RUTGERS–NEW BRUNSWICK
Molecular Biosciences
Graduate Student Organization

18th Annual MBGSO Research Symposium

Friday March 14, 2025

9:30 AM-4:30 PM

Life Sciences Building Atrium

Busch Campus

Rutgers University

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A Letter from the Organizers

Welcome to the 18th Annual Graduate Student Research Symposium hosted by the Rutgers University Molecular Biosciences Graduate Student Organization (MBGSO). We are delighted to have you join us today to support the outstanding research produced by graduate students in the Molecular Biosciences Graduate Program and related graduate programs. We are fortunate to be able to foster a scientific community here at Rutgers.

As a student-led organization, the goal of MBGSO is to facilitate the professional development of graduate students and provide opportunities for continued growth, learning, and networking. By hosting the MBGSO Annual Symposium we hope to not only showcase graduate student research but also to encourage collaboration and interdisciplinary discourse. With support from the university community our presenters receive valuable feedback and input on their work as well as an opportunity to disseminate their research to a broader audience. With these goals in mind, we organize the annual symposium and look to the university community to make it a success.

We would like to express our gratitude to our faculty advisor, **Dr. Janet Alder**, for her tireless work on behalf of the graduate students and for providing valued guidance and support. We would also like to thank **the administrative personnel supporting the Rutgers School of Graduate Studies** for their role in helping the MBGSO coordinate this and several other events throughout the year. We gratefully acknowledge the **Molecular Biosciences faculty** for their ongoing support and commitment to our graduate program and especially to those of them that volunteered their time to participate in the symposium to judge student presentations and offer valuable feedback and insight. We are also grateful to our keynote speaker, **Dr. Zhiping Pang**. And finally, this event would not be possible without the participation of the graduate student presenters, and so **we offer a hearty thanks to our peers** for helping create and nurture the vibrant intellectual and social community within the Molecular Biosciences Graduate Program. We are proud and honored to be at the service of the Molecular Biosciences community.

Sincerely,

MBGSO Executive Board 2024-2025

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Program Coordinator: **Noah Mac**

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Symposium Schedule

9:30AM - 10:00AM……..**Registration and Introductions**

10:00AM - 11:00AM……**Oral Presentations I**

11:00AM - 12:00PM……**Poster Presentations I**

12:00PM - 1:00PM……**Keynote Address**

1:00PM - 2:00PM……..**Lunch & Networking**

2:00PM - 3:00PM……..**Poster Presentations II**

3:00PM - 4:00PM……..**Oral Presentations II**

4:00PM - 4:30PM…..……**Award Ceremony**

4:30PM - 5:45PM…..……**Networking Event**

Keynote Address

“Mechanisms of Synaptic Regulation: from Stem Cells to the Brain”

Dr. Zhiping Pang, PhD

Dr. Zhiping Pang is a Professor in the RWJMS Department of Neuroscience and Cell Biology and the Child Health Institute (CHI) at Rutgers University, New Brunswick. Dr. Pang has a broad background in neurobiology and stem cell biology, and joined CHI NJ in 2011. His graduate and postdoctoral training was under the supervision of Dr. Thomas C Südhof at the University of Texas Southwestern Medical Center and Stanford University, where he focused on exploring the molecular mechanisms underlying calcium-triggered synaptic vesicle release.

Dr. Pang’s current research focuses on mouse and human neurons, studying the molecular underpinnings of neuropsychiatric disorders, as well as eating disorders. His research interests may provide valuable insights into the neural causes and consequences of childhood obesity. Through his lab’s work, Dr. Pang has developed novel techniques for deriving neuronal cells from primary skin cells and pluripotent stem cells, providing opportunities to study the pathogenesis of neurological disorders, including pediatric developmental disorders and autism spectrum disorders.

Today, Dr. Pang is a leader in his role here at Rutgers. Recently awarded the Presidential Outstanding Faculty Scholar Award in 2023, he continues to serve the Rutgers community and beyond with his exemplary research and teaching experience. Dr. Pang has amassed over 5,000 citations in his career and is relentless in his pursuit of high-quality science, demonstrated by recent publications in Cell, Nature and Science-affiliated journals.

Most importantly, and in accordance with the theme of this symposium, Dr. Pang has a profound record with mentorship. Dr. Pang writes, “I am devoted to empowering the next generation of scientists to excel and contribute profoundly to the realm of biomedicine. This commitment extends to creating a dynamic and inclusive research community where diversity is celebrated and every individual is afforded the opportunity to thrive.” He is actively involved in mentoring students and professionals at Rutgers, including undergraduates, PhD candidates, Research Assistants, and postdoctoral scholars.

*Adapted from the Pang lab website

ORAL PRESENTATIONS

Morning Presentations

10 AM-10:20 AM: HP1 Recruits the Chromosomal Passenger Complex to the Chromosome for Acentrosomal Spindle Assembly in Meiosis
Presenter: Siwen Wu
Chromosome segregation fidelity during female meiosis is critical for genome integrity, with aberrations causing infertility, miscarriages, and congenital anomalies. The chromosomal passenger complex (CPC)—composed of inner centromere protein (INCENP), Borealin, Survivin, and Aurora B kinase—regulates spindle assembly and ensures accurate chromosome segregation during meiotic cell division. In Drosophila oocytes, the CPC is required for microtubule recruitment to chromosomes, enabling acentrosomal spindle formation post-nuclear envelope breakdown during meiotic metaphase I. However, the mechanisms of CPC chromosomal recruitment and its interaction with spindle microtubules remain unclear. INCENP is a scaffolding component of CPC interacting with microtubules (MTs) and heterochromatin protein-1 (HP1). From our previous study, we hypothesized that HP1 recruits the CPC to chromosomes to initiate acentrosomal spindle assembly and chromosome biorientation. We developed HP1 RNAi reagents and generated Incenp mutants with deletions in HP1 binding sites. In HP1 RNAi Drosophila oocytes, we observed increased chromosome segregation errors, suggesting HP1 has a crucial role in regulating chromosome biorientation. 30% of HP1 RNAi oocytes failed to assemble spindles, indicating that HP1 has a role in spindle assembly. Incenp mutants lacking the HP1 binding domain showed increased chromosome segregation errors, but normal bipolar spindle formation, indicating that HP1-INCENP interaction is not responsible for spindle formation but has a role in chromosome biorientation. Strikingly, we observed a complete failure of spindle assembly and CPC chromosomal recruitment in oocytes by deleting two domains, HP1 and SAH, suggesting that multiple INCENP domains may be required to interact with HP1 and initiate spindle assembly in oocytes.

10:20 AM-10:40 AM: Protein-Membrane Interactions in Cell-to-Cell Transmission of Huntingtin Protein
Presenter: Nora Jaber
Many proteins associated with neurodegeneration are intrinsically disordered proteins (IDPs) that exhibit dynamics and “prion-like” behaviors. There is currently little knowledge of the molecular factors that influence how organization of their microenvironment controls IDP function. Evidence shows IDP-membrane interactions modulate the formation of IDP inclusions, dynamics, and functions. However, the role that these interactions play in the context of neurodegeneration, specifically how it influences aggregation and propagation of IDPs, is poorly understood. The goal of this research is to characterize the functional roles of membranes in transmission of IDPs, using mutant huntingtin (mHtt) as a model protein. When huntingtin’s poly-glutamine (polyQ) tract is expanded, one is at risk for Huntington’s Disease. We take an interdisciplinary approach by combining correlative light and electron microscopy (CLEM), cryo-electron tomography (cryoET), and biochemical and biophysical assays to elucidate molecular mechanisms of huntingtin transmission and to understand how interactions with membranes affect mHtt aggregation and transmission. Deciphering the fundamental characteristics that influence neurodegeneration will allow for making more informed decisions for therapeutic approaches down the line.

10:40 AM-11:00 AM: RIG-I Antiviral Signal Transduction is Mediated by Conditional CARD Interactions
Presenter: Mihai Solotchi
RIG-I is an essential cytosolic receptor of the innate immune system whose modular structure enables a series

of intricate mechanisms to regulate its activation. 5'ppp viral dsRNA products activate the exposure mechanism of RIG-I CARDs, thereby initiating the downstream type I interferon antiviral response. Downstream signal transduction is mediated through CARD-CARD interactions, K63 ubiquitination, and interactions with MAVS. However, evidence surrounding these molecular events is limited, and the precise order and dynamics of RIG-I CARD-CARD interactions and ubiquitination remain to be determined. Here we use NanoBiT bioluminescent protein-complementation to develop a novel high-throughput cellular screening assay for RIG-I CARD:CARD interactions. Additionally, site-specific-labeled fluorescent RIG-I proteins were generated to develop a complementary in vitro assay for measuring CARD:CARD interactions using single-molecule FRET for studying CARD-CARD interactions. Our biochemical assays combined show that shorter, monomeric RNA ligands activate RIG-I with lesser potency than longer RNA ligands which can accommodate two or more RIG-I binding events, and that activation of RIG-I correlates with CARD-CARD interactions observed by NanoBiT. Furthermore, our results demonstrate that the E3 ligase RIPLET stabilizes oligomeric RIG-I complexes, which may potentiate more CARD-CARD interactions. These results provide a framework for further characterizing these CARD-CARD interactions in the context of RIG-I activation and signal transduction. While this project is a work in progress, our preliminary findings shed light on the underlying complexity of RIG-I's signal transduction pathway.

Afternoon Presentations

3 PM-3:20 PM: Hypoxia-induced metastatic reprogramming through the suppression of KDM8 histone demethylase function in pancreatic cancer

Presenter: Pradeep Moon Gunasekaran

Pancreatic ductal adenocarcinoma (PDA) is a common and deadliest malignancy of the pancreas. Owing to poor vascularity, desmoplasia, and extensive consumption of oxygen, hypoxia is a general feature of PDA. To adapt to hypoxia, malignant cells undergo major genetic and epigenetic reprograming that promotes epithelial-to-mesenchymal transition (EMT), metastasis, and treatment resistance. Despite the established knowledge of hypoxia-induced factors or HIFs, the role of other oxygen-sensing regulators in hypoxic response remains elusive. We show that Kdm8, a histone 3 lysine demethylase carrying a Jumonji-C, suppresses the pro-metastatic program in PDA. Genetic depletion of Kdm8 promotes metastasis across multiple transplanted tumor models and unleashes a transcriptional state that closely resembles EMT and the neuroendocrine-like subtype of PDA. Mechanistically, the cell state change following Kdm8 inactivation can be attributed to global changes in histone 3 lysine 36 dimethylation (H3K36me2) and lysine 27 trimethylation (H3K27me3). Interestingly, re-expression of the Kdm8 hypermorphic variants that demonstrate increased resistance to hypoxia diminishes hypoxia-induced gene expression changes and metastasis, suggesting the critical role of the Kdm8 demethylase function in suppressing PDA progression. We pioneered an innovative genetically-engineered mouse (GEM) model of PDA and showed that Kdm8 depletion reduces the expression of genes defining the classical PDA subtype and drives a profound loss of the differentiated state. Collectively, our results support a model by which hypoxia induces a major phenotypic change and metastatic progression of PDA through the suppression of the demethylase activity of Kdm8 and the subsequent reprogramming of the chromatin state, namely the "hypoxia-Kdm8-chromatin" axis.

3:20-3:40 PM: Characterizing the Impact of Developmental Cc2d1a Reduction as a Sex-Specific Mouse Model of ASD/ID

Presenter: Abigail Heller

Intellectual disability (ID) and Autism Spectrum Disorder (ASD) exhibit notable male diagnostic bias (4:1 for ASD, 2:1 for ID) with complex genetic heterogeneity. Previous research identified CC2D1A loss of function (LOF)

as a cause of 100% penetrant ID, and highly penetrant ASD. While existing Cc2d1a conditional knockout (cKO) mouse models avoid early postnatal lethality of global knockouts, their conditional limitations inadequately represent patients with developmental CC2D1A LOF. We generated mice with V5-HA epitope tags knocked into Cc2d1a, resulting in protein degradation. Homozygous V5-HA mice (Cc2d1aVH/VH) survive despite ~86% CC2D1A reduction but do not show ASD/ID-like behaviors as forebrain cKOs do. To explore phenotypic penetrance thresholds, we crossed the Cc2d1aVH line with a null allele, creating a more severe hypomorph (Cc2d1a-/VH) with ~90% protein reduction. These mice are viable and fertile without major sensory-motor deficits. Cc2d1a-/VH females show developmental growth stunting but normal behavior. In contrast, Cc2d1a-/VH males exhibit deficits in sociability, social novelty preference, and spatial memory acquisition. In addition, Cc2d1a-/VH males show cortical CaMKII activation deficits. These males also display a trend of reduced feeding and lower NPY/AgRP mRNA expression in the arcuate nucleus, suggesting hypothalamic signaling dysregulation. This severe developmental hypomorph model reveals unique neuronal mechanisms driving sex-specific ASD/ID-like phenotypes within Cc2d1a reduction and sex-specific impacts on feeding and growth, offering novel insights into what factors may be at play within the ASD and ID diagnostic sex bias.

3:40 PM-4:00 PM: Cell-Type-Specific Contributions of Sensory and Motor Cortical Inputs to Striatal Plasticity and Behavior

Presenter: Branden Sanabria

The striatum, a key input structure of the basal ganglia, contributes to learning by sorting information from our sensations, movements, and rewards. Projections from the sensory (S1) and motor (M1) cortex target striatal spiny projection neurons (SPNs) and parvalbumin fast spiking interneurons (FSIs) in the dorsolateral striatum (DLS). However, their capacity for plasticity and functional role in shaping behavior is less known. We hypothesized that S1 and M1 synapses onto SPNs and FSIs exhibit cell-specific differences driving sensorimotor integration. To investigate anatomical differences, we injected AAVs encoding spaghetti monster fluorescent proteins (sm.FPs) into S1 and M1 of mice, and generated 3D reconstructions of synapses to identified SPNs and FSIs. To examine baseline capacity for plasticity, we optogenetically stimulated S1 or M1 corticostriatal terminals in ex-vivo slices with a theta burst stimulation (TBS) while recording from SPNs or FSIs. Lastly, we tested a reward-based paradigm in which mice learned to report the stimulation of M1 or S1 corticostriatal terminals by licking for water. Our results indicate that SPNs receive significantly more synaptic contacts from M1 than S1, but FSIs receive similar contact from both regions. Additionally, S1 and M1 synapses onto FSIs are equally potentiated by TBS, suggesting equal plasticity. Preliminary behavioral data demonstrates that mice can learn to report S1 corticostriatal stimulation, enabling us to assess learning induced plasticity. Altogether, our results reveal cell-type specific differences that drive plasticity in the DLS and sensorimotor integration, providing insight into how cortical inputs shape striatal circuits to generate adaptive behaviors.

POSTER PRESENTATIONS

Morning Session

Presenter: Ghata Nandi

Poster #1: Regulation of mitochondrial metabolism and energetics by the LONP1 protease in human iPSC-derived neural progenitor cells

Authors: Nandi G., Shetty R., Noland R., and Suzuki C.

Mitochondrial LONP1 is an ATP-driven protease and chaperone essential for regulating mitochondrial proteostasis, energy metabolism, and cellular stress responses. Our recent work showed that a rare bi-allelic mutation in LONP1 (Lon-P761L) causes severe neurological dysfunction and impaired pyruvate dehydrogenase (PDH) activity, a key enzyme linking glycolysis to the tricarboxylic acid (TCA) cycle. In patient-derived fibroblasts, we demonstrated that Lon-P761L leads to the accumulation of phosphorylated PDH E1α, resulting in PDH inhibition and elevated intracellular lactate levels. This dual metabolic dysfunction is likely to severely impair neuronal energy production, as neurons predominantly rely on glucose oxidation through the TCA cycle to generate ATP. Given the limitations of studying primary human neurons, we generated iPSC-derived neural progenitor cells (NPCs) from fibroblasts of two affected siblings homozygous for Lon-P761L and their unaffected heterozygous mother. Sibling NPCs exhibited elevated levels of phosphorylated PDH E1α at serines -232, -293, and -300, reduced spare respiratory capacity (SRC), and a stronger reliance on glycolysis for ATP production than maternal controls. Additionally, sibling NPCs showed loss of mitochondrial membrane potential, increased oxidative stress, and elevated levels of mtDNA-encoded proteins and transcription factor A (TFAM), suggesting impaired LonP1-mediated degradation. Interestingly, both sibling NPCs and fibroblasts displayed increased extracellular glutamate release, indicating a possible stress adaptation mechanism. Our findings suggest that Lon-P761L disrupts mitochondrial proteostasis and energy metabolism, driving metabolic reprogramming and cellular stress responses. Our future work will focus on neuron-astrocyte interactions to further elucidate how Lon-P761L impacts mitochondrial health, with broader implications for neurodegeneration, cancer, and cardiovascular diseases.

Presenter: Xia Qiu

Poster #2: BRAFV600E mutation driven CRC initiation

Authors: Xia Qiu, Michael Verzi

Serrated colon tumors account for up to 20% of colon tumors, and have a poor prognosis relative to conventional adenomas. A “sawtooth” pattern of epithelium infoldings in histopathology characterizes these tumors, and molecularly, Serrated colon tumors are characterized by the presence of BrafV600E mutation. However, the BrafV600E mutation inefficiently drives tumor formation on its own in mouse models, no tumor observed in 16 months after tamoxifen injection, herein we call Serrated tumor resistant condition. To effectively induce the development of serrated colon carcinomas, susceptibilities must be in place. Our lab found that the loss of the transcription factors Smad4 in epithelium, can create susceptible conditions for Serrated oncogenesis, large tumors in the intestine can be observed as soon as 2 months. In the susceptible condition, it seems that the number of stem cells remains relatively unchanged. Mitogen-activated protein kinase (MAPK) cascades are important pathways that orchestrate intestine development, homeostasis and cellular fate. Serrated colorectal cancers are hypothesized to be initiated by Braf V600E mutation and subsequent activation of MAPK/ERK pathway.There is a gap in understanding of the cellular origins responsible for initiating serrated carcinomas, and their regulatory mechanisms downstream of ERK activation (phosphate ERK1/2). This proposal seeks to elucidate the cellular dynamics following activation of BRAF-V600E in

conditions of susceptibility to serrated tumors. Mechanistically, I also aim to understand the transcriptional regulatory mechanisms of downstream events by BRAF-V600E mutation during Serrated oncogenesis.

Presenter: Masuda Akther

Poster #3: Enhancing the antitumor efficacy of nucleotide synthesis inhibitor by targeting DNA replication stress response

Authors: Akther M, Valvezan A

Loss of function mutations in the tumor suppressor genes TSC1 and TSC2 cause the genetic tumor syndrome Tuberous Sclerosis Complex (TSC), and are also associated with some cancers. TSC1/2-deficient tumors exhibit increased cellular anabolism driven by the mechanistic Target of Rapamycin Complex 1 (mTORC1). We previously discovered that TSC2-deficient cells and tumors are highly dependent on rate limiting enzyme in de novo guanine nucleotide synthesis, inosine-5′-monophosphate dehydrogenase (IMPDH). This metabolic vulnerability can be exploited using clinically approved IMPDH inhibitors which selectively induce DNA replication stress and DNA damage in TSC2-deficient cells, culminating in cell death. However, these cells can also adapt to IMPDH inhibitor therapy by activating the replication stress response (RSR) and DNA damage response (DDR) pathways, which can promote their survival and reduce IMPDH inhibitor efficacy. We hypothesized that inhibiting RSR and DDR pathway effectors can enhance the efficacy of IMPDH inhibitors. We combined the clinically approved IMPDH inhibitor Mizoribine with inhibitors of the ATM, ATR, CHK1, CHK2, DNA-PK, and WEE1 kinases, to determine which combinations are most effective at selectively killing TSC2-deficient cells relative to wild-type. Our preliminary findings indicate that combining Mizoribine with the ATR inhibitor AZD6738, which is currently in clinical trials for oncology, significantly increases apoptotic cell death in TSC2-deficient cells compared to Mizoribine treatment alone, while maintaining selectivity. Additionally, inhibitors targeting WEE1 (AZD1775) and a dual CHK1/ CHK2 inhibitor (AZD7762) also enhanced mizoribine-induced cell death. Thus, we propose a novel combinatorial treatment strategy targeting the RSR/DDR pathways in conjunction with IMPDH inhibition to enhance the anti-tumor efficacy of these therapies.

Presenter: Laura Byron

Poster #4: Impact of high sugar diet on lifespan and health in a Drosophila Model of Alzheimer’s disease

Authors: Byron, L. Estores, B. Villa, J. Oh, M. Lyu, Y.

With increased life expectancy, age-related neurodegenerative disorders are becoming more prevalent, significantly burdening society. Alzheimer's Disease (AD), the leading cause of dementia, is one of the most costly and deadly diseases in developed countries. Addressing lifestyle-related risk factors could potentially delay or even prevent up to 40% of AD cases. Over the past two decades, the overconsumption of high-sugar foods has been linked to an elevated risk of AD. However, the precise mechanisms underlying the connection between high-sugar diets and AD remain unclear. We proposed that high sugar diets influence AD-relevant dysfunctions, such as increased mortality through currently unknown mechanisms. To explore these connections, we utilized a Drosophila AD model, where flies express humanized amyloid-beta pan-neuronally. We found that wild-type flies and flies modeling AD on a high sugar diet did not show a change in locomotion compared to those on a control diet. However, WT and AD-modeling flies did show a decrease in climbing ability with age. In addition, we discovered that expressing humanized amyloid-beta in flies does not impact mortality on a normal diet, but increases mortality on a high sugar diet. Dietary influences are more pronounced in amyloid-beta-expressing female flies, consistent with the greater risk of AD in women than men. Our findings indicate D. melanogaster as an effective model for studying dietary effects on AD-associated neuronal dysfunction and provide a simpler system to elucidate the complex mechanisms by which a high-sugar diet impacts health-related traits in the presence of amyloid-beta.

Presenter: Sree Varshini Murali

Poster #5: Fractalkine signaling regulates the levels of several chemotactic cytokines after acoustic trauma
Authors: Sree Varshini Murali, Astrid Cardona, Tejbeer Kaur
Fractalkine (CX3CL1) is a chemokine produced in spiral ganglion neurons (SGNs) and binds to its receptor, CX3CR1, expressed by macrophages in the cochlea. Mice lacking CX3CR1 show decreased macrophage density and increased SGN loss after cochlear injury. These findings suggest that intact fractalkine signaling is required for regulating macrophage density and SGN survival in the injured cochlea. This study aimed to examine the effects of fractalkine signaling on cochlear inflammation by measuring cytokine levels after acoustic trauma to understand how fractalkine play neuroprotective role after cochlear injury. We utilized mice with intact fractalkine signaling (wildtype) and that lack or express human polymorphic variant of fractalkine (CX3CR1hM280). 5-6 weeks old mice per genotype were exposed to 112 dB SPL noise at 8-16 kHz for 2 hours or unexposed. Following euthanasia; cochleae were isolated at different days post noise exposure (DPNE). Extracted protein samples were loaded in triplicates and subjected to protein multiplex assay for cytokines and chemokines. Cytokine levels were comparable between unexposed wildtype and fractalkine signaling mutant mouse models. Chemotactic cytokines like CXCL1, CXCL2, CXCL10, CCL2, CCL7, CCL3, and CCL4 were found to be significantly reduced in mice lacking CX3CR1 receptor compared to wildtype mice at 1-DPNE. These data suggest that such acoustic trauma causes an acute inflammation due to spontaneous resolution of elevated cytokine levels. Suggesting that fractalkine signaling regulates the chemotaxis of immune cells in the noise-injured cochlea. Future studies will address if infiltration of blood circulating immune cells influence SGN survival after acoustic trauma.

Presenter: Maddy Terry
Poster #6: Investigating kinetochore – microtubule attachments and chromosome movement in Drosophila Meiosis
Authors: Terry, M Gunturu, S Garg, D McKim, K
During female meiotic cell division, the interactions between the kinetochores (KT) and the spindle are responsible for the correct partition of chromosomes. The establishment of end-on attachments of homologous KTs to opposite spindle poles is known as biorientation and is critical for maintaining genomic integrity. The KT is a proteinaceous complex that connects centromeric DNA to the spindle. This research focuses on the KMN network – SPC105R, NDC80c, and MIS12c – which forms the outer KT and contains microtubule (MT) binding activity. The outer KT can interact laterally with antiparallel spindle MTs before transitioning to a stable end-on attachment through the formation of KT MTs (k-fibers). However, the capture of spindle MTs to KTs is error prone, which can lead to mis-segregation of chromosomes. This can result in spontaneous abortions, birth defects, and infertility. We are interested in determining the mechanisms behind the transition of lateral to end-on attachments, as well as what motors are responsible for chromosome movement when establishing biorientation. KT subcomplex NDC80 is required for end-on attachments and is a proposed target of Aurora B kinase (AURKB) during attachment error correction. Protein phosphatase 2A (PP2A) is then needed to dephosphorylate the KT, allowing for NDC80 to establish stable end-on KT-MT attachments. We have developed a tool to study both k-fiber dynamics and MT attachments at the KT; Spc25INbox; Incenp RNAi. This transgene expresses AURKB only at the KT, with endogenous AURKB knocked down, leading to the formation of a monopolar spindle of only k-fibers. Additionally, our lab has previously shown that loss of NDC80 or PP2A results in primarily lateral attachments, which we will use for the basis of our study. Therefore, Spc25INbox; Incenp RNAi paired with Ndc80 RNAi or PP2A RNAi allows us to observe k-fiber formation, as well as kinase influence on KT-MT attachments. We have found that k-fibers are captured, not grown, at the KT and converted to end-on attachments. Secondly, we found that KT localized AURKB alone is not sufficient for destabilizing KT-MT end-ons, and likely relies on a central spindle localized kinase. Furthermore, previous work has shown that lateral attachments are sufficient for chromosome movement. How KTs know which direction to move after forming a lateral attachment is unknown. Therefore, future work

includes live imagining of motor protein mutants with Ndc80 and PP2A RNAi to determine the relationship between lateral attachments and chromosome movement.

Presenter: Yue Wu
Poster #7: Bioactivity of Microbial Metabolites Derived from B-type Proanthocyanidins
Authors: Wu, Y; Duran R.M; Roopchand, D.E.
B-type proanthocyanidins (PACs) are major polyphenol constituents found in grape berries and seeds and are associated with protection against chronic metabolic disease. While parent PAC compounds are poorly absorbed, they are biotransformed by the gut bacteria into more bioavailable microbial metabolites (MM) that may contribute to their metabolic health benefits. Most studies have focused solely on the effects of PAC parent compounds rather than PAC-derived microbial metabolites and their effective physiological doses. To compare the anti-inflammatory activity of PACB2 vs. known PAC-derived MMs, we performed in vitro experiments in murine ileal organoids and RAW264.7 macrophages challenged with pro-inflammatory mediators. In organoids, PACB2 or a mixture of seven PAC-derived MMs reduced inflammatory markers and showed target-based and dose-dependent responses. In RAW264.7 cells, both PACB2 and a mixture of seven PAC-derived MMs exhibited dose-dependent anti-inflammatory responses. Notably, four out of seven MMs effectively suppressed inflammatory markers, while the remaining three MMs showed inactivity, although they may have synergistic effects when combined with other MM. Further experiments will investigate potential synergistic interactions among MMs in RAW264.7 cells and investigate whether PACB2 and/or the MM mix can promote the secretion of the incretin glucagon-like peptide-1 (GLP-1) for glucoregulation in murine ileal organoids.

Presenter: Derek Cavallo
Poster #8: C. elegans as a novel model for microbiome interactions reveals synergistic health-promoting effects of natural products
Authors: Cavallo, D
Plant-derived natural products have the potential to serve as novel, accessible, and effective treatments for chronic inflammatory diseases, such as diabetes, obesity, heart disease, cancer and Alzheimer's disease. One such product, monk fruit extract, has been used in traditional Chinese medicine to treat inflammation for centuries. The intensely sweet taste and low caloric content of mogrosides, the terpenoid compounds found within monk fruit extract, originally gained the attention of diabetes researchers looking for a potential low glycemic sugar substitute. Surprisingly, studies in rodent models and cell cultures found effects independent of simple sugar restriction, including improvements in insulin homeostasis, glucose metabolism and oxidative stress. However, the mechanism of these effects is not yet known. Furthermore, recent studies suggest that the human gut microbiome can metabolize mogrosides and produce anti-inflammatory secondary metabolites, including short chain fatty acids. This is especially important as diabetes, like other chronic inflammatory conditions, is associated with dysbiosis of gut microbe communities. Thus, a positive prebiotic effect of mogrosides may exist concurrently with the observed modulation of host metabolic pathways. Using the nematode model Caenorhabditis elegans, we investigated the effect of mogroside treatment on the gut microbiome and host metabolic pathways to determine the mechanism of action as a potential therapeutic for diabetes in humans.

Presenter: Hayley Palmer
Poster #9: Cannabidiol may improve exercise capacity in ovariectomized mice
Authors: Palmer, H., Roopchand, D**.**

The reduction of 17β-estradiol (E2) in postmenopause is associated with a range of metabolic disorders. Hormone replacement therapy (HRT) is not appropriate for everyone therefore other options are needed. Cannabidiol (CBD) is a non-psychotropic phytocannabinoid derived from the industrial hemp plant (Cannabis sativa L.). CBD supplementation may be beneficial for post-menopausal women as it has been shown to reduce inflammation, improve gut barrier integrity, limit bone loss, and improve cognitive function. Prior work showed that ovariectomized (OVX) mice supplemented with CBD (25 mg/kg delivered perorally in a sesame oil and peanut powder vehicle) had improved metabolic phenotypes and an increase in relative abundance of fecal Lactobacillus species. In the present work, we investigated the effects of CBD on exercise capacity in female mice. OVX and sham surgery mice were perorally administered hemp extract containing 25 mg CBD/kg daily for 12 weeks. They were subjected to forced exercise on a treadmill and run to exhaustion. Running endurance is estrogen dependent – ovariectomized mice showed decreased time to exhaustion which was improved with CBD supplementation.

Presenter: Sesha Rajeswari Talluri

Poster #10: Pharmaceutical Applications of Mango Seed Kernel Starch Nanoparticles.

Authors: Talluri SR, Dr. Michniak- Kohn B.

PURPOSE:

The purpose of this study is to prepare and characterize diclofenac-loaded nanoparticles using starch isolated from mango seed kernels. Few studies have explored Mango Seed Kernel Starch (MSKS) in pharmaceuticals. This agro-industrial waste-derived starch is cost-effective and may serve as a valuable pharmaceutical excipient.

METHODS:

MSKS was extracted using the alkaline method and lyophilized. It was characterized for solubility, pH, moisture content, swelling index, gelatinization temperature, and flow properties and compared to corn starch. MSKS nanoparticles (MSKSNPs) were synthesized using mild alkali hydrolysis and ultrasonication. Drug-loaded MSKSNPs were prepared via ethanol injection method using diclofenac sodium as a model drug. Drug-loaded MSKSNPs were characterized for physicochemical properties by Dynamic Light Scattering (DLS), X-ray Diffraction (XRD), Differential Scanning Calorimetry (DSC), Transmission Electron Microscopy (TEM), and Fourier Transform Infra-Red (FTIR). Encapsulation efficiency (%EE) was analyzed using High-Performance Liquid Chromatography (HPLC).

RESULTS:

MSKS yield varied with solid: solvent ratio and drying method. MSKS solubility was 17±2.8%, pH 7.0±1.2, moisture content was 7.4±0.8%, swelling power 3.2±0.16 g/g, and gelatinization temperature 60°C. Particle size was 6.5±0.1 with a polydispersity index (PDI) of 0.70±0.0. FTIR confirmed starch integrity. Drug-loaded MSKSNPs with particle size 140±3.6 nm and PDI 0.42±0.03 were amorphous, with 82.34±5.2% EE. XRD and DSC confirmed reduced crystallinity. TEM showed a globular morphology.

CONCLUSION:

MSKSNPs were successfully synthesized using a simple, time-efficient process. These amorphous nanoparticles hold promise as drug delivery systems for various therapeutics.

Presenter: Prarthana Gowda

Poster #11: Exploring mechanism of TRIO-Linked Cytoskeletal Defects in the Pathophysiology of Neuropsychiatric Disorders

Authors: Gowda, P; Diaz de Leon Guerrero, S; El Achwah, M; Zhang, H; McCarroll, A; Chen, J; Duan J; Pang, Z

Neuropsychiatric disorders (NPDs) like autism spectrum disorder and schizophrenia involve altered neural development and brain function, impacting cognition and behavior. Increasing evidence points to the critical

role of cytoskeletal remodeling in maintaining neuronal structure and synaptic function—its dysregulation has been closely linked to NPD pathology. Several whole genome sequencing studies have identified TRIO as one of the strongest associated genes with NPDs. The guanine exchange factor TRIO is known to interact with Rho family GTPases, which are considered master regulators of cytoskeleton. This study investigates the effects of TRIO heterozygous loss of function mutations on cytoskeletal dynamics, by examining changes in neuronal morphology, synaptic activity, axonal transport, transcriptomics, and cellular energetics. Using human-induced neurons derived from six distinct induced pluripotent stem cell backgrounds, we provide a robust and relevant model to explore TRIO's role in NPD pathology. I have generated and validated TRIO heterozygous mutation in iPSCs and iNs, then analyzed alterations in neuronal morphology, synaptic function, downstream signaling, and transcriptomics. My findings demonstrates that TRIO impairs activity of cytoskeletal remodelers, leading to abnormal neuronal architecture and deficits in mitochondrial dynamics, which are linked to defects in synaptic activity. This research aims to deepen our understanding of cytoskeletal dysregulation in NPDs. Future work will include live imaging to track axonal transport and distribution of mitochondria, alongside OCR and ROS assays to explore changes in cellular energetics. Pharmacological manipulation will further establish contributions of actin filaments and microtubules in observed phenotypic changes, providing valuable insight into molecular mechanisms driving NPDs.

Presenter: Prateeksha Rout

Poster #12: Transcription factor network shifts in intestinal regeneration

Authors: Rout, P., Amer, H., Verzi, M.

Under normal conditions, the small intestine undergoes cell turnover every 3-5 days. When injury or damage is inflicted upon the intestinal epithelium, a subset of rare, highly enriched regenerative genes are activated, and facilitate repair and regeneration. Distinct from genes involved in homeostatic turnover, we see that this injury induced change in gene expression leads to unique intestinal organoid and tissue morphology. Additionally, the transcription factor (TF) led regulatory networks that facilitate regeneration are poorly understood. By stimulating a wound healing state in intestinal tissue through irradiation (IR) exposure, we observe the emergence of key regenerative gene signatures, and visualize these changes using bulk and single cell RNA-seq and ATAC-seq. Using chromatin accessibility information, we identify regenerative TFs that are differentially active during wound healing, and empirically test their activity and target binding in vivo and in vitro. New knowledge of gene regulatory mechanisms driving the regenerative stem cell fate switch will point us to pathways with which to manipulate and improve regeneration of the intestine following injury from chemotherapy, radiation damage, and inflammatory bowel diseases.

Presenter: Jay Joshi

Poster #13: Cell cycle phase-specific regulation of mTOR complex 1 activity

Authors: Joshi J, Lerner A, Scallo F, Grument A, Valvezan A

Mechanistic Target of Rapamycin Complex 1 (mTORC1) is a master metabolic regulator that integrates nutrient and growth factor signals to promote anabolic cell growth and proliferation. mTORC1 dysregulation contributes to the development and progression of many diseases, including most human cancers. mTORC1 is activated in most, if not all, proliferating eukaryotic cells, but whether mTORC1 is regulated in a cell cycle-phase specific manner is unknown. We hypothesized that mTORC1 activity changes throughout the cell cycle to meet the unique metabolic and biosynthetic demands of each cell cycle phase. Using multiple independent methods to track mTORC1 activity throughout a complete cell cycle, we find that mTORC1 activity oscillates from lowest in mitosis/G1 to highest in S and G2. The interphase oscillation in mTORC1 activity is mediated through changes in the subcellular localization of an essential negative regulator of mTORC1, the TSC Complex. By contrast, in mitosis, mTORC1 activity is suppressed in a CDK1-dependent manner in both control and TSC Complex-deficient cells,. We demonstrate that mTORC1 promotes progression through S and G2, and promotes entry into mitosis

by satisfying the Wee1-/Chk1-dependent G2/M checkpoint. Taken together, our data uncover cell cycle-dependent oscillations in mTORC1 activity, with important functional consequences for cell growth and proliferation.

Presenter: Katherine Duseau
Poster #14: Exploring CPEB1 mediated translational control in spermatogenesis
Authors: Duseau, K.
Gametes are formed by meiosis, a specialized cell cycle that reduces genomic ploidy and introduces genetic variance. Progression through meiosis involves complex spatiotemporal gene expression that modulates RNA by transcriptional and translational regulatory mechanisms. Errors in gene regulation often result in meiotic arrest and infertility. One crucial mechanism of gene regulation during gametogenesis occurs via cytoplasmic polyadenylation of mRNAs. CPEB1 is a sequence-specific RNA-binding protein that is essential for cytoplasmic polyadenylation and is critical for meiotic progression. Much of what is known about the role of CPEB1 in meiosis focuses on female oocyte maturation, however, several studies suggest that this protein also has a major function in early meiotic prophase. Previous work in our lab has identified a unique point mutation within the RNA binding domain of CPEB1 that results in an early meiotic arrest in both male and female mice. An in-depth characterization of this mutant will allow us to decipher the role of CPEB1 in early meiotic prophase. Through a systematic evaluation of meiotic progression in this point mutant, I have identified errors within several meiotic processes that lead to cell death and impaired fertility. Future work on this project will identify the mRNA targets of CPEB1 in early prophase and illuminate the mechanisms by which CPEB1 regulates meiosis.

Presenter: Rachel Ofer
Poster #16: Mapping the spatial transcriptomic changes during intestinal regeneration over a 6-day time course
Authors: Ofer, R., Tran, T., Verzi, M.
The intestinal epithelial cells lining exhibits a remarkable regenerative capacity in response to injury, yet the spatial and temporal regulation of this process remains poorly understood. In this study, we utilize spatial transcriptomics in conjunction with a time series of intestinal regeneration to capture the dynamic gene expression changes occurring across distinct stages of tissue repair. By integrating tissue sections with spatially resolved transcriptomic profiling, we track the molecular events driving regeneration in response to injury over a 6-day time course, from the early apoptotic phase to tissue remodeling and epithelial repair. Our data generated over 1.5 billion unique reads across three distinct biological samples, and data output is at a 2 µm resolution. Analysis reveals a shift in tissue differentiation during regeneration, corresponding to altered cellular migration rates, and identifies temporal changes in niche factors and cytokine gradients that guide the regenerative response - particularly in mesenchymal and immune cell populations. By mapping these processes over the 6-day time course, we offer a high-resolution, dynamic view of intestinal regeneration, uncovering how tissue architecture and cellular interactions evolve during repair. This work lays the foundation for future strategies aimed at enhancing intestinal regeneration and develop targeted therapies for inflammatory bowel diseases (IBD) and other gastrointestinal disorders.

Presenter: Jingyun Qiu
Poster #17: CHD7 Binds Insulators to Regulate Gene Expression During Neuronal Differentiation
Authors: Qiu, J; Jadali A; Ni J; Martinez, E; Song, Z; Kwan, K
Spiral ganglion neurons (SGNs) in the cochlea are essential for sound transmission, and their death leads to hearing loss. Guiding fate-restricted progenitors into SGNs offers the potential for hearing restoration by replenishing lost SGNs through cell replacement therapies. Understanding the molecular mechanisms driving SGN differentiation will advance stem cell therapies. Using the immortalized multipotent otic progenitor (iMOP)

cell line, we investigated the role of chromodomain helicase DNA-binding protein 7 (CHD7), a nucleosome repositioner, in neuronal differentiation. We found that CHD7 knockdown prevented neuronal differentiation. To identify the genome-wide binding sites of CHD7, we performed Cleavage Under Targets & Tagmentation (CUT&Tag) in proliferating iMOPs and iMOP-derived neurons. Analysis showed that CHD7 is enriched at H3K4me3 (promoter), EP300 (enhancer), and CTCF (insulator). While CHD7 is known to function at promoters and enhancers to specify cell fate, its role at insulators is less understood. To explore CHD7's function during neuronal differentiation, we identified CTCF+CHD7+ regions based on the enrichment of both CTCF and CHD7. We annotated CTCF+CHD7+ sites at a boundary between two topologically associating domains (TADs). Using CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa), we targeted each CTCF+CHD7+ site to determine its effect on transcription of a nearby gene, Mir9-2. Targeting these sites at the early stage of neuronal differentiation increased miR9 levels, regardless of the CRISPR method. The results suggest that these CTCF+CHD7+ sites act as insulators to prevent promiscuous promoter-enhancer interactions between TADs. Our results implicate CHD7 function at insulators to during neuronal differentiation.

Presenter: Byron Avihai

Poster #18: Longitudinal Single-Cell Genomic and Transcriptomic Analysis of Pediatric AML

Authors: Avihai B, Singh A, Khiabanian H, Herranz D

Background and hypotheses: Little is known about the mutations driving therapeutic resistance in pediatric AML, and diagnostic and therapeutic options for relapsing patients, only 30% of whom survive, are lacking. We hypothesize that relapsed pediatric AML is associated with distinct molecular signatures that are detectable at the single-cell resolution at diagnosis or at remission, and that resistance-conferring mutations correlate with changes in transcriptional profiles.

Methods: Using novel bioinformatics pipelines, we integrated single-cell DNA (MissionBio) and RNA (10x Genomics) data from 78 bone marrow samples collected from 40 patients at diagnosis, remission, and/or relapse (including 9 trios), and identified genomic/transcriptomic features associated with relapse.

Preliminary results: Genomic data from one case revealed strong associations between a pathogenic KRAS mutation and leukemic subclones, with the main diagnosis leukemic clone KRAS heterozygous, later eclipsed at relapse by a clone KRAS homozygous. This suggests either the homozygous KRAS mutation conferred chemoresistance, or that resistance-conferring mutations arose in a homozygous KRAS subclone. In the same patient, transcriptomic data revealed an expression profile of a minor diagnosis subclone (7% cells) that mapped to an expanded relapse population (37%). Associated marker genes were enriched for leukemic pathways and FLT3, indicating that relapsed cells correspond to a prominent leukemic clone originating from a minor diagnosis leukemic subclone

Conclusions: We will next integrate such clonal (DNA) and biological pathway (RNA) findings for each patient and across patients to highlight the underlying mechanisms of therapy resistance in relapsing pediatric AML.

Acknowledgments: New Jersey Commission of Cancer Research (NJCCR) grant (COCR23PRG006).

Presenter: Yijia Chen

Poster #19: Transcriptional Regulation of Spinal Motor Neuron Maturation and Subtype Specification

Authors: Yijia Chen, Tulsi Patel

Spinal motor neurons (sMNs) control movement by innervating muscles and are subdivided into alpha, gamma, and beta subtypes in adulthood. Although neuronal specification occurs during embryonic development, the transcriptional mechanisms that drive postnatal maturation and establish subtype identity remain poorly understood. Notably, in amyotrophic lateral sclerosis (ALS), alpha sMNs degenerate while gamma sMNs remain resistant, underscoring the importance of understanding subtype-specific regulatory pathways. Using single-nucleus RNA and ATAC sequencing (snMultiome-seq) across developmental stages, we found that sMN subtypes emerge during postnatal maturation, characterized by the activation of distinct transcription factor

(TF) networks and chromatin accessibility changes. Among candidate TFs, Creb5 is uniquely enriched in gamma sMNs, which innervate muscle spindles.
To investigate these regulatory mechanisms, we developed enhancer-driven adeno-associated viruses (AAVs) based on open chromatin regions specific to alpha, gamma, or beta sMNs, enabling selective labeling and manipulation of these subtypes. We are now developing enhancer motif perturbation AAVs to functionally assess the role of key TF binding sites in regulating sMN subtype identity. Additionally, we generated a Creb5 conditional knockout mouse model to determine whether Creb5 loss alters muscle spindle formation or gamma sMN innervation patterns. By combining enhancer-driven AAVs and genetic models, our approach establishes a powerful platform to interrogate subtype-specific transcriptional regulation and its implications for MN diseases.

Presenter: Saurav Doshi
Poster #20: Targeting Mitochondrial Structural Protein OPA1 In Acute Myeloid Leukemia
Authors: Doshi S., Kundu T., La Vecchia S., Antonoglou P., Glytsou C.
Acute Myeloid Leukemia (AML) is the most fatal leukemia, commonly observed in adults with a survival rate of less than 20%. In 2018, a new treatment combining the BCL-2 antagonist Venetoclax with hypomethylating agents, was introduced for AML. However, therapy resistance and disease relapse remain significant challenges, necessitating the development of more efficacious therapies. Mitochondrial functions are crucial for the survival of AML blasts and previous studies in our lab have highlighted the role of the mitochondrial cristae structure regulator, OPA1, in developing Venetoclax resistance. However, the effect of genetic and pharmacologic targeting of OPA1 in AML remains unexplored.
Our in vivo studies incorporating flow cytometry analysis show that combining OPA1 genetic knockout with Venetoclax in an AML cell line xenograft model suppresses cancer spread and significantly increases animal survival. Moreover, pharmacological inhibition of OPA1 using a novel OPA1 inhibitor, MYLS22, significantly enhances Venetoclax efficacy in patient-derived xenograft models and Venetoclax-resistant cell line models. In addition, to identify novel combinatorial treatments based on targeting OPA1, we performed a genome-wide CRISPR/Cas9 screen in human AML cells. Our approach revealed genes participating in synthetic lethality with MYLS22 or drug-resistance, proposing new therapeutic strategies for AML treatment.
The combined inhibition of OPA1 and BCL-2, along with the search for newer therapeutic candidates, holds significant promise for AML patients, offering hope for more effective targeted therapies against AML.

Presenter: Kimberly Izarraras
Poster #21: Kisspeptin alleviates human hepatic fibrogenesis by inhibiting TGFb signaling in hepatic stellate cells
Authors: Izarraras, Kimberly; Prasad, Kavita; Bhattacharya, Dipankar; Friedman L., Scott; Bhattacharya, Moshmi
The hormone kisspeptin attenuates steatosis, metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis in mouse models, by signaling via the kisspeptin 1 receptor (KISS1R). However, whether kisspeptin impacts fibrogenesis in human liver is not known. We investigated the impact of a potent kisspeptin analog (KPA) on fibrogenesis using human precision cut liver slices (hPCLS) from fibrotic livers from male patients, in human hepatic stellate cells (HSCs), LX-2, and in primary mouse HSCs. In hPCLS, 48 h and 72 h of KPA (3 nM, 100 nM) treatment decreased collagen secretion, and lowered expression of fibrogenic and inflammatory markers. Immunohistochemical studies revealed that KISS1R is expressed and localized to HSCs in MASH/fibrotic livers. KPA treatment reduced transforming growth factor b1 (TGFb)-induced expression of fibrogenic and inflammatory markers in LX-2 cells and in primary mouse HSCs. KPA treatment also decreased TGFb-induced collagen secretion, cell proliferation and colony formation. Mechanistically, KISS1R signaling downregulated TGFb signaling by decreasing SMAD2/3 phosphorylation, and SNAIL expression, via activation of protein-phosphatases PP2A, a binding partner of KISS1R that dephosphorylates SMAD 2/3. Additionally, KPA treatment upregulates KISS1/KISS1R mRNA levels in hPCLS and LX-2 cells, suggesting another mechanism by

which KPA is mediating its protective effect. This study revealed a novel pathway of suppressing human hepatic fibrogenesis through anti-fibrogenic actions of kisspeptin signaling, thus identifying it as a new therapeutic target to treat hepatic fibrosis.

Presenter: Gustavo Rios

Poster #22: The Staphylococcus aureus non-coding RNA IsrR regulates TCA cycle activity and virulence

Authors: Rios Delgado,G, Zheng, V, Boyd, J

Host tissues sequester iron to protect against infections in a process known as nutritional immunity. In response, pathogenic bacteria alter gene expression to adapt to iron starvation. In the human pathogenic bacterium Staphylococcus aureus, this change in gene expression is mediated, in part, by the ferric uptake regulator (Fur), which acts as an iron-dependent transcriptional repressor. We demonstrate that an S. aureus Δfur mutant has decreased expression of acnA, which codes for the Fe-dependent enzyme aconitase. This prevents the Δfur mutant from growing with amino acids as sole carbon and energy sources. We used a suppressor screen to exploit this phenotype and determined that a mutation that decreases the transcription of isrR, which produces a regulatory RNA, increased acnA expression, thereby enabling growth. Directed mutation of bases predicted to facilitate the interaction between the acnA transcript and IsrR, decreased the ability of IsrR to control acnA expression in vivo and IsrR bound to the acnA transcript in vitro. IsrR also bound transcripts coding the alternate TCA cycle proteins sdhC, mqo, citZ, and citM. Whole-cell metal analyses suggest that IsrR promotes Fe uptake and increases intracellular Fe not ligated by macromolecules. Lastly, we determined that Fur and IsrR promote infection using murine skin and acute pneumonia models.

Afternoon Session

Presenter: Connor Mattivi
Poster #23: Allele Specific Knockout of HLA
Authors: Mattivi, C, Oconer, F, Cao, J
Identification of the interaction between specific heavy chain alleles of the Human Leukocyte Antigen (HLA) and tumor antigens is critical for the success and advancement of cancer immunotherapies. Current strategies for the identification of therapeutically relevant T-cell receptors (TCRs) require the prediction of Human Leukocyte Antigen (HLA) identity based on knowledge of the tumor antigen. However, if the tumor specific antigen is unknown or putatively identified without functional validation, CRISPR-Cas9 knockout studies of individual HLA alleles may provide an efficient pathway to TCR identity. While many tools exist to generate the small guide RNAs (sgRNAs) necessary for CRISPR-Cas9 knockout studies, none currently allow for allele-specific targeting of HLA. Here, we developed and validated a unique bioinformatic tool to generate sgRNA's against individual HLA alleles, a capability outside of current, publicly available sgRNA design tools. Our tool allows for a streamlined generation of targeting constructs, removing the necessity of manually aligning HLA sequences, and providing a consistent algorithm for identifying potential off-target interactions. This tool will be an asset to the continued research efforts on cutting-edge cancer therapies.

Presenter: Mansi Gokani
Poster #24: Computational evaluation of polypeptide candidates for nanoplastic capture
Authors: Gokani, M; Guo, A
Micro- and nanoplastics pose significant health concerns due to their increased likelihood of consumption as they break down from larger plastic waste. Freshwater is a primary source of plastic ingestion, as current water filtration methods are ineffective for capturing nanoscale plastics. To address this issue, new materials and methods are needed to capture and remove nanoplastics from water. Protein-based materials are ideal candidates due to their ability to perform functions with highly specific molecular recognition. However, the vast design space of amino acid sequences necessitates computational methods for screening and identifying peptide sequences capable of selective binding to target plastics. We approach this challenge by using molecular dynamics simulations with neural network-based enhanced sampling methods to identify peptide sequences that can be used in capture of nanoscale polystyrene and understand the thermodynamics and design principles underlying successful polystyrene capture. We present a series of free energy calculations and analysis of binding configurations for multiple polystyrene-binding candidates, providing a thermodynamic understanding of successful polystyrene capture that may inform optimized design of nanoplastic-sequestering materials.

Presenter: Sebastian Gallon
Poster #25: Distinct Flavivirus Exposure Sequences Differentially Prime the Adaptive Immune Response
Authors: Gallon, S. Tonto, PB. Herrera, BB.
The co-circulation of flaviviruses such as dengue 1-4 (DENV-1-4), Zika (ZIKV), yellow fever (YFV), and West Nile (WNV) presents significant public health challenges due to cross-reactive immune responses that can influence disease severity. Antibody-dependent enhancement (ADE) remains a major concern, as prior immunity to one flavivirus may exacerbate subsequent infections. Using human serum samples with known infection histories, we examined the relationship between neutralizing antibody titers and ADE potential in an Fcγ receptor-bearing human monocyte cell line. We found that prior YFV immunity did not predispose individuals to ADE, whereas prior DENV-1-4, ZIKV, and WNV infections generated highly cross-reactive antibodies capable

of enhancing subsequent infections. To further investigate the impact of infection sequence on adaptive immunity, we employed a murine model to compare primary YFV-secondary DENV-1 (pYFV-sDENV-1) versus primary DENV-1-secondary YFV (pDENV-1-sYFV) infections. Both sequences led to reduced neutralizing antibody titers against the secondary infection and expansion of neutralizing antibodies against the primary infection, indicative of original antigenic sin. However, the pDENV-1-sYFV sequence resulted in a greater expansion of cross-reactive, enhancing antibodies against DENV-2 in vitro. Additionally, functional T-cell responses to DENV and YFV peptides were more robust in the pYFV-sDENV-1 group, suggesting an asymmetrical immune imprinting that could influence disease outcomes. These findings highlight how flavivirus exposure history shapes adaptive immunity, with implications for vaccine strategies and risk assessment in flavivirus-endemic regions.

Presenter: Ahmad Salman Sirajee

Poster #26: Cell-free DNA fragmentation patterns reveal functional contexts of their origin

Authors: Sirajee, AS., De, Subhajyoti

Cell-free DNA is emerging as a non-invasive biomarker of health and diseases such as cancer. Various cell types from hematopoietic and other tissues release cfDNA into the bloodstream via apoptosis, necrosis, or active secretion, which then undergoes non-random degradation based on their epigenetic contexts-of-origin and nuclease activities. Analyzing liquid biopsy sequencing data from healthy donors (n = 243), we show that cfDNA originating from different epigenomic and functional genomic contexts undergo differential processing that affects their size distributions, GC content, end motifs, and other molecular characteristics. Combining multiple fragmentation characteristics into a composite index, dubbed the FRAGILE score, we establish context-specific fragmentomic signatures. The FRAGILE score of cfDNA can predict their functional genomic contexts of origins with high precision and recall, and those originating from the transcriptional start sites, CpG islands, and proximal regulatory regions can predict the expression status of their proximal genes. Variations in the FRAGILE score derived from the tissue-specific (blood vs non-blood) functional elements indicate that most cfDNA fragments in healthy donors are predominantly of hematopoietic origin. Taken together, the FRAGILE score establishes a genome-wide baseline fragmentation pattern and provides a non-invasive window into the functional genomic profiles.

Presenter: Kaitlyn Snyder

Poster #27: Gut Microbiota is Different between Gender Affirming Hormone Therapy Compared to Gender Affirming Surgery

Authors: Snyder K, Yasrebi A, DeSio D, Wu G, Ghosh S, Zheng A, Gao S, Donlon A, Joseph L, Roepke T, Campbell S

The effects of gender-affirming hormone therapy (GAHT) on gut microbiota and goblet cells are unknown. Here we propose a rodent study design to understand the gut, to accurately reflect the reality of the trans experience, as trans women do not all seek or undergo orchiectomy (ORX). Instead, supplement estrogen with an androgen blocker. PURPOSE: Characterize 1) the gut microbiota and 2) goblet cells in estrogen-GAHT. METHODS: Forty C57 male mice were grouped (n=10/group) as follows: 1) intact with oil, 2) intact with estradiol benzoate (EB, 150 µg/kg) and finasteride (F, 0.25 mg/kg), 3) ORX with oil; and 4) ORX with EB (150 µg/kg). Each mouse was dosed daily for 8 weeks. Gut microbiota was analyzed using 16S rRNA gene V4 amplicon sequencing and colon samples stained using Alcian Blue Periodic Acid Schiff (ABPAS) for goblet cell counts. Alpha diversity (Shannon Index and Faith's Phylogenetic Distance) and Beta-diversity (Bray-Curtis, Jaccard, weighted and unweight UNIFRAC) were analyzed. PERMANOVA was used to see differences between groups. Procrustes and correlation analysis were used to show associations between co-abundance groups (CAG) and estrogen levels. ANOVA was used to determine differences in goblet cell count. RESULTS:

Microbiome analysis revealed no differences in alpha diversity. However, beta-diversity showed that Intact:EB+F and ORX:EB had significantly different gut microbiota compared to their oil controls ($p<0.05$), and Intact:EB+F had significantly different gut microbiota compared to ORX:EB ($p<0.05$). CAG analysis both showed marked differences between ORX:EB vs Intact:EB+F groups (<0.05), with concordance correlations at 96% ($p=0.001$). Two functionally similar CAGs, CAG15 and CAG22, showed statistical significance in abundance in ORX:EB vs Intact:EB+F ($p<0.05$), respectively. CAG15 and CAG22 also correlated highly with estrogen levels ($p<0.05$). ABPAS revealed ORX:EB mice showed a marked increase of goblet cells per colon crypt vs the Intact:EB+F group ($p<0.05$). CONCLUSION: Gut microbiota and goblet cell count is significantly different between Intact:EB+F and ORX:EB. Furthermore, both Intact:EB+F and ORX:EB had its own CAG linked to estrogen metabolism. SIGNIFICANCE/NOVELTY: These are the first data of its kind and could be critical for trans women weighing the choice of treatment.

Presenter: Jordan Lee

Poster #28: Inhibition of Casein Kinase 2 Decreases cAMP Egress and Promotes Human Airway Smooth Muscle Cell Relaxation

Authors: Kim, N; Cao, G; Panettieri, R; An, S

In human airway smooth muscle (HASM), activation of the cell surface beta2-adrenoceptor (B2AR) evokes cAMP efflux to the extracellular space via an ATP-binding cassette (ABC) membrane transporter, ABCC1. The mechanistic basis for ABCC1 activation remains unknown, however. Using HASM cells in culture as a model, here we identified Casein Kinase 2 (CK2) as an intracellular cAMP sensor and a homeostatic regulator of ABCC1. By western blot, we showed that HASM cells expressed CK2 alpha and beta subunits and that beta2-agonist stimulation increased the phosphorylation levels of CK2. Pharmacologically inhibiting CK2 with TBB (4,5,6,7-Tetrabromo-1H-benzotriazole) decreased homeostatic cAMP egress and substantially ablated B2AR-evoked release of cAMP from HASM cells. Consistent with these results, TBB acutely decreased basal tone and potentiated beta2-agonist-induced generation of intracellular cAMP levels ([cAMP]i) and HASM cell relaxation as measured by optical magnetic twisting cytometry. Interestingly, a prolonged inhibition of CK2 increased mRNA expression levels of B2ARs and corroborated increased beta2-agonist mediated HASM cell relaxation–even under experimental conditions of B2AR desensitization. Collectively, these data support a previously unrecognized role of CK2 in the B2AR signaling pathways and put forth homeostatic regulation of cAMP via B2AR/CK2/ABCC1 axis as new disease-modifying targets in the treatment of airflow obstruction in asthma.

Funding: HL164404, HL114471

Presenter: Lucas Foster

Poster #29: RMAPS-Gamma and RMAPS-Alpha, novel thermophilic, chemolithoautotrophic, thiosulfate-oxidizing members of the Pseudomonodota isolated from a deep-sea hydrothermal vent

Authors: Foster L and Vetriani C

RMAPS-Gamma and RMAPS-Alpha are newly isolated members of the Gammaproteobacteria and Alphaproteobacteria respectively. During a research expedition on the R/V Atlantis to the East Pacific Rise, an experimental colonizer was retrieved from the Riftia Mound vent site using the deep-submergence vehicle Alvin. A biofilm-covered fragment of mesh from the colonizer was suspended in anaerobic artificial seawater to create a slurry, which was then used to inoculate various types of media for enrichment cultures. After performing multiple end-point dilutions, two pure cultures were obtained and named RMAPS-Gamma and RMAPS-Alpha. These bacteria are thermophiles that grow at 55℃, oxidize thiosulfate, reduce nitrate, and fix carbon dioxide. The 16S rRNA genes of these isolates were amplified by polymerase chain reaction from their genomic DNA, and the amplicons were subsequently purified and sent out for Sanger sequencing. Following Blast searches on EzBioCloud and NCBI, the closest relative to RMAPS-Gamma was identified as Thiolapillus

brandeum, while the closest relative to RMAPS-Alpha was Tepidamorphus gemmatus. Since the 16S sequence of RMAPS-Gamma shares 94% sequence similarity with its closest relative and RMAPS-Alpha shares 92% similarity with its closest relative, these isolates both belong to new genera. The genomes of RMAPS-Gamma and RMAPS-Alpha were then sequenced on Illumina and Nanopore platforms, providing insights into their biochemical capabilities. This information will be used to conduct a series of experiments to further characterize the metabolism of these two isolates and investigate their ecological roles in hydrothermal vent biofilms.

Presenter: Lingjun Lu

Poster #30: Mathematical Modeling of Dietary Timing- and Protein Quality-Responsive Liver Circadian Clock and its Function on Ribosome Biogenesis

Authors: Lu, L., Levy, J.L., Anthony, T.G., and Androulakis, I.P.

Circadian rhythms are critical in regulating various physiological processes and maintaining homeostasis. Disruption of circadian rhythms is related to diverse pathological conditions, including metabolic and neurological diseases. Independent of the central clock, peripheral circadian clocks can be strongly entrained by metabolic cues through integrated signal sensing and stress response pathways, which in turn maintain downstream metabolic activities. The effect of metabolic inputs on clock function and dysfunction is the action of multiple signals, such as dietary timing and quality (nutrient variation). However, the principles and dynamics of nutrient entrainment and its regulation of circadian metabolism remain poorly understood.

Essential amino acids (EAAs) are vital nutrients fundamental to regulating metabolic events such as protein synthesis. As they are not endogenously synthesized in mammals, their dietary manipulation is of significant interest. The primary sensory mechanism of (dietary) EAA availability is composite. Its deficiency triggers integrated stress response (ISR), specifically, the GCN2-eIF2α-ATF4 pathway, while its abundance is sensed through the mTORC1 pathway. These two axes are intertwined and can act oppositely (suppress and stimulate, respectively) on translation-regulatory processes such as ribosome biogenesis (RiBi). Interestingly, experimental evidence shows that either of these EAA signaling pathways interacts with the core clock network and similarly affects its intrinsic properties, and as such, clock genes and proteins control RiBi both directly and indirectly. Based on this, we propose a semi-mechanistic mathematical model to describe the dietary timing- and EAA availability-responsive liver circadian clock and downstream ribosomal protein (RP) expression while considering only dietary timing relative to the internal clock time. Our preliminary results corroborate that (i) mutant EAA sensory mechanisms alter intrinsic circadian characteristics, with mTORC1 activity inhibition or Gcn2 knockout lengthening the period and reducing the amplitude of the clock, and (ii) the tissue clock is induced by a normal stress response while maintaining to be functional (i.e., synchronized) when dietary EAA is deprived. We will also predict the potential effects of EAA sensory imbalances on hepatic clock synchronization, which may be synergetic or antagonistic to the pre-existing impact of dietary EAA manipulations (unperturbed or perturbed oscillations) on endpoint RP production. This work can enhance the understanding of the dynamics of peripheral circadian rhythms under coexistent multiple entrainers and their links to metabolism, laying the foundation for studying the mechanisms driving multi-entrainer entrainment that underlies health homeostasis and for designing effective personalized nutrition recommendations to alleviate circadian disruption-related chronic diseases.

Presenter: Seepra Rath

Poster #31: The role of carbomer concentration on physicochemical properties and product performance of 0.5% w/w diclofenac sodium topical gels

Authors: Rath S, Abdulhafid K, Michniak-Kohn B

Introduction: Differences in the formulation composition and/or the manufacturing process, may influence the physicochemical and structural (Q3) properties, and thereby, the performance of topical products. The aim of

the current study is to assess the impact of quantitative differences in carbomer on a topical gel's Q3 properties and performance such as in vitro drug release.
Methods: Gels containing 0.5% w/w diclofenac sodium were prepared by varying the amount of gelling agent, carbomer homopolymer type C. The reference formulation contained 0.5% w/w carbomer. Four modified formulations contained 0.55%w/w (reference+10%), 0.45%w/w (reference-10%), 0.625%w/w (reference+25%) and 0.375%w/w (reference-25%) of carbomer. The Q3 properties of the gels were evaluated. In vitro release test (IVRT) was performed and the release rates for the five gels were compared.
Results: Q3 properties such as appearance, pH, and water activity were similar across all five gels. The microscopic images showed that the drug was fully dissolved. Viscosity increased with the increase in carbomer concentration. The IVRT method, developed with the reference gel, was linear, precise, and reproducible. The gel with 0.375% carbomer showed a slightly higher release rate, but the 90% confidence intervals (75-133.33%) indicated no significant difference in release rates compared to the reference gel.
Conclusion: All five gels exhibited similar Q3 properties except viscosity, and similar drug release. This suggests that altering the quantitative amount of carbomer (i.e. to the extent of 25% difference compared to the reference gel), does not appear to significantly affect the drug release across these diclofenac sodium gels evaluated in this study.

Presenter: Sarah Potgieter
Poster #32: Nucleophosmin couples nucleolar remodeling to the cell cycle during male meiosis
Authors: Potgieter, S Nayyab, S Uccello, M Snyder, E
Ribosomes are made in a phase separated nuclear subdomain, the nucleolus. Over 70 years of analyses have demonstrated meiotic male germ cell nucleoli have unusual morphology and a close association with the XY-body, a heterochromatic region containing the sex chromosomes. However, a mechanistic understanding of this relationship has remained a mystery. Using high resolution microscopy, this work revealed a key nucleolar protein, NPM1, is observed in two nuclear domains: the nucleolus proper and within the XY-body. Further, NPM1 localization was correlated with phosphorylation state as phosphorylated NPM1 (p-NPM1) localized to the XY-body throughout prophase I before translocating to the nucleolus shortly before nucleolar breakdown in late prophase I. Additional analyses demonstrated NPM1's dual localization also corresponds to NPM1 protein isoform: a canonical form primarily localized to the nucleolus and a truncated form in the XY-body. RNA FISH against pre-rRNA demonstrated p-NPM1 translocation into the nucleolar core coincided with the shutdown of rRNA transcription demonstrating a potential role for p-NPM1 in signaling nucleolar dissolution. As phosphorylation of NPM1 is reliant on cell-cycle dependent kinases (CDKs), this further suggests p-NPM1 signals cell-cycle state to the nucleolus, coupling ribosome biogenesis events to the meiotic cell-cycle. Current efforts are aimed at defining the specific CDK driving NPM1 phosphorylation. Together, these studies demonstrate that the nucleolus and the XY-body share molecular components that are regulated in a cell-cycle dependent manner suggesting their close proximity facilitates temporal coordination of nucleolar function and the meiotic cell cycle thus answering the long-standing mystery of meiotic nucleolar localization.

Presenter: Ryan Fink
Poster #33: Identifying the Interactome of the key regulator, H2-O, in the MHC-II Antigen Presentation Pathway
Authors: Fink, R
Extracellular pathogens are recognized by specialized antigen-presenting cells (APCs), which process and present peptides via major histocompatibility complex II (MHC-II) to CD4 T cells, thereby initiating antibody-mediated immunity. Peptide loading of MHC-II is catalyzed by H2-M and its negative regulator H2-O. However, recent evidence reveals that the understanding of H2-O function is incomplete. Specifically, I/LnJ mice clear mouse retroviruses while C57Bl/6J mice are susceptible. Gene mapping studies revealed that four single nucleotide polymorphisms (SNPs) in the H2-Ob gene of I/LnJ mice result in four amino acid substitutions that

mediate the retroviral response via increased production of neutralizing antibodies. Notably, knock-in of three of the I/LnJ Oβ amino acid substitutions into C57Bl/6J mice were sufficient to induce neutralizing antibodies and viral resistance. Critically, the knock-in Oβ protein maintains wild-type expression levels, cellular localization, and maintains binding with H2-M yet fails to inhibit H2-M. These observations suggest that the 3 amino acid substitutions may facilitate novel protein interactions with H2-O that modulate the MHC-II pathway. To elucidate these potential interactions, two complementary approaches were used: immunoprecipitation coupled with mass spectrometry and a biotin ligase proximity labeling system. IP-mass-spec identified several novel binding partners, including the v-ATPase, which was confirmed by western blot. The proximity labeling system is expected to provide additional evidence of H2-O protein interactions, potentially revealing transient interactions not captured by traditional IP-mass-spec methods. Ultimately, a comprehensive understanding of this pathway will provide critical insights into how inter-individual genetic polymorphisms in the antigen presentation pathway modulate viral pathogenesis and susceptibility.

Presenter: Mudassir Lodi

Poster #34: Identifying Risk Genes Associated with Neural Progenitor Cell (NPC) Hyper-proliferation in mTOR and p53 Pathways

Authors: Lodi, M., Millonig, J., Xing, J.

ASD patients exhibit statistically larger head circumference and brain volume than healthy individuals, and macrocephaly (head circumference above the 97th population percentile) is found in ~20% of ASD individuals. One possible mechanism to explain the enlarged brain and macrocephaly is increased proliferation of neural progenitor cells (NPCs). NPC hyper-proliferation has been associated with some common etiologies of ASD, including 16p11.2 Deletion Syndrome (16pDel). Previous analyses of iPSC-derived NPCs from macrocephalic individuals with idiopathic ASD and 16pDel consistently show NPC hyper-proliferation phenotypes, which is mechanistically associated with p53 and mTOR pathway dysregulation. We hypothesize that studying the genetic architecture of neurodevelopmental phenotypes associated with NPC hyper-proliferation, such as macrocephaly, within the p53 and mTOR pathways can provide insight into the genetic architecture of ASD. In this study, we focus on the genomic variation within idiopathic ASD and 16pDel patients with macrocephaly. To identify genes that are unique to macrocephaly, we also analyzed genomic variation within normocephalic idiopathic ASD and 16pDel patients, and compare the resulting candidate genes to the one from macrocephalic patients. Within idiopathic ASD patients, our analysis identified two genes within the mTOR pathway associated with macrocephaly with statistical significance: SOS2 and PPP2R3C. Within 16pDel patients, we identified five genes associated with macrocephaly. One of the genes, PRKAB2, was identified in macrocephalic but not normocephalic patients. Examination of these genes through molecular experimentation can provide further insight into their impact on neurodevelopmental disorders.

Presenter: Gabby Panayotakis

Poster #35: Geothermal Bioreactor to Model the Evolution of Multi-Species Interactions

Authors: Panayotakis, G., Stephens, T., Bhattacharya, D.

The multi-kingdom microbes (eukaryotes and prokaryotes) in biofilms from Yellowstone National Park (YNP) geothermal hot springs are highly resistant to the local inhospitable conditions (e.g., elevated temperature, acidity, heavy metals). However, the cellular and ecological drivers behind this resilience remain unclear. Although bacterial biofilms are well studied, multi-kingdom biofilms remain overlooked, even though they have higher genetic flexibility and metabolic capacity. The YNP biofilms are dominated by eukaryotic Cyanidiophyceae red algae (Galdieria and Cyanidioschyzon), with previous research focused on environmental multi-omics sequencing or manipulation of liquid monocultures; both of which do not address how individual environmental conditions may affect the genomic content, cellular morphology, and biotic interactions at these sites. In particular, published data indicates diploid and haploid forms of Galdieria in liquid culture, however,

this is yet to be observed in the environment. The same study also suggests (without direct observation) the presence of diploid Cyanidioschyzon. The environmental conditions driving these shifts in ploidy are unknown. In our study, we cultured an environmental sample of the YNP biofilm in the lab to enable various advanced microscopy techniques, which when combined with nuclear staining and omics analyses, will enable the investigation of morphology and ploidy changes in nature. We have found that, compared to liquid monocultures, Galdieria and Cyanidioschyzon display distinct changes in cell structure, size, shape, and ploidy in our environmental cultures. These results present an opportunity to explore biofilm functionality and formation, genetic novelty, and the origin of speciation through biotic interactions in complex microbial biofilms.

Presenter: Eleanor Agosta

Poster #36: Genomic Instability and Novel Complexity of Human-HPV DNA Structures in a Squamous Carcinoma Cell Line

Authors: Agosta, E. , Chang, Y. , Lenz, J. , Montagna, C.

Human papillomaviruses (HPV) cause most cervical carcinomas and substantial fractions of oropharyngeal, anal, vulvar, penile, and vaginal carcinomas. HPV DNA replicates as extra-chromosomal episomes during infection and integrates into the human genome in nearly all cancer cases. In tumors, it can exist as extra-chromosomal DNA (ecDNA) circles and/or as hetero-concatemer tandem repeats covalently linked with human DNA. The presence of ecDNA is associated with poor patient prognosis across cancer types. However, distinguishing whether particular amplified DNAs in tumors are ecDNA and/or intrachromosomal tandem repeats (such as hetero-concatemers) is challenging based solely on DNA sequencing. Therefore, to accurately characterize HPV integration structures, we applied a battery of DNA analysis techniques to the HPV16-positive human oropharyngeal squamous cell carcinoma cell line UM-SCC-47. We precisely elucidated the structure of the integrated HPV16 DNA, determined the human-virus DNA junctions, and mapped a repeated, 23 kbp hetero-concatemer at single-base-pair resolution. Unexpectedly, optical genome mapping revealed that the 23 kbp hetero-concatemer occurred in tandem arrays of various lengths ranging from a single unit to greater than 27 tandem units. These large-scale arrays (up to 700 kbp) were further rearranged with adjacent human DNA in even larger-scale structures. Additionally, single-cell FISH analysis revealed that HPV16 DNA exists both intra- and extra-chromosomally in individual cells. These findings highlight extensive genomic instability and novel, complex heterogeneity of HPV16-human concatemeric DNA structures in this cell line, including previously undescribed higher-order organizational patterns. Characterizing the complexity of HPV integrations may enable patient stratification or inform the development of targeted therapeutic strategies.

Presenter: Xinyu Hu

Poster #37: Accurate Cell Segmentation Unlocks Single-cell Spatial Transcriptomics

Authors: Jackie Y, Xinyu H

Spatial transcriptomics (ST) enables gene expression profiling with spatial context, making it invaluable for studying development, neuroscience, and diseases like cancer. ST methods fall into two categories: image-based techniques, such as Xenium, which offer high spatial resolution by detecting individual RNA molecules, and sequencing-based approaches, like Visium HD, which capture more transcripts but with lower spatial precision.

To enhance the spatial resolution of sequencing-based ST, computational methods have emerged. Bin2Cell maps gene expression to individual cells using nuclei segmentation of H&E-stained images but is computationally intensive and prone to boundary inaccuracies due to fixed-distance nuclear expansion. STHD, a machine-learning approach, predicts cell types in Visium HD data using single-cell RNA sequencing as a reference. While more efficient, it lacks cell segmentation and suffers from low transcript counts in individual Visium HD bins, reducing classification accuracy.

To overcome these limitations, we integrate Bin2Cell and STHD, combining their strengths. Instead of fixed nuclear expansion, we refine more accurate cell boundaries using gene expression similarity. Additionally, rather than classifying single bins as in STHD, we aggregate multiple bins to increase count number therefore improve cell type identification. Evaluated against a ground truth dataset from Xenium and Visium HD on the same tissue slide, our method significantly improves cell segmentation and downstream analysis compared to existing approaches.

Presenter: Zoe Mastromihalis

Poster #38: Updated examination of commercially available infant and toddler foods in the United States available for purchase using WIC

Authors: Mastromihalis, Z., Peterson, O., Masood, B., Moding, K. J., Ferrante, M. J.

Background: US children do not meet recommendations for vegetable intake. The American Academy of Pediatrics (AAP) and The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) recommend introducing a variety of single vegetables during complementary feeding to facilitate children's acceptance of a wide variety of vegetables across their lifetime. It is unclear whether commercially available infant and toddler foods (ITFs) meet these recommendations.

Objective: To describe the content and variety of commercially available vegetable-containing ITFs and their availability for WIC participants in New Jersey and Indiana.

Study Design: A database of commercially available ITFs containing vegetables was created using product websites gathering ingredient lists and nutrient information. Types of vegetables (e.g. carrots), US Department of Agriculture vegetable categories (e.g. Red/orange vegetables), and WIC availability in New Jersey and Indiana were coded using product information. Descriptive statistics were used to analyze vegetable variety and WIC availability.

Results: Vegetable-containing products (n=755) from 37 US companies were identified. Of these, only 46% (n=349) were available through WIC New Jersey and 16% (n=119) through WIC Indiana. Across all products, 46 different vegetables appeared; the most prevalent were carrots (n=287), sweet potatoes (n=166), and spinach (n=134). Red/orange vegetables appeared the most (n=780), followed by vegetables from the "other" category (n=426) and dark green vegetables (n=264). Vegetable variety decreased when examining WIC availability in New Jersey (n=30 different vegetables) and Indiana (n=22 different vegetables).

Conclusions: Exposure to a variety of vegetables may be limited in commercial ITFs available for purchase using WIC.

Presenter: Eton Victor

Poster #39: Exploring the location and novel interactors of KDM5C in ccRCC

Authors: Victor, Eton, Chen, Zilu, Jian, Cao

Lysine demethylase 5C (KDM5C), a member of the KDM5 family of histone demethylases, removes tri-, di-, and mono-methyl groups from lysine 4 on histone H3. KDM5C is among the top mutated genes in clear cell renal cell carcinoma (ccRCC), the most prevalent type of kidney cancer, indicating its tumor-suppressive function. However, its mechanism is still unknown. We have found KDM5C loss in ccRCC cells increased the secretion of the cytokine, CXCL5, recruited immune suppressive neutrophils into the tumor environment, inhibited cytotoxic T-cells, and accelerated tumor growth in a ccRCC tumor transplantation model. Surprisingly, we have found that KDM5C is predominantly expressed within the cytoplasm of a variety of cell lines and tissues. This is against KDM5C's known function as a histone demethylase. In contrast, other members of the KDM5 family, which are not highly mutated in ccRCC, are found in the nucleus. This then raises the question as to the function of KDM5C in this cellular compartment. We hypothesize that KDM5C regulates CXCL5 expression via a non-histone interactor in cytoplasm. This study aims to identify this non-histone interactor of KDM5C, investigate its role in KDM5C's tumor suppressor function in kidney cancer, and potentially identify novel targets for therapeutic

intervention.

Presenter: Komal Mandleywala

Poster #40: Unleashing the therapeutic potential of dietary interventions in Leukemia

Authors: Mandleywala, K, Da-Silva Diz, V , Thai C, Herranz D.

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematological malignancy, accounting for 10-15% of pediatric and up to 25% of adult ALL cases. Despite advancements in treatment, 20-50% of patients relapse, leading to poor prognosis, while survivors face long-term side effects such as metabolic disorders, neurocognitive impairments, and cardiovascular complications. These challenges highlight the critical need for safer and more effective therapeutic strategies. Oncogenic mutations in the Notch signaling pathway drive over 60% of T-ALL cases, but targeted therapies like γ-Secretase inhibitors have shown limited clinical success due to toxicity. Emerging evidence suggests that systemic factors, including metabolism, the immune system, and the microbiome, play pivotal roles in shaping therapeutic responses, underscoring the potential of host-directed interventions.

In our study, we explore the therapeutic potential of dietary interventions in T-ALL by modulating systemic nutrient availability. Using a NOTCH1-induced T-ALL mouse model, we conducted high-throughput survival screening with various dietary regimens. Remarkably, we found that dietary restriction of the amino acid - histidine significantly impaired T-ALL progression and extended survival.

Our findings reveal a previously unrecognized vulnerability of T-ALL to histidine deprivation, opening new avenues for metabolic reprogramming through dietary modulation. Our goal is to address key questions such as, How does histidine deficiency affect T-ALL progression? To what extent does diet influence cellular metabolism and metabolite availability in T-ALL? And can dietary interventions enhance the efficacy of existing therapies? By elucidating the mechanisms underlying the therapeutic effects of histidine restriction, we hope to develop a novel, non-toxic strategy for T-ALL treatment. Our research has the potential to transform cancer therapy by integrating dietary interventions with conventional treatments, improving patient outcomes, ensuring quality of life, and extending survival for T-ALL patients.

Presenter: Sayoni Chatterjee

Poster #41: Genetic underpinnings of the proximo-distal elaboration of pectoral appendages during the fin-to-limb transition

Authors: Chatterjee S, Shanabag A, Mansour T, Turner N, Senevirathene G, Okamoto A, Miryala M, Shubin N, Nakamura T

The origin of the tetrapod limb remains an enigmatic puzzle in evolutionary biology. The elaboration of skeletal elements along the proximodistal axis is a hallmark of the fin-to-limb transition, marking the emergence of the tetrapod limb. While fish fins consist of proximal radials and distal fin rays, tetrapod limbs exhibit a distinct segmentation pattern, with three progressively specialized regions: a single proximal bone, two middle bones, and multiple distal bones. This segmentation pattern, absent in fins, defines tetrapod limb evolution. Despite recent advancements in paleontology and embryology, the fundamental mechanisms governing skeletal elaboration remain elusive. We address this gap by analyzing the functions of Hox genes, homeobox transcription factors that play pivotal roles in establishing the proximodistal positional information. Our initial transcriptomic analyses revealed that Hoxa13, which is indispensable for patterning distal extremities of pectoral appendages, represses a cohort of chondrogenic genes for patterning the distal bones of the zebrafish pectoral fin. Interestingly, Hoxd9a, a gene implicated in chondrocyte differentiation in tetrapods, emerged as a key player in this regulatory network. To explore the interaction between Hox9 and Hox13 genes in zebrafish fin patterning, we generated a paralogous knockout of Hoxa13 in combination with Hoxd9a. Our initial findings indicate that this combinatorial knockout leads to increased proximal to distal segmentation in the fin

endoskeletal elements. This intriguing pattern may reflect a recapitulation of skeletal elaboration observed during the fin-to-limb transition. Building on these findings, my thesis will investigate how the emergence of the distinct pattern of segmentation of the tetrapod limb is coupled with specific changes to the Hox regulatory network. By doing so, we aim to uncover the genetic mechanisms that drive the elaboration of skeletal structures, a process central to the fin-to limb puzzle.

Presenter: Nusrath Yusuf

Poster #42: The role of Tex15 in shaping stochastic olfactory receptor gene choice

Authors: Yusuf, N, Kahiapo, J, Brann, D, Danoff, J, Irvine, A, Veera, P, Boutros-Ghali, N, Datta, B, Monahan, K

Each mature olfactory sensory neuron (OSN) expresses a single olfactory receptor (OR) allele, which encode the proteins that bind chemical odorants. However, the OSN progenitors that give rise to OSN co-express multiple OR genes during differentiation. The regulatory mechanisms that govern the transition from multiple to monogenic, monoallelic choice of an OR remain to be elucidated. We show that testis expressed 15 (Tex15), a protein that has only been studied in the testes where it regulates methylation and silencing of transposons, is transiently expressed during this critical gene regulation window in OSN progenitors. By examining Tex15 KO mice, we show that Tex15 is crucial for stochastic OR gene choice. Using single cell RNAseq, we find that when Tex15 is knocked out OR choice is still singular, but there is a dramatic reduction in the diversity of expressed OR genes with a few OR genes dominating stochastic choice. Strikingly, the upregulated OR genes are the first to be transcriptionally activated in wild-type OSN progenitors and tend to be located relatively close to OR enhancer elements. Based upon its role in transposable element regulation, we hypothesized that Tex15 is regulating monoallelic OR gene choice through either methylation patterns or through its effect on chromatin state of developing OSNs. Through enzymatic methyl-seq experiment, we observe changes in methylation along several CpG sites and through our ChIP-seq experiments we see a decrease in heterochromatin deposition over OR clusters and OR genes. This project elucidates a novel aspect of how OSNs come to stochastically choose a single OR and how Tex15 gene and protein guides this specific yet diverse choice.