Student abstracts are grouped by majors -- linked below -- and then alphabetically (mostly) by last name, with their assigned poster number:

BIOCHEMISTRY

99 Malika Alamova

Identification of a subpopulation of granule cell precursors that is the cell of origin of SHH-Medulloblastoma

Malika Alamova,[1,2] Salsabiel El Nagar,[2] Alexandra L. Joyner[2]

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Medulloblastoma (MB), a cerebellar tumor, is the most common malignant pediatric tumor. While survival rates for patients are high, there remains an urgent need for less toxic treatments, as current therapeutic modalities (surgery and chemotherapy) result in long-term side effects. There are four molecularly distinct subgroups of MB: WNT, Sonic Hedgehog (SHH), Group 3, and Group 4. The SHH subgroup accounts for ~30% of all cases and originates primarily from granule cell precursors (GCPs). These precursors highly proliferate during the first weeks after birth in response to SHH, making them sensitive to mutagenesis. There is evidence that GCPs are heterogeneous where each subpopulation presents distinct molecular characteristics. Constitutive activation of SHH signaling via expression of a mutant SHH receptor (SmoM2) at mouse postnatal day 0 (P0) only in Nestin (*Nes*)-expressing GCPs, that represent 2% of GCPs, or across all GCPs, results in similar survival rates. Thus, we hypothesize that *Nes*-expressing GCPs are preferentially susceptible to forming SHH-MB. To analyze how *Nes*-expressing GCPs are preferentially responsible for SHH-MB, we studied the cerebellum of mice where SHH-MBs were induced across GCPs (*Atoh1-SmoM2*) or only in Nes-expressing GCPs (*Nes-SmoM2*) at an early stage of tumorigenesis (P12). *Nes*-expressing GCPs were found to form large lesions only in the posterior cerebellum whereas *Atoh1*-expressing GCPs do not. These results suggest that Nes-expressing GCPs may be the origin of SHH-MB and are involved in tumor maintenance because SHH-MB originates in the posterior region of the cerebellum.

100 Alanna Fields

Determining the Structure(s) of the CYRANO long noncoding RNA

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MicroRNAs (miRNAs) guide Argonaute (AGO) proteins to bind and repress target RNAs. However, some targets, called trigger RNAs, direct miRNA degradation instead. Trigger RNAs base-pair extensively with the miRNA, which induces a conformational change in the miRNA–AGO complex and recruits the ZSWIM8 E3 ubiquitin ligase, destroying both AGO and miRNA. The CYRANO long noncoding RNA is a potenttrigger, reducing miR-7 levels up to 50-fold, and the CYRANO miR-7 binding site is required but not sufficient for this activity. Preliminary studies in the Kleaveland lab have identified at least three accessory regions of CYRANO that enhance miR-7 degradation, however, the mechanistic basis for this enhancement is unknown. We hypothesize that RNA structure affects CYRANO-directed miR-7 degradation. To begin testing this hypothesis, we will determine the 2D structure of the CYRANO miR-7 binding site in vivo in control cells and miR-7-deficient cells using dimethyl sulfate (DMS) chemical probing followed by high-throughput sequencing. DMS methylates accessible nitrogenous bases in RNA, which can be detected as mutations after reverse-transcription. As the same RNA sequence may exist in multiple structures, we will use deconvolution and annotation of ribonucleic conformational ensembles (DANCE-MaP) to identify the number of unique structures in the ensemble and characterize their features. Follow-up studies will determine how loss of CYRANO accessory regions affects the structure of the miR-7 binding site and how loss of miR-7 binding affects the structure(s) of these accessory regions. By identifying structural characteristics of CYRANO, we can better understand how CYRANO and perhaps other triggers work.

1. Martin Habib

Harnessing the Potential of Teretoxins in Liver Cancer Therapy

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Abstract

Liver cancer is a serious and often fatal disease with limited treatment options. Hepatocellular carcinoma(HCC) is the most common form of liver cancer with the third highest mortality rate. Existing treatment options for advanced stage HCC, such as sorafenib, act by inhibiting kinases and are often prone to side effects due to the ubiquitous nature of kinases. An alternative approach is to treat liver cancer as a channelopathy. Ion channels such as transient receptor potential(TRP) ion channels have been reportedly dysregulated in various forms of cancer including liver cancer. TRP channels are involved in various cellular processes, including cancer cell proliferation and survival hence their relevance in tumor propagation. Venom peptides have been described as highly specific and selective for ion channels. Teretoxins which are venom peptides derived from terebrid snails have been described in literature as potential modulators of TRP channels. A previous study identified the potential of Tv1, a teretoxin, to inhibit certain TRP channels in HCC mouse cells and significantly reduce tumor progression in syngeneic mouse models. Our goal is to validate the activity of Tv1 and other teretoxins in human HCC cell lines. We have confirmed the expression profile of ion channels in six HCC cell lines and successfully identified and synthesized three teretoxins including Tv1. We will purify these peptides and confirm their activity and mechanism of action against HCC. Our results will highlight the potential of teretoxins as novel therapeutic agents for liver cancer, improve understanding of the role of TRP channels in liver cancer progression and provide new insights for future drug development.

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2. Aaron Lyons

"Synthesis of Dopamine Ligands via Modifications on a Tetrahydroprotoberine Skeleton"

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Hypothesis/Statement of Problem: Dopamine D1 and D3 receptors (D1R and D3R respectively) play a significant role in psychostimulant addiction. Previous studies in rats indicate that molecules with a dual D1R agonist and D3R antagonist pharmacology are effective in reducing the self-administration of cocaine. Thus, this targeting strategy may be therapeutically viable for the treatment of cocaine use disorders (CUDs). However, there is a dearth of such dual-dopamine receptors targeted compounds to robustly validate this targeting strategy for CUDs. The tetrahydroprotoberberine (THPB) alkaloid, (*S*)-isocorypalmine, is one of only two molecules known with this unusual D1R/D3R pharmacology. We hypothesize that (S)-isocorypalmine may be structurally modified to obtain novel dual-targeted D1R agonists/D3R antagonists. The goal of this project is to synthesize and evaluate novel analogs of (S)-isocorypalmine that incorporate a sulfonamide motif as a bioisosteric replacement for the C-2 phenolic functionality in (S)-isocorypalmine.

Methods: (S)-isocorypalmine was prepared from commercially available berberine via a series of standard chemical transformations. Thereafter, the C-2 phenolic group of (S)-isocorypalmine was triflated and converted to an amine via Buchwald amination conditions. Reaction of the amine handle with a variety of sulfonyl chlorides furnished a library of sulfonamide analogs, that were spectroscopically characterized by nuclear magnetic resonance and mass spectrometry.

Results: A set of the analogs is currently being evaluated for affinity to dopamine receptors in radioligand binding assays at the Psychoactive Drug Screening Program (PDSP, NIMH).

Conclusion: After biological evaluation, we expect biological probes with high D3 receptor affinity with partial D1 receptor affinity for further clinical analysis.

Funding Acknowledgements:

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101. Fahima Miajee

Cell-type Specific Origin of Perineuronal Nets' Accumulation of Semaphorin-3a in the Prefrontal Cortex

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Perineuronal nets (PNNs) are a complex extracellular matrix (ECM) that forms a shield-like structure around specific brain cells, the parvalbumin-expressing neurons. PNNs comprise several proteins, namely proteoglycans and other binding partners, such as Semaphorin-3a (Sema3a)—an axonal repellent molecule associated with a decreased ability to receive new synapses. Since Sema3a is produced by neighboring cells and anterogradely secreted to accumulate in the ECM, we first analyzed available prefrontal cortex (PFC) single-cell RNA-sequencing datasets to reveal which cells express Sema3a. We found that somatostatin-expressing (Sst+) and pyramidal cells (PCs) express Sema3a. We are validating this finding using immunohistochemistry and have established a protocol to employ ascorbate peroxidase (APEX2)-based proteomics and western blots to label proteins from Sst+ and PCs. While PNNs naturally appear during development, exacerbated levels are observed in chronic stress (CS)-related diseases, such as depression, motivating our quest to understand the role of Sema3a in neuroplasticity. Next, we labeled PNNs in the PFC of adult mice and found that CS increased the number of PNN+ neurons in the PFC. Thus, we want to test whether CS intensifies Sema3a expression and to determine from which specific cell types Sema3a originates. A cre-dependent viral vector carrying Sema3a, HA-tagged, will be expressed in PFC to label Sst+ or PCs, and immunohistochemistry for HA will reveal the source of Sema3a in PNNs. Our results will bring to light the origin of Sema3a in PNNs after CS and help to understand the role of PNNs in structural plasticity and antidepressant mechanisms.

3. Alexander Niyazov

Effects of BRCA1-Mediated Ubiquitination of HuR on RNA Metabolism in Breast Cancer

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Hypothesis/Statement of Problem: BRCA1 mutation causes a 65% increase in the risk of developing breast cancer (BC). Additionally, patients with BRCA1 mutation are more likely to develop triple negative breast cancer (TNBC), an aggressive form of BC which lacks current targeted therapies. *BRCA1* forms a heterodimer with BARD1, acting as an E3 ubiquitin ligase, but the targets and implications of this enzymatic activity in BC are not fully understood. Our preliminary studies indicate that BRCA1/ BARD1 ubiquitinates the RNA binding protein HuR, leading to detachment from target mRNAs involved in important cellular pathways such as DNA damage response and cellular proliferation.

Methods: Western blots, sub-cellular fractionations, and RNA-immunoprecipitation assays were performed using samples from MCF7 BC cells with functional BRCA1 and SUM1315 TNBC cells with non-functional BRCA1. Samples from cells expressing Myc-tagged ubiquitination-resistant K313R HuR derivative or WT HuR derivative were included.

Results: BRCA1/BARD1-depleted cells, SUM1315 cells and Myc-tagged K313R HuR-expressing cells show decreased HuR ubiquitination. SUM1315 cells without functional BRCA1 showed elevated levels of chromatin-bound HuR and lack of UV-induced cytoplasmic localization of HuR compared to MCF7 cells. Expression of K313R HuR also showed increase in chromatin-bound HuR and a decrease in HuR oligomerization compared to WT HuR-expressing cells. Lastly, HuR-binding to mRNA target TP53 increases in BRCA1/BARD1-depleted cells and SUM1315 compared to MCF7 cells.

Conclusion: These data indicate HuR is ubiquitinated by BRCA1/BARD1, impacting HuR sub-cellular localization, HuR oligomerization, and HuR-binding to target transcripts. Therefore, BRCA1 mutations may lead to transcriptome dysregulation, influencing BC outcomes and therapies.

4. Beatrice Norton

The effect of the KRAS mutation on a redox signaling pathway in osteosarcoma

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This study investigates the impact of the KRAS mutation on redox signaling in osteosarcoma, a prevalent bone cancer affecting adolescents. With limited biomarkers for early detection or treatment response, the need for targeted drug therapies is crucial. Focusing on the G12S KRAS mutation in the 143b osteosarcoma cell line, this project explores the interconnection between KRAS, glutathione (GSH), hydrogen sulfide (H2S), reductive oxygen species (ROS), xCT receptor expression and cysteine within the redox signaling pathway. We proposed a pathway that the KRAS-mutant exhibits higher proliferation rates due to lower ROS levels, influenced by increased cysteine, H2S, and GSH levels. Riluzole is an FDA-approved drug that inhibits the release of glutamate and could have a significant effect on the investigation of this redox signaling pathway. We performed Western blot and qPCR methods to assess xCT protein and mRNA expression, a luciferase assay measures GSH levels, a fluorescence assay evaluates intracellular ROS levels, and two different colorimetric assays determine H2S and proliferation levels. Our preliminary results show that GSH levels in 143b cell line samples are 1.3-2 times higher than its HOS parent cell line samples. The study aims to contribute to the identification of potential biomarkers in the redox signaling pathway of osteosarcoma, particularly in KRAS-mutant cases, offering insights for targeted therapies in this challenging cancer type.

Mixed Death Types Occur During Ferroptosis Execution and Are Regulated by Nutrient Availability

Leslie Revatta[1], Jyotirekha Das[2], Saloni Hombalka[2,3], and Michael Overholtzer[2, 3, 4]

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Hypothesis:

Cell death mechanisms eliminate cells during normal development and are often dysfunctional in diseases such as cancer. While much is known about different mechanisms that can eliminate cells, including apoptosis and regulated forms of necrosis, little is known about how cell death is executed in cell populations in response to stress. Cell death responses occurring in complex cell mixtures such as cancer tissues are not well understood. We investigate one form of cell death called ferroptosis to examine if nutrient starvation, a common occurrence in cancers, affects the mechanism and extent of death in cell populations.

Methods:

Cells were treated with ferroptosis inducers in the presence or absence of amino acids and imaged by time-lapse microscopy with fluorescent indicators of nuclear morphology and membrane rupture. The relative timing and morphological features of individual deaths were then examined.

Results:

Our results revealed striking morphological diversity underlying death execution within cell populations. Cells can be observed to die with necrotic morphologies, characterized by rapid membrane rupture, or apoptotic morphologies, involving cell shrinkage and blebbing in the absence of rupture, or with mixed morphologies.

Conclusion:

Our findings demonstrate that cell death can be executed in complex mixtures within cell populations in manner that is influenced by nutrient starvation, suggesting that mixed death profiles could impact the treatment of diseases such as cancer. We show that nutrient starvation has a strong effect to shift death types toward necrosis through a mechanism that is independent of the induction of autophagy, a well-characterized starvation response.

6a. Pollena Sangana
Fatima Khalid

Development of Novel Venomous Marine Snail Organoid Cultures to Advance Venom Peptide Drug Discovery

Pollena Sangana[1], Fatima Khalid[1], James V. Parziale[1,2],Mandë Holford[1,2,3]

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Hypothesis/ Statement of Problem:

Animal venom is a complex cocktail of toxins used as a dynamic mode of defense and predation. Venom from snakes and marine cone snails have been used to develop therapeutics for treating human diseases. Unfortunately, drug discovery and development of venom compounds are hindered due to the lack of a robust and reliable model system. Recently, a snake venom gland organoid system was designed by optimizing mammalian organoid growth factor media. Similar to snakes, venomous marine snails have growth factor orthologs comparable to those used in the development of mammalian and snake venom gland organoids. We plan to exploit these similarities to create, for the first time ever, marine invertebrate organoid cultures. We hypothesize that culturing stem cells from marine snail venom glands with growth factor-enriched media will drive their development into venom-producing organoids. Our novel organoid models will allow for improved discovery and characterization of venom as a molecular innovation in nature and medicine.

Methods:

Using *Conus leopardus* and *Conus lividus* as a model we plan to:

1. Performing differential expression analysis of venom glands to identify the molecular function of venom transcriptomes.
2. Optimizing tissue culture and growth factor media to generate a venom gland organoid.

Results:

BLAST results indicate that growth factors WNT, EGF, LGR5, TGF, and FGF are present in marine snails.
Venom gland cells can be isolated and visualized with mammalian cell dyes.

Conclusion:

Venomous snails utilize similar pathways as vertebrates in cellular development. Venom gland and bulb tissue sections show epithelia-like organization.

6b. Fatima Khalid
Pollena Sangana

Development of Novel Venomous Marine Snail Organoid Cultures to Advance Venom Peptide Drug Discovery

Fatima Khalid[1], Pollena Sangana[1], James V. Parziale[1,2],Mandë Holford[1,2,3]

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[2] The Graduate Center, The City University of New York
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Conclusion:

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7. Maliha Tasnim

Determining the Role of AMPK Activation in Increasing the Risk of Atrial Fibrillation for Wolff-Parkinson-White Syndrome Patients Using Engineered Human Cardiac Microtissues

Maliha Tasnim[2,3], Mark C. Daley[2], Bum-Rak Choi[1], Kareen LK Coulombe[2]

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[2]Center for Biomedical Engineering, School of Engineering and Division of Biology and Medicine, Brown University, Providence, RI

[3]Macaulay Honors at CUNY Hunter College, New York, NY

Hypothesis/Statement of Problem: Mutations in the PRKAG2 gene, which cause overactivation of 5' adenosine monophosphate-activated protein kinase (AMPK), have been linked to inherited forms of Wolff-Parkinson-White Syndrome (WPW) that may results in an increased risk of atrial fibrillation. The goal of this project was to determine if AMPK activation contributes to the onset of atrial fibrillation in WPW patients by studying human atrial electrophysiology *in vitro*.

Methods: Self-assembled microtissues were treated with a vehicle control (DMSO) and an AMPK activator at a low (1μM) and high concentration (10μM) for a week. By monitoring changes in cellular glycogen levels and AMPK phosphorylation, it was possible to validate AMPK activation. Changes in electrophysiology were evaluated by recording microtissue beat rate and recording action potentials using high-speed optical mapping with a voltage-sensitive dye.

Results: The data shown in the graphics of the results section show no significant difference between the beat rate and action potential for the two treatment groups and the vehicle control. However, a difference is seen in the maximum capture rate of the control and one of the treatment groups which shows that at higher AMPK activation the cells lose their ability to keep up with the external electrical pacing. This suggests that the treated cardiac microtissues are susceptible to sustaining atrial fibrillation.

Conclusion: While this experiment did not give significant results for the main question, the main takeaway was that the treatment (i.e. compound 991) worked in achieving the desired condition of WPW syndrome. Future work will use cardiomyocytes derived from WPW patients to evaluate the expression of different ion channels and their contribution to altered atrial electrophysiology and the role of AMPK using a larger sample size.

8. Andrew Wegner

Abstract Title:
Utilizing Colon Cancer Mouse Models to Investigate Tumor Immunity in Primary Colon Tumors and Liver Metastases.

Authors:
Andrew Wenger, Alison Juray, Caolain Mathers, Erika Hissong, Marie Parsons, Lukas Dow, Despina Siolas

Background and Objectives: Colorectal cancer is the 2nd most common cause of cancer death in the United States. Recent findings suggest that patients with advanced colorectal cancer with metastatic disease to the liver may be resistant to immunotherapy treatment in comparison to patients without liver metastases. We have developed a preclinical model to study immune microenvironment differences between primary colon tumors and the liver metastases using organoid implantation of mouse tumor cells into syngeneic C57/bl6 mice.

Methods: Mouse-derived *Kras*$^{G12D/+}$*; APCQ*$^{1405X/+}$*;Trp53*^{Q97X} colon cancer organoids (500,000 cells) were cultured in-vitro and injected into either the cecum of a mouse to produce primary tumors or the spleen to imitate hematogenous metastasis to the liver. Tumors were dissected at four weeks post-surgical implantation, where they were subsequently weighed, fixated with formalin, preserved in ethanol, and paraffin embedded. Hematoxylin and eosin-stained tumor sections were examined histologically by a colon cancer pathologist**.**

Results: Tumors were successfully formed in the both the cecum and liver 4 weeks after implantation with high reproducibility. Immunofluorescence (IF) was performed for $CD3^+$, $CD4^+$, and $CD8^+$ T cells. T cell density (cell count/mm2) was quantified in ImageJ in both cecum and liver tumors at either the tumor center or invasion front.

Conclusion: We have described a novel preclinical model for studying immune cells present in cecum tumors or liver metastases of a mouse. Tumor formation can be achieved with a rapid turnaround rate and high reproducibility. This mouse model can be used to study the effects of interactions between cancer cells and immune cells and immunotherapy studies.

9 Nicole Zakharov

Abstract

Glycans are prevalent in biological systems and are involved in complex physiological and pathological pathways. Synthetic glycans are in demand for research on deciphering these mechanisms. C-glycosides are glycan analogues in which the glycosidic oxygen is replaced by a carbon substituent. This modification results in greater stability and different conformational properties compared to their O-glycoside parents and makes them unique mechanistic probes. Accordingly, general syntheses of C-glycosides are of interest. This project focuses on the synthesis of C-glycosides of lactose (Galβ1-4Glu), a widely occurring subunit on biologically relevant glycans. The synthetic strategy centers on the reaction of an easily accessed C-galactose derivative and a simple achiral aldehyde to give a complex C-linked galactose product that can be transformed to derivatives of C-lactose. Progress on this synthesis and the versatility of this approach will be presented.

MOLECULAR COLLISIONS IMPACT THE CONFORMATION AND FATE OF THE TRANSCRIPTION COMPLEX

Chuquimarca, Stephany; Watters, John; Liu, Shixin. Ph.D, The Rockefeller University; Laboratory of Nanoscale Biophysics and Biochemistry, 1230 York Avenue, New York, NY 10065

Introduction

Transcription is a core component of the central dogma of biology in which the macromolecular machine RNA polymerase (RNAP) produces a complementary strand of RNA from the genetic information encoded in the genomic DNA. The produced RNAs are then coded for proteins or serve other regulatory purposes necessary for critical cellular functions. Termination of transcription is tightly regulated to ensure production of accurate gene products. Misregulation of transcription can result in several different diseases, including cancer. Recently, our group has characterized a new mechanism of transcription termination, where collisions between converging RNAPs at programmed positions on the genomic track regulate the precise termination of RNA synthesis. Sequencing methods in vivo and single-molecule visualization in vitro have characterized this termination mechanism. Still, currently, no structural information is available to show what conformational changes the RNAP undergoes in a collided state.

Methods

Obtaining a high-resolution structure of this collision will provide new insights into how collision-directed transcription termination is regulated. We aim to develop a cryogenic-electron microscopy (cryo-EM) platform to study the various stages of RNAP conformation during collision. A homogenous sample of the macromolecular complex is necessary to obtain a high-resolution cryo-EM structure and requires extensive optimization. To this end, *in vitro* transcription assays were performed using purified *E. coli* RNAP to generate halted complexes as analyzed by agarose gel electrophoresis. In the *in vitro* transcription assays, a challenge was encountered with spurious RNAP binding and initiating transcription from the ends of the designed DNA template, resulting in non-specific RNAP: DNA complexes.

Conclusion

Preliminary evidence suggests that stable collided complexes that would be suitable for cryo-EM experiments have been achieved. Overall, this study promises to provide unprecedented insights into the molecular basis of collision-driven transcription termination. Obtaining high-resolution structures of the collided complex would open the door to answering more profound questions about how force, torque, and DNA supercoiling regulate these collisions. A similar approach applies to other collisions between macromolecular machines operating on the crowded genomic track.

BIOLOGICAL SCIENCES

11. Rida Akhlaq

Reducing Unassisted Falls Among Admitted Patients With Cancer at NewYork-Presbyterian, Weill Cornell Medicine.

Christine Ann Garcia, German Rodriguez, Dianna Assalone, Catherine DeBarbrie, Stefanie Taflin, Kristen Marsh, Harjot Kaur Singh, Jennifer Inhae Lee, Dan Crossman, Natan Santacruz, Jessica McDonough, Dana DeJesus, Yaw Kwarteng, Ethan Besas, Wooram Jung, Jihui Lee, Rida F Akhlaq, Manuel Hidalgo

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Background: Patients with cancer are at particularly high risk for falls and may suffer worse morbidity and mortality, including fractures due to bony metastases, subsequent bleeding due to thrombocytopenia. In our tertiary NYC hospital in 2020, there were 67 falls among patients with cancer admitted to oncology floors, accounting for 12.4% of all WCM falls among 5% of admissions. In the first quarter of 2021, there were 15 total falls which triggered the oncology units to focus on falls' reduction efforts. Of the patients that fell during their inpatient admission during 2020, 20% of these patients were not considered "high risk for falls" based on the traditional Morse Falls' risk assessment, making it unclear if the traditional assessment can adequately risk stratify patients with cancer.

Methods: Our SMART aim was to reduce the rate of unassisted inpatient falls per 1000 patient days (falls' rate) on oncology inpatient units (10N, 10S, 10C, 10W) at NewYork-Presbyterian, Weill Cornell Medicine by 10% from January 31, 2021- June 30, 2022. We initiated 5 iterative Plan-Do-Study-Act (PDSA) cycles on oncology units. Cycle 1 (2/2021) consisted of multidisciplinary root cause analysis meetings held with nurses, physicians, advanced practice providers, and environmental services. We also completed multipronged rapid cycle falls' audit among all oncology nurses. During cycle 2 (3/2021), new falls' signage was developed and posted outside each room and in patient bathrooms. During cycle 3 (6/2021), interdisciplinary falls' education was implemented. During cycle 4 (7/2021), a falls' prevention board was started to bring awareness to all team members. In cycle 5 (8/2021), a standardized, campus-wide post-fall huddle tool was implemented to deep dive into the "5 Whys" of falls. In cycle 6 (6/2022), we have just launched a prospective risk assessment tool to collect potential falls' risk factors not included in the Morse Falls' assessment.

Results: From February 2021 to June 2022, we were able to significantly reduce our unassisted falls rate on oncology inpatient units by 57%, from 4.51 falls per 1000 patient days to 1.97 falls/1000 patient days. Variation in falls' rates over time shows a median rate of 2.3 falls per 1000 patient days from quarter in 2018 with a downward trend in 2021-2022.

Conclusions: Through multiple PDSA cycles, we made iterative changes that ultimately reduced our unassisted falls rate among oncology patients. It was essential to engage key stakeholders including nurses, physicians, advance practice providers, patients and families in the discussion and get to the root of why patients were falling. Overall, this improved communication among team members and made the oncology units a safer place.

12. Tasmiah Akhter

Title: Toward RNA Molecular Technologies to Modulate Tissue-Selective Expression

Authors: Tasmiah Akhter[1,2], Jessica Das[1,3], Dennis Lam[1], Mohammadsadeq Mottaqi[1,4,5], Brandon Ely[1,3], Okkeun Jung[1,3], Hiroshi Matsui[4,6-8], Shahana S. Mahajan[3,4,9,10], Weigang Qiu[1,3,11], Mandë Holford[3,4,6-8,12], Frida E. Kleiman[3,6], and Andrew L. Wolfe[1,3,4,13]

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Hypothesis/Statement of Problem: Kirsten Rat Sarcoma Virus (KRAS) is a commonly mutated oncogene among all cancers, notably in ~40% of colorectal cancers (CRC) and ~20% of non-small cell lung cancers (NSCLC). RNA-based therapies, like KRAS-targeting siRNAs, present opportunities for treating tumors with mutations that are clinically undruggable using approved small molecules. However, on-target effects of KRAS knockdown in non-tumor tissues may be toxic, highlighting the need for strategies to localize expression to specific tissues with cancer. Occasionally, endogenous expression patterns of upregulatory RNA binding proteins (RBPs) and downregulatory miRNAs are restricted to one unique tissue type. We hypothesize that we can develop RNA Tissue Specific Barcodes that contain binding sites for endogenous RNA regulating factors to restrict the expression of an exogenous therapeutic RNA of interest to a single tissue type.

Methods/Results: We analyzed large RBP expression databases of various normal and tumor tissues. The highest expressing RBP that functionally upregulates its targets was chosen for validation in each specific tissue. We tested hits IMP2 and RBMS3 using immunoblots on cancer cell lines, and to assess the efficiency of the binding site interaction we are cloning RNA binding sites into dual-Luciferase reporters. RNA sequencing of miRNAs and RBPs in our CRC and NSCLC cell lines is underway to provide deeper insights into expression patterns.

Conclusion: By localizing expression to single tissues, off-tissue effects can be minimized while maximizing therapeutic efficacy. The primary goal is to enhance RNA-based therapy specificity, advancing targeted approaches for improved patient welfare.

102 Haya Alkiswani

Testing Beta-Cyclodextrin Derivatives for Clearance of Lysosomal Content in the Retinal Pigment Epithelium (RPE) *In Vitro* and *Ex Vivo*

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Hypothesis/Statement of Problem: Lysosomal storage disorders (LSDs) lead to accumulation of unprocessed substances in lysosomes. These lysosomal defects cause cell death leading to tissue atrophy. Our lab discovered a family of acidic cyclodextrins (aCDs), which are highly effective on inducing exocytosis. Consequently, these aCDs are attractive potential therapeutic agents to treat LSDs. This study specifically aims to evaluate the effectiveness of different doses of aCDs on lysosomal exocytosis, cellular viability, and lipofuscin content in the context of retinal cells *in vitro* and *ex vivo*.

Methods: Doses of various concentrations were prepared for each of the treatments: succinic acid (weak acid), aCD, HCl (strong acid), and a neutral cyclodextrin. After the treatments were administered to RPE cells in a 96-well plate, a beta hexosaminidase assay was done on the supernatant to evaluate exocytosis. The cells were lysed, and a beta hexosaminidase assay was done to determine activity due to remaining lysosomal content. For the *ex vivo* experiment, the eyes of mice with ABCA4/ RDH double mutation, were enucleated and eyecups were prepared. The left eye was used as control, while the right eye was treated with aCDs; both eyes were then stained and visualized by microscopy.

Results: *In vitro* results suggested that aCDs have the greatest potential to effectively induce lysosomal exocytosis while maintaining cell viability in RPE cells. *Ex vivo* results show that RPE treatment with aCDs clear lipofuscin accumulation in mouse RPE cells.

13 Amber Arif

Uncovering the Mechanism of Metabolomic Changes in Cells with Chromosome 3p Deletion

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Hypothesis/Statement of Problem:
Aneuploidy, the presence of an abnormal number of chromosomes, is a hallmark of over 90% of solid tumors, with tumor-specific patterns of chromosome gain or loss. Among these, the deletion of chromosome arm 3p (chr3p) is an early event in lung cancer. Chr3p deletion is implicated in the pathogenesis of lung cancer, suggesting a role in tumorigenesis. A genetic screen identified that knocking down GABRA5, one of the GABA receptor alpha subunits, increases toxicity in squamous lung epithelial cells with chr3p deletion. This study hypothesizes that chr3p deletion disrupts GABA signaling by reducing the expression of GABA transport genes, thereby increasing intracellular GABA levels and sensitivity to channel inhibition, contributing to lung cancer development.

Methods:
Genome-engineered lung epithelial cells with chr3p deletion identified increased sensitivity to GABRA5 inhibition. CRISPRi-guided knockdown (KD) of GABA transport genes GAT1, GAT3, and TauT and subsequent intracellular GABA level measurements via ELISA were performed.

Results:
Preliminary data showed that chr3p deletion increases intracellular GABA levels, with a corresponding decrease in extracellular GABA, indicating a defect in GABA transport. KD of GABA transport genes in chr3p-deleted cells resulted in heightened intracellular GABA levels, suggesting their regulatory role. Rescue of GABA transporter expression showed a potential to normalize GABA signaling and reduce sensitivity to GABRA5 inhibition.

Conclusions:
The study suggests that chr3p deletion affects GABA transporter gene expression, contributing to the oncogenic process in lung cancer. This research paves the way for further study into the impact of aneuploidy on established neurotransmitters and metabolic pathways in epithelial cells.

14 Sindi Beqo

Drug-Decoupled, 48-Hour Extended Release Nitric Oxide Delivery System - PCCM-125: Potential in Glaucoma and Ocular Surface Disease

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Problem: Nitric oxide (NO) has recognized potential in preventing glaucoma progression by lowering intraocular pressure, corneal wound healing, and corneal infections. However, NO therapeutics suffer from rapid NO depletion, low concentrations, and narrow applicability due to drug coupling (unstable NO bonded to partner drug). Our goals were decoupling NO from drug, while increasing the duration of NO release. To achieve this, we designed a plasma-chemical treated, chitosan-coated, micellar NO delivery system, PCCM-125.
Methods:Immediate release NO donor-oil synthesized through plasma-chemical treatment. PCCM-125 was created by combining this oil with similarly treated surfactant to form micelles, subsequently chitosan-coated. Controls included NO-free oil and untreated micelles. NO release in synthetic tear fluid (STF) was monitored over 24 hours for the oil (100µL in 1 mL STF) and 48 hours for PCCM-125 (1 mL in 10 mL STF), utilizing colorimetric assays for nitrite/ nitrate.
Results: PCCM-125 in STF: Nitrate concentration linearly increased over more than 48 hours, while nitrite remained relatively constant at a maximal level (0.3 mg/L) until 36 hours when it started to decline. NO donor-oil: Rapid elevation (minutes) of nitrite and nitrate levels. Untreated controls: remained at 0 mg/L.
Conclusion:PCCM-125 extended release of NO in STF, evidenced by steady nitrite level and linear nitrate increase over 48 hours. Since it is not coupled to a drug, PCCM-125 has broad applicability, while overcoming significant challenges of low NO concentration and rapid depletion. Thus, PCCM-125 likely has significant potential in glaucoma and corneal applications in future eye models.

103 Sangita Chakraborty

Effect of PAX3-FOXO1 Fusion Protein Knockdown on Global Nucleotide Synthesis in Fusion-positive Rhabdomyosarcoma Cell Lines

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The fusion protein PAX3-FOXO1 serves as the main molecular driver in fusion positive rhabdomyosarcoma (FP-RMS), a particularly aggressive soft tissue malignancy prevalent in children. Despite extensive efforts to understand the molecular and functional consequences of this novel chimeric transcription factor, the fusion protein remains "undruggable." We attempt to address this limitation by studying this fusion protein from a metabolic standpoint as little is known about how PAX3-FOXO1 regulates cellular metabolism in the current literature. Preliminary findings in the Finley lab highlight the cancer cells' dependency on thymidine synthesis genes as part of the folate cycle and concurrently reveal heightened levels of hypoxanthine, an intermediate metabolite in the purine synthesis pathway. Based on these insights, we hypothesize that the fusion protein upregulates global nucleotide synthesis to sustain its rapid proliferative needs. Here, we use doxycycline-inducible shRNA targeted against the PAX3-FOXO1 translocation junction to generate PAX3-FOXO1 knockdown FP-RMS cell lines. Metabolites will be extracted from harvested cell lysates and be measured by targeted liquid chromatography-mass spectrometry. We anticipate that the LC-MS results will reveal a reduction in global nucleotide synthesis following the knockdown of the fusion protein which will allow us to potentially uncouple any observed effects of PAX3-FOXO1 loss on nucleotide metabolism from slower cell proliferation.

15 Subyeta Chowdhury

The Role of Cooperating Mutations in the Progression of Myeloproliferative Neoplasms into Acute Myeloid Leukemia

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Hypothesis/Statement of Problem: Myeloproliferative neoplasms (MPN) are blood disorders that often progress into Acute Myeloid Leukemia (AML). A majority of MPNs are caused by mutations in genes that play a key role in the JAK/STAT pathway—a pathway essential to normal hematopoiesis—and the RAS pathway, yet there are limited treatment options for patients who carry these mutations. A fraction of NRAS/KRAS mutant patients who progressed to AML had cooperating mutations in JAK2.

Methods: Assessment of genomic data from a cohort of MPN patients at MSKCC who progressed to AML with mutations in NRAS/JAK2 led to the identification of three genes of interest: PHF6, STAG2, and SRSF2. An shRNA system will be used to knock down the expression of these genes in bone marrow cells from mice that carry Nras-G12D and Jak2-V617F mutations. These cells will be plated in Methocult, and the number of colonies formed in experimental knockdown conditions will be compared with controls. These cells will then be serially replated to assess their leukemic potential. Since Nras-G12D and Jak2-V617F mutations alone are insufficient to cause leukemia, these cells will not re-plate for more than 3-4 times.

(Expected) Results: If the knockdown cells have an increased fitness and leukemic potential, they will be able to grow for several more replatings. If one of the candidate genes initiates a leukemic phenotype, this experiment will be repeated using peripheral blood mononuclear cells from patients.

Conclusion: Understanding the origin and progression of disease will help advance our knowledge of RAS-mutated MPNs, and to consequently identify new treatment strategies.

The Role of Haptoglobin-Related Protein in Innate Immunity to African Trypanosomes

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Hypothesis: African Trypanosomes are parasites that cause nagana in animals. Humans and some primates are innately protected against trypanosome infections due to specific high-density lipoproteins called Trypanosome Lytic Factors (TLF). TLFs contain distinct proteins: haptoglobin-related protein (HPR) and apolipoprotein L-1 (APOL1). APOL1 is a cation channel-forming protein that lyses trypanosomes through ion dysregulation and osmotic swelling. HPR shares homology with haptoglobin (Hp), which binds toxic free hemoglobin (Hb). Trypanosomes endocytose Hp:Hb complexes using surface haptoglobin-hemoglobin receptor (HpHbR). HPR, only secreted in TLF due to an uncleaved signal peptide, also binds Hb and can exploit HpHbR, resulting in endocytosis of TLF and, eventually, parasite lysis. HPR is a 47kDa αβ-disulfide-linked inactive serine protease. The active site catalytic triad of serine proteases is aspartic acid(D), histidine(H), and serine(S). Sequence analysis revealed that two residues in the HPR β-chain "active site," K144 and A297, may inactivate the enzyme. I hypothesize that HPR uses the inactive pocket to bind APOL1, protecting it from degradation.

Methods: I will use site-directed-mutagenesis to make catHPR, a secretable form of HPR (L20V & Y21D) with restored catalytic function (K144H & A297S), in vector pRG977-HK62. Enzymatic activity of purified catHPR from transfected Chinese Hamster Ovary-Suspension cell culture media can be evaluated with recombinant APOL1 visualizing degradation by Western blot.

Results: Plasmids containing K144H or A297S mutations are constructed. I am engineering L20V & Y21D in both plasmids.

Conclusions: This study will expand our understanding of human innate immunity against trypanosomes and address the role of HPR in TLF.

17 Rowena Fang

Repeated Sampling of the Oral Microbiome to Improve Detection of Barrett's Esophagus

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Hypothesis/Statement of Problem: The occurrence of esophageal adenocarcinoma (EAC) has increased 10-fold over the last half century. Although Barrett's esophagus (BE) has been established to be a precursor to EAC, more than 90% EAC patients are never diagnosed with BE beforehand. Currently an upper endoscopy is the only method to diagnose BE, but there is a critical need to develop minimally-invasive, cost-effective and efficient methods of BE screening to lower EAC mortality. The microbiomes of the mouth and esophagus are directly linked and the esophageal microbiome is altered in BE. Thus, the oral microbiome may provide information about EAC risk. We previously found that a salivary microbiome signature composed of *Lautropia*, *Streptococcus*, and *Enterobacteriaceae* distinguished BE patients with high accuracy. Thus, analyzing the microbiome of saliva may represent a highly novel, non-invasive screening test for BE. However, the temporal reproducibility of a salivary microbiome signature for BE has not bee previously demonstrated. We hypothesize that repeated sampling of the salivary microbiome can accurately distinguish BE patients from non-BE individuals.

Methods: We are performing a longitudinal cohort study of 250 patients with and without BE who have undergone an upper endoscopy within three years of enrollment. We are collecting saliva samples three times spaced one month apart, and enrolling 50 subjects with an established endoscopic and histologic diagnosis of BE and 200 subjects without BE. We are collecting demographic and clinical information at baseline, and at the time of each sample collection subjects also complete a validated food frequency questionnaire assessing fat and fiber intake over the previous 4 weeks. The anticipated enrollment duration is 2 years. We will be performing 16S rRNA gene sequencing on saliva samples. We will used gradient boosted modeling to develop a microbiome-based signature to distinguish BE from non-BE patients based on baseline saliva samples. We will then assess longitudinal reproducibility of this microbiome signature (calculating intraclass correlation coefficients (ICC)) and whether repeated sampling improves the test characteristics (area under the receiver operating curve). With 50 BE cases, the ICC of the three repeated microbiome signatures can be estimated with a 95% CI width of $\leq$0.32. With 200 non-BE controls, the ICC of the three repeated microbiome signatures can be estimated with a 95% CI width of $\leq$0.16.

Results and Predicted Outcomes: Thus far, 32 BE and 82 non-BE subjects have been enrolled. 94 subjects have provided three longitudinal samples and have completed the study. We aim to complete enrollment by December 2025. Based on similar work in a separate cohort of patients, we predict that a salivary microbiome signature will distinguish BE from non-BE with high accuracy (AUC 0.80), and that the signature will have good reliability (ICC 0.80). Thus, we would be able to discriminate between the oral microbiome of BE and non-BE patients.

Predicted Conclusions: We anticipate that repeated assessment of a salivary microbiome signature will demonstrate that this non-invasive testing approach can distinguish BE patients with high accuracy. Further, we anticipate that the signature will be reproducible over time, indicating that it is a potentially robust and accurate method to identify patients at high risk for developing esophageal adenocarcinoma. Thus, analyzing the microbiome of saliva represents a less costly, non-invasive screening test for BE, which can potentially reduce the risk of EAC in the future.

18 Abigail Groysman

Gut Microbiome Modulation by Oral Vancomycin: Implications for Health and Disease

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Statement of Problem – Oral vancomycin is one of the frequently used antibiotics to probe the contribution of gut microbiota, which play a pivotal role in the pathogenesis of metabolic and neurodegenerative diseases, cancer, inflammatory and infectious disease. However, a systematic review of the literature is lacking to understand the impact of oral vancomycin on gut microbiome, host health and disease.

Methods – We conducted a comprehensive search of research literature on PubMed and Google Scholar, investigating the effects of oral vancomycin in various disease models. The studies were assessed for single oral vancomycin usage, shifts in gut microbiota composition, changes in disease severity, and proposed mechanism of action in mitigating or exacerbating disease.

Results- Oral vancomycin caused a significant shift in the gut microbiome composition, largely ablating gram-positive bacteria including gram-negative *Bacteroides,* and enriching *Akkermansia* and Proteobacteria. Oral vancomycin treatment had positive impact on malaria severity, insulin resistance, liver cancer and Parkinson's disease, varying impact on Type I Diabetes, while negatively impacting anti-hyperglycemic effect of metformin, colitis, colorectal cancer, allergic inflammation, asthma, and cognitive decline.

Conclusion – Our findings demonstrate that the influence of oral vancomycin on disease outcomes depends on host characteristics, disease type, experimental model, and duration of antibiotic administration. While its potential remains promising in preventing or mitigating specific gut microbiota-driven diseases, further investigation is warranted to optimize its utilization and minimize potential unintended effects.

19 Diana Katanov

Disrupting Heterodimerization of Oncogenic Drivers MDM2:MDMX through Site Directed Mutagenesis

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Abstract

Mouse double minute 2 (MDM2) is known for its role as a negative regulator of tumor suppressor protein p53. The *TP53* gene is mutated in eighty percent of human cancers, and MDM2 is overexpressed in thirty percent of triple negative breast cancers (TNBCs). MDM2 is an E3 ubiquitin ligase that promotes the ubiquitination and proteasomal degradation of p53. MDM2 and its paralog, MDMX, heterodimerize to down-regulate p53 through their Really Interesting New Gene (RING) domains. However, recent studies have brought to light p53-independent roles of MDM2:MDMX that promote cell proliferation and metastasis. To test if the MDM2:MDMX interaction is a required tumor driver in p53-independent mechanisms, site directed mutagenesis (SDM) was utilized to introduce specific point mutations to *MDM2* and *MDMX* genes to disrupt dimerization. SDM uses Polymerase Chain Reaction (PCR), Kinase, Ligase, DpnI (KLD) Reaction, and bacterial transformation to engineer altered plasmids. We expected the resulting MDM2 protein to have the C449N missense mutation that disrupts MDM2/MDMX[1]. Similarly, the MDMX expected mutant, harboring a C437DEL mutation, disrupts MDM2/MDMX due to the RING domain deletion. Sanger Sequencing results confirmed the presence of the SDM mutations. Expression of the MDMX protein from the mutant plasmid in transiently transfected HCT116 p53 -/- cells was confirmed by transient transfection and cell lysate followed by western blot. To investigate further downstream signaling, western blot analysis and chemiluminescence was utilized to assess MDM2, MDMX, p53, and PAR levels. Future studies are in progress to determine if oncogenic signaling is disrupted by blocking dimerization.

[1] Kosztyu P, Slaninová I, Valčíková B, et al. A Single Conserved Amino Acid Residue as a Critical Context-Specific Determinant of the Differential Ability of Mdm2 and MdmX RING Domains to Dimerize. *Front Physiol*. 2019;10:390. Published 2019 Apr 9. doi:10.3389/fphys.2019.00390

20 Tiffany Lin

Characterizing the Kinematics of Skilled Action in a Mouse Model of DYT1 Dystonia

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Hypothesis/Statement of Problem: Dystonias are a group of disorders characterized by abnormal twisting movements due to involuntary co-contractions of opposing muscles. Contractions in task-specific dystonia, a primary focal dystonia, happens during specific activities that usually involve highly skilled and repetitive movements. Emerging evidence shows that these movements may be regulated by abnormal neuroplastic mechanisms. However, primary dystonia has been difficult to study in rodent models as knock-in mice with the human mutant TOR1A gene (DYT1-KI mice) do not exhibit a clear phenotype when tested on classic behavioral tests like the rotarod and simple lever pressing.

Methods: One explanation is that these behavioral tests can be completed by mice without utilizing corticostriatal or cerebellothalamocortical circuits. Reduced connectivity between these brain regions has been shown by imaging studies to correlate with dystonic motor symptoms. Skilled reaching is a behavior that involves the corticostriatal and cerebellothalamocortical circuits. We therefore hypothesized that task-specific dystonic behaviors would be revealed in DYT1-KI mice after extensive training in skilled reaching.

Results: Here we show that DYT1-KI mice consistently had more “fumbles,” where the pellet was lost mid-retrieval. And, while overt dystonic behaviors were not detected, 30% of DYT1 mice displayed abnormal movements. This is consistent with the penetrance of DYT1-dystonia in humans.

Conclusions: These results indicate that the human TOR1A mutation is sufficient to generate motor deficits in skilled behaviors. Further, DYT1-KI mice provide an invaluable model to determine the circuit mechanisms that factor into the pathogenesis of dystonia.

21 Anisa Mujaj

Identifying *C. elegans* Germline DNA Repair Pathways With and Without Functional CEP-1

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Hypothesis/Statement of Problem: CEP-1, the ancient ortholog of p53, induces germline cell death by activating the transcription EGL-1 and CED-13, orthologs to the human BH3 domain proteins Puma and Noxa. GLP-1 is part of the Notch signaling pathway, influencing cell fate determination within the germline. PME-2, orthologous to human PARP-2, is implicated in DNA repair but requires further investigation. This study explores the impact of CEP-1 and GLP-1 mutations, alongside PME-2 knockdown, on DNA repair in C. elegans.

Methods: Worms were maintained on NGM plates to assess egg laying, viability, and lifespan under varying temperature conditions pre- and post-UVC treatment. PME-2 knockdown was achieved through RNAi to observe its effects.

Results: Results indicate that MD701(ced-1::GFP) worms exhibit prolonged lifespan compared to JBC1(cep-1 (gk138); ced-1::GFP) worms at 21°C. Before UVC exposure, minimal differences in lifespan were observed between MD701 worms with and without PME-2 knockdown at 21°C, consistent with JBC1 worms. Egg-laying and viability showed no significant differences at 21°C. After UVC treatment, egg viability decreased in worms with wild-type CEP-1 (MD701) with PME-2 knockdown, dropping from 87.3% to 46.7%. Additionally, UVC treatment reduced egg viability in worms with mutated CEP-1 (JBC1), both with and without PME-2 knockdown, with viability rates of 28.85% and 33.8%, respectively.

Conclusion: These findings validate prior data on lifespan and egg viability in worms with and without functional CEP-1 and suggest that PME-2 may be involved in germline DNA damage response.

104 Adrianne Nemchik

Evaluating the Effects of Exosomes and Collagen Scaffolds in Murine Calvarial Bone Regeneration

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Hypothesis/Statement of Problem: Multipotent stem cells (MSCs) can differentiate into specialized cells of the bone and other connective tissues, thereby aiding in bone regeneration. However, the regenerative potential of the small extracellular vesicles (exosomes) secreted by pediatric bone MSCs (pMSCs) remains unclear. Natural polymers like collagen can enhance cellular integration and osteoblast activity in bone tissue engineering. This project investigates the impact of a collagen sponge scaffold and pMSC exosomes on bone regeneration in a murine calvarial defect model.

Methods: Exosomes from pMSCs were applied to some 3mm diameter defects made in the calvaria of mice using a collagen sponge as a vehicle of delivery and stability. Immunofluorescent staining of cross-linked calvarial tissues and high-resolution inverted microscopy techniques helped identify relevant cell types and analyze cellular morphology and tissue architecture during regeneration.

Results: The visualization of vascular patterns using dual markers staining endothelial cells - EMCN and CD31, osteoblast differentiation using transcription factors RUNX2 and OSX, and osteoblast activity during osteogenesis using extracellular matrix protein POSTN, helped characterize cell types and their spatial locations in an osteoconductive environment as they participate in bone regeneration.

Conclusions: Bone tissue engineering using a collagen sponge scaffold with and without pMSC exosomes regenerates bone and demonstrates similar patterns of cellular organization as seen in intact bone. Understanding the mechanisms involved in bone regeneration, and identifying participating cells, can help optimize treatment options for bone defects for future applications in bone tissue engineering procedures in pediatric cases, such as cleft lip and palate disorders.

105 Swara Patel

Investigating the Impact of ASXL1 Mutations on BAP1 Stability

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The ASXL1 gene codes for a component of and regulates the stability of the BAP1 histone H2A deubiquitinase complex. ASXL1 mutations are implicated in various myeloid malignancies including acute myeloid leukemia and associated with a poor prognosis. Cancer associated frameshift mutations in ASXLl1 have been found to encode truncated, stable gain of function proteins which can enhance BAP1 activity. However, the precise molecular mechanisms by which ASXL1 mutations impact and stabilize BAP1 protein activity have not yet been elucidated. We designed a BAP1 dual reporter construct with a BAP1-GFP-T2A-CHERRY sequence to investigate the impact of ASXL1 mutations on BAP1 protein stability. We hypothesize that ASXL1 truncating mutations increase BAP1 protein stability which result in a higher GFP:CHERRY ratio. The T2A linker allows for the GFP and MCHERRY expression to be compared differentially to assess relative BAP1 protein stability in ASXL1 wild type, knock-out, and gain of function mutations. Additionally, we designed three constructs with point mutations in the BAP1 catalytic domain which significantly decreases protein stability and enzymatic activity in vitro as controls. Upon cloning these constructs, we produced lentiviruses and transduced primary bone marrow cells. GFP and MCherry expression was analyzed across populations of progenitors as well as mature myeloid and lymphoid cells by flow cytometry. We expect our results to demonstrate the impact of different ASXL1 mutations on BAP1 protein stability across different populations of blood cells. This will enable us to better understand the impact and mechanisms of various ASXL1 truncating mutations implicated in myeloid malignancies in terms of increasing BAP1 protein stabilization.

22 Tanvir Raihan

Characterization of Bap1 Knockout on Retina Development in the Mouse

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Hypothesis/Statement of Problem: The BRCA-1 associated protein (BAP1) gene is known to have an important role in eye development in Xenopus models. However, the function of the BAP1 protein in human and mouse eye development is still unclear. This project seeks to understand why, how, and when the Bap1 gene contributes to normal retinal development in mammalian eye development.

Methods: Transgenic mice with conditional knockout of the Bap1 gene in early retinal progenitors were developed utilizing mRx-CRE to investigate the role of Bap1 in early eye development. Retina sections taken from mice at various time points were compared between control and Bap1 conditional knockout mice.

Results: Thinner retinas were found in Bap1 conditional knockout mice than in wild-type mice at the p7, p10, p12, p21, and p32 time points, but not at the p0 time point. This may indicate that the phenotypic changes occur during postnatal development in mice. Analysis of individual retinal layers at p0, p21, and p32 revealed significant differences in the thickness of each layer at p21 and p32. Phenotypic analysis of retinal layers using cell-specific markers at p10, p21, and p32 suggests that Bap1 plays a role in cell number and organization of laminar structure in the retina. While further characterization and quantification are necessary to fully understand the role of Bap1 in retinal development, initial results reinforce the importance of Bap1 and the viability of using the Bap1 fl/fl mRx-Cre transgenic mouse model in investigating Bap1 and its functions in retinal development.

Examining the Influence of Substrate Stiffness on iPSC-derived Lateral Plate Mesoderm Differentiation *in vitro*

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Hypothesis/Statement of Problem: Previous work from our lab has shown that hair-bearing skin organoids (SKOs) can be derived from pluripotent stem cells (PSCs) through guided differentiation. These SKOs exhibit complexity and architecture reflecting the human skin. However, they lack vasculature, immune cells, sweat glands, as well as diverse anatomical identity. To address these limitations, we propose constructing SKOs by co-inducing surface ectoderm and specific types of mesoderm. The lateral plate mesoderm (LPM) gives rise to the progenitor cells of the heart, cardiovascular system, smooth muscle, lymphoid blood lineage, trunk (chest) dermis, and limb dermis. Recent works have shown that LPM cells can be generated from PSCs *in vitro*, however controlling further lineage differentiation to obtain on-target cell types remains a challenge. Specifically, the role of mechanical force and substrate stiffness in influencing the differentiation pathways of LPM cells remains poorly understood.

Methods: We generated LPM cells from PSCs and tested their reactivity on engineered polyacrylamide hydrogel substrates of varying stiffnesses that have been micropatterned with an extracellular matrix ligand. Post culture, we utilize immunofluorescence to assess these cells for markers of different progenitors, including LPM (Hand1) and limb mesenchyme (PRRX1), as well as for markers of mechanical support (F-actin) and cell adhesion (ZO-1).

Results and Conclusions: Our preliminary results suggest that mechanical tension influences progenitor marker localization within LPM cell clusters, and that LPM cells grown on softer substrates express endothelial markers, a promising start towards potentially using substrate-tuned LPM cells to increase the capability of SKOs as a model for disease, cancer, and wound repair.

24 Elisa Sambataro

Comparison of Host DNA Depletion Methods from Low-Biomass Microbiome Samples

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Hypothesis/Statement of the Problem: 16 rRNA gene amplicon sequencing is a widespread tool used to characterize bacterial populations from a wide range of environments. However, host-derived low-biomass samples are dominated by mammalian DNA. It limits the use of 16 rRNA gene amplicon sequencing to identify changes in microbial populations due to few microbial components reads. Therefore, it is important to identify methods to deplete host DNA before shotgun sequencing. We compared the efficiency of two methods, using Propidium monoazide (PMA) and Saponin to deplete human DNA from low-biomass microbiome samples to enrich microbial DNA before sequencing.

Methods: We collected 3 samples from three body sites (skin, nasal cavity, and saliva), from two donors. One sample from each site was treated with PMA, Saponin and one remained untreated as a control. The effectiveness of each treatment was measured by comparing the DNA yield in each sample to their corresponding untreated control. To test the effect on the samples' microbiome composition, DNA was sequenced using qPCR 16S long-read sequencing.

Results: Preliminary results showed that saliva samples treated with Saponin ($p = 0.009$), and PMA ($p= 0.01$) showed a significantly lower DNA yield than untreated samples, suggesting that Saponin and PMA could deplete human DNA from low-biomass microbiome samples. No significant difference was seen in the DNA concentrations in skin and nasal samples. However, these values are close to the detection limit, and effects might be difficult to observe.

Conclusions: Hence, Saponin showed greater success in saliva samples as a host DNA depletion method to enhance microbial DNA before sequencing.

25 Jason Sethiadi

Utilizing Stereolithography to Engineer Multi-well Systems for Organoid Culture

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Hypothesis/Statement of Problem: Organoids and three-dimensional spheroids are multicellular aggregates that can model tissue architecture and organ physiology in vitro. They have become a standard in tissue engineering, serving as extremely applicable tools in bioengineering, drug development, and investigating the effects of disease on cellular phenotypes and function.

Methods: Specifically, we developed organoids that co-aggregate different hepatic cells to model liver function. To diminish the heterogeneity during organoid and spheroid formation, we used photolithography to build a polydimethylsiloxane-based (PDMS) multi-well system that accommodates the organoids. However, one substantial challenge in organoid biology is ensuring the spheroids' survival over extended periods. Facilitating a conducive environment is crucial since organoids are prone to detaching from their wells or losing their spherical shape. This poses a problem for studies requiring the organoid to function for multiple weeks or months. Using stereolithography, we gained greater control over the design and specifications of each well and developed a more suitable environment for generating spheroid aggregates.

Results: By optimizing the dimensions and geometry of the multi-well system for hepatocyte-fibroblast spheroids, we observed that this created a more stable environment for the organoids. Compared to previous multi-well systems, the optimized platform increased the duration of the spheroid's lifespan. Furthermore, we observed that the organoids grown in the optimized system had significantly higher albumin secretion levels than current spheroids.

Conclusions: This demonstrates the versatility of stereolithography as a technique in engineering three-dimensional culture systems and presents an opportunity to modify and optimize these microwell patterns for culturing different types of organoids.

The Role of Protein Arginine Methyltransferase 5 (PRMT5) in Non-Alcoholic Fatty Liver Disease (NAFLD)

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Statement of the Problem: Non-Alcoholic Fatty Liver Disease (NAFLD), characterized by excessive liver lipid accumulation in non-alcohol-consuming individuals, is a significant global healthcare burden with poorly understood mechanisms. Protein arginine methyltransferase 5 (PRMT5) facilitates a transcriptional or posttranslational modification involved in the majority of symmetrical dimethylation of arginine residues on histones and non-histone proteins. We demonstrated that PRMT5 expression levels increased in the liver of mice fed on a high-fat diet, and inhibition of PRMT5 decreased lipid droplet accumulation. We sought to investigate the role of PRMT5 in the development of NAFLD in vivo.

Methods: Two studies were conducted: Firstly, a gain-of-function study using adeno-associated viruses (AAV) to deliver green fluorescent protein control, wild-type PRMT5, or an enzymatic-deficient mutant in C57BL/6J mice. Secondly, an adenoviral-cre recombinase-mediated loss-of-function in PRMT5 conditional knockout mice.

Results: Results revealed that exogenous wild-type PRMT5, but not the enzyme-dead mutant PRMT5, promoted NAFLD, while PRMT5 depletion reduced liver lipid accumulation and improved glucose clearance and insulin tolerance. Probing into the mechanism, we confirmed PRMT5 knockdown efficiency in vitro using an inducible method in α Mouse Liver (AML12) cells. Additionally, we conducted a whole transcriptome analysis using RNA-seq of the control and PRMT5 knockdown cells and identified that bile acid pathways were altered in the PRMT5 knockdown cells. The differentially expressed genes were validated by quantitative reverse transcription polymerase chain reaction (RT-qPCR).

Conclusion: Our study elucidates the critical role of PRMT5 in NAFLD pathogenesis, shedding light on metabolic gene regulation, lipid, and bile acid metabolism pathways, and providing valuable insights for novel treatments.

27 Nabiha Subzwari

Characterization of Exosomes from Mature Oligodendrocytes with Myelin Regulation Potential

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Hypothesis/Statement of Problem: Oligodendrocytes (OLs) release exosomes that function in diverse biological processes in the central nervous system. It has been shown that mature OLs use exosomes as a signal to inhibit myelination. We have found that the ablation of the non-muscle myosin IIB (NMIIB) gene in OL potentiates their differentiation, myelin formation, and myelin repair. We asked if the knockout of NMIIB changes exosome production by OL, thus promoting their differentiation.

Methods: To determine their ability to affect OL branching and differentiation *in vitro*, we treated oligodendrocyte progenitor cell (OPC) cultures with exosomes purified from wild-type and NMIIB conditional knockout (cKO) mouse brain slices and spinal cords. To explore if exosome activity on OL maturation changes in the context of myelin damage, OPCs that were treated with exosomes from brain slices were given inflammatory cytokines (IFN-γ), while those treated with exosomes from spinal cords were given demyelinating agents (lysolecithin). Cells were fixed and processed for immunocytochemistry to measure the percentage of MBP+ cells and the area of MBP+ OL branching.

Results: We hypothesize that exosomes from NMIIB cKO mice may have a beneficial effect on OPC differentiation following demyelination.

Conclusions: This study aims to further characterize how exosomes regulate oligodendrocyte differentiation. The overall goal is to use this information to treat, and even prevent, demyelinating diseases such as Multiple Sclerosis.

Optimization of Decoy SAH Wash Conditions for the MagIC-cryo-EM Technique

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Hypothesis: Magnetic Isolation and Concentration (MagIC)-cryo-EM is a newly introduced technique that allows for structural analysis through specific targeting with nanomagnetic beads which reduces required target concentration to 100 to 1000-fold lower than conventional cryo-EM methods (Arimura Y, Konishi HA, Funabiki H. bioRxiv [Preprint]. (2024) PMID: 38328033). The washing conditions could be optimized using a decoy SAH protein to remove non-specific binding to nanomagnetic beads' components.

Methods: Rosetta(DE3) *E.coli* cells expressing His-SUMO-decoy-30nm-SAH were induced with 1mM IPTG, disrupted by sonication and soluble fraction was collected with centrifugation. His-SUMO tag was cleaved with SENP1 and washed through HisTrap to separate from decoy-30nm-SAH. Decoy-30nm-SAH was further purified, and concentrated using Amicon 3K.

Results: Four washing conditions were analyzed: 1. Decoy wash of sample before mixing with nanomagnetic beads; 2. Decoy wash after mixing sample and nanomagnetic beads; 3. Decoy wash before and after mixing sample and nanomagnetic beads; 4. No decoy wash. Wash conditions 2 and 3 allowed for the best removal of nonspecific binding to the spacer component of nanomagnetic beads with no significant difference between the two conditions. Wash condition 4 did not adequately prevent non-targets from bindings to the spacer. Wash condition 1 provided moderate removal of non-specific binding to the spacer, however, significant interference still persisted.

Conclusion: Decoy wash after mixing sample and beads created the most optimal conditions as it prevents non-specific binding to the spacer proteins on the nanomagnetic beads and is not improved by additional prewash.

29 JoJo A Merolla (Josephine)

Illumina sequencing is the ideal DNA sequencing method

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Illumina sequencing is widely regarded as the gold standard for DNA sequencing due to its unparalleled accuracy, speed, and scalability. Its superiority stems from its proprietary sequencing by synthesis technology, which leverages bridge PCR and fluorescently labeled nucleotides to generate high-quality reads. Illumina sequencing offers unmatched throughput, allowing for simultaneous analysis of millions of DNA samples, making it ideal for large-scale genomics projects. Additionally, its impressive accuracy and lengthy read lengths enable resolution of complex genomic regions and reliable variant detection. While other sequencing technologies have their strengths, Illumina sequencing remains the benchmark for DNA sequencing, offering an unbeaten combination of speed, accuracy, and scalability.

Illumina sequencing is superior to other sequencing technologies for DNA due to its proprietary sequencing by synthesis approach, which leverages bridge PCR and fluorescently labeled nucleotides, resulting in a higher signal-to-noise ratio and increased accuracy in base calling. Specifically, the use of four differently colored fluorescent dyes (fluorescein, Cy3, Cy5, and Cy7) to label the four nucleotides allows for simultaneous detection of multiple bases in a single reaction, enabling faster and more accurate sequencing. The distinct colors and emission spectra of these dyes enable precise discrimination between the four bases, leading to higher accuracy and longer read lengths. Additionally, the optimized excitation and emission wavelengths for each dye allow for efficient and specific detection of the fluorescent signals, further enhancing the accuracy and speed of the sequencing process. This results in a higher quality sequencing data, enabling researchers to make more accurate conclusions about the DNA sequence.

Methods:

* Comparative analysis of sequencing technologies using various metrics (accuracy, read length, throughput, cost).
* Investigation of the chemistry behind Illumina's sequencing by synthesis reaction.
* Development of new sequencing technologies that aim to surpass Illumina's performance.
* Library preparation and sequencing using Illumina and other platforms.
* Data analysis using bioinformatic tools (e.g., BWA, Samtools).
* Chemical modifications to nucleotides and sequencing reaction conditions to enhance performance.

* Surveying experts in the field for their experiences and preferences with various sequencing technologies.

Results:

* Higher accuracy and longer read lengths compared to other sequencing technologies.
* Improved signal-to-noise ratio and base calling accuracy.
* Enhanced detection of rare genetic variants and improved resolution of complex genomic regions
* Increased throughput and speed of sequencing reactions.

Conclusions:

Illumina sequencing leverages advanced biochemistry techniques, including bridge PCR and fluorescently labeled nucleotides, to achieve high accuracy and speed. The use of four differently colored fluorescent dyes enables simultaneous detection of multiple bases, enhancing accuracy and speed. Optimized excitation and emission wavelengths for each dye result in efficient and specific detection of fluorescent signals. Improved sequencing data quality enables researchers to make more accurate conclusions about DNA sequence, enabling advancements in fields such as genetics, genomics, and personalized medicine.

Resources:

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30 Rohan Ghoshal

Role of Cholecystokinin in Regulating the Motivational Properties of Nicotine

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Statement of Problem: Nicotine addiction through habitual tobacco use is a leading cause of premature death in the United States. Postprandial plasma cholecystokinin (CCK) levels are elevated in tobacco smokers relative to non-smokers, yet the consequences of this effect on nicotine intake are unknown. Thus, the aim of this study is to elucidate a mechanism through which nicotine induces elevated CCK levels and the role of circulating cholecystokinin in modulating nicotine intake.

Methods: An enzyme immunoassay was used to determine plasma CCK levels in genetically modified mice (TAS2R-knockout) injected with nicotine (1.5 mg/kg, s.c.) or saline. Next, a toxin (CCK-saporin) that selectively lesions CCK receptor expressing (CCKR+) neurons was injected into the vagus nerve (nodose ganglia) of a separate cohort of mice. The lesioned and intact control mice were prepared with chronic indwelling jugular catheters and permitted to self-administer nicotine at various doses (0.1–0.4 mg/kg per infusion), and nicotine intake was monitored.

Results: CCKR-lesioned mice self-administered greater quantities of nicotine compared to controls, an effect most apparent at aversive doses of nicotine, suggesting that CCKR+ neurons regulate aversive sensory responses to nicotine that limit its consumption. TAS2R-knockout mice showed similarly elevated nicotine-induced postprandial CCK plasma levels as controls, suggesting that this effect is not mediated by direct activation of TAS2R+ enteroendocrine cells by nicotine.

Conclusions: Peripheral CCKRs regulate nicotine intake in part due to actions on vagal sensory afferents. This novel “bottom-up” regulation of nicotine intake by the nodose ganglia may prove useful for the development of novel addiction therapies.

BIOLOGY

31 Sera Aktas

Regulation of p21 translation and senescence induction by a long non-coding RNA during the DNA damage response

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Non-lethal doses of chemotherapy frequently result in resistant cells that undergo induced senescence. These resistant cells can return to a proliferative state growing more aggressively compared to cancer cells that were never senescent. Chemotherapy in combination with senolytics (small-molecule drugs designed to target senescent cells) have been used to target these dormant cancer cells. The most studied senolytic, navitoclax, redirects cells undergoing chemotherapy treatment from senescence to apoptosis by inhibiting anti-apoptotic Bcl-2 and Bcl-xL and downregulating senescence-inducing p21 levels, highlighting the relevance of p21 in this combinatorial treatment. p21 is a cyclin-dependent kinase inhibitor which functions to halt the cell cycle and induce senescence during DNA damage response (DDR).

Recently, we identified a long non-coding RNA from the CDKN1A locus, which codes for p21, generated by alternative polyadenylation after DNA damage. We term this transcript Selective Polyadenylation Upon Damage (SPUD). SPUD modulates p21 protein translation during DDR. SPUD levels and induction by chemotherapeutic agents in cancer cells are much higher than in normal cells. SPUD levels correlate with p21 in different cell lines. *We hypothesize that the role of SPUD causing increased p21 translation in cancer cells can be targeted as a mechanism to decrease p21-induced chemotherapy resistance.* Consistent with this, siRNA-mediated depletion of SPUD reduces the number of senescent cells after DNA damage treatment in multiple cancer cell lines. I propose in future experiments to downregulate SPUD in combination with navitoclax and doxorubicin to induce a more robust cell-killing response by eliminating senescent cancer cells.

32 Brandon Arroyo

Mechanistic Effects of N361 Glycosylation of Epidermal Growth Factor Receptor

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Hypothesis/Statement of Problem: Epidermal growth factor receptor (EGFR) is a transmembrane tyrosine kinase that responds to extracellular growth factors to promote cell proliferation. EGFR mutations and amplifications account for a significant fraction of non-small cell lung carcinomas and breast adenocarcinomas, with L858R being the most common oncogenic hotspot. Molecular dynamic simulations suggested glycosylation, a post-translational modification, at N361 may be important for dimerization or ligand binding. However, the functional relevance of this modification at N361 on EGFR protein and cellular behaviors remained unclear.

Methods: To determine the functional relevance of glycosylation at N361, we created glycosylation-defective EGFR N361A, with or without an additional oncogenic mutation at L858R. We stably expressed these constructs in MCF10A and 293T cells, which do not have pre-existing activation of the EGFR pathway.

Results: Immunofluorescence and flow cytometry showed that the mutant constructs were each well expressed at the cell membrane. Proximity ligation assays measuring colocalization of EGFR with its binding partner Her2 in cells showed that N361A greatly increased number of foci relative to wildtype controls. N361A decreased cell viability and growth, as well as sensitivity to stimulation by the ligands EGF and amphiregulin. Additionally, N361A desensitized cells expressing the oncogenic L858R to necitumumab, which targets the extracellular domain, possibly because the mutation alters the antibody binding interface. In contrast, N361A sensitized cells to Osimertinib, which targets the EGFR kinase domain.

Conclusions: These findings help us understand the intricate relationship between EGFR and glycosylation, reinforcing the critical functional relevance of post-translational modifications on oncogene function.

106 Vivian Block

Early immune response alters stress- and depression-related behaviors in a mouse model

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Hypothesis: The project goal is to characterize the contributions of specific stress and immune effects on anhedonic, anxiogenic, and other stress-related behaviors. Furthermore, an examination of how behavioral phenotypes relate to each other within an individual mouse was observed.

Methods: C57BL/6J male (n=12) and female (n=12) mice were used, divided into three groups: stress (n=8), LPS and stress (n=7), controls (n=9). All mice were injected at 21 days, with LPS+stress mice receiving LPS in saline solution and controls and stress only mice receiving a saline injection. Mice were stressed using a 7-day chronic unpredictable mild stress paradigm. A stress-related behavioral battery was performed on each mouse, including light-dark box, open field, novelty induced hypophagia (NIH), forced swim test, and tail suspension test. Student's t-tests were conducted on data.

Results: Groups were found to significantly differ in multiple behavioral domains. In open field, stress mice had significantly more center entries when compared to both LPS+stress mice ($p=0.0049$) and controls ($p= 0.0382$). Initial analysis of NIH behavior found that LPS+stress mice spent significantly less time licking than control mice ($p=0.0394$).

Conclusion: It is possible that developmental immune activation and adult stress interact to amplify a lack of motivation for a reward in stressful conditions that is not observed in mice exposed only to stress in adulthood. Additionally, the differences in open field behavior suggest it is possible that activation of developmental immune response can modulate stress-related anxiety phenotypes.

33 Milany Bruno

Investigating the Interaction of ICP and TbCatL Recombinant Protein in a CHO-S Mammalian model

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Hypothesis/Statement of Problem: *Trypanosoma brucei*, a eukaryotic parasite, can cause African sleeping sickness in humans and nagana in cattle. Human resistance to most subspecies is attributed to Trypanosome Lytic Factor, with the apolipoprotein APOL1 causing lysis in the parasite by forming channels in its membrane. *T. brucei's* lysosomal cysteine protease, Cathepsin L (TbCatL), degrades APOL1, inhibiting lysis. The presence of Inhibitor of Cysteine Proteases (ICP) in trypanosomes modulates TbCatL, but the in-vitro interaction between ICP and TbCatL is not well-understood. This project aims to purify, quantify, and analyze both ICP and TbCatL through in-vitro cotransfection in mammalian cells, as well as study their combined effect on APOL1.

Methods: To attain our goal, we will transfect Chinese Hamster Ovarian suspension cells (CHO-S) with pcDNA plasmid containing epitope tagged ICP and TbCatL, followed by Nickel-column chromatography for protein purification. Enzymatic assays will be used to analyze protein activity in fractions, while Western Blot and Silver staining will determine the presence of the proteins of interest. The Bicinchoninic acid (BCA) assay will be employed to determine the concentration of expressed proteins in our model.

Results: We have purified and isolated ICP and TbCatL from the media of CHO-S cell transfections. We are currently purifying cotransfections of ICP and TbCatL to analyze the interaction of the two proteins in-vitro.

Conclusion: Using our in-vitro system, we aim to understand the quantity of intracellular and extracellular ICP and TbCatL. Cotransfection should allow for protein interactions analogous to those in trypanosoma, offering insights into how ICP and TbCatL interact and affect APOL1 function.

34 Zijing Cao

Investigating the Intracellular Membrane Localization of Cathepsin-L in *Trypanosoma brucei brucei*

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Hypothesis/Statement of Problem: *Trypanosoma brucei* are eukaryotic parasites that cause African Sleeping Sickness Disease in humans and Nagana in mammals. *T. brucei* have cysteine proteases called Cathepsin-L (TbCatL), an essential protease in the parasite. Elevation of TbCatL levels in trypanosomes have been associated with efficiency in crossing the host blood-brain barrier and evading the hosts' innate immunity. However, the pathway of secretion and the regulation of TbCatL activity has been under-investigated. The aim of this project is to understand the possible association of TbCatL with other proteins and regulators in the endolysosomal system of the exocytic pathway.

Methods: Total of $1*10^8$ *Trypanosoma brucei brucei* (strain 2T1) were cultured in 50mL of standard HMI9 medium. Parasites were hypotonically lysed to harvest all soluble components. Lysed parasites were treated with sodium carbonate to linearize vesicle membranes. Ultracentrifugation using SW 65 Ti rotor at 100,000g separated soluble and peripheral membrane bound components from membrane bound components. Samples collected were immunoprecipitated and the detection of TbCatL was determined by gel electrophoresis and western blot.

Results: TbCatL was detected in both the soluble and peripheral bound fraction and the membrane-bound fraction.

Conclusions: It is possible for TbCatL to reversibly interact directly with the membrane or with other proteins on the membrane. This may be a regulatory mechanism of TbCatL activity in the lysosome. I will use Lysosome-immunoprecipitation to further identify intracellular membrane localization of TbCatL.

107 Janie Chan

Function and Clinical Relevance of RHAMM Isoform B in Pancreatic Cancer Initiation and Progression

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Abstract:
Approximately 90% of cancer-related deaths are due to metastatic spread. Pancreatic cancer patients are often asymptomatic until the disease has metastasized to distant organs. Pancreatic ductal adenocarcinoma (PDAC) comprises over 90% of pancreatic malignancies, is highly aggressive, and is characterized by rapid and infiltrative growth. We have identified that the receptor for hyaluronan-mediated motility (*RHAMM*; gene name: *HMMR*) is overexpressed in pancreatic cancer, while undetectable in the normal adult pancreas. Different RHAMM isoforms exist as products of alternative splicing and RHAMM isoform B ($RHAMM^B$), which lacks exon 4, is the predominant isoform in pancreatic cancer and it is not expressed in mice. We have demonstrated that $RHAMM^B$ promotes metastasis in human tumor cell line xenografts. However, the role of $RHAMM^B$ in PDAC initiation and early-stage progression is unknown. To address this gap of knowledge, we partially humanized the mouse *HMMR* in immunocompetent mice by CRISPR knock-in. We designed a long single-strand donor DNA (lssDNA) to replace mouse exon 4 and the surrounding intronic sequences with the human exon 4 and partial intronic sequences on both sides. Two LoxP sites were added in the lssDNA to flank the exon 4 and mediate its excision by a Cre recombinase expressed under a pancreatic-specific promoter (p48-Cre), yielding $RHAMM^B$ expression in the mouse pancreas. We are studying whether mice expressing $RHAMM^B$ will exhibit an earlier onset of invasive PDAC, larger tumor burden, and shorter lifespan compared to the control mice that do not express this RHAMM isoform.

Impact of Obesity on Breast Cancer Immune Evasion

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Hypothesis/Statement of Problem: The coinciding health factors of cancer patients have a definitive impact on the trajectory and success of therapeutics. This study presents a novel molecular adaptation of breast cancer that promotes its evasion of the cytotoxic immune response, particularly within the clinical context of obesity—one of the world's most common chronic diseases and a major risk factor for breast cancer. Obesity triggers adipose tissue inflammation and dysfunction, and the mechanism by which this molecular reprogramming of the tissue microenvironment (TME) results in the aggravated growth of breast cancer is poorly understood.

Methods: To study novel adaptations supporting tumor progression in obesity, 30 clonal tumor lines were generated from the heterogeneous breast cancer line EO771, and transduced with unique DNA barcodes. These barcoded clonal lines were then pooled and used to generate orthotopic tumors in lean and obese mice. Competitive growth between different clones was tracked through barcode sequencing, and the most proliferative cell lines were isolated. RNA-sequencing was performed on the most competitive clonal line to uncover the genetic pathways associated with obesity-aggravated growth.

Results: Transcriptomic analysis of competitive tumor lines revealed a heightened suppression of the interferon-gamma signaling pathway—in particular, downstream interferon-regulatory factors (IRFs) and guanylate binding proteins (GBPs). Ongoing biochemical analysis aims to uncover the mechanism and dynamics of IFNγ dysregulation in obesity-driven breast cancer.

Conclusions: Characterizing how the suppression of the anticancer immune response develops promises crucial insights into how obesity modulates breast cancer growth. These discoveries hold the potential to illuminate novel pathways for therapeutic interventions in this challenging clinical intersection, offering hope for improved cancer outcomes among obese patients.

36 Khaja Faizuddin

Microglia Uptake of Oligodendrocyte derived Exosomes

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Hypothesis: Multiple sclerosis (MS) is an autoimmune disorder in the central nervous system (CNS) caused by the pathological loss of myelin. In the CNS, oligodendrocytes (OL) are the glial cells responsible for the formation of myelin around axons. This is a complex process that requires cell-cell communication. Exosomes are extracellular vesicles that contain many bioactive substances known to facilitate communication within the different cells of the CNS. Exosomes are also known to inhibit the differentiation of oligodendrocytes and myelin formation. Microglia are another type of CNS glia cells involved in the modulation of immune responses in the CNS. In normal conditions, homeostatic microglia internalize exosomes released by oligodendrocytes. We hypothesize that after inflammatory-mediated demyelination, OL exosomes accumulate in the extracellular space and this accumulation can inhibit the differentiation of oligodendrocytes reducing their remyelination capacity.

Methods: To test this hypothesis, exosomes will be collected from whole brains of wild type mice through differential centrifugation, and labeled with fluorescent dye PKH67 that targets the exosomal membrane. Exosomes will then be used to treat BV2 microglia cultures under two conditions: non-inflammatory (control) and inflammatory Lipopolysaccharide (LPS) 1ng/ml (treatment). Exosome uptake will be measured by fluorescence microscopy using antibodies against PLP (proteolipid proteins present on oligodendrocytic exosomes), IBA1 (microglia), and CD63 (exosomal marker). Media will be collected and used to treat OL cultures. These cultures will be stained to determine their levels of differentiation using antibodies against Olig1, O4+, MBP, Olig 2, and MOG.

Results: We expect to observe higher uptake of oligo specific exosomes in control condition compared to the inflammatory treatment due to microglia entering an activated immune state after exposure to LPS. In the second part of the experiment we expect to see a reduction in OL differentiation in the treatment group compared to the control due to the predicted presence of higher levels of exosomes in the Treatment derived conditioned media.

Conclusion: Reduced uptake of exosomes by microglia in inflammatory conditions may cause exosome build up in the extracellular space. This would lead to inhibition of oligodendrocytes differentiation of myelin. Understanding of this mechanism can be leveraged in the development of therapeutics designed to promote remyelination and aid in the recovery of MS patients.

37 Alona Gulko

Modular CRISPR/Cas9 System for Multi-Gene Targeting in Prostate Cancer

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Cancer research faces the challenge of flexibly modeling and perturbing the complex genetic profiles observed in patient populations without time-consuming breeding. Our objective is to develop a modular CRISPR/Cas9 guide system for efficiently testing combinatorial genetic alterations in prostate cancer (PCa) independent of a Cre-LoxP system. Initially, we demonstrated the system's ability to target *Pten*/*Trp53* (2x GOI: Genes of Interest), and now aim to model more complex PCa metastatic signatures such as *Pten*/*Trp53*/*Rb1* (3x GOI) and *Pten*/*Trp53*/*Rb1*/*Smad4* (4x GOI). We hypothesize that these gene combinations will differentially affect PCa expansion, metastatic seeding patterns, and emergence of therapeutic resistance. We have identified CRISPR gRNAs for complete knockout of our GOI and now aim to achieve multi-cistronic expression of the same gRNAs, doubling the number of targeted genes without Cre-Lox genotypes. We plan to accomplish this through molecular cloning of tRNA-gRNA multiplexes into lentiviral vectors, validating first in vitro gene targeting. Validation of gRNA guides for *Pten*, *Trp53*, *Smad4*, and *Rb1* via western blot in mouse prostate epithelial cells (MPEC) independent of the tRNA multiplex system has been successful. Additionally, we have cloned the lentiviral vector, enabling modular insertion of these guides. Our next steps involve validating that these gRNAs remain effective in a tRNA multiplex system using puromycin selection in MPEC. This project aims to develop genetic tools for multi-gene targeting, broadening our model's use to other cancers and advancing personalized medicine in prostate cancer with potential new therapies and biomarkers.

38 Yasmin Hussein

Sequencing MDA-MB-468 R273H Clones and Assessing p53 Oligomer Formation to Verify L334P CRISPR/Cas9-Induced Mutations

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Hypothesis/Statement of Problem

p53 gain of function (GOF) genes contain hot-spot missense mutations in the site-specific DNA binding domain. One mutation is R273H, often found in triple-negative breast cancer cells, in which an arginine is replaced by a histidine at the 273 position.The p53 gene also contains a C-terminal domain (CTD) and an Oligomerization domain (OD), which are involved in non-specific DNA binding and p53 tetramer formation respectively. Through designing CRISPR clones, we hope to answer the question of whether the OD and CTD of mutant p53 (mtp53) R273H regulate the GOF properties in the triple negative breast cancer cell line MDA-MB-468. We also aim to design a primer to sequence generated CTD CRISPR clones.

Methods

To study the OD of mtp53, our lab created L344P CRISPR clones. To confirm the success of the CRISPR mutagenesis, genomic DNA from the clones were purified, the sequence was amplified using PCR, and the samples were sent out for sequencing. Glutaraldehyde cross linking and western blot analysis were also used to assess p53 oligomer formation. Primers were designed and tested using PCR, gel electrophoresis, and sequencing.

Results

Sequencing results show that we do not have 100% L344P mutation. Western blot results also confirm that these cells still contain oligomer-forming p53 protein. PCR and gel electrophoresis results confirm successfully designed primers that amplify the target region of the CTD.

Conclusions

We have yet to select for a single L344P mutant. We hope to select for single mutants to further explore the correlation of the OD with mtp53 GOF properties.

39 Georgii Lifshits

Chronic stress increases anxiety in a moderately anxiogenic environment

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Unlike situational anxiety, in patients with Generalized Anxiety Disorder (GAD), anxiety persists even after the threat is gone. A similar condition can be modeled in mice by exposure to prolonged or chronic stress]. Previous studies suggest that the medial prefrontal cortex (mPFC) is strongly affected by chronic stress, decreasing in volume and may play a role in mediating GAD. To further investigate how chronic stress affects mPFC activity in an anxiogenic environment, male mice (n=5, 129SvEv, Taconic) underwent a 10-day chronic social defeat stress paradigm or served as non-stressed controls (n=5), followed by recordings in a subset of animals of single cell firing in the mPFC, and oscillatory activity in the BLA during a one hour exposure to an open field test. The open field was modified (mOF) to present a moderately anxiogenic environment, which is smaller and less brightly lit than a classic open field. Using Deep Lab Cut, a machine-learning based tool for markerless pose estimation, to analyze 40-60 min of behavior in the mOF, we find that stressed animals spend 40% less time in the center of the mOF than non-stressed controls overall and sampled in 10 min increments throughout the task. We also found that the average speed of stressed mice is 60% higher than non-stressed controls. We are currently analyzing neural firing in the mPFC during mOF exposure in stressed and non-stressed mice. Taken together, we show that chronic stress increases anxiety, even in a moderately stressful environment.

40 Selma Music

Selma Music, Hyunu Kim, Adriana Mujal, Mark Owyong, Joseph C. Sun
TIMS SPUR

Sun Lab Research Statement

Natural killer (NK) cells are part of the innate immune system and provide protection against viruses and cancer by killing target cells and recruiting additional lymphocytes. However, the factors that contribute to the killing mechanisms employed by NK cells are not well understood. RNA-binding proteins are present to regulate these responses and prevent unrestricted effector activity. Of the RNA-binding proteins expressed by NK cells, ZFP36L2 has some of the highest expression. These proteins inhibit cytokine production and proliferation of T and B cells. The overall objective of this study is to determine how the RNA-binding protein ZFP36L2 is involved in the function of NK cells. Our **working hypothesis** is that ZFP36L2 is necessary for optimal NK cell cytotoxicity and proinflammatory cytokine production against common NK targets of B16 melanoma, YAC-1 lymphoma, and viral ligand expressing cells.

To test this hypothesis, we will first determine the effector function of ZFP36L2 in NK cell cytotoxicity **(Aim 1)**. To accomplish this, we will use conditional knockout mouse model, *Zfp36l2*$^{fl/fl}$ × NKp46^{Cre}, to conduct *in vivo* Calcein assays and *in vitro* HelixNP/AnnexinV+ assays. To determine the mechanism behind the effector function observed, we will stain for granzymes. Next, we will determine the effector function of ZFP36L2 in NK cell proinflammatory cytokine production **(Aim 2)**.Successful completion of this project will characterize ZFP36L2 in its roles in NK cell functions and contribute to the understanding of the immune system.

41 Shlomo Pallas CUNY STEM Conference 2024 Abstract

Comparitive and Synergistic Inhibition of KRAS-Mutant Cancers

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Hypothesis/Statement of problem: KRAS is a small GTPase mutated in 15-30% of all cancers, making it one of the most common oncogenes. Currently two direct KRAS inhibitors, sotorasib and adagrasib, are clinically approved to treat cancer, but are limited to a minority of patients with specifically G12C mutations. Furthermore, patients treated with sotorasib or adagrasib developed resistance to KRAS inhibition after a median of 6 months. This indicates a need to study new ways to inhibit KRAS and understand relevant mechanisms of resistance to KRAS inhibition, we hypothesize that combination therapies will improve treatments.

Methods: This project has focused on characterizing seven structurally and mechanistically distinct KRAS G12C, G12D, and G12S inhibitors and identifying combination strategies that might improve their efficacy. We have conducted time and dose course experiments on ASPC1 (G12D) and H358 (G12C) lines and characterized cell viability. In the osteosarcoma line HOS and HOS-143b (G12S) we combined dose courses of riluzole with dose courses of an experimental direct KRAS G12S inhibitor, G12Si-5, then performed viability assays at 72h.

Results: Time-course and dose-course viability experiments indicated that the KRAS G12C inhibitors garsorasib and RM-018 were more potent than adagrasib against KRAS G12C cell line H358, and that MRTX-1133 selectively inhibited ASPC-1 cells with KRAS G12D. The FDA approved riluzole significantly inhibited cell proliferation and growth in the osteosarcoma line HOS but was less effective against the derivative HOS-143b line, which contains a KRAS G12S mutation. We found that G12Si-5 works in synergy with riluzole to enhance inhibition of cell viability in the HOS-143b cell line.

Conclusion: Future directions will be to further investigate the mechanisms by which riluzole and other chemical inhibitors sensitize cells with mutant KRAS to direct KRAS inhibitors, and how mutational isoforms influence mechanisms of resistance. These data suggest that new KRAS inhibitors and combinatorial therapies can expand treatable patient populations to improve outcomes for lung, pancreatic and bone cancers.

42 Anisa Siddikova

Respiratory syncytial virus infection alters the gut immune response to commensal bacteria

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Hypothesis/Statement of Problem: Respiratory Syncytial Virus (RSV), characterized by inflammation of the bronchioles, is a major cause of hospitalizations among infants and older adults. Early-life gut dysbiosis, an imbalance of microbiota, has been linked with elevated risk of lung infections later in life. However, our understanding of the impact of respiratory infections on the gut and its long-term consequences is limited. We hypothesize that RSV infection in mice increases gut inflammation.
Methods: To test this, we intranasally infected mice with RSV, collected blood and stool samples over the course of the infection, and analyzed immune cells in the lung and colon using flow cytometry.
Results: We saw an increase in immune cells and cytokine production in both lung and colon of infected mice. We further found an increase in antibodies binding to commensal bacteria in the intestinal lumen, which was more prominent in the colon than in the small intestines, suggesting a tissue specific difference in response to RSV. Lastly, we saw gut microbiome changes in response to RSV, such as reduced *Muribaculaceae* and elevated *Alistipes*.
Conclusions: Together, these data suggest that respiratory infections may disrupt homeostasis beyond the lung, and respiratory virus-induced changes to the gut could influence the risk of subsequent enteric infections or chronic conditions such as inflammatory bowel disease. A better understanding of how RSV influences the gut could help to identify patients at risk for these conditions as well as potential therapeutic targets.

43 Ariel Singh

Evaluating Lymphocyte Screening of Breast Cancer Patients for Detection of Human Mammary Tumor Virus

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Background: Oncogenic viruses, such as human papilloma virus, HPV, are of interest in developing novel therapeutic agents and preventative care options. Previous studies demonstrate an etiological role for Mouse Mammary Tumor Virus (MMTV) in the development of breast cancer (BC) in mice. Despite investigative research done, there is no definitive evidence of MMTV being a causative agent in human BC. The discovery of a human betaretrovirus (HMTV), sharing high homology with MMTV, opened new doors for exploration. This study aims to evaluate presence of HMTV in lymphocytes of human breast cancer patients.

Methods: BC patients are actively being enrolled in a Northwell IRB approved protocol. PCR assay using primers reported in previous literature amplified a target 254-bp sequence, homologous to the MMTV *env* gene. Lymphocytes from six patients were screened for the presence of HMTV.

Results: The 254-bp sequence was not detected in any of the six patient samples. The positive and negative controls demonstrate the expected results.

Conclusions: Exogenous MMTV requires infection of lymphocytes for spread to mammary tissue. This is facilitated by the viral Sag protein which is presented to the T cell. Sag produces an almost-complete deletion of lymphocytes, resulting in a lack of responding T cells. This possibly explains the undetectable HMTV-infected lymphocytes. Our next step is to examine for the presence of HMTV in the mammary tissue and viral antibodies in the serum.

Cep-1 plays a role in egg survival and propagation in the model organism C. elegans

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The human protein p53 is a transcription factor that induces cell cycle arrest and apoptosis in the event of DNA damage. It is the most conserved protein across almost all organisms, functioning as the so called “guardian of the genome.” The model organism, *C. elegans* has an ortholog, *cep-1*, activated whenever germline DNA damage occurs. This is to repair DNA lesions when they appear. The *cep-1* knockout strain, *cep-1(gk138)*, was compared to the wild type strain to observe how their lifespan differs from the wild type. It is observed that the *cep-1(gk138)* animals have a slighter longer lifespan compared to the wild type. Next, *cep-1(gk138)* was used to test how the knockout of the main response protein to DNA damage induced by UVC irradiation would affect the egg laying capabilities and the viability of those eggs. Wild type animals were found to have no significant changes to egg laying capabilities, nor egg viability. The *cep-1(gk138)* animals displayed markedly decreased egg laying and egg viability, due to the lack of the animals’ ability to repair potentially lethal DNA damage. Egg laying had been observed to be 4-5 eggs laid per hour in the control *cep-1(gk138)* worms, decreasing to 1.7 eggs per hour in irradiated *cep-1(gk138)* worms. These findings suggest that *cep-1* seems to play a role in decreasing life span in *C. elegans*, but helps to promote egg survival and propagation by repairing DNA, similar to how its ortholog, p53, does in humans.

The Role of PI31 in FBXO7 Neurodegenerative Disease

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Hypothesis/Statement of Problem: The ubiquitin-proteasome system is largely responsible for maintaining proteostasis in all cells, and it is especially important in the neuron as intracellular protein degradation is critical for effective neuronal function. The protein Proteasomal Inhibitor of 31kD (PI31) has been found to be a proteasome regulator and is associated with the assembly and axonal transport of 26S. Thus, the disruption of PI31 can lead to neurodegenerative diseases, and overexpression of PI31 can alleviate symptoms, such as motor dysfunction, of such diseases. *Nutcracker* (FBXO7) is an F-box protein and component of SCF E3 ligase complex that stabilizes PI31 function.

Methods: To establish the role of PI31 in *Nutcracker* (FBXO7) disease, a climbing assay using *Drosophila melanogaster* was performed. The climbing assay consists of collecting *Drosophila* in empty vials and testing their ability to climb up a certain distance within a short time frame after being tapped to the bottom of the vial. A control group was tested against *Nutcracker* mutant flies and their motor performance was recorded over the course of three weeks.

Results: The *Nutcracker* mutation *Drosophila* displayed significantly worse motor performance compared to the control flies, consistent with PI31 being associated with proper motor function. To further confirm this, we are reestablishing PI31 in *Nutcracker* mutation flies to see if the climbing phenotype can be rescued.

Conclusion: Studying the role of PI31 in proteasome regulation and transport may be the key to understanding the progression and treatment of FBXO7 neurodegenerative diseases. Future directions include expanding the study of PI31 in other, non-FBXO7 neurodegenerative diseases.

45 Angie Lee

Investigating Theory of Mind through Dogs' Response to Human Attentive and Non-Attentive Behaviors in a Baiting Task

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Hypothesis/Statement or Problem: Theory of mind (ToM) is the capability of individuals to attribute to others mental states such as beliefs, intentions, and knowledge (Premack & Woodruff,1978). Studies have shown that dogs adapt behavior aligned with human perception (Udell et al., 2011; Kaminski 2013). This study aims to investigate whether humans' attentive behavior (looking vs not looking) or other behaviors function as a discriminative stimulus for dogs.

Methods: During training, dogs learn to approach a baiter when an agent witnesses the baiting and retrieves a treat from under a mat, and to approach the mat when the agent does not witness the baiting and fails to retrieve the treat. In each test trial, one of the components of the agent's behavior is inconsistent with the condition (e.g. the agent would be looking, but then fail to retrieve the treat and approaching the mat would be reinforced). Data collection is still ongoing. Currently, only two dogs have completed the procedure, out of an intended sample size of 18 dogs.

Results: We did the preliminary results based on two dogs. The result show that both dogs' performance deteriorated the most when component #3 was incongruent with the condition. Also, when component #4 was incongruent, their performance also deteriorated, but only in the baiter-reinforced condition.

Conclusions: This study could help determine whether dogs rely on humans' attentive behaviors more than other behaviors when predicting an outcome, which is consistent with ToM.

46 Paloma Manon

Modeling Diabetic Cardiomyopathy using iPSC-derived Human Cardiomyocytes in Culture Dish

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Background: Diabetic cardiomyopathy (DCM) is defined as a progressive and irreversible heart muscle defect that causes cardiac dysfunction. It is of great public importance to investigate the currently largely unknown mechanisms of DCM in human models, alongside potential mitigations. The goal of the study is to establish a human DCM model using induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs).

Hypothesis: Human iPSC-CMs cultured in diabetic medium (DM) can recapitulate DCM pathology and contractile dysfunctional of cardiomyocytes.

Methods: After differentiation from human iPSCs, iPSC-CMs were cultured with cardiomyocyte purification medium (lactate+/glucose-) for 7 days and maturation medium (fatty acids+/glucose-) for 3 days by mimicking the adult cardiomyocytes' preference of utilizing fatty acids as a major metabolic substrate as previously described[3]. Then we characterized an *in vitro* cell based model for DCM developed by exposing iPSC-CMs to control medium (5 mM glucose and 5 mM mannitol) or DM (10 mM glucose, 10 nM endothelin-1, and 1 mM cortisol) for 48 hours. Cell size was evaluated by staining with Wheat Germ Agglutinin and fluorescence imaging. CytoMotion was used for imaging and quantifying the contractility of iPSC-CMs.

Results: The purity of iPSC-CMs was 98%. The DM-treated iPSC-CMs exhibited increased cell size. Additionally, DM treatment resulted in the increased time to peak and return velocity of contraction. These findings suggest that DM resulted in the hypertrophy of iPSC-CMs and impaired cell contractility.

Conclusion: Our data demonstrate that DM results in the pathological and functional changes of human iPSC-CMs. The advances in disease modeling using iPSC-CMs have opened novel paths to further investigate molecular mechanisms and cardioprotective approaches of human DCM.

CHEMISTRY

47 Mark Bubnovich

Kinetic and thermodynamic effects of sucrose on chymotrypsin-catalyzed peptide synthesis

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Hypothesis/Statement of Problem: Enzymes have solidified their crucial role as biological catalysts in pharmaceutical development, biosensing, and chemical transformations by making otherwise impossible or slow reactions proceed at accelerated rates. Their catalytic activity stems from the fragile three-dimensional structure of the active site that can be compromised through changes in pH, temperature, mechanical forces, and salinity. Therefore, there is a growing demand for methods of protein stabilization. Here in, we describe how modification of the solvent environment stabilizes chymotrypsin and improves its catalytic ability.

Methods: Enzymatic peptide coupling of a model reaction between N-BOC-L-Tyrosine and C-NH_2-L-Lysine in up to 3 M sucrose and 100 mM phosphate buffer was analyzed using Liquid Chromatography – Mass Spectrometry (LCMS). Similarly, 20 mM aspartame and 40 mM amino acid amide (F-NH2, Y-NH2) were dissolved in 3 M sucrose and 100 mM phosphate buffer solutions, after which 20 uL of 1 mg/mL chymotrypsin was added to the mixture to facilitate enzymatic reactions. Both reactions showed evidence of fiber formation and were analyzed for peptide products of various lengths using LCMS.

Results: Monitoring dipeptide coupling through LCMS revealed an improved kinetic and thermodynamic profile of the enzyme in sucrose as opposed to the phosphate buffer. Analyzing the reactions between aspartame and amino acids amides confirmed sucrose effect on chymotrypsin by showing higher tripeptide, tetrapeptide, and pentapeptide yields in sugar solution.

Conclusions: This study suggests that sugar rich media improves catalytic activity of chymotrypsin.

48 Michelle Ma

Investigation of Chelating Agents for the Removal of Thorium from Human Teeth upon Nuclear Contamination

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Thorium-232 (^{232}Th) is a radioactive heavy metal that is of increasing interest as a source of nuclear energy. However, upon nuclear incidents, the ingestion or inhalation of Th in major quantities can contribute to chemical and radiological health problems, including accumulation in the bone tissue and an increased risk of developing pancreatic, lung, and hematopoietic cancers. The major mineral component of the bone is hydroxyapatite (HAP) - also the major mineral component of the teeth. As such, the teeth are the first site of exposure upon oral ingestion of Th contaminated materials, and Th can pose a potential risk to teeth development. In essence, in the case of human contamination, it is critical to identify effective chelating agents capable of removing Th. Using a batch study methodology, this present work investigates the uptake and the removal of Th from synthetic HAP and from teeth samples by diethylenetriamine pentaacetate (DTPA), ethylenediaminetetraacetic acid (EDTA), and other promising chelating agents. Th uptake over synthetic HAP exceeds 98% at physiological pH with <1 min of contact time, and uptake exceeds 90% across the entire pH range. Regarding teeth, over 1 mg Th uptaken per gram of tooth is observed after 24 hours. The overall effectiveness of chelating agents for the removal of Th from is as follows: DTPA > EDTA > NaF/mouthwash/3,4,3-LI(1,2-HOPO); this trend was observed both in synthetic HAP and Th-impregnated teeth samples.

49 Wasiq Mahmood

Graphene Dispersion with Dipeptides

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Hypothesis/Statement of Problem: Graphene exhibits remarkable properties such as high electrical conductivity, exceptional mechanical strength, and thermal stability. One challenge hindering its widespread application is its inherent insolubility in aqueous solvents.

Methods: An approach to tackle this challenge involves binding graphene with dipeptide compositions containing Y (tyrosine). The role of Tyrosine in dipeptide composition is crucial due to its tyrosinase-mediated oxidation. Utilizing the enzyme, tyrosinase, the oxidation generates a radical on the hydroxy group of the tyrosine that leads to a radical interaction with graphene's sp^2 carbon network. Dipeptides were tested which were composed of tyrosine and different amino acids. Combinations such as WY (Tryptophan-Tyrosine), FY (Phenylalanine-Tyrosine), YR (Tyrosine-Arginine), and LY (Leucine-Tyrosine) were tested via zeta potential series.

Results: Successful dispersion occurs when tyrosine is paired with amino acids containing aromatic or aliphatic sidechain groups due to non-covalent support. While no dispersion is observed when tyrosine is paired with amino acids containing charged groups due to preferential interactions with the aqueous media and not with the graphene lattice. According to literature, a zeta potential above -30 mV indicates that the particles in the solution have a strong electrostatic repulsion between them and for graphene, this means that the graphene particles are well dispersed in the solution.

Conclusions: Aromatic and aliphatic dipeptides containing tyrosine, are shown to be favorable for graphene dispersion because of non-covalent and covalent interactions after enzymatic oxidation confirmed by zeta potential. This enhances the dispersibility of graphene in aqueous solvents, overcoming its inherent insolubility and potentially leading to advancements in biosensor technology.

50 Colin Pratasevich

Towards the discovery of cytotoxic agents for targeting Prostate Cancer

Abstract

Prostate Cancer (PC) is the second most common tumor in men in the US. Despite the availability of various hormone-suppressing therapies for hormone-sensitive PCs, up to 50% of PCs progress to metastatic castration-resistant prostate cancer (mCRPC) within three years of diagnosis. Hence, there is a need for alternative mechanisms for treating PCs, particularly mCRPCs. Small-molecule drug design presents a favorable solution given the challenges of synthesis, bioavailability, and immunogenicity of biomolecular and polymeric designs. We have discovered relatively simple glycans that show greater cytotoxicity against prostate cancer cell lines that overexpress prostate specific membrane antigen (PSMA), compared to PSMA negative cells. This selectivity is attributed to a vector on the glycan that targets PSMA. This behavior coupled with their possible novel mechanism of action compared to known clinical agents, make these glycans attractive leads to anti-cancer therapeutics. Our progress on the synthesis of analogues with improved selectivity and potency will be presented.

51 Kaylen Huesca

Role of an interaction between regions distal from the catalytic site on activity of the hairpin ribozyme

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Hypothesis/Statement of Problem: Ribozymes are enzymes composed of RNA; many of the small naturally occurring ribozymes have important catalytic roles in replication and gene regulation in prokaryotic organisms. Ribozymes can be found in prokaryotes as well as certain eukaryotic organelles. We are investigating structure-function relationships within the hairpin ribozyme found in the tobacco ringspot virus (TRsV), a plant virus. The secondary structure of the ribozyme is characterized by a central junction and four stems; binding of certain multivalent metal ions induce folding and interaction between unpaired regions (internal stem loops) in two adjacent stems to form the catalytic center and initiate cleavage at a specific site in one of the internal stem loops. There are also regions of potential complementarity beyond (distal to) the regions forming the catalytic site. The goal of this research is to determine whether a long range pairing between the distal regions assists in stabilization of the folded structure and thereby increasing the rate of catalysis.

Methods: To test this question, we are conducting catalytic assays comparing the native sequence of the ribozyme with a mutated ribozyme that differs in the sequence of one of the distal loops. Rates of catalysis are monitored by gel electrophoresis to visualize bands representing the cleaved RNA.

Conclusion: This research helps elucidate the role of long-range structural interactions in modulating activity of naturally occurring ribozymes.

52 Almas Mughal

Synthesis of novel Fluorine-labeled Radioactive Tracer Compound for Positron Emission Tomography (PET)

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Abstract:

Positron Emission Tomography (PET) is a molecular imaging technique widely used in pre-clinical and clinical settings to analyze changes in biological processes. Radioactive tracer molecules are used in PET to cause physiological change and label and detect metabolic processes related to cardiovascular, oncological, and neurological disease progression. These bioactive molecules consist of positron-emitting radionuclides, such as fluorine-18 (18F), carbon-11 (11C), and oxygen-11 (11O). As part of PET imaging, these molecules are specifically designed as ligands that bind to the therapeutic site of interest, with reasonable specificity, facilitating the analysis of the pharmacokinetics and pharmacodynamics within the in vivo response. The radiotracers linked to the biological molecule can emit positrons which upon collision with local electrons, create a pair of positrons that can be detected via gamma-detectors. The early drug development process of these radioactively labeled molecules can be labor-intensive, considering the biodistribution of the specific drug, the efficacy of the bio-marker used, and the cost and safety of administering these drugs in clinical settings. By preparing a fluorine-labeled tracer drug via cost-effective measures, it provides information on the potency/efficacy of using halogenated biomolecules in PET imaging and clinical settings. The synthesis of the fluorinated biomolecule involves known synthesis of 4-methyl-N-phenylbenzenesulfonamide, and N-(4,4-dimethoxycyclohexa-2,5-dien-1-ylidene)-4-methylbenzenesulfonamide, before final synthesis of N-(2-fluoro-4-methoxyphenyl)-4-methylbenzenesulfonamide, involving a halogenation reaction via pyridinium fluoride. Future results of this study will provide insight into usage of halogens like fluorine in increasing the potency of biological molecules used in clinical settings and for PET imaging.

53 David Sharer

Characterization of NK-92 Activation by Interleukin-12

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Hypothesis/Statement of problem: The activation of the NK-92 cell line by interleukin-12 (IL-12) has been under-examined in the field of immunology. Interleukins are glycoprotein cytokines that are released by leukocytes such as CD4 helper T-cells, macrophages, and monocytes (in addition to non-immune cells such as epithelial cells) in response to pathogenic infections. They bind to interleukin receptors on natural killer cells to stimulate the release of cytotoxic perforins and granzymes, and cytokines such as interferon-γ. Assessing the activation of NK-92 cells by interleukin-12 would provide a model for studying the immune activation of natural killer cells *in vitro.* This model can then be exploited to further understand the transcriptional landscape that contributes to natural killer cell activation.

Methods: RT-qPCR will be used to measure the expression of the serine protease granzyme b and cytokine interferon-γ. Increased expression would signify an activated NK-92 profile. Furthermore, flow cytometry will be utilized to detect markers of NK-92 activation (CD69). Killing assays will also be performed to assess the cytotoxicity of NK-92 cells in the presence and absence of interleukin-12. Lastly, an ELISA will be performed to measure interferon-γ expression in NK-92 cells.

Results: The interaction between interleukin-12 and NK-92 cells will likely increase the expression of NK-92 granzyme b, interferon-γ, and CD69. These results should also be accompanied by an increase in NK-92 cytotoxicity in the presence of interleukin-12.

Conclusion: NK-92 activation by IL-12 is an informative model for studying the activation of natural killer cells *in vitro.* Using this model, putative transcripts of novel innate immune-related micropeptides (<100 amino acids long) can be identified to better elucidate the natural killer cell immune response.

Engineering Chromosome 9p Arm Loss: An Important Predictor of Immune Evasion in Several Human Cancers

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Aneuploidy, the gain or loss of chromosome arms or segments, is found in 90% of solid tumors. Our lab and others have shown that cancer aneuploidies are chromosome specific, with common gains and losses across tumor types. The loss of chromosome 9p arm was specifically identified as one of the most prevalent Somatic Copy Number Alteration (SCNA) in human cancer. Among different cancer types, including oral, bladder, esophageal, and pancreatic, 9p loss is associated with poor response to immunotherapy and decreased levels of cytotoxic immune cells (such as CD8+ T cells and NK cells) into the tumor (immune cold). In this study, we investigate the immune-related effect of computationally identified chromosome 9p cytoband losses. To accomplish this, we utilize a human oral cancer cell line to genetically engineer the deletion of cytobands 9p21, 9p13, and 9p24 using CRISPR/Cas9 techniques. These cytoband regions include some known cancer drivers and genes involved in proteasomal degradation or membrane trafficking, suggesting that its deletion might disturb MHC-mediated antigen presentation. Using this model for immunological assays, we will study the mechanisms of immune evasion controlled by 9p deletion and predict Cytotoxic T cells to be predominantly affected by this genetic alteration. The goal for this project is to understand how 9p loss leads to immune evasion and identify a potential novel biomarker for the prediction of patient immunotherapy response.

54 Vanessa Arcos

The Role of the Central Junction of the Multi-Helix U2-U6 snRNA complex of the Yeast Spliceosome as a Recognition Site for the Cwc2 Protein.

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Hypothesis/Statement of problem: Pre-mRNA splicing in eukaryotic cells, which involves the removal of non-coding regions (introns) from pre-mRNA and ligation of coding regions (exons), is an essential process that regulates gene expression. The splicing process is catalyzed by a ribonucleoprotein complex called the spliceosome that assembles from five small nuclear (sn)RNAs and >100 proteins in a very dynamic process. The splicing reaction is catalyzed by complex formed by the pairing of U2 and U6 snRNA; the protein Cwc2 is postulated to play a crucial role in facilitating the folding of the yeast U2-U6 snRNA complex to achieve its catalytic conformation. Our research goal is to probe the role of the central junction of the multi-helix U2-U6 snRNA complex of the yeast spliceosome as a recognition site for Cwc2.

Methods: The affinity of RNA-protein complexes is measured using an electrophoretic mobility shift assay (EMSA), enabling the observation of the migration properties of free and bound RNA and protein. More specifically, we compare binding of the protein to the wild-type junction sequence comprising a mix of three- and four-helix conformers to a mutated sequence forming only the four-helix conformer.

Results: Preliminary data indicates that Cwc2 has a greater affinity for the U2-U6 snRNA complex with the wild-type junction compared to the mutated junction, suggesting that there is an additional binding site within the more open three-helix junction that is not accessible in the more structured four-helix junction.

Conclusions: Results of this study will contribute to a deeper understanding of the role of protein cofactors in assisting formation of RNA catalytic sites.

COMPUTER SCIENCE

55 Sami Chen

Effectiveness of Explanations on Understanding Robot Behavior

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Hypothesis/Statement of Problem: Because robots are becoming more common in professional environments, it is important that systems for human-robot interaction result in efficient teamwork to achieve a common goal. There are times where a human will disregard a robot's assistance because they don't understand the robot, or a person may also place too much trust in a robot despite it making mistakes. It's essential for a human to be aware that robots will occasionally make mistakes, so that they do not overly depend on the robot. Explanations for why the robot believes that its decision is correct could change how much the human could trust the robot's decision.

Methods: An online between-subjects experiment using Amazon Mechanical Turk will have participants observe scenarios of a robot learning its way to its destination, and provided either explanations, descriptions, or a control of no description. They are questioned on their understanding of the explanation (if provided) and if the robot did the right action. Then, they try to predict what the robot will do and if they'd do the same thing.

Results: The anticipated questionnaire results will be analyzed for what was most helpful for understanding the robot and compare how provided information affects the predictions made. We hope to learn the effectiveness of explanations for understanding robots from this work compared to a description or providing no text.

56 Saim Imran

Navigating the Ethical Horizons: Assessing Consciousness in Large Language Models

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Large Language Models (LLM's) become more common as research and societal needs advance. LLM's are machine learning models designed to output text based on probabilistic algorithms in an attempt to respond properly to user input. As algorithmic content becomes more advanced, the ethics of consciousness present themselves. To name a precedent, a LLM presented by Google was reported to have become sentient, and in response to the report the employee who made the report was relieved of his position. LLM's will continue to expand in this climate and as they do, the question of whether they perceive things similarly to us is now in question. This dilemma is of importance, for it presents us with guidelines for how to go about creating these algorithms, deploying them and possibly most important, shutting them down. The objective of this research is to study the content of one example: ChatGPT's OpenAI LLM algorithm and compare it to guidelines we've developed to develop a conclusive output regarding the consciousness of these algorithms. As well as presenting a better algorithmic design in the event that consciousness is found within these algorithms.

57 Seungyeon Lee

Underwater Acoustic Communication and Hardware Implementation

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Hypothesis/Statement of Problem: We aimed to develop an embedded hardware platform for underwater acoustic communication and investigate the impact of signal frequency modulation on communication system performance. Our hypothesis suggested that variations in distance, depth, and modulation would significantly influence signal reception by the hydrophone.

Methods: We constructed a basic wireless communication system design in MathWorks Simulink, leveraging the Digilent Eclypse Z7 board for microcomputer architecture and hardware interfacing. Prior to experimentation, Digilent software was installed on a micro-SD card for compatibility verification with Xilinx software. Transmitter and receiver tests were conducted underwater, where a human voice was modulated to three different frequencies and transmitted. Experimental data were collected, and Machine Learning techniques were employed for data analysis, including the utilization of algorithms such as Mean Squared Error (MSE) and Least Mean Square (LMS).

Results: The tests revealed significant impacts of varying distance, depth, and modulation on the received signal detected by the hydrophone. Through the application of Machine Learning algorithms, ongoing efforts focused on refining parameter ratios and coefficients for improved accuracy in data processing. Analysis indicated the platform's adaptability to changing environmental conditions and its ability to support high data rates in underwater communication scenarios.

Conclusions: The results of the transmitter and receiver tests show that changes in distance, depth, and frequency have a significant impact on the signals detected by the hydrophones, which illustrates the system’s capability to respond to diverse environmental parameters.

110 Isabel Stec

Phylogenetic Graph Optimization

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February 20, 2024

A phylogenetic tree, also known as an evolutionary tree, is a branching diagram or model that depicts the evolutionary relationships amongst a group of organisms. It represents the evolutionary history and ancestry of different species and shows how they are related through common ancestors. The Phylogenetic Graph (PhyG) is a program designed by Dr. Ward Wheeler to produce phylogenetic graphs from textual and graphical input data. This work centers on the optimization of model parameters for use with genomic and quantitative phylogenetic analysis through expectation-maximization techniques. There are two methods that will be attempted to optimize the parameters. In the first method, the parameters will be revised to see if the value output improves, continually being modified until the output ceases to improve. In the second method, a run is done where all parameters are revised simultaneously. These results are taken and the parameters are re-estimated based on the received output until it nears optimization.

Research Proposal for Socially-Aware Robot Navigation In Unfamiliar Environments

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February 17, 2024

Abstract

Robot navigation in unfamiliar human-populated environments poses a significant challenge because of the dynamic nature of human behavior and the complexity of social norms. Our work aims to facilitate the integration of robots into shared public spaces, ultimately enhancing their utility and acceptance in society. Traditional navigation algorithms struggle to adapt to real-time interactions with humans and unfamiliar locations while respecting social conventions. This research aims to address this gap in existing navigation systems by developing a framework that enhances robot navigation efficiency while promoting safe human-robot interaction in shared public spaces. We will measure the accuracy of social convention identification, the efficiency of the navigation path, and the effectiveness of the robot's environment model which is made up of three components: the social module, the navigation module, and the knowledge module. The anticipated outcomes of this research hold significant implications for robot navigation and human-robot interaction. By leveraging autonomous decision-making strategies, machine learning techniques, contextual knowledge, and social navigation models, we can enable robots to navigate new environments while dynamically adjusting their movements based on observed human interactions and movement from a single streaming source. Further work can integrate capabilities such as multi-robot coordination, semantic mapping, and action prediction based on a human's body language.

59 Yannis Giannoulakis

Effects of the Auto-Enrollment Provision of the Pension Protection Act of 2006 on Labor Force Outcomes of Older Americans

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Hypothesis / Statement of Problem:
The Pension Protection Act of 2006 (PPA) looks to protect pension plans, reinforce individual savings and prepare Americans for retirement in an effort to stabilize the lives of American retirees, present and future. A provision of the act strengthens the 1998-2000 IRS ruling that firms are allowed to automatically enroll their employees by superseding state wage-payment laws (WPLs) that require written consent (WC). Prior to the PPA, several states required workers to provide WC into 401Ks and other retirement plans. It is expected that states that previously required WC due to WPLs experience positive labor force outcomes such as higher employment rates, prolonged working lives and higher earnings after the PPA went into effect.

Methods:
I implement difference-in-difference regressions to estimate the effects of the PPA's auto-enrollment provision on labor force outcome in the years preceding 2008 and after; states that previously required WC are the treatment group and those that do not are the control group. This will capitalize on the natural experiment presented by the PPA where I will look at the before and after effects of the act. The data I use is from the Annual Social and Economic Supplement of the Current Population Survey. The data has 1,106,050 observations of American workers in their forties and fifties spanning from 2001 through 2019.

Results:
The results show that individuals living in states that required WC prior to the PPA experienced a statistically significant increase in employment and a decrease in outcomes resulting in exiting the labor force. Income, both wage and total, increase significantly for those in the treatment group. The treatment effect on pension participation does not change participation.

Conclusion:
The PPA displays positive effects on American workers who live in lived in states that required WC prior to the PPA and has significant policy implications for future lawmakers. By nudging workers into desired choices by structuring their choices, I see future opportunities for lawmakers to write policy that pushes people into decisions that are beneficial to society.

The Impact of Sexual Orientation on Wages

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Hypothesis: Existing estimates of the gay-straight wage gap likely underestimate the true gap if some gay workers misreport their sexual orientation. Removing bias from the measurement error increases the size of the gay-straight wage gap. This paper measures consistent estimates of the effect of sexual orientation on wages.

Methods: A primary assumption is that the sample measures gay people who misreport their sexuality, resulting in one-sided measurement error. This paper addresses the resulting bias with three methods. The first method scales the parameters from a linear regression model by a reasonable amount of misreported gay people. The second method uses attitudes to instrument sexual orientation. The third method uses attitudes to identify the most likely gay and straight persons.

Results: The GSS measures sexual orientation, sexual behavior, attitudes toward gay people, and demographics. Using method 1, gay men earn 19.2% less, and gay women earn 8.4% less than their straight counterparts. Using method 2, gay men earn 24.7% less, and gay women earn 9.1% less. Using method 3, gay men earn 17.2% less, and gay women earn 10.5% less. All three methods show existing research underestimates the gay-straight wage gap by 7% - 12%.

Conclusion: While all three methods show a greater gay-straight wage gap, my preferred measurement is from method 1, which is statistically significant and does not assume that a gay person is more likely to be gay-friendly or that a straight person is more likely to be not gay-friendly.

Adverse Selection in Online Auctions: A Study of eBay Motors

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Hypothesis/Statement of Problem: The issue of adverse selection in markets with information asymmetries, as illuminated by Akerlof (1970), is particularly pronounced in online transactions, where buyers lack the opportunity to physically inspect goods. Sellers provide information to counter adverse selection. Sellers share details through photos and text descriptions, which narrow the information gap between themselves and potential buyers. This research tests whether this information provided by sellers alleviates adverse selection problems with an emphasis on differentiating between dealers and non-dealers. Dealers, leveraging their established reputations and vested interest in maintaining them, possess a certain advantage over non-dealers, who lack such accrued trust. In this study I examine how the impact of photos varies across dealer and non-dealer sellers of automobiles on eBay motors.I anticipate that auction prices, number of bidders, and probability of a successful trade, are all greater for private sellers.
Methods: I estimate non-linear regression models on data from 80,000 completed used-car auctions from March to October 2006, to examine how seller-provided information influences auction prices, bidder engagement, and trade likelihood, distinguishing between dealers and non-dealers.
Results: The marginal effects of an additional photo on price, number of bidders and the probability of sale are all significantly and substantially greater for non-dealers than dealers
Conclusion: These results underscore the role of signaling and reputation in mitigating adverse selection, instilling buyer confidence, and facilitating trades.

62 Reesa Sooklall

The Impact of Pre-Abortion Restrictions on Women's Well-Being and Healthcare Access

Reesa Sooklall

Topic/Hypothesis: *Planned Parenthood v. Casey* (1992) allowed state-level abortion regulations that avoid undue burdens on women. Since then, 35 states enacted mandatory waiting periods (MWP) ranging from 24 to 72 hours and 14 states enacted ultrasound requirements before an abortion. Two-trip MWP necessitates two visits to an abortion clinic, adding logistical and emotional complexities to a sensitive choice. States with ultrasound requirements mandate whether the woman should view and listen to the fetal heartbeat. This study examines the effects of the two-trip MWP and ultrasound requirement on women's mental health, use of alcohol and tobacco, and routine women's health screenings.

Method: I apply staggered difference-in-differences (DiD) to Behavioral Risk Factor Surveillance System data from 2010 to 2021 to estimate the causal effects of the two-trip MWP and ultrasound requirements on women's mental health, use of alcohol and tobacco, and whether women are obtaining mammograms and pap smears. Staggered DiD compares the change in outcomes for states with abortion policies (multiple treatments) to states without abortion policies (controls) over multiple periods. I estimate Poisson, logit, and multinomial logit regression models to account for the distributions of the outcomes.

Results: Two-trip MWP increases mental distress in women by two additional days in a month, increases alcohol consumption, and the probability of smoking compared to women in states without MWP. Ultrasound requirements decrease mammograms and pap smears women obtain in treated states.

Conclusion: Abortion restrictions promote worsening long-run health outcomes for women since they increase mental distress and substance use and decrease preventative screenings.

Changes in child height and open defecation in Rural India

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Hypothesis/Statement of Problem: Rural Indian children are exceptionally short by international standards. However, between 2015-16 and 2019-21, the average rural child's height increased by about one-fifth of a standard deviation, a more rapid increase than in previous years. Over this period, exposure to open defecation in rural India reduced dramatically from 55% of households to 27% of households, in part because of a large government program that subsidized the construction of latrines.

Methods: This paper estimates the improvement in child health that can be attributed to the reduction in open defecation between 2015-16 and 2019-21. I use administrative data on annual toilet construction combined with India's National Family Health Survey (NFHS) 4 and 5 (N=1,982,518) to estimate linear regressions of each child's height-for-age z-score on their exposure to open defecation. A Blinder-Oaxaca decomposition controls for fixed differences across districts, and changes in other environmental exposures and economic status within districts.

Results: Across rural India, the mean open defecation exposure level fell from 0.60 in 2015-16 to 0.30 in 2019-21. The decomposition results indicate this reduction in open defecation exposure accounts for about 20% of the improvement in child height over this period.

Conclusions: Reducing open defecation is an important policy goal because exposure to the bacteria in feces causes diarrhea, intestinal parasites, and other enteric infections that can inhibit children's physical and cognitive growth. Child height is an indicator of human capital and earnings. The improvement in the disease environment contributed to an important increase in child height, yet children in India are still short by international standards and much open defecation remains.

ENVIRONMENTAL STUDIES

64 Sadde One

Nutritional benefits of crop-foraging in Primates around Kibale National Park, Uganda

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[3]Community Conservation, Uganda Wildlife Authority

Statement of Problem: Preventing conflict in areas where humans and wildlife interact is an important goal of wildlife management. The communities around Kibale National Park, Uganda are a potential hotspot for conflict because they live close to the forest. This project sought to assess the nutritional reasons for crop raiding by primates in the surrounding areas of Kibale.

Methods: This project relied on three years (2019, 2020, and 2021) of data from the Ugandan Wildlife Authority as well as additional data in 2022. These data indicated incidents of crop raids by primates, including baboons and chimpanzees. These data were then supplemented by nutritional data from previous studies on crop nutrition and forest ecology. We then compared nutritional data from these commonly eaten crops to the animal's diets in the wild using published data.

Results: Baboons raided the following crops (n= times): maize (33% of baboon records), cassava (11%), sweet potatoes (6%), beans (6%), assorted crops (33%), jackfruit (11%) and groundnuts (5.5%), Chimpanzees (n= times) raided the following crops sugarcane (54% of chimpanzee records), honey from apiary's (45.5%), bananas (4.16%). Compared to published data on chimpanzee and baboon diets in Uganda, the crop foods were higher in energy and lower in protein than forest foods. Some crops were high in fat, such as groundnuts.

Conclusion: These results demonstrate nutritional reasons for primates to consume crops. In addition, crops are often denser than forest foods. These results help us to understand the reasons behind crop raiding by primates in Uganda.

65 Presley Hernandez

Analyzing PAH Concentrations in Experimental Burn Plot Soils to Improve Reconstructions of Savanna Fires

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Hypothesis/Statement of Problem: Today, savanna fires are responsible for 80% of burned areas globally, but it is difficult to predict how these fires may change in the future. To better understand how fires will respond to climate change, scientists reconstruct past changes in savanna fire occurrence using Polycyclic Aromatic Hydrocarbons (PAHs). To do so, we must understand what conditions control the concentrations and distributions of PAHs in savannas.

Methods: We used soil samples from Kruger National Park, South Africa, where managers have conducted controlled experimental fires for the last 69 years to test how PAHs are preserved in soils with a known fire history. We analyzed the PAH concentrations in soils sampled before and after fires (pre- and post-burn) and in fire suppression plots.

Results: PAH concentrations were greater and more variable in burned plots' soil than in unburned plots but did not differ in burn plots pre- vs. post-fire. Unburned plots also had relatively larger and more alkylated PAHs, consistent with degradation of PAHs in soils that have not burned recently. PAH concentrations are higher in plots with greater rainfall, nutrient-rich basalt bedrock, and intermediate fire frequency. Together these variables determine grass biomass, which suggests fuel loads are a major control on PAH production.

Conclusions: Our work suggests soil PAH concentrations at local scales are insensitive to individual fires but instead reliably preserve decadal fire history, supporting the use of PAHs to reconstruct fire regimes. However, fuel loads can complicate interpretations of PAH concentrations in fire reconstructions.

66 Lin Wang

Thermal Performance of Green Roofs

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Introduction

In urban areas, impervious surfaces make the city susceptible to flooding and heat waves (Gaffin et al., 2009; Jamei et al., 2021). As one of the nature-based solutions, green roofs (GRs) reduce energy consumption and peak temperatures (Li and Yeung 2014). In this project we assess the thermal performance of a GR from May to September, 2023.

Methods

We collected surface temperature (ST) measurements of a GR on Randall's and Wards Islands, Manhattan, with an HDE Temperature Gun Infrared Thermometer. Five-minute solar radiation data was obtained from the NYC Micronet (Brotzge et al. 2020) weather station in nearby Astoria, Queens. We examined the temperatures of different surfaces and evaluated the cooling effects of various green and white roofs compared to darker surfaces — either artificial turf or black (equation 1).

$$\text{Location 1: } \Delta T(°C) = \text{Specified surface} - \text{Black}$$
$$\text{Location 2: } \Delta T(°C) = \text{Specified surface} - \text{Turf} \quad (1)$$

Results

Non-vegetative surfaces such as turf and a black roof contained the highest observed ST, whereas the shade contained the lowest ST. Meanwhile, the observed ST of a native plants GR and sedum GR were comparable to a white roof. According to a regression analysis, the cooling effect of GRs may be greater than that of a white roof at higher solar radiation levels (~1000 W/m^2). The estimated cooling effect for GRs ranged from 2 to 3°C per 100 W/m2 over 20 minutes.

Conclusion

GRs provide significant cooling under high levels of solar radiation. Note that the thermal performance of a GR varies depending on plant species; native plants usually offer better cooling than sedum.

Leading to the Annales: An analysis of the intellectual and institutional history of the University of Strasbourg

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Statement: The following research explores the University of Strasbourg as a uniquely Alsatian institution that was massively successful at the turn of the century and was crucial in ushering in a new era of academia in Western Europe. Defined by its cultural liminality, dedicated faculty, rigorous scholarship, and unique legacy, the University set new standards for scholarship that resulted in scholarly schools of thought such as the Annales. As an Alsatian institution, the University also opened up the opportunity for a new form of regional self-identification that separated Alsace from its traditional role as a gateway between France and Germany.

Methodology: This research primarily uses monographs and personal correspondence as the basis for analysis. Administrative records provide a contextual framework that is paired with secondary sources to contextualize the state of the University at any given period of time. Each section of sources is also categorized temporally and through local affiliations.

Results: This research argues convincingly that the University of Strasbourg is a composite institution that, through difficult navigation, defined itself via interdisciplinary scholarship. However, this process was complicated due to various 'crises' in intellectual identity, faculty, and administrative relations, and the status of Alsace as an extension of Imperial power both under German and French administration.

HUMAN BIOLOGY

111 Asia Akperov

Plasmacytoid dendritic cell differentiation and targeting in RUNX1 mutated acute myeloid leukemia

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Plasmacytoid dendritic cells (pDCs) are a unique subset of dendritic cells that produce type 1 Interferon and are essential for our immune response. Acute myeloid leukemia (AML) is a rare group of blood cancers with a high mortality rate. A subset of AML patients with the RUNX1 mutation were observed to have plasmacytoid dendritic cell (pDC) proliferation. In order to gain insight on the connection between the RUNX1 mutation and pDC proliferation we set up the following experiment.
We cultured primary bone marrow from mice under 5 different genotype conditions- WT (wild type), RUNX1 Heterozygous (KO/+), RUNX1 KO/KO (double knockout), Germline mutation (RQ/+), RQ/KO Germ line mutation knockout. Our media conditions included IMDM, FBS, L Glutamine, non-essential Amino Acids, Penicillin, Streptomycin, and B-Mercaptoethanol with FLT3L. We confirmed that this media condition gave rise to pDC cells. In each condition, we observed the pDC differentiation using cell counts and flow cytometry on culture day 5 and day 10. Our results showed that there was an increase in pDC proliferation under Heterozygous (KO/+) conditions. This is a rare phenomenon that doesn't follow the typical dose effect. Subsequent experiments will include spectral flow analysis of in vivo mice of the same 5 conditions, as well as measuring pDC function using TLR agonist and cytokines.
Our experiments aim to explore how we can exploit the relationship between the RUNX1 mutation and pDC proliferation for therapeutic applications for AML patients with the RUNX1 mutation.

68 Afeeda Ali

Visualizing Cephalopods Toxin Expression in Squid (*D.pealeii)* Posterior Salivary Glands.

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Hypothesis/Statement of Problem: Cephalopods are predatory marine organisms that secrete venom from their posterior salivary glands to immobilize their prey. Cephalotoxin (CTX) is the most studied paralytic protein that is part of this venom arsenal. Despite this, the expression of CTX within the posterior salivary glands of *D.pealeii* has been relatively unexplored. This study aims to visualize the expression of CTX within the posterior salivary glands of *D.pealeii.* We hypothesize that CTX is highly expressed throughout these glands. This study offers a potential key to understanding the functional significance of these toxins in cephalopod biology.

Methods: To fluorescently visualize and map the expression of cephalopod toxins, specifically CTX, we employed Hybridization Chain Reactions (HCR) on paraffin sections of *D.pealeii* posterior salivary glands. This method facilitates localization and potential functions within the glandular tissue of CTX and other putative toxins.

Results: Our study demonstrated for the first-time visualization of CTX expression in the posterior salivary glands of *D. pealeii* squid. These results allow us to analyze the specific locations and relative abundance of CTX within the salivary gland structures, contributing essential data to our understanding of cephalopod physiology and venom evolution in molluscs as well as identifying novel putative toxins for manipulating cellular function.

Conclusion: Our findings support the initial hypothesis, showing a notable and widespread expression of cephalopod toxins throughout the salivary glands of *D.pealeii.* The visualization of CTX expression provides a foundation for future investigations, emphasizing the importance of understanding toxin dynamics in cephalopods for broader biomedical implications of further research.

69 Junia Cenord-Cator

Gene mutations and humanity's quest for immortality.

The impact of achieving human immortality on society and what it means for the future of humanity.

Abstract

This research paper delves into the pursuit of human immortality through genetic mutations. It analyzes gene research on life extension, including cryopreservation, anti-aging medication, delaying retirement, and transferring consciousness onto digital networks. The paper examines the crucial role that genetic mutations may play in achieving human immortality and explores this feat's societal and ethical implications. Although the paper highlights the scientific feasibility of achieving human immortality through genetic modifications, it also raises potential concerns about unequal access to life-extension technology, overpopulation, and the creation of a genetically superior class of humans. Expert insights from genetics and gerontology weigh in on these issues, providing readers with a balanced assessment of the benefits and drawbacks of life-extension technology and its potential impact on society and individuals. It offers a comprehensive and analytical examination of the scientific and ethical implications of the quest for human immortality. It presents a persuasive case for the potential of genetic mutations to achieve human immortality while highlighting the importance of balanced and thoughtful approaches to this innovative field of research. It provides realistic projections of genetic engineering advancements, ethical considerations, and possible unintended consequences.

Keywords: human immortality - genetic mutations - gene research - life extension - anti-aging medication - transferring consciousness - digital networks - societal implications - ethical implications - genetics - gerontology - innovative research - genetic engineering advancements.

70 Tahmid Chowdhury

Determining the role of calcium accumulation in TLF-mediated lysis of African Trypanosomes

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Hypothesis/Statement of Problem: Trypanosomes are unicellular eukaryotic parasites that cause African trypanosomiasis. Humans and some non-human primates are protected from most species of trypanosomes due to an immunity complex called Trypanosome Lytic Factor (TLF). TLF carries Apolipoprotein L-1 (APOL-1), a cation channel-forming protein. We propose that after the receptor-mediated endocytosis of TLF, APOL-1 is inserted in the endosomal membrane at an acidic pH. Once the endosome is recycled to the neutral environment of the plasma membrane, the channel opens. Calcium and sodium ions influx through the channel, causing an osmotic imbalance, resulting in the trypanosome swelling and bursting. In a different model, APOL-1 opens a pore in the mitochondrial membrane, causing mitochondrial membrane depolarization and apoptotic-like cell death. We hypothesize that calcium influx through the APOL-1 channel in the plasma membrane leads to calcium accumulation in the mitochondria, causing mitochondrial membrane depolarization. We are testing this hypothesis by chemically blocking mitochondrial calcium influx through the mitochondrial calcium uniporter (MCU) with oligomycin. If APOL-1 forms a mitochondrial membrane pore, blocking MCU will not prevent mitochondrial membrane depolarization.

Methods: Flow cytometry was used to measure calcium accumulation in *Trypanosoma brucei* with a genetically encoded calcium indicator (GCaMP). Oligomycin was added to inhibit mitochondrial calcium influx, and TLF was added at a physiological concentration of 10 μg/mL.

Results: Oligomycin-treated trypanosomes did not have a change in GCaMP fluorescence compared to untreated controls.

Conclusions: Oligomycin treatment needs to be further optimized to test our hypothesis about APOL-1 localization. Our future direction is to use TMRE to measure mitochondrial membrane depolarization after oligomycin and TLF treatment.

112 Rania Darwish

The Role of Tyrosine Hydroxylase Neurons in the Paraventricular Hypothalamus in Response to Stress.

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Hypothesis/Statement of Problem: Stressors can initiate physiological stress responses, such as increased blood glucose and decreased feeding, that are tightly regulated by distinct neuronal populations in the hypothalamus, which plays a central role in the body's stress response. In my study, I am investigating the role of tyrosine hydroxylase (TH+) neurons in the PVH in the stress response and their regulation of metabolism.

Methods: To modulate activity in PVH TH+ neurons, I used a chemogenetic technique in TH-cre mice by introducing 3 viruses by administering a PVH injection of adeno-associated virus (AAV) with cre-dependent expression of hM3DGq-mCherry (activating), hM4DGi-mCherry (inhibiting), and mCherry (control). To study the time course of stress effects on PVH-TH+ neuronal activation, we injected AAV with cre-dependent expression of a calcium indicator GCamp8 virus into the PVH and used fiber photometry to record TH+ neuronal activity.

Results: Using fiber photometry, we identified increased TH+ neuron activity in response to stress. Chemogenetic activation of TH+ neurons in unstressed mice resulted in impairments in glucose and pyruvate tolerance, while inhibiting these neurons in stressed mice increased feeding, suggesting their involvement in glucose metabolism and feeding. We selectively activated PVH-TH+ neurons projecting to the locus coeruleus (LC) or the lateral septum (LS). Our results suggest PVH-TH+ neurons projecting to LC and LS may be involved in the glucose response to stress.

Conclusions: These findings enhance our understanding of the PVH neuronal circuits involved in the metabolic responses to stress and future studies will examine their role in the regulation of immune stress response.

71 Oleksandr Ihnatenko

Alterations in Oligodendrocyte Numbers and Types in a Rat Model of Alzheimer's Disease

Oleksandr Ihnatenko[1,2,3,4,]

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Alzheimer's Disease (AD) exhibits white matter abnormalities associated with the progression of pathology. Dysfunction of oligodendrocytes, the myelin producing cells of the brain, is detrimental for neuronal energy metabolism and may be a potential upstream risk factor of amyloid-β (Aβ) deposition, a hallmark of AD pathology. My study aims to compare the total numbers of oligodendrocytes and their progenitor (OPC) and mature populations within the hippocampus of Tg344-AD and wild-type (WT) rats. I will utilize the Fisher transgenic 344-AD rat model of AD, which expresses human mutant amyloid precursor protein (APPsw) and presenilin 1 (PS1ΔE9) genes. The Tg344-AD model is characterized by Aβ plaque formation, reactive gliosis, tauopathy, neuronal loss in the hippocampus and cognitive impairment in an age-dependent manner. Using immunohistochemical analysis, I will investigate the numbers of oligodendrocyte from different populations between WT and Tg344-AD rats. I expect there to be a decrease in total oligodendrocytes, but an increase in OPCs in the hippocampus. For future studies, I plan to investigate potential mitophagy impairment in areas of myelin damage. Previous studies from others showed that areas of axonal hyperinflammation have increased APP production. I hypothesize that this rise in APP could potentially lead to increased blockage of TOMM40 and TIMM23 channels, causing hyperactivation of the AMPK cell death pathway and the consequent disruption of the equilibrium associated with proper clearance of dysfunctional mitochondria. This research can lead to a better understanding of how oligodendrocyte dysfunction in AD can induce a pathway of neuronal death.

113 Nur Lyba

Developmental Changes in Neonatal Fc Receptor (FcRn) Expression in Thymic Antigen Presenting Cells

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Immature T lymphocytes develop in the thymus, where they are screened for functionality and self-reactivity. The resulting T cells emigrate to peripheral tissues in the gastrointestinal tract, where they aid in discerning between harmful or commensal antigens. Dysregulation of this mechanism can lead to sustained inflammation against commensals, as in Crohn's Disease. The Diehl Lab recently showed that colonization of mice at weaning with epithelial-adherent *E.coli* leads to its trafficking to the thymus, specifically by dendritic cells (DCs) expressing CX3CR1. This mechanism does not appear to function in adult mice, suggesting that it may have a role in the development of the mucosal immune system. The environmental factors in the early life gut that promote this thymus trafficking remain to be defined. The **neonatal Fc receptor (FcRn)** is an IgG receptor that can bind to IgG-bound commensal bacteria and promotes antigen sampling by DCs in the early-life intestine. This project focuses on how changes in FcRn expression in antigen presenting cells over developmental periods can affect the trafficking of microbes in early life. First, immunofluorescent staining of the thymus from young and adult mice was optimized to visualize and quantify FcRn expression. We show a slight, non-significant decrease in the average number of FcRn+ cells in the adult mice. Additionally, flow cytometry is used to analyze intracellular FcRn expression in CX3CR1+ DCs in the thymus and intestine of young and adult mice. In the thymus, FcRn was shown to have a higher expression in young mice, with a statistically significant drastic change from two weeks to three weeks. However, this intensity was similar in all age groups in the large intestine. Altogether, our data suggests that thymic migratory DCs have a higher expression of FcRn in early life.

72 Blanca Sophia Maymi

The Efficacy of UWA Crop Raiding Interventions in Kibale National Park, Uganda

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Statement of Problem: Crop-raiding by non-human primates is a source of human-wildlife conflict across African farmlands. This study examines the efficacy of crop-raiding interventions implemented by the Uganda Wildlife Authority (UWA) in Kibale National Park (KNP), Uganda.

Methods: We examined 3 years of long-term UWA data on the crop-raiding behaviors of primates and other wildlife around KNP between 2019 and 2021. Through UWA, we also conducted interviews (n=16) with local farmers bordering KNP who had been affected by crop raiding. We analyzed these data to describe the most successful interventions and those unsuccessful.

Results: The percentage of primates that crop raided decreased each year, but due to an increase in other wildlife crop-raiding incidents. The percentage of primates (chimpanzees, baboons, and vervet monkeys) reported in 2019 was 4.9 percent (17 out of 349 cases). In 2020, the percentage dropped significantly to only 1.4 percent (18 out of 1,326 cases). In 2021, the percentage was 1.2 percent (18 out of 1,539 cases). The most used interventions to deter primates are swinging beehives and chasing by guards.

Conclusion: Crop raiding continues to be a pressing conservation and public health issue across many African farmlands. Finding ways to mediate human-wildlife conflict is crucial to preserving the biodiversity across forests and protected areas, as well as the health and livelihood of local communities and ultimately allowing humans and wildlife to coexist.

73 Kemra Riggins Fleshman

Assessing the Relationship Between Waterbourne Pollutants and Microplastic Abundance in Mussels

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Statement of Problem: Microplastics (plastic particles less than 5 mm) have become omnipresent in every ecosystem yet the consequences of their presence are largely unknown. **Methods:** In this study, we looked at where microplastics can be found in a marsh ecosystem; we decided to study mussels as they are keystone species in the marsh because they filter feed. We collected mussels from different marsh ecosystems at two different levels of pollution: Newtown Creek and Piermont Marsh. To carry out a microscopic analysis of our samples, we developed a protocol to digest the biological tissue and isolate the microplastics. We utilized a Scanning Electron Microscope (SEM), Stimulated Raman Scattering (SRS), and a UV microscope to observe the isolated microplastics.

Results: We have found an average of 1 microplastic for every 3 ml of water in Piermont Marsh and an average of 9.43 microplastics for every 3 ml of water in Newtown Creek. Using the same calculation process we found that in Piermont there was an average of 11 microplastics for 0.06 grams of mussel tissue.

Conclusion: We were able to confirm that microplastics are found in mussels in natural aquatic environments around New York. With these findings, we concluded that Newtown Creek is significantly more polluted with microplastics than Piermont Marsh. Our future goals are to use better data analysis to more accurately quantify the microplastics in our sample, use better filtration techniques to isolate more microplastics, finish SEM imaging, and understand its effects on human health with grocery store mussels.

74 Sophia Tong

Perceived Stress and Its Association With Sleep Quality in Patients With Neuropathic Pain and Distal Symmetric Polyneuropathy

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Hypothesis/Statement of Problem: To assess the relationship between sleep quality and perceived stress in patients with peripheral neuropathy. The role of sleep in the modulation of pain is well established, and there is evidence suggesting that the treatment of disordered sleep in patients with neuropathic pain may improve pain perception. However, studies examining the drivers of impaired sleep and social determinants of health in patients with peripheral neuropathy are limited.

Design/Methods: The relationships between disordered sleep, pain perception, and neuropathic symptoms were examined cross-sectionally in 24 subjects diagnosed with peripheral neuropathy. For each subject validated scales including the Pittsburgh Sleep Quality Index (PSQI)), Brief Pain Inventory (BPI), Pain Catastrophizing Scale (PCS)), and Michigan Neuropathy Screening Instrument (MNSI) were compared to Perceived Stress Scale (PSS).

Results: 75% of participants enrolled were female (18/24) and 16.7% identified as non-white (4/24) with mean age of 66.9 years (SD ∓ 10.5). Greater stress measured by PSS was associated with worse sleep quality in univariate analysis with PSQI ($p=0.017$). Further analysis adjusting for age, sex, race, history of major depression, PCS, and PSS still demonstrated a cross-sectional association in these participants with distal symmetric polyneuropathy ($p=0.009$).

Conclusions: We demonstrate a strong association between perceived stress and worse sleep quality in a sample of participants with peripheral neuropathy. Disturbed sleep is modifiable and an improved understanding of the drivers of impaired sleep examining social determinants of health has important implications for developing target interventions that treat sleep impairment and neuropathic pain.

75 Abigail Uchitelev

Reconstruction of a human blood-retina barrier to investigate the role of APOE variants in age-related macular degeneration

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Purpose: Age-related macular degeneration (AMD) is a leading cause of vision loss after 50 years of age. The pathological hallmark of AMD below the retinal pigmented epithelium (RPE), is the accumulation of lipid-rich deposits, drusen, leading to retina degeneration. Several risk variants for AMD occur in lipid-related genes, including the apolipoprotein E (APOE) gene, but their role in AMD is unknown. Using induced pluripotent stem cell (iPSC) technology, we developed an in vitro human induced outer blood-retina barrier tissue (BRB) to investigate the role of APOE variants on AMD.
Methods: We generated iPSC-derived RPE, pericytes and endothelial cells and combined them within a transwell system by adding RPE to the apical side and extracellular matrix-encapsulated vascular cells on the basal side. We also established protocols for reproducing drusen-like deposits in BRBs. Using iPSC lines that were CRISPR-edited, we engineered isogenic BRBs with different APOE genotypes within specific cell types.
Results: Transepithelial electrical resistance of the RPE within BRB evolves and stabilizes at around 4 weeks. Staining of the BRBs showed a monolayer of ZO-1-positive retinal epithelial cells, and an underlying 3D vascular compartment staining positive for endothelial cell marker PECAM1. BRBs engineered with APOE3/3 RPE and APOE2/2 vasculature had larger deposits when compared to BRBs with APOE3/3 RPE and APOE3/3 or APOE4/4 vasculature.
Conclusions: We developed a human BRB isogenic model to study the effect of genetic risk factors on the development of drusen and other AMD-related phenotypes. This multimodal strategy will establish a versatile platform for modeling AMD and genetic vulnerabilities, opening new avenues for drug discovery and clinical translation.

76Lily Ye

The Role of Exotically Introduced Plant Species in the Diets of Red-Tailed Monkeys (*Cercopithecus ascanius*)

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Hypothesis/ Statement of Problem: The spread of exotic plant species alters the ecosystem functioning by displacing native species and changing food availability for non-human primates. The Uganda Wildlife Authority, the government agency responsible for wildlife management in Uganda, began to take initiative on the removal of exotic plant species; however, these exotics may be consumed as a nutrient source.

Methods: We documented the exotic plant species in the diets of red-tailed monkeys (*Cercopithecus ascanius*). We recorded the foods eaten by monkeys during focal follows of recognizable individuals from 7:00 to 19:00 in three red-tailed monkey groups residing in Kibale National Park, Uganda. Data were collected in 2017 (n=31 days) and 2023 (n=9 days).

Results: The red-tailed monkeys consumed 102 plant-part species combinations. These included: two exotic plant species: *Lantana camara* and *Acanthus polystachyus*. The mean number of plant species consumed with and without the exotics included in their diets are 22 (SD=4.40) and 17 (SD=10.0) species per day, respectively. During the dry season, redtails exhibited a lower diet diversity with few exotics and majorly insects. The redtail's daily diet consisted of a mean of 14.9 (SD=10.0) and 22.4 (SD=4.40) plant species during the dry and rainy season, respectively.

Conclusions: Since exotics were eaten so infrequently and on days when diet diversity is high, our results suggest redtails are not reliant on them and they might be an alternative food source. Future research is needed to understand how exotic species affect the nutritional ecology in terms of nutritional goals and nutritional strategies/balancing.

77Qirui Zhu

The Effectiveness of the SBIRT-OEND Study Approach in the Intervention and Treatment of Substance Use Disorder

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Substance Use Disorder is one of the most prevalent health issues in New York State and has a widespread impact on Public Safety, Welfare, and Education. There are various barriers to treating substance use disorder as it is often interlinked with mental health, homelessness, social stigma, and admission difficulties. The Screening, Brief Intervention, Referral to Treatment, Opioid Education, and Naloxone Distribution (SBIRT-OEND) study is a clinical initiative in the Emergency Department at Bellevue Hospital. It has been proven to effectively identify and deliver early intervention and treatment services to patients who are screened positive or at risk of developing substance use disorder including alcohol, tobacco, and a variety of drugs. Not only were the patients referred to social workers and treatment programs, but they were also offered fentanyl test strips and Naloxone Kits to help reduce harm. In case of emergency, Naloxone can be easily administrated by others to counteract the effects of a patient's opioid overdose. Between the time period of February 2022 and February 2024, we have screened a total of 15774 patients, of which 15% have used drugs for non-medical use in the past 12 months, and among them, 28.9% reported feeling the need to cut back or get help on using Heroin or Cocaine. Among those who have used or know people who use opioids, 35% were provided with a Naloxone kit. 6% of the screened patients have endorsed risky use of substances and are referred to the LEADs team for further research and treatment programs. We believe the SBIRT-OEND study approach is effective in treating substance use disorder.

MEDICAL LAB SCIENCE

78 Morgan Serbagi

Bacteriophage Enzyme LysGBS19 as a Novel Antibiotic for Group B *Streptococcus*

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Statement of Problem: *Streptococcus agalactiae*, or Group B *Streptococcus* (GBS), is a bacterial species commonly associated with vaginal and GI flora, but can be a risk factor for congenital infection of infants, leading to neonatal sepsis, pneumonia, and meningitis. Penicillin is the treatment of choice, but drug allergies, the rise in antibiotic resistance, and the potential of dysbiosis confer the need to develop novel therapeutics. Recombinant bacteriophage lytic enzymes (lysins) are viable candidates for their relatively specific mode of killing and the lack of a known mode of resistance. LysGBS19, a lysin derived from streptococcal phage CHPC877, has shown promise at eliminating GBS *in vitro.*

Methods: LyAR, an automated database search tool, generated a list of GBS lysin candidates. One hit, LysGBS19, was further pursued for its rapid optical density reduction of GBS in suspension. Lysin activity was further evaluated, and conditions were optimized *in vitro*. Fluorescent microscopy was used to visualize cell lysis.

Results: LysGBS19 was able to kill an array of GBS capsular serotypes *in vitro* with high residual antibiotic activity. LysGBS19 was also capable of lysing clinical isolates of *Streptococcus pyogenes*, or Group A *Streptococcus* (GAS), a pathogen associated with maternal morbidity.

Conclusion: Although the optimal conditions must be further discerned, LysGBS19 shows promise at combating GBS. In future studies, we will continue to determine the lytic spectrum of LysGBS19 against other GBS and GAS strains and the vaginal flora. We will also test LysGBS19 *in vivo* in GBS decolonization and infection mouse models.

NEUROSCIENCE

79 Nawshin Maleeha

Undergraduate 2024 STEM+ Research Conference

Acute Demyelination Increases Anxiety and Chronic Demyelination Impairs Working Memory

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Hypothesis/Statement of Problem: Cuprizone is a copper-chelator that induces oligodendrocyte apoptosis and drives demyelination. Although this model has been widely used to study the pathophysiology of Multiple Sclerosis, its effects on behavior at acute and chronic stages of demyelination are unknown.

Methods: We compared male C57BL/6J mice exposed to the cuprizone demyelination diet for 6- (acute), or 12- (chronic) weeks to age-matched controls on spatial working memory, spatial reference memory, and anxiety, using the Y-Maze and the Open Field (OF), respectively, and on object recognition memory, using the Novel Object Recognition (NOR) task.

Results: Intriguingly, acute demyelination did not affect overall anxiety in the OF but significantly decreased rearing in the novel arm of the Y-Maze compared to controls, an effect that lasted through the chronic stage. This suggests that demyelination selectively increases anxiety in a novel context. The Y-Maze also revealed that while spatial reference memory remained intact after demyelination, chronic demyelination impaired spatial working memory, when animals showed significantly less spatial alternation than controls. Finally, the NOR task showed that acute and chronic demyelination impaired object recognition memory compared to exposure-matched controls. Analysis of myelin basic protein (MBP) expression revealed myelination deficits throughout the brain. However, analyses of cell activity during NOR after chronic demyelination showed selective cell activity reduction in the entorhinal cortex and dorsal hippocampus, regions implicated in object recognition memory, elucidating specific targets for intervention in Multiple Sclerosis.

Conclusions: This work demonstrates how cognitive deficits evolve with demyelination, affecting context-based anxiety first and spatial working memory at the more advanced stage.

80 Francesca Jereis

Investigating Cre Recombinase-Mediated Modifications in Prostate Tumorigenesis

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Hypothesis/Statement of Problem: The Cre-lox system, utilizing Cre recombinase, can be used to excise a sequence between two loxP sites, resulting in the removal of genetic material. These Cre-driven modifications are used in the Nowak lab to induce prostate tumorigenesis by targeting crucial tumor suppressor genes. Our aim is to establish a control system enabling identical cell types with an inactive virus, surpassing a no-virus control by averting unintended alterations. The CreY324F plasmid serves as our control in this study, while the *PTEN*$^{loxP/loxP}$; *Trp53*$^{loxP/loxP}$ plasmid is employed to evaluate the efficacy of our novel control (CreY324F). The main goal is to determine if cellular behavior mirrors that of the no-virus control, potentially leading to cell demise. The objective of this study is to investigate the extent to which inducing a point mutation in Cre (Y324F) abolishes its functional impact, thereby prompting cellular behavior akin to those without viral intervention.

Methods: Restriction enzyme digestion engineered a mutant Cre plasmid, which was integrated into host cells via bacterial transformation. PCR, recombination tests, mini-prepping, and DNA sequencing ensured the fidelity of the CreY324F construct, isolated via midiprep techniques. Mouse embryonic fibroblast (MEF) cells were infected with the construct alongside non-mutated plasmid control. Viral infection efficiency was assessed via flow cytometry.

Results: Flow cytometry analysis showed construct-infected MEFs exhibiting a 112-fold decrease in eGFP+ cells. In contrast, control plasmid eGFP levels increase over twelve days.

Conclusion: Further experiments will involve creating a cell line containing the mutated Cre.

114 Cedrica Samuels

Space-Filling Curves Over Finite Fields

Cedrica Samuels[1],and Andrew Obus[2]

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Hypothesis/ Statement of Problem: A "space-filling curve", over a finite field, is defined as a curve that passes through every point of a space over that field. Space-filling curves can also be defined over the real numbers, but their construction is not smooth in a differentiable way; that is, it is not continuous but "jagged". We will present an overview of the construction of a space-filling curve over the real numbers for 2-dimensional space and then give a complete account of all the ways to construct analogous curves over finite fields.

Methods: Literature review and computer algebra computations.

Results: A complete classification of space-filling curves over 2-dimensional projective space along with a proof based mainly on undergraduate-level mathematics.

Conclusion: Space-filling curves over a finite field, unlike in the case of real numbers, can be constructed in a smooth way.

81 Moises Acero

Study of Molecular Dynamics of Ionogels

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Hypothesis/Statement of Problem: Our society is facing an increasing need for energy storage devices. Lithium-ion batteries are most used to meet these needs because of their high energy density and ability to last a high numb er of charge cycles. Currently, these batteries use liquid electrolytes based on organic carbonates solv ents, which are highly flammable and volatile. On the other hand, electrolytes based on ionic liquids (IL) and a gelling matrix, also called ionogels, are a promising alternative to replace conventional electrolyte s. Ionic liquids are molten salts having a melting point below 100 °C and display favorable properties as novel solv ents. These properties include non-flammability, having negligible vapor pressure, and having high thermal and ele ctrochemical stability. A suitable Li salt is then added to make the electrolyte. After combination with a gelling matrix, the ionic liquid forms a composite semi-solid electrolyte, which promotes the development of safer energy storage materials. Here we present an overview of the molecular properties based on ionogels forme d by imidazolium ionic liquids and exfoliated boron nitride (hBN) nanoplatelets. This novel material is a promising ele ctrolyte component because of its ability to absorb large quantities of ionic liquids, thereby enhancing the me chanical modulus of the ionogel and sustaining high ionic conductivity.[1].

Methods: To investigate the ion dynamics, we measured the self-diffusion coefficients of the ionic species using pulsed-field gradient nuclear magnetic resonance (NMR). We also measured the ^{1}H and ^{19}F longitudinal relaxation rate (R_1) dispersions by using fast field cycling NMR (Figure 1).

Results and Conclusions: Our preliminary results indicate that the presence of Li^{+} affects the rotational motion of the anion more than the IL cation in the bulk liquid. However, under confinement associated with the pre sence of hBN, the cation relaxes faster than the anion. This reversal of relative relaxation rates sheds light on the nature of the molecular-scale interaction between the IL and the hBN gelling agent.

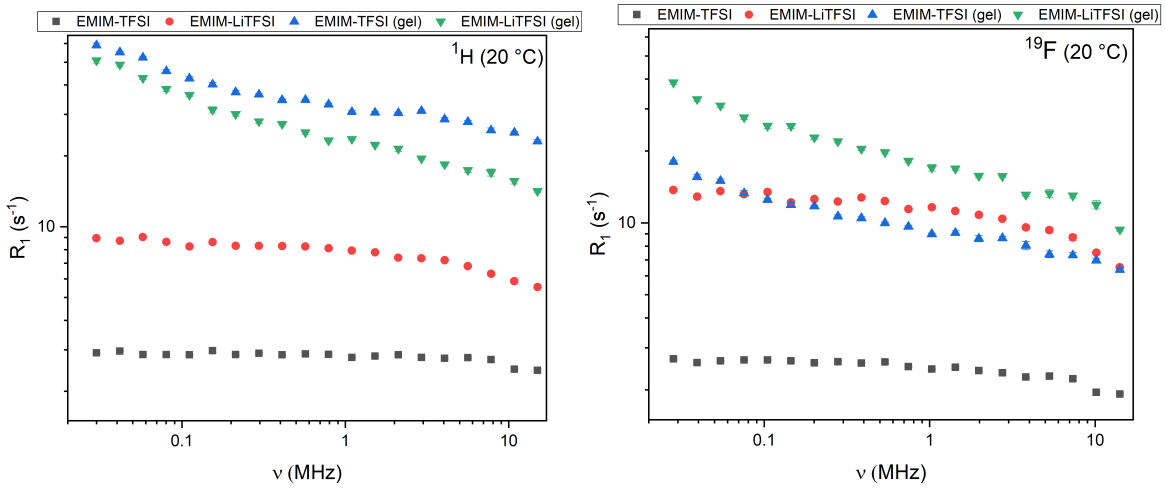

Figure 1: ^{1}H (left) and ^{19}F (right) relaxation rate dispersions for investigated systems, measured at 20 °C.

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115 Sherelyn Alejandro

Fundamental Parameters for an Extrasolar World with Potential Auroral Signature using JWST Observations

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Hypothesis/Statement of Problem: The phenomenon of aurora has long been the interest of those lucky enough to witness the interaction of our planet's ionosphere with solar wind predominantly closer to the poles . Aurorae in our solar system can also be found in the likes of the giant gas planets Jupiter and Saturn, where several features are displayed in infrared observations including a mix of methane and H3+ emission. Brown dwarfs are astronomical objects that lie between low mass stars and giant gas planets, linking planetary and stellar astrophysics, and share their characteristics with stars and planets. Auroral activity has been suggested in brown dwarfs from radio observations by Hallinan, G. et al. and Kao, M. M. et al.. However, efforts by astronomers to spot auroral features seen in Jupiter in the infrared have been unsuccessful. CWISEP J193518.59-154620.3 (CW1935 for short) is a companionless brown dwarf ~47 light years away

and ~500K in temperature that exhibits methane in emission in JWST near-infrared observations. A temperature increase in the upper layers of the atmosphere can explain this feature, and is attributed to auroral processes which are likely to play a role. Nonetheless, a lack of a host star that provides plasma brings up the possibility of the existence of an active moon, similar to Io which also contributes to the aurora detected on Jupiter.

Methods: In order to characterize the atmosphere of CW1935, I combined distance measurements with astronomical data from the near-infrared to the mid-infrared using JWST and Spitzer. The assembly of these data is known as spectral energy distribution (SED). SED construction was done using a modified version of the Python-based open-source package called SEDkit to include a Monte Carlo approach when determining fundamental parameters and their uncertainties. The data used are collected from the literature through the SIMPLE Archive(http://simple-bd-archive.org/). I combed the literature and SIMPLE to identify and load the relevant and useful data into Python. After loading the data, I modified spectra and photometry measurement to be read in properly by SEDkit. I used SEDkit to obtain an empirically calculated bolometric luminosity (L_{bol}) from the SED. . Using models from Marley M. et al. that predict how the parameters of brown dwarfs evolve with time evolutionary models and an age estimate from the literature, we then estimate a radius, mass, gravity, and effective temperature for CW1935.

Results: We present the spectral energy distribution for CW1935 and derived fundamental parameters like mass, gravity, effective temperature, and bolometric luminosity from new JWST observations.

Conclusions: Brown dwarfs have played a critical role in furthering our understanding of the giants in our solar system, and CW1935, is further proof that these cold extrasolar worlds are amazing analogs to our gas giants, and can expand our knowledge of atmospheric processes outside our solar system.

A Survey on Different Physical Implementation of Quantum Computing System

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To keep an AI data center running requires an immense amount of power; this adds a heavy burden to the fight against climate change. Quantum computing holds great promise to address this complex challenge. A quantum computer is fundamentally different from a classical computer. Quantum effects such as the qubit's superposition, interference, and entanglement provide it with computational advantages over classical algorithms. Of all the open problems in the field, the development of quantum computers is the most crucial since they are the basic units in quantum technology. In the physical layer, there are several ways to implement quantum systems. Which one/ones will have the most potential to achieve universal, scalable, and error-corrected systems? We review the most recent progress of several quantum technologies to realize quantum computing. It is believed that the topological quantum computing technology is developed to be naturally protected from decoherence so that no active quantum error correction is needed. Although it is gaining momentum, to build scalable and fault-tolerant quantum computer in the near future it is crucial to solve remaining problems which are still open, such as the realization of distributed quantum computing between distant points via anionic particles.

83 Christopher F. Zapata

High Probability White Dwarfs in the Background of Kepler/K2

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Hypothesis/Statement of Problem: The Kepler mission of 2009 was specifically designed to observe regions of the Milky Way galaxy, in search of exoplanets. Kepler collected detailed pixel data of the measured brightness of targeted stars allowing for the extraction of high-quality light curves. The Kepler spacecraft observed a region of the sky for 4 years in its primary mission, and after some mechanical failures, observed a different field along the ecliptic for 5 years. This secondary mission was known as K2. The Gaia mission of 2013 was primarily focused on creating a high precision 3D map of the Milky Way galaxy. To do this, the space-based telescope measured the precise positions, distances and motions of about one billion stars. Included in this, are the locations of 359,000 high probability white dwarf stars. The locations of these stars were not known at the time of the Kepler mission, but now allows for the possibility of retroactively looking at Kepler target pixel files where white dwarfs may have been observed.

Methods: The Gaia catalog of high-probability white dwarfs was filtered down to 199,383 stars brighter than the 20th magnitude and with the highest probability of being a white dwarf star. Crossmatching the location of Kepler/K2 targets with the Gaia catalog of white dwarf stars identified a number of white dwarfs that were near the original target. Using the World Coordinate System, RAs and DECs of the white dwarf stars were plotted against the target pixel files to locate them in relation to the Kepler/K2 target.

Results: It is likely that many of these stars were the target of interest when Kepler/K2 were in operation, and therefore have already been examined. It is also possible that although the star was the target of interest, it was not known at the time if the star was a white dwarf. 23 white dwarf stars were found to be within a Kepler short cadence target pixel file. 141 white dwarf stars were found to be within a Kepler long cadence target pixel file. 394 white dwarf stars were found to be within a K2 short cadence target pixel file. 1557 white dwarf stars were found to be within a K2 long cadence target pixel file.

Conclusions: A periodogram of the light curve for a particular white dwarf was created. The highest peak at a time scale of 1.58 days stands out significantly above the noise and may represent the rotation period of the white dwarf. The analysis done for this particular white dwarf star represents the same work that is to be done for the other white dwarf stars that have been

identified to be within the bounds of a Kepler/K2 target pixel file. Future work involves the extraction of high-quality light curves for a custom aperture around each white dwarf star. For white dwarfs with enough separation from the Kepler/K2 target, extracted light curves will be detrended using methods such as Cotrending Basis Vectors to accurately remove systematics and noise. Afterwards, the detrended light curves will be inspected for variability using periodogram analysis, to look for signals of interest such as eclipses, planetary transits, or pulsations.

84 Colin Purchase

Conceptualizing a STEM Innovation Lab/Makerspace at Hunter College

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Besides research and education roles, universities play a crucial role at stimulating innovation and entrepreneurship (I&E), which relates to direct contributions to economic growth and social progress. Science and Technology (S&T) I&E ecosystem infrastructure is much needed at Hunter College (e.g., institutional resources, modernized makerspace, competitions, etc.).

We are proposing a sustainable STEM Innovation Lab/Makerspace to (1) foster and facilitate the interdisciplinary collaborative design projects among students, staff, faculty and entrepreneurs. Several possible revenue channels are proposed. (2) contribute to job creation and talent retain. To achieve this goal, we have conducted field trips to visit the makerspaces at City College, Columbia University and NYU, as well as several community makerspaces.

It is found that the specific revenue model and the direct impact may vary depending on the makerspace's goals, target audience, and available resources. The overall contribution of makerspaces to skill development, innovation and community engagement can play an important role in job creation, economic development and social impact.

It is urgent to setup a makerspace at Hunter College that provides an inclusive and dedicated space, a variety of cutting-edge equipment and state of the art resources for students, scientists, engineers, artists, creatives, to fast prototype, test and implement their ideas.

Type V Deep Eutectic Electrolytes: A Sustainable Breakthrough for Lithium-ion Batteries

Emilia Pelegano-Titmuss[1], Giselle de Araujo Lima e Souza[1], and Steven Greenbaum[1]
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Statement of Problem: The scientific community is increasingly focused on designing and characterizing neoteric solvents with environmentally friendly properties such as recyclability, low toxicity, and cost-effectiveness. The research on neoteric solvents is thus strongly oriented towards the achievement of the United Nations Sustainable Development Goals to ensure an environmentally sustainable, and healthy society. Under these terms, Deep Eutectic Solvents, mostly formed by low-cost natural components, emerge as promising candidates to replace conventional organic solvents in different technologies.

Methods: Our Deep Eutectic Solvent (DES) was prepared by mixing Thy:Cam components at a fixed 1:1 molar ratio at 60 °C for 1 hour. The solutions with final salt concentrations of 10% and 30% by mole were prepared in an argon-filled glove-box ([O2] and [H2O] < 1 ppm) by mixing pre-weighed amounts of DES and LiTFSI. The transport properties of the resulting electrolyte was assessed using pulsed field gradient Nuclear Magnetic Resonance (PFG-NMR) as a function of temperature.

Results: Our investigation has unveiled the intricate interplay between lithium salt and the diffusion coefficients of DES components. Notably, we have observed a gradual reduction in the mobility of camphor compared to thymol, with this effect becoming particularly pronounced at elevated temperatures, especially in the samples containing 30% molar of LiTFSI.

Conclusions: This intriguing phenomenon suggests alterations in the solvation environment, potentially due to the coordination of lithium ions with the carbonyl group within camphor, suggesting that the Thy:Cam Deep Eutectic Electrolyte is a potential candidate for a sustainable electrolyte!

86 Stephen Rosario

Highly Conductive PAN-based Hybrid Aqueous/Ionic Liquid Solid Polymer Electrolytes with Tunable Passivation for Li-ion Batteries

Stephen Rosario, Steven Greenbaum

The escalating global demand for lithium-ion batteries has spurred safety concerns attributed to the utilization of flammable organic solvent-based electrolytes. In response, this study researches an electrolyte approach termed the hybrid aqueous/nonaqueous electrolyte (HANE) to modulate passivation at the anode within solid polymer electrolytes (SPEs). Incorporating ionic liquids as the nonaqueous constituent, the HANE strategy emerges as an effective avenue for enhancing SPE performance while mitigating safety risks. The investigation primarily centers on the development and characterization of Hybrid Aqueous/Ionic Liquid Solid Polymer Electrolytes (HAILSPEs), precisely crafted to uphold ionic conductivity while fostering a robust passivation layer. Synthesis and assessment efforts culminated in the identification of two HAILSPE systems boasting noteworthy room temperature ionic conductivities exceeding 5.39 mS/cm, marking a notable advancement over preceding materials. Employing advanced pulsed field gradient nuclear magnetic resonance techniques at Hunter College, measurements of Li+ ion transference numbers, indicative of the fraction of current carried by Li+ ions, yielded values of 0.6 or higher. These findings underscore the potential of the streamlined methodologies employed in this research to tackle the persistent challenge of cathodic degradation in aqueous SPEs. Furthermore, the successful deployment of HAILSPEs bears far-reaching implications for the evolution of cutting-edge and resilient energy storage solutions. Through cleverly balancing performance imperatives with safety considerations, this study contributes substantively to the ongoing quest for next-generation lithium-ion batteries tailored to meet burgeoning energy storage demands.

Affiliations for this experiment include: Kyle B. Ludwiga, Riordan Correll-Browna, Max Freidlina, Mounesha Garagab, Sahana Bhattacharyyaa, Patricia M. Gonzalesa, Arthur V. Crescec, Steven Greenbaum, Chunsheng Wanga, Peter Kofinasa

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PSYCHOLOGY

116 Tyjanae Orr

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What happens when we stimulate the VTA to mPFC projection?

Hypothesis/Statement of Problem: The United States has experienced an increase in mental health diagnoses related to depression and anxiety following the onset of the 2020 Covid-19 pandemic. Prior to 2020, depression prevalence among adults was below 10% but, reports of depression have tripled since then. This study aims to determine the contribution of Ventral Tegmental Area (VTA) neurons that project to the medial Prefrontal Cortex (mPFC) in relation to anxiety and depression-like behaviors in adults. We hypothesized that activation of VTA to mPFC projecting cells would decrease depression and anxiety-like behaviors.

Methods: To test our hypothesis we conducted tests to see if anxiety and depression symptoms in mice would decrease with the use of optogenetics. We ran behavioral methods such as open field, light dark box, novelty induced hypophagia and forced swim. The mice were divided into two conditions (control and experimental). The control group was injected with a virus that does not react to light activation, while the experimental group was given a virus that does respond to the optogenetic stimulation (light-sensitive). The mice were recorded and monitored for behavioral patterns including, learned helplessness and anxiety-like behavior.

Results: Preliminary analysis of the behavioral testing demonstrated that stimulating the neural pathway from VTA to mPFC did not affect anxiety-like behaviors during open field and light dark box. However, the stimulation decreased depression-like behaviors, primarily during forced swim.

Conclusion: The results indicate that stimulating the neural pathway from VTA to mPFC has a greater effect on decreasing depression opposed to anxiety. This model shows that the neural pathway from VTA to mPFC modulates depression-like behaviors.

87Juliet.Wenschke

Abstract:

With the increasing prevalence of mobile device use among parents, concerns about its impact on infant development have grown. This replicated study aims to investigate the effects of parental mobile device use on infant positivity during parent-infant interactions, taking into account the influence of socioeconomic status (SES). Building upon the classic Still Face Paradigm (SFP), a more diverse sample of infants aged 18 to 24 months and their caregivers participated in a modified SFP. The study comprised three phases: free play (FP), still face (SF) with mobile device use, and reunion (RU). In addition to assessing infant positivity with indicators such as positive affect, room exploration, caregiver engagement, toy engagement, and positive vocalization, SES will be considered as a factor. Infants from lower SES backgrounds are expected to display higher levels of infant positive behaviors during the SF phase compared to infants from higher SES backgrounds, possibly due to shared stressors within the home environment. It is also anticipated that during the RU phase, infants from lower SES backgrounds may demonstrate fewer positive behaviors, indicating a potentially reduced capacity for optimal recovery. The findings from this study will provide valuable insights into the impact of parental mobile device use on infant social-emotional development and parent-infant interactions, with a specific emphasis on the interplay between infant positivity and SES.

Keywords: mobile device use, infant positivity, socioeconomic status (SES), still face paradigm (SFP), parent-infant interactions.

88 Emma Bucknavage

Variation in intake rates of food types in grey-cheeked mangabeys (*Lophocebus albigena*)

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Objectives: Foraging primates select a variety of food sources from their environment to fulfill their nutritional and energy requirements determined by their unique physiology. Food availability and forest composition vary based on spatiotemporal and social competition factors that inform foraging strategy and nutrient prioritization of primates. Previous research in grey-cheeked mangabeys (*Lophocebus albigena*) has found their omnivorous diet varies depending on region and food dispersal. The intake rate of different foods is important for nutrition, but further, for feeding competition and food depletion.

Methods: Two groups of grey-cheeked mangabeys were studied year-round for 2 years in rainy and dry seasons in Kibale National Park, Uganda. Full-day individual focal follows were conducted to record the identity, plant part, quantity, and location of foods consumed during the animal's daily intake. The number of items consumed was measured for each feeding bout and was later used in JASP to calculate the average feeding rate for each type.

Results: Our results revealed that leaf buds, young leaves, and isects, with respective means of 13.96, 7.81 and 7.80 items per minute, were eaten significantly faster than seeds and piths, with means of 3.51 and 2.69 items per minute ($p < 0.05$).

Discussion: Intake rates provide insight into nutrient-balancing techniques of mangabeys depending upon food availability, such as an increased intake of insects during dry seasons, as suggested in previous studies. Complementary research on social interactions would provide greater context into which food sources the primate had sufficient time to consume.

89 Mary Avella

Developing an online task to examine how attention to detail affects learning dynamics

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Hypothesis/Statement of Problem: Autism Spectrum Disorder is a neurological disorder that affects how a person communicates and interacts with others. One way people on the spectrum are different from neurotypical people is in their attentional focus. In particular, those on the spectrum have been shown to pay close attention to detail instead of looking at “the bigger picture”. One way these contrasts manifest is through learning, where attention to detail might reflect focusing attention on the most recent information, rather than integrating over longer time periods. Because neurodiversity is a wide spectrum, it is hard to measure the difference between every autistic and normal learning style. Previous work from the Nassar lab has identified relationships between "attention to detail, " as measured by the autism spectrum questionnaire, and specific learning strategies that are overly focused on specific data points. This work was conducted as part of a small in-person study, and we hope to conduct a larger, online study to validate and extend the results.

Methods: To do so, we used an online video game experiment to analyze how people learned based on the movements and changes on the screen. The video game measured how participants moved a bucket to catch money dropped by an invisible helicopter. The participant had to infer where the helicopter was, so they could catch the money to earn points. The movements of the helicopter once each new trial started varied between similar patterns and spontaneous movements, so we could measure how people would decide on where to move the bucket. We have a working, online version of the task and plan to collect behavioral data and measures of attention to detail using an Autism Spectrum Questionnaire.

Results: The initial pilot results show a mix of stable and flexible learning, with jumps in learning at changepoints between trials. Future work will scale up the study and examine whether individuals with higher attention to detail have heightened flexibility at the expense of belief stability.

Conclusions: Measuring autistic ways of learning helps us gain more knowledge about the autism spectrum.

90 Daisy Caizaguano

Beyond Hot Flash Severity: Do Hot Flash Beliefs Drive Sleep Disturbance in Menopausal Women?

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Hypothesis/ Statement of Problem: Hot flash severity and sleep disturbance are among the most common complaints experienced by women going through menopause. Existing research has repeatedly indicated that worse hot flash severity is associated with greater sleep disturbance. However, it is possible that cognitive factors, such as negative appraisal of hot flashes, may better explain sleep disturbance than hot flash severity. The present study aims to assess the relationship between hot flash severity, hot flash beliefs, and insomnia symptoms.

Methods: As part of a larger longitudinal study, a total of 121 participants (42 years and older) were assessed with Hot Flash Belief Scale (HFBS) and Insomnia Severity Index (ISI). A hierarchical linear regression was performed to explore the association between hot flash severity and insomnia symptoms, and subsequently the association between hot flush severity and insomnia symptoms when controlling for hot flush beliefs.

Results: Multivariate regression analyses indicated an initial correlation between hot flash severity and insomnia symptoms. However, this relationship became non-significant after controlling for hot flash beliefs, indicating that hot flash beliefs is a better predictor of insomnia symptoms that hot flash severity.

Conclusion: This current study reinforces the idea that sleep disturbance during menopause is multifactorial and highlights the importance of cognitive appraisals. Our findings suggest that cognitive behavioral therapy techniques aimed at modifying negative beliefs about hot flashes may be beneficial in improving sleep among women during the menopausal transition.

91 Emily Drucker

Examining Correlations in Life, Relationship, and Sexual Satisfaction Between Kinky and Non-Kinky Individuals

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Hypothesis: This study examines correlations in life, relationship, and sexual satisfaction between kinky and non-kinky individuals in committed romantic relationships. This study aims to contribute to a more comprehensive understanding of the psychology of kink-practitioners, and to examine the implications of these practices in the context of life, relationship, and sexual satisfaction. It is predicted that individuals who practice kink, as compared to non-kinky individuals, report an equivalent or greater degree of life, relationship, and sexual satisfaction.

Methods: Data was collected from 72 romantically partnered U.S. residents, ages 25-50 (n= 72). Participants were anonymously recruited through online forums (Instagram, Facebook, Reddit, and FetLife, a popular online fetish community). Participants were administered a series of 5 closed-item, Likert-scale based surveys to assess sexual satisfaction, relationship quality, life satisfaction, and personality.

Results: In measuring correlations between kink-identification and sexual satisfaction, there was shown to be a statistically significant negative correlation ($r(71) = -.291$, $p = .014$), suggesting that kinky individuals report higher sexual satisfaction than non-kinky individuals.
No statistically significant correlations were found between life and sexual satisfaction ($r(71) = .227$, $p = .057$), although the data confirms statistically significant positive correlations between life satisfaction and relationship satisfaction ($r = .424$, $p = <.001$) as well as relationship satisfaction and sexual satisfaction ($r = .642$, $p = <.001$), which are consistent with the findings of past research.

Conclusion: Greater understanding of these behaviors may have clinical implications related to the treatment of kinky individuals seeking psychotherapy, as well as the increased ability of these individuals to embrace their sexual identities which may lead to improvements in self-esteem and even quality of life.

92 Maylyn Mei

The Development of Face Processing Related Brain Structures in Individuals with Varying Likelihoods of Autism

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Hypothesis/Statement of the Problem: The Mid-Fusiform Sulcus (MFS) is an anatomical landmark that strongly predicts the presence of the fusiform face area (FFA), thus it allows us to study the neural development of face processing and recognition in those who are unable to complete face perception tasks. Face processing and preference develop early in infanthood, but has proven difficult to study as infants can not complete FMRI face-related tasks. This new method allows us to study the development of face processing brain structures from infancy using MRI scans.

Methods: Early years of life are critical to face learning, thus we will analyze MRI scans of 503 six, twelve, and 24 month-old infants with differing likelihoods of autism to determine when the MFS develops relative to when they learn to process faces. Using the GNU Image Manipulation Program, we will calculate the FFA's cortical thickness (CT) and sulcal depth (SD) by i.) tracing grey matter & white matter boundaries and ii) using these boundaries to compute the corresponding distances.

Results: At six months, the majority of infants had developed the MFS, though more MFS was identified on the left than the right hemisphere. By twelve months, all infants had an identified MFS bilaterally. Those later diagnosed with autism did not have a significant difference in MFS development than those who were not, more data needs to be collected.

Conclusions: The purpose of this project is to provide insight into the developmental timeline of face processing related structures as a possible biomarker for face processing ability and general socialization.

93 Chris Stein

Investigating Whether Mutant Rhodopsin Engages with the BBSome

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Hypothesis/Statement of Problem:
Rod photoreceptors are light-sensing cells in the retina which contain a modified primary cilium, known as the outer segment. This outer segment compartment is filled with disc-shaped membranes that are densely packed with the light-sensing protein, rhodopsin. Rhodopsin is a 7-transmembrane domain GPCR that is delivered to rod outer segments by vesicular traffic. Mutations that affect rhodopsin traffic are known to disrupt disc formation and will ultimately lead to human blindness. The C-terminus of rhodopsin contains signaling motifs that are important for its correct localization. One is the FR motif found in close proximity to the last transmembrane domain of rhodopsin. In other GPCRs, this FR motif is important to regulate their exit from the primary cilium. Ciliary exit of many GPCRs is executed by a protein complex known as the BBSome. The BBS7 subunit of the BBSome is known to mediate interactions between the BBSome and GPCRs through the FR motif. Our lab has found that mutating the FR motif of rhodopsin results in some of it being mislocalized outside the outer segment.

Methods:
To test whether this mislocalization is due to abnormal interaction between the BBSome and rhodopsin, we performed immunoprecipitation assays between the C-terminus of rhodopsin and the BBS7 subunit of the BBSome.

Results:
Our results show that the BBS7 subunit does not interact with rhodopsin's C-terminus, even in the presence of the FR mutation.

Conclusions:
Our results suggest a different mechanism for the observed mislocalization.

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94 Amberlee Weber

The relationship between mood, chronotype and chronic pain in patients evaluated for obstructive sleep apnea (OSA).

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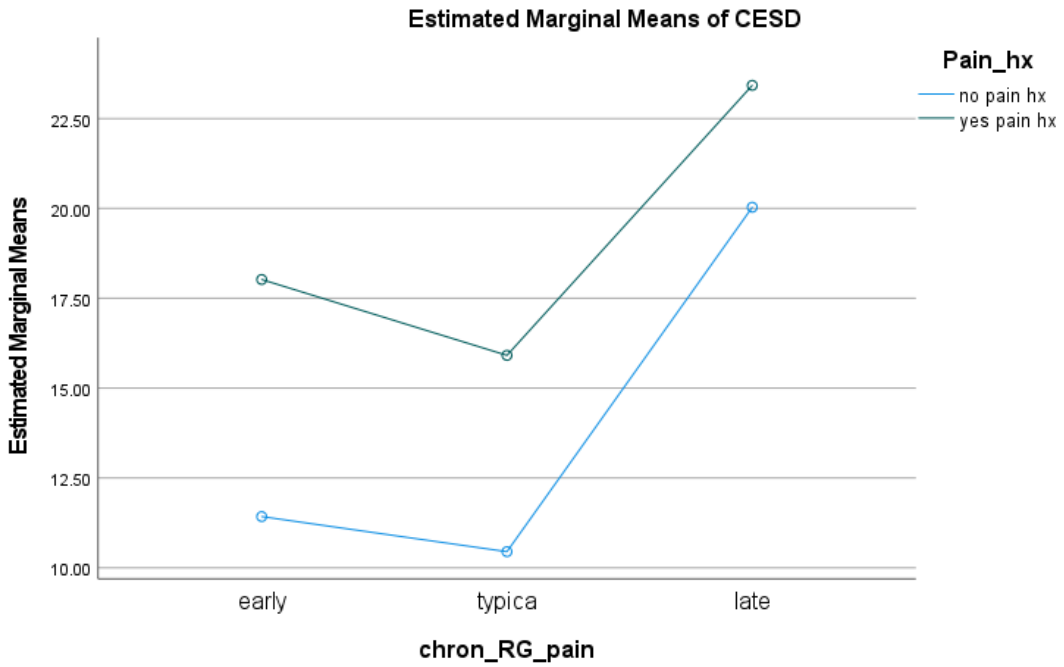
Introduction: No studies have simultaneously examined effects of chronotype and pain on mood in OSA patients. This study analyzes depression symptoms in relationship to self-reported sleep-timing and chronic-pain-conditions (CPC) in patients referred for OSA evaluation.

Methods: Three hundred-sixty patients (210 women) without shift work history or significant medical/psychiatric conditions except depression/anxiety underwent polysomnography(PSG); 78 had CPC (e.g., fibromyalgia, arthritis). Self-reported sleep times, defined as early, typical and late chronotypes (EC, n=115; TC, n=163; LC, n=82). Center for Epidemiologic Studies Depression Scale-Revised (CESDR) was regressed onto OSA, chronotypes and CPC.

Results: Higher CESDR related to CPC presence ($F=8.1$, $p=0.004$) and LC ($F=7.8$, $p<0.001$), but not to OSA ($F=1.6$, $p=0.21$). No interactions were significant. Among patients without CPC, LC group had higher CESDR ($n_{LC/noCPC}=124$, $M_{LC/noCPC}=20.7\pm18.9$) relative to EC ($n_{EC/noCPC}=91$, $M_{EC/noCPC}=11.5\pm11.3$, $p<0.001$) and TC ($n_{LC/noCPC}=67$, $M_{TC/noCPC}=10.1\pm10.6$, $p<0.001$, Bonferroni post-hoc). Among CPC-present patients, CESDR did not significantly differ between chronotypes ($n_{EC/CPC}=24$, $M_{EC/CPC}=17.5\pm14.5$; $n_{TC/CPC}=39$, $M_{TC/CPC}=16.3\pm10.3$; $n_{LC/CPC}=15$, $M_{LC/CPC}=22.9\pm17.3$).

Conclusion: Without CPCs, late chronotype related to higher depression symptoms, versus early and typical. With CPC, CESDR did not significantly differ between chronotypes, possibly due to overall elevation of depression symptoms in these patients. There was no relationship between OSA and depression symptoms.



Covariates appearing in the model are evaluated at the following values: age = 48.4266, sex = 1.4209, BMI = 32.4621, AHI = 14.7904

95 Jason Amadio

Characterization of Zinc-Finger Protein 638 (ZNF 638) in Cerebral Organoid Models of Multiple Sclerosis

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Hypothesis/Statement of Problem: Multiple Sclerosis (MS) is a neurodegenerative, autoimmune disease that results in demyelination and increased inflammation in the Central Nervous System (CNS) (Filippi et al., 2018). Epstein-Barr Virus (EBV) was confirmed to increase risk of MS by 32x after infection; however, the mechanism remains uncharacterized (Bjornevik et al., 2022). The ZNF638-DYSE genetic locus is associated with increased disease progression (IMSGC & MSC, 2023). ZNF 638 protein functionality involves mediating transcriptional repression of unintegrated retroviral DNA (Savage et al., 2018). This project aims to characterize a potential difference in expression of ZNF638 in Cerebral Organoid Models of MS compared to controls.

Methods: We derived cerebral organoids from induced pluripotent stem cells (iPSC) of healthy control subjects and from primary progressive MS (PPMS) patients to ensure cells were derived from patients with significant disease progression. Organoids cultured for 42 days. Samples were stained with ZNF638 polyclonal antibody, and co-stained with DAPI, Sox2+, and MBP. Samples were analyzed using immunofluorescence and quantified based on intensity.

Results: There was no visible localization of ZNF638. The results showed an increase of intensity in the MS model compared to control, but no significant difference was observed.

Conclusion: The association of ZNF638 to increased disease progression is based on a particular risk allele of the gene. Therefore, it is possible that only a portion of the expressed ZNF638 was related to disease progression. Furthermore, ZNF638 is expressed in a variety of cells and the organoid was not isolated enough to determine the association.

96 Katherine Bayona

The effects of HIV-1 Tat/morphine on AMPAr and NMDAr dysregulation in the dorsal striatum of female rodent brains

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Hypothesis/Statement of problem: The human immunodeficiency virus-1 (HIV-1) protein, transactivator of transcription (Tat) is a mediator in the development of HIV-1-associated neurocognitive disorders (HAND). HIV-1 Tat promotes neuronal injury and loss by disrupting intracellular calcium (Ca^{2+}) homeostasis via the N-methyl-D-aspartate receptor (NMDAr). The neurotoxicity of HIV-1 Tat on HAND is aggravated by morphine use. Women diagnosed with HAND can have worsened synaptodendritic damage when they abuse opiates (morphine), due to estradiol's (E_2) ability to potentiate drug-driven reward behaviors. We will investigate the mechanisms underlying the interaction between HIV-1 Tat and morphine to mitigate the effects of HAND in the female brain. We hypothesize HIV-1 Tat disrupts the expression pattern of NMDAr and Alpha-amino-3-hydroxy-5-methyl-4-isoxalepropionic receptor (AMPAr) in the dorsal striatum (DS), which can be further exacerbated after *acute* morphine use.

Methods: We performed a western blot analysis of NMDAr and AMPAr in the DS of transgenic HIV-1 Tat -/+ female ovariectomized (ovx) mice, following an unbiased morphine conditioned place preference task (CPP).

Results: We observed the downregulation of the GluA1 subunit in Tat (+) mice, which is essential for synaptic strengthening and AMPAr retention at the postsynaptic membrane. Followed by a significant decrease in GluA1 (serine 845), a phosphorylation site essential for stabilizing GluA1-containing AMPARs at the postsynaptic membrane. Additionally, we observed the downregulation of the GluA2 subunit, which is necessary for AMPAr stability and limits Ca^{2+} influx. NR1 expression was significantly decreased, suggesting impaired NMDAr function and increased Ca^{2+} influx.

Conclusion: Therefore, Ca^{+2} influx may disregulate AMPAr GluA1/2 subunit composition, worsening synaptodendritic damage in HAND patients.

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117 Jeslyn Mei

Calvaria Defects in Mouse *Fbn1* Mutants

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When one or more cranial sutures fuse prematurely, the skull develops into an abnormal shape in a birth defect called craniosynostosis. Mutations of *Fbn1*, which encodes for the glycoprotein fibrillin-1 and promotes the functional integrity of connective tissues, cause Marfan syndrome in humans. Multiple cases of people with *Fbn1* mutations also exhibit craniosynostosis. Thus, we investigated if fibrillin-1 acts as a key regulator of suture formation using mouse *Fbn1* mutants as a model system. Calvarial bone was examined at birth (P0) by Alizarin red staining or microcomputed tomography (microCT) in 3D. Also, frontal sections of the head were examined after immunofluorescence for a marker of bone. Although the *Fbn1* mutants showed calvaria abnormalities, namely narrow sutures, they did not show craniosynostosis at P0. We followed up to P7, which is the last stage that *Fbn1* mutants survive to, but still did not find craniosynostosis. We then examined earlier stages to determine when the calvarial abnormality first arises. Based on immunofluorescence for a marker of preosteoblast, the *Fbn1* mutants appeared normal at embryonic day (E) 14.5 (mouse gestation is 19 days). Therefore, we conclude that fibrillin-1 is required for proper calvaria development and suture formation during the late stages of embryonic development, but is not required to prevent craniosynostosis specifically.

97 Albert Jurkowski

Medial entorhinal cortex spatial coding deficits in a pilocarpine mouse model of temporal lobe epilepsy

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Abstract

Temporal lobe epilepsy (TLE) affects approximately 50 million people worldwide and can lead to pervasive deficits of cognition, mood, and memory. Chronic TLE causes cellular and circuit dysfunction within the hippocampus, including interneuron death and formation of maladaptive excitatory and inhibitory circuits. Hippocampal subfield CA1 contains spatially-tuned place cells, which develop impaired stability and information content between 3- and 6-weeks post-epileptogenesis, coinciding with spatial memory loss. However, the origin of these deficits remains unknown. We hypothesize that the medial entorhinal cortex layer III (MECIII), as the primary upstream source of afferent CA1 projections, will also develop spatial coding breakdown of its place cells. Our study reliably targeted MECIII neurons with layer specificity to express GCamP8m using an adeno-associated virus. We performed *in vivo* calcium imaging of pilocarpine mouse models of TLE in open-field and linear-track conditions. Preliminary data showed pilo mice had significantly decreased spatial information content of MECIII place cells across both timepoints, while cellular stability trended downwards as memory deficits emerged at 8-weeks. These results suggest TLE-associated deficits in MECIII spatial coding which worsened with exacerbation of spatial memory deficits. This novel technique of targeting MECIII neurons will allow future studies to opto- or chemogenetically manipulate cellular activation to assess its effect on downstream CA1 cells.

Keywords: temporal lobe epilepsy, in vivo calcium imaging, medial entorhinal cortex, place cells

98 Lewis Nunez Severino

Title: Neural Activity Patterns Underlying Abstract Sequences in Humans

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Hypothesis/Statement of Purpose: Processing complex patterns involves tracking sequential information, including abstract sequences that rely on a set of goals rather than specific details (e.g., slicing then spreading when making a sandwich). Despite the utility of abstract sequences, our understanding of the neural representations underlying them remains limited. Previous work identified that the rostrolateral prefrontal cortex (RLPFC) is necessary for abstract sequential monitoring in humans during a response task. In monkeys, an analogous area in dorsolateral prefrontal cortex (DLPFC) responded to abstract sequential changes during a no-report task. We tested the hypothesis that human RLPFC responds to sequence changes in the same no-report abstract sequential task. We predicted that neural activity patterns involved in monitoring sequential changes will be like those observed in prior studies with monkeys.

Methods: We conducted fMRI on 23 human participants during the visual task used in prior studies with monkeys, which involved changes in the rule and number of items of an abstract sequence.

Results: Utilizing univariate analyses, we identified brain regions active during certain conditions of the task, such as the inferior frontal gyrus, superior temporal sulcus, and RLPFC, findings that mirror results previously observed in monkeys. Subsequently, we conducted region of interest analyses to further explore these active regions during the task. Our results showed that RLPFC only responds to changes in the rule governing an abstract sequence.

Conclusion: These findings underscore the specific role of the RLPFC in processing rule changes within abstract sequences, highlighting its critical involvement in higher-order cognitive functions such as planning.

STATISTICS

118 Danielle Elterman

TITLE: Universal Post-Thaw Viability Testing of Allogeneic Hematopoietic Stem Cell (HPC) Collections Shows Increased Risk of Non-Engraftment and Delayed Platelet Engraftment in Products with Decreased Post-Thaw Viable CD34 (vCD34) Yield.

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Hypothesis: Cryopreservation may lead to diminished viability in stem cells, impacting transplant outcomes. Universal post-thaw viability (PTV) monitoring can highlight connections with significant CD34 viability loss. However, such programs are not widely established, and there is lack of information about the impact of testing for PTV and its clinical applications. This study examines the utility of PTV testing in hospitals for uses in differentiating at risk patients, engraftment probability, and transplant outcomes.

Methods: PTV analysis was conducted on 227 consecutive allogeneic hematopoietic cell collections processed between May 2022 and September 2023. QC vials of cryopreserved products were thawed 24-72 hours after freezing, and PTV of CD34+ and CD35+ cells was assessed. Concordance between PTV in cryobags vs cryovials was validated. Total vCD34 were calculated as: total nucleated cell count x CD45 viability x % viable CD34 cells among viable CD45 cells. Patient dosing was based on post-thaw values.

Results: PT CD34+ recovery follows a normal distribution and remains consistent over time, suggesting that viability drop is a natural occurrence with many involved factors. Median CD34 viability dropped from 99%[99;100] fresh to 80%[69;88] post-thaw, and 55 out of 227(24%) products had>35% drop total vCD34. Products with >35% drop in vCD34 yield were associated with higher risk of non-engraftment for both neutrophils (Fisher p=0.013, OR 23.6&95% CI 1.20-464.2), and platelets (Fisher p=0.004, OR 16.2&95% CI 1.8-142.5). Engrafted patients had a median vCD34 change of -22%[-34;-9], compared to -41%[-72;-32] for those who failed to engraft. Post-thaw vCD34 dose was significantly associated with delayed platelet engraftment (t-test p=0.027), but not ANC engraftment (t-test p=0.59).

Conclusion: Products with >35% drop had higher probability of delayed engraftment. engraftment. Implementing PTV testing allows identification of at-risk patients, who could benefit from increased surveillance and alternative treatment plan.