Ossimetha, Ashley; Ossimetha, Angelina; Kosar, Cyrus; Rahman, Momotazur. (2020), Socioeconomic Disparities in Community Mobility Reduction and COVID-19 Growth. [Status: revision requested at May clinic journal]

A systematic review of testosterone status and ill health in Black populations

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Abstract: Testosterone is not just a “male sex hormone” but a biomolecule with a broad spectrum of demonstrated physiological functions as well as a wide variety of physiological and pathophysiological associations about which we are just learning. In particular, the level of testosterone is thought to impact the general wellbeing and outcomes of individuals. Consequently, testosterone levels influence disparity in health outcomes and its variation is determined by gender, age, and racial differences. There is, however, a dearth of empirical evidence regarding whether there are geographical variations in the level of testosterone and whether this variation is associated with ill health in different Black populations across the world. It is therefore hypothesized that the level of testosterone varies across Black populations and that this variation affects health outcomes. The current study elucidated the documented levels of testosterone in African or African American demographics. This will build the foundation for understanding the genomics of the within-group differences in testosterone-one-associated prognosis in diseases like COVID-19, diabetes, cancer, and hypertension.

Methodology: A systematic search was conducted following the PRISMA guidelines, with a combination of terms including “testosterone” and nationality/ancestry descriptors. The search included studies from the last 10 years using databases including Google Scholar, Web of Science, Scopus, PubMed, EBSCOHost, and ProQuest.

Results: We retrieved over 300 peer-reviewed original research publications across Africa and Americas and our preliminary evaluation suggests variation in the level of testosterone across Black populations.

Conclusion: It is hoped that our findings will provide biological evidence for the physiological dissimilarity among Black populations and the impact of such differences on disease risk.

How well does a point-of-care hemoglobin A1C screening machine identify patients with pre-diabetes?

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The aim of this study is to investigate the ability of the machine to identify pre-diabetes (HbA1c between 5.7-6.4%), compared to a “gold standard,” to identify individuals who would benefit from diabetes prevention interventions. Participants were recruited through a diabetes prevention parent trial and were determined eligible if they: (1) were at least 19 years old; (2) not currently diagnosed with diabetes; (3) had a Body Mass Index (BMI) of 25kg/m2 or higher; and (4) were prediabetic. HbA1c was measured by a finger stick using the PTS Diagnostics machine. Participants with levels within 5.7-6.4% attended a blood draw via venipuncture (LAB). The samples then underwent a HbA1c test by the “gold standard” lab assay.

242 participants were sampled in this study. The POC measurement had a mean value of .32% higher than the LAB. This differential was consistent across gender and age but was .75% and .58% higher for American Indian/Alaska Natives and females, respectively, and .16% higher in Black/African Americans.

A paired-samples t-test comparing the POC and LAB measurements was conducted. There was a significant difference (ES=0.25) for all groups except for females (ES=0.01). Participants with levels above 6.5% had a higher HbA1C measurement by the POC than the LAB (ES=0.05).

Effect of Chronic Stress on School-Aged Children: Self-Regulation During the Disappointing Gift Task

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Previous research has revealed that, for young children, stress can influence self-regulation (the ability to manage behav-

iors and emotions), which has been related to social adjustment and academic achievement. Hair cortisol concentration (HCC) is an indicator of chronic stress and has been associated with cognitive and behavioral performance. Although there have been examinations into the association between stress, cortisol, and self-regulation in children, current findings are inconsistent as to the relationship between cortisol and cognitive performance. This is mainly due to differences in how cortisol was measured, participants’ age, and the cognitive tasks used. This cross-sectional study examined the impact of physiological chronic stress (HCC) on self-regulation during the Disappointing Gift Task (DGT). We hypothesize that children’s HCC levels will be inversely related to their ability to regulate their behavior during the DGT. This research proposal would use data collected and coded from 100 children (56% female) aged 7–9 years old (mean age=8.2, standard deviation=0.7) as part of a larger longitudinal study. Self-regulation was measured by the DGT, an observational task that measures the emotional displays of children after they receive an undesirable gift following the completion of a stress-inducing task. To measure HCC, hair samples of approximately 30-50 strands were collected from the posterior of the participants’ heads and processed via immunoassy. One centimeter of hair corresponds to the average free cortisol for 1 month. Data will be analyzed using linear regression models with DGT scores as the dependent variable and HCC as the independent variable. If the results confirm our hypothesis, this study will suggest that chronic stress negatively influences self-regulation in children. In addition, these results will contribute to the clarification of previous inconsistencies in the literature and will be essential for broadening our understanding of how chronic stress impacts children. Regardless of the results, this study will be critical in designing interventions aimed to promote self-regulation techniques in children, supporting their social adjustment and academic achievement.
The Disproportionality Phenomena: How African Americans and the Latinx Population are predisposed to Higher Rates of COVID-19

Marshaun Love, Alexander Yentumi, Junoria Worthy, Amoni Madison, Keisha Avery University of Missouri – Columbia, Harris-Stowe, Saint Louis University

COVID-19 cases in America include over 2.7 million infected individuals with nearly 130,000 deaths. Despite minority communities occupying a smaller portion of the overall population, the Latinx population has experienced infection four times the average rate. In comparison, African Americans have experienced disease at five times the rate of average. This study investigates what issues are linked to this significant variance in these distinctive ethnic groups’ rates of contraction and death from the pandemic within New York City, which consists of five boroughs; (Brooklyn, Staten Island, Queens, Bronx, Manhattan) that have a disproportionate amount of COVID-19 infections in comparison to the rest of the state. By creating a reference archive of stats on the phenomena, experts gain insight into where to intervene. At-risk individuals (African American & Latinx) receive an informational overview of why they are disproportionally affected. Exploring related problems can be separated into three categories: living conditions, pre-existing health conditions, and work circumstances. Methods involve tapping data sources for the necessary statistical analysis of possibly linked issues, and keyword article search to find other reports on this issue. Results will show which key trends have been studied and analyzed for
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