2ND ANNUAL
POSTDOC RESEARCH
Symposium

Brought to you by:

OHSU Postdoc Society and Office of Postdoctoral Affairs

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OCTOBER 27, 2023

12:30-6:30 PM
Auditorium Building and BICC Library
Oregon Health & Science University
Portland, OR

2ND ANNUAL POSTDOC RESEARCH SYMPOSIUM

Oregon Health and Science University

October 27th, 2023

Auditorium
12:30- 3:10 PM

BICC Library
3:10 - 6:00 PM

Invited speakers

Dr. Steph Bernell
Oregon State University

Dr. Monte Westerfield
University of Oregon

Dr. Aqilah McCane
Oregon Health & Science University

12:30 - 1:00: Check-in and Opening (Auditorium)

1:00 - 1:40: Dr. Steph Bernell – Orgeon State University
Associate Professor, College of Health and Human Sciences

1:45 - 2:25: Dr. Monte Westerfield – University of Oregon
Professor, Institute of Neuroscience

2:30 - 3:10: Dr. Aqilah McCane – Oregon Health & Science University
Assistant Professor, Oregon National Primate Research Center

3:10 - 3:30: Break and poster hanging (BICC Library)

3:30 - 5:30: Poster session and Happy hour

5:30 - 6:00: Prizes and Closing remarks

Oregon State University · University of Oregon · OHSU

POSTER PRESENTATION LIST

3:30-4:30 pm: odd posters presenting

4:30-5:30 pm: even posters presenting

Name of presenting author	Poster Number	Institution
Abrar Samiea	1	OHSU
Alejandro Damian Serrano	2	UO
Alexander P Rockhill	3	OHSU
Alexander J. Schachtner	4	UO
Aravinth Ekamparam	5	OSU
Amy Webster	6	UO
Arianna Scalco	7	OHSU
Aude Chiot	8	OHSU
Christian Schmid	9	UO
Corinna Kulicke	10	OHSU
Damayanti Bagchi	11	OHSU
Darren E. Ginder	12	OHSU
Michael M. Wade Wolfe	13	UO
Elizabeth K. Wood	14	OHSU
Fernanda Sandes de Lucena	15	OHSU
Gauthami Sulgey	16	OHSU
Hayleigh Ast	17	OHSU
Hung Nguyen	18	OHSU
Ishaq Wadiwala MBBS	19	OHSU
Jennifer Eng	20	OHSU
Jessica F. Hebert	21	OHSU

Jianhao Cao	22	OHSU
Justin Anderson	23	OHSU
Laura Desban	24	UO
Marissa Co	25	OHSU
Paige C. Arneson-Wissink	26	OHSU
Paula Sanchez-Molina	27	OHSU
Po-Han Yeh	28	OHSU
Prem Singh	29	OSU
Rashi Yadav	30	OHSU
Rebecca A. Frederick	31	UO
Reuben Hoffmann	32	OHSU
Sarah Bernhardt	33	OHSU
Sarah Zerimech	34	OHSU
Sayandeep Gupta	35	UO
Sherry Bell	36	UO
Shiva Moaven	37	UO
Sivashankari Rajasekaran	38	OHSU
Sophia Lambert	39	UO
Tenzin Ngodup	40	OHSU
Vidhi Shah	41	OHSU
Vignesh Ravichandran	42	UO
Yoshio Funahashi	43	OHSU

POSTER JUDGING GUIDELINES

Thank you for judging poster presentations at the 2nd Annual Postdoc Research Symposium! This year, every attendee has the opportunity to cast their "vote" for each poster to ensure the diversity of the judges reflects the diversity of postdoctoral research topics represented by OHSU, OSU, and UO. Poster numbers can be found on the poster board and in the abstract book. Each poster will be evaluated on the following categories:

- **Communication/Presentation** –The central argument or idea of the poster is clearly communicated, even to a non-specialist audience.
- **Content/Innovation** –The display conveys compelling information that supports the research argument or objective. Conclusions are put into perspective of the larger field or discipline.
- **Visual** –The display is visually engaging, attractive, and easy to read.

The top posters in each of the three categories will be honored at the conclusion of the symposium.

Vote Here!

Poster 1

Defining the Role of Skin Resident B cells in Early Cancer Development

Abrar Samiea

B cells are vital players in immune function. They give rise to antibody secreting cells, present antigen, and can secrete both inflammatory and immunoregulatory cytokines. While general B cell functions have been investigated in detail, the role of these cells in the context of cancer and dermatology has until recently received relatively little attention. Key new studies demonstrated a positive association between B cell tumoral accumulation and patient response to checkpoint blockade immunotherapy in melanoma patients. Similarly, B cells can be driven by various microenvironmental signals to acquire an immunoregulatory phenotype defined by expression of potent immune modulating cytokines, including IL-10, IL-35, and TGF-ß. Presence of a regulatory B cell signature is associated with more aggressive tumor growth and reduced response to checkpoint immunotherapy. In order to harness B cells in melanoma immunotherapy we must both encourage their expansion within the tumor microenvironment and ensure they are driven towards a productive anti-cancer cell state. Here, my research will be focusing in the functional biology of resident memory B cells in the tumor microenvironment and introducing new tools to determine if these cells are a suitable target for therapeutic intervention.

Poster 2

The development, evolution, and locomotory hydrodynamics of salp colony architecture

Alejandro Damian-Serrano, Kaiden Walton, Anneliese Bishop-Perdue, Kelly Sutherland

Salps are tunicates that filter-feed on microbial production in the plankton in marine pelagic ecosystems. Salps form colonies of asexually-budded individuals that swim by multi-jet propulsion. Colonies develop into species-specific architectures with distinct zooid orientations. These architectures vary in frontal drag, thrust ratio, and locomotory efficiency. We (1) define the salp colony morphospace, (2) characterize the developmental pathways that build the different architectures, (3) assess their hydrodynamic consequences for locomotion, and (4) reconstruct their evolutionary history. First, we defined a universal comparative set of axes and planes based on the transversal double chain arrangement found in the early-developing stages of all colonies and defined adult zooid architectures as developmental transitions from this shared stage. Development shows that the morphospace is constrained to three transformation pathways, where all architectures are either final or intermediate stages towards bipinnate, cluster, or helical forms. To measure these architectures and their hydrodynamic properties, we collected and photographed specimens of adult and developing colonies via SCUBA diving, and measured the swimming speed of different species using in situ stereo-videography. To study the evolutionary history of these architectures, we inferred a new 18S gene phylogeny, reconstructed the ancestral states using models informed by developmental constraints, and identified categorical shifts in the evolutionary change of zooid orientations. We find that the ancestral salp architecture is most likely oblique or linear, with every other state being derived. Linear architectures are the fastest, most hydrodynamically efficient, and have evolved independently more often than any other architecture. Each of the three slowest-swimming architectures was derived at least once, suggesting that swimming speed is not strongly selected for across salps, and might be driven by ecological trade-offs with other traits.

Poster 3

Referencing Schemes and Their Effect on Oscillations and Broadband Power Spectral Shifts in Stereoelectroencephalography

Alexander P. Rockhill, Michael A. Jenson, Nicole C. Swann, Ahmed M. Raslan, Dora Hermes, and Kai J. Miller

Measurements of electrical potential must be in relation to a reference. ECoG researchers report several referencing schemes: recordings with low variance (Crone, 1998), an average of all recording channels (Miller, Zanos, et al., 2009) and pairwise bipolar (Miller, Sorensen, et al., 2009). sEEG researchers use these references (Li et al., 2021; Rockhill et al., 2023) but the geometry of the recordings relative to cortical columns and the location of recording contacts in white as well as gray matter effects interpretation of these signals. We hypothesized that bipolar referencing would facilitate detection of oscillations and broadband spectral changes, leading to higher classification accuracy between movement and rest.

Twelve sEEG patients at Mayo Clinic Rochester, Minnesota volunteered to participate in a movement research task where they were asked to move their hand, foot or tongue for three seconds at a time with 20 repetitions for each movement. Data were sampled at 1200 Hz with a g.tec HIAMP amplifier (Gerlingen, Germany) using BCI2000 (Schalk et al., 2004). Power spectral density for each channel was computed using the Welch method (Welch, 1967) and then classified using a linear SVM after PCA dimensionality reduction.

We found that bipolar, average and low variance referencing schemes improved classification accuracy over the native reference of a single white matter contact. Average referencing improved classification accuracies in all bands whereas bipolar referencing sacrificed accuracy at higher frequencies that reflect broadband shifts in the power spectrum (Miller, Sorensen, et al., 2009).

Our future work will determine more precisely where trade-offs occur (i.e. if average referencing makes movement-related changes more diffuse) and the effect of the orientation of the electrode relative to cortical geometry on signal characteristics.

Poster 4

3-D Direct Laser Written Intraneural Microelectrode Arrays

Alexander J. Schachtner, Diana Ostojich, Rachel Yuan, Rebecca Frederick, Ana V. Garcia-Caraveo, Morgan A. Brown, Melissa Bemrose, Felix Deku, Timothy J. Gardner

Neurostimulation and recording are important tools for studying fundamental peripheral nerve function and the development of therapeutic interventions. To date, there exist few devices capable of stable, high-quality interfacing with nerves on the scale of common small animal models (< 200 µm diameter). Existing devices often deploy electrodes on the exterior nerve surface and are thus subject to low signal to noise ratios due to weak electric field penetration and excessive movement noise. In this work, we present progress toward a flexible biocompatible polymer-based device with compliant, intraneural penetrating, 3D-printed microelectrodes for electrical recording and stimulation of peripheral nerves in small animals.

Poster 5

Evaluating Urban Stormwater Treatment Systems for Effective Managed Aquifer Recharge: A Comprehensive Framework

Aravinth Siva Subramaniam Ekamparam, Salini Sasidharan

Water is a vital resource for all living beings. However, the increasing population, urbanization, and industrialization have led to a surge in freshwater demand. Climate change has further exacerbated the situation by impacting already-stressed freshwater sources. The atmospheric rivers bring short-duration rainfall extremes that can cause flash floods in urban areas, posing a threat to densely populated regions. To mitigate urban flooding, engineered structures such as bioretention cells, grass swales, infiltration basins, etc., are being installed to capture, treat, and infiltrate excess runoff and stormwater. However, these stormwater treatment facilities and their treatment efficiencies are primarily evaluated for infiltration. In many urban areas, the growing population depend on groundwater for public drinking, adding additional stress into already depleting aquifers. Therefore, discharge water from these structures can be utilized to recharge aquifers using managed aquifer recharge (MAR) techniques such as drywells. However, while these treatment systems are quite helpful in mitigating floods, the discharged water quality from these systems sometimes fails to meet drinking water standards. Therefore, estimating the treatment efficiency of these systems becomes essential before integrating a treatment train into various MAR practices. Failure, in the treated water quality could lead to the contamination of the potable groundwater causing public health concern, clog the aquifer pores or deteriorate the aquifer water quality by disturbing the local water chemistry.
This study investigated the treatment efficiencies of various pretreatment systems employed as best management practices (BMP) across the United States. The data was collected from BMP dataset. Various BMPs have been grouped based on their treatment mechanism, and their inflow and outflow water characteristics have been evaluated for significant water quality parameters, with a special focus on heavy metals. The categorization will help to develop a decision framework and implement site-specific treatment techniques to produce output water that meets regulatory standards.

Poster 6

Epigenetic context predicts gene expression variation and reproductive traits across genetically identical individuals

Amy Webster, John Willis, Erik Johnson, Peter Sarkies, Patrick Phillips

In recent decades, genome-wide association studies (GWAS) have been the major approach to understand the biological basis of individual differences in traits and diseases. However, GWAS approaches have proven to have limited predictive power to explain individual differences, particularly for complex traits and diseases in which environmental factors play a substantial role in their etiology. Indeed, individual differences persist even in genetically identical individuals, although fully separating genetic and environmental causation is difficult or impossible in most organisms. To understand the basis of individual differences in the absence of genetic differences, we measured two quantitative reproductive traits in 180 genetically identical young adult Caenorhabditis elegans roundworms in a shared environment and performed single-individual transcriptomics on each worm. We identified hundreds of genes for which expression variation was strongly associated with reproductive traits, some of which depended on prior environmental experience and some of which was random. Multiple small sets of genes together were highly predictive of reproductive traits across individuals, explaining on average over half and over a quarter of variation in the two traits. We manipulated mRNA levels of predictive genes using RNA interference to identify a set of causal genes, demonstrating the utility of this approach for both prediction and understanding underlying biology. Finally, we found that the chromatin environment of predictive genes was enriched for H3K27 trimethylation, suggesting that individual gene expression differences underlying critical traits may be driven in part by chromatin structure. Together, this work shows that individual differences in gene expression that arise independently of underlying genetic differences are both predictive and causal in shaping reproductive traits at levels that equal or exceed genetic variation.

Poster 8

Elevated expression α5-integrin by myeloid cells in motor areas provides a potential target for therapeutics in ALS.

Aude Chiot, Shanu F. Roemer, Lisa Ryner, Alina Bogachuk, Katie Emberley, Dillon Brownell, Michael Leviten, Dennis W. Dickson, Lawrence Steinman, Bahareh Ajami

Amyotrophic lateral sclerosis (ALS) is a fatal disease affecting upper and lower motor neurons and leading to progressive paralysis. While motor neurons are the main cells affected in ALS, the microglial cells, the macrophages of the central nervous system, and peripheral macrophages in the nerve react strongly to the disease and become reactive. Previous studies have shown that microglial cells influence the progression of the disease by maintaining inflammation and interacting directly and indirectly with the motor neurons. In addition, modulating microglial cells and peripheral nerve macrophage profiles have been shown to influence disease progression. In a previous study from our lab, single-cell mass cytometry (CyTOF) analysis revealed a prominent expression of α5 integrin in microglia and macrophages in a superoxide dismutase-1 G93A mouse model of ALS (SOD1G93A). Our new analysis revealed that α5 integrin- positive microglial cells and sciatic nerve macrophages display a very inflammatory phenotype. Interestingly, in post-mortem tissues from ALS patients with various clinical ALS phenotypes and disease duration, α5 integrin was expressed in motor pathways of the central and peripheral nervous system and highly upregulated compared to controls, making it a relevant target to modulate microglial cell and macrophage inflammatory profile. In an attempt to assess the downregulation of alpha 5 as a potential therapeutic target for ALS, we administered a monoclonal antibody against α5 integrin to SOD1G93A mice. Targeting α5 integrin in SOD1G93A mice, reduced microglial cell reactivity, improved motor functions and increased survival compared to an isotype control. Together these findings in mice and humans suggest that α5 integrin is a potential therapeutic target for ALS.

Poster 9

Passive exposure to task-relevant stimuli enhances categorization learning

Christian Schmid, Muhammad Haziq, Melissa M. Baese-Berk, James M. Murray, Santiago Jaramillo

Learning to perform a perceptual decision task is generally achieved through sessions of effortful practice with feedback. Here, we investigated how passive exposure to relevant stimuli, which is relatively effortless and does not require feedback, influences active learning. First, we trained mice in a sound-categorization task with various schedules combining passive exposure and active training. Mice that received passive exposure exhibited faster learning, regardless of whether this exposure occurred entirely before active training or was interleaved between active sessions. We next trained neural-network models with different architectures and learning rules to perform the task. Networks that use the statistical properties of stimuli to enhance separability of the data via unsupervised learning during passive exposure provided the best account of the behavioral observations. We further found that, during interleaved schedules, there is an increased alignment between weight updates from passive exposure and active training, such that a few interleaved sessions can be as effective as schedules with long periods of passive exposure before active training, consistent with our behavioral observations. These results provide key insights for the design of efficient training schedules that combine active learning and passive exposure in both natural and artificial systems.

Poster 10

MR1 ligands efficiently exchange from soluble to host MR1 in post-ER compartments

Corinna Kulicke, Gwendolyn Swarbrick, Nicole Ladd, Meghan Cansler, Megan Null, Aneta Worley, Chance Lemon, Tania Ahmed, Joshua Bennett, Deborah Lewinsohn, Erin Adams, David Lewinsohn, Melanie Harriff

MR1 restricted T (MR1T) cells have the potential to be important players in both microbial and non-infectious inflammatory disorders and cancer. Similar to other antigen presentation molecules, evidence continues to build for multiple, complementary MR1 antigen presentation pathways. To further investigate post-ER pathways for loading of MR1 molecules, we used a novel antigen delivery method employing MR1 monomers and tetramers loaded with 5-(2-oxopropylideneamino)-6-d-ribitylaminouracil (5-OP-RU). We demonstrate that MR1 ligands are efficiently presented to MR1T cells when delivered in the context of soluble MR1 molecules. Using MR1-deficient cells reconstituted with wild-type MR1 or MR1 molecules that cannot bind 5-OP-RU, we show that this presentation is dependent on host MR1 and requires the transfer of ligand from the soluble molecule onto MR1 expressed by the antigen presenting cell. Experiments using 6-formylpterin and brefeldin A indicate that the exchange occurs in post-ER compartments. Interestingly, however, we do not see evidence that the exchange requires endosomal acidification. Instead, we propose a model where chaperones direct the exchange of covalently bound ligands from one MR1 molecule to another. This new mode of delivery strengthens the evidence for a post-ER exchange pathway for MR1, which could represent an important avenue by which MR1 acquires antigens derived from endocytosed pathogens.

Poster 11

Using volumeEM methods to understand changes in corneal nerves after injury

Damayanti Bagchi, James R. Carroll, Deborah M. Hegarty, Catherine W. Morgans, Sue A. Aicher

The cornea contains the highest density of sensory nerves of any tissue in the body. The ophthalmic branch of the trigeminal ganglion contains somas of neurons that innervate the corneal epithelium and also transduce and transmit sensory information from the cornea to the brain. The sensory nerve endings within the corneal tissue are called intraepithelial corneal nerves. Our previous studies used immunocytochemistry, confocal microscopy, and image analysis to examine changes in intraepithelial corneal nerve density, morphology, and neurochemistry after a corneal abrasion injury. However, these methods do not provide adequate resolution to fully understand the subcellular relationships between corneal nerves and epithelial cells, and how these relationships change after injury.
In the present study, we are applying different electron microscopy-based approaches to further investigate the morphological changes in corneal nerve density after abrasion and examine nerve and epithelial recovery over time. Using previously described methods, rats were anesthetized with isoflurane and heptanol was applied to the center of the left eye and the corneal epithelium was removed to produce a corneal abrasion. One week later, rats were euthanized and perfused transcardially with 4% paraformaldehyde and 0.25% glutaraldehyde in 0.1 M phosphate buffer, pH 7.4. Abraded and unabraded whole-mount corneas were immuno-processed to detect corneal nerves using an antibody to beta-tubulin. Tissues were post-fixed in osmium tetroxide, dehydrated, and embedded in EPON resin using two distinct protocols. Transmission electron microscopy (TEM) was used to confirm immuno-labeling of intra-epithelial corneal nerves. To get an overview of nerve density one week after abrasion injury, we created a montage of images collected using a FEI Helios G3 DualBeam™ scanning electron microscope (SEM) and compared epithelial cell area and nerve density in abraded and unabraded corneas, confirming reductions in both epithelial thickness and nerve density after abrasion. We also noted changes in the type and number of epithelial cells. Our next steps will be to compare volume EM methods for SBF -SEM and array tomography to determine whether corneal nerves course between or through epithelial cells during nerve recovery. Overall, immuno EM and volume EM based approaches are expected to provide a more intricate and detailed description of injured corneal nerve recovery.

Poster 12

Adolescent prairie vole ethanol seeking and affiliative behavior are reduced based on sex following early-life sleep disruption.

Darren E. Ginder, Carolyn E. Jones-Tinsley, Miranda M. Lim

Early-life sleep is critical for neuronal development and maturation. One critical neurodevelopmental timepoint in rodents is during the pre-weaning period, postnatal day (P) 14 to 21. Using prairie voles, we have reported that early-life sleep disruption (ELSD) at this timepoint results in adult interference with social bonding and increases ethanol consumption following a stressor. Furthermore, we have reported increased parvalbumin expression and reduced glutamatergic neurotransmission in prefrontal cortical regions in adult prairie voles that experienced this paradigm. To understand the impact of ELSD on the lifespan, examination of an earlier time in life is necessary. Thus, the aim of the present study was to examine the behavioral outcomes of ELSD on adolescent prairie voles. Here we hypothesized that anxiety and reward related behaviors, as measured by 2-bottle choice and social interactions, would be negatively impacted by ELSD in adolescent male and female prairie voles. Male ELSD voles were no different from control voles in measures of anxiety and ethanol preference or consumption, but social interactions were significantly reduced. ELSD differentially impacted female prairie voles, with increased anxiety-like behavior and reductions in ethanol consumption, but no impact on ethanol preference or social interactions. Together, these results suggest both male and female prairie voles experience differential changes to reward seeking behaviors, but only female prairie voles showed increases in anxiety-like behavior. These results further suggest that early-life sleep is critically important for neurotypical behaviors in adolescence, a time where reward-seeking and risky behaviors are adaptive for learning and promoting survival.

Poster 13

Exploring the Differential Oxidative and Nucleophilic Reactivity of Sulfur Anions with Phosphine Electrophiles

Dr. Michael M. Wade Wolfe and Dr. Michael D. Pluth

Reactive Sulfur Species (RSS) are crucial molecules in biological systems that play key roles in signaling in vivo. Thionitrite (SNO-) and perthionitrite (SSNO-) are of particular interest, as they are known cross-talk species between the H2S and NO which belong to the gasotransmitter family. Due to the wide range of accessible oxidation states for sulfur (2- to 6+), reactions involving RSS are more chemically complex than those involving analogous reactive oxygen species. To investigate the differential oxidative and nucleophilic reactivity of a series of sulfur and oxygen containing anions (SSNO-, SNO-, NO2-, (S4)2-, and HS-) we selected PPh2Cl as simple, reducing electrophile. Reaction between -SSNO and PPh2Cl resulted in a complex mixture of mono and diphosphorus species in the P(V) oxidation state that was elucidated by 31P NMR spectroscopy. We were able to tune the selectivity for the P and P2 products by modulating the stoichiometry of PPh2Cl. Interestingly, sulfur and oxygen were incorporated into the phosphorus products, but not nitrogen. Instead, N is liberated from the reaction in the formation of NO gas. Finally, we demonstrated that even the less oxidizing anions, (S4)2- and HS-, reacted with PPh2Cl due to the strong driving force of forming P=S bonds.

Poster 14

Consumption of Prenatal Vitamin C Intake Mediates the Association between Pregnancy-related Anxiety and Offspring Negative Affect at Six Months of Age

Elizabeth K. Wood, Olivia K. Nomura, Amanda N. Howery, Hailey Volk, Joel T. Nigg, Hanna C. Gustafsson, & Elinor L. Sullivan

Trait-like negative affect reflects tendencies to experience negative emotions and is an early risk marker for future psychopathology. Self-reported pregnancy-related anxiety among birthing parents is linked to increased dietary intake and offspring risk for higher negative affect, but the mechanisms are not well understood. Given its anti-inflammatory properties and propensity to influence cortisol regulation during chronic stress, prenatal vitamin C consumption may be associated with offspring neurobehavioral outcomes. To examine the role of prenatal vitamin C intake on the relationship between pregnancy-related anxiety and infant negative affect, 293 pregnant individuals completed six nonconsecutive 24-hour dietary recalls conducted by trained dietitians during their second and third trimesters (three recalls/trimester), as well as questionnaires regarding dietary supplement usage and dosage. Birthing parent pregnancy-related anxiety was assessed during the second trimester using the Pregnancy-Related Anxiety Questionnaire. Infant negative affect at six months was captured via the Infant Behavior Questionnaire-Revised. Higher pregnancy-related anxiety regarding concerns about the developing baby's health was associated with increased infant negative affect at six months (β=.13, p<.05). This effect was mediated by prenatal dietary and supplemental vitamin C intake (βindirect=-.04, p=.04), such that higher pregnancy-related anxiety was associated with greater vitamin C intake (β=.17, p<.05). Vitamin C intake was associated with lower infant negative affect (β=-.24, p<.01). Results suggest that higher pregnancy-related anxiety leads to higher prenatal vitamin C consumption, which is associated with lower infant negative affect at six months. Increasing prenatal vitamin C intake may be a promising protective factor against pregnancy-related anxiety and subsequent offspring outcomes.

Poster 15

Drug repurposing for glycosyl-transferase inhibition and dental biofilm disruption

Fernanda Sandes de Lucena, Matthew G. Logan, Marcelo Yudi Icimoto, Steven Lewis, Hua Zhang, Hui Wu, Carmem Pfeifer

Purpose/Aim. Streptococcus mutans play a crucial role in caries formation, and form a biofilm whose cohesion depends on exopolysaccharides (EPS), synthesized by glucosyl transferases (Gtfs). Several small-molecule Gtf inhibitors have been investigated, though many are active at relatively high concentrations. The objective of this study is to repurpose FDA-approved drugs for GTF inhibition using in silico docking, and validation with molecular biology approaches.
Materials and Methods. The PDB structure of S. mutans Gtf-C was used to screen a library of drugs, 32 of which demonstrated reduction of biofilm biomass assessed by crystal violet assay. Further screening via a renilla reporter assay (luciferase IdhRenGSm strain) was used to select the drugs with the best cell viability, one of which was tested for cell adhesion strength (impingement test) and viability of the planktonic cells on the well at concentrations ranging from 6.25-50 µM. Data were analyzed with one-way ANOVA/Tukey tests (alpha=5%).
Results. Data for the initial screening is omitted. Results for 6 drugs are presented in Figure 1. Drugs 3.2, 3.4, 3.7, 3.8, 5 and 5.4 affected the biofilm formation at least for one of the concentrations tested, as can be observed through the morphology of the crystal violet stained biofilm (Fig. 1-A). Exposure of biofilm to the molecules reduced the bacterial viability of all the drugs, except for drug #3.8 (Fig. 1-B).
Conclusions. One of the tested molecules, #3.8, showed potential in disrupt the biofilm formation without reducing its viability. Further tests will be necessary in order to evaluate the binding affinity of this compound to the Gtfs.
Funding. NIH-NIDCR (R35-DE029083; K02-DE025280)

Poster 16

Study to identify heteroaryl amide as a broad-spectrum antiviral

Gauthami Sulgey, Nicole Haese, Samuel Medica, Craig Kreklywich, Zachary Streblow, Corinne E Augelli-Szafran, Omar Moukha-Chafiq, Daniel N Streblow

A heteroaryl amide (SRI-36418) compound class was identified using an antiviral high throughput screening (HTS) assay and further structure-activity relationship (SAR) studies were performed to generate the lead compound SRI-45148. The compound, SRI-45148 was tested in-vitro and found to have inhibitory effect against both DNA (human cytomegalovirus) and RNA (Chikungunya virus (CHIKV) and Venezuelan equine encephalitis virus (VEEV)) viruses. The compound showed low cytotoxicity in Vero cells and normalized human dermal fibroblasts (NHDF). Further, at a concentration of 10 micro molar, the compound was able to induce a reduction in titer of CHIKV, VEEV and HCMV by 7.7, 8.7 and 3.5 logs, respectively. In CHIKV infected cells the compound inhibited both transcription and gene expression of the viral envelope glycoprotein (E2). In HCMV, while an efficient shut down of glycoprotein B (gB) expression was observed, a moderate effect was seen on the expression of UL44 and pp28 proteins. Our time of addition studies showed that the drug was effective in inhibiting HCMV replication even when added 48 hours post infection. However, in case of CHIKV, pre-treatment or treatment at an early time point during infection appeared to be necessary to inhibit viral replication. Further studies are underway to identify the drug target and to elucidate the mechanism of action of a potential broad-spectrum antiviral.

Poster 17

Changes in the Gut Microbiome Following Micronutrient Supplementation in Children with ADHD: The MADDY Study

Ast, Hayleigh and Hammer, Matthew; Bruton, Alisha; Robinette, Lisa; Hatsu, Irene; Leung Brenda; Arnold, L. Eugene; Karstens, Lisa; Johnstone, Jeanette

Micronutrients have demonstrated promise in managing emotional dysregulation in children with ADHD. The mechanism for why micronutrients are effective remains unknown. Given the micronutrients' direct contact with the gastrointestinal microbiome we analyzed the change in the composition of the microbiome before and after treatment and in responders and nonresponders. A pairwise analysis on 16sRNA gene sequencing was completed on a sub sample of stool from the MADDY study. Results demonstrate two families *Rikenellaceae* and *Oscillospiraceae* were significantly changed in the responder versus nonresponder. Similar to a previous study, the phylum *Actinobacteriota* decreased with no change in alpha diversity in the micronutrient versus placebo groups. These observations indicate that micronutrients have an impact on the gastrointestinal bacteria of the microbiome and point towards specific bacterial changes being correlated with response to treatment and micronutrients themselves.

Poster 18

Imaging modality of selective focal white mater injury in rodents

Hung Nguyen, Martin Pike, and Selva Baltan

White matter injury (WMI) is associated with disabilities after stroke, and the mechanisms of WMI differ from gray matter. To verify the potential benefits of therapeutic approaches it is essential to follow the course of ischemia progression and the correlated behavioral outcomes in longitudinal studies. We have developed an in vivo selective focal WMI model to further investigate WM changes. Therefore, we aim to develop a novel MRI modality to detect selective WMI that is correlated with behavioral assessments. 2-month-old C57BL/6 males were used in the study. Three injections each of 200 nL of L-NIO (130µM) were deposited at the previously identified coordinates. Sham mice underwent the same procedure but were injected with saline. Behavioral deficits were assessed using cylinder test, and pasta eating test at baseline, day 1 and 7 post-injury. MRI of the mice were taken on days 2 and 10 post-injury to assess WM changes in corpus callosum (CC). Mice were anesthetized with Ketamine/xylazine in combination with low isoflurane (0.75%) in 100% oxygen and positioned with heads immobilized on an animal cradle while body temperature and respiration are monitored. We quantified the total edema volume and fractional anisotropy (FA) using T2-weighted imaging and diffusion tensor imaging respectively.
We detected persistent focal edema without significant changes in volume and a reduction FA signaling in the ipsilateral CC. These imaging modalities correlated with behavioral deficits.
In conclusion, we established a MRI protocol to longitudinally assess WM integrity and the resultant behavioral deficits after selective focal ischemic injury.

Poster 19

Hepatic Artery Aneurysm Embolization Inducing Cholecystitis

Robin Osofsky, MD; Ishaq Wadiwala MBBS; Reid Mahoney, MD; Amani Politano, MD

HISTORY
A 40-year-old man with a history of hypertension, hyperlipemia, and active tobacco and opiate abuse who presented to a referring facility with acute abdominal pain with melenic stools, and 120-pound unintentional weight loss in the last year. An CT abdomen and pelvis demonstrated a 2.2 cm fusiform common and proper hepatic artery aneurysm with mural thrombus. On hospital day (HD) 2, he developed worsening melena, new hematochezia, and hematemesis, requiring multiple blood transfusions. An EGD demonstrated clot in the gastric cardia. Due to persistent transfusion requirements, the patient was transferred to our tertiary care center on HD 5. A repeat CT demonstrated an enlarging saccular outpouching in the distal portion of the proper hepatic aneurysms. (Figure 1A)

PLAN
On HD 6, the patient underwent a hepatic artery angiogram with the common, proper, and left hepatic arteries embolized. (Figure 1B) Furthermore, contrast extravasation into the biliary system was noted, consistent with haemobilia. Post-procedurally, his hematocrit stabilized. However, the patient developed moderate transaminitis. On HD 10, he developed new RUQ tenderness, prompting abdominal ultrasound and HIDA demonstrating acalculous cholecystitis. Later he underwent an uncomplicated percutaneous cholecystostomy tube placement.

DISCUSSION
Though rare, HAAs are clinically crucial due to their potential for rupture, with mortality rates reported at 33%. SVS guidelines for treating HAAs include any symptomatic aneurysm, and aneurysms > 2 cm, and with growth rate > 0.5cm/yr. Both open and endovascular approaches can be utilized, our patient’s HAA was extensive, thus embolization was done. It is not unexpected that the patient developed hepatic ischemia and cholecystitis. Similar outcomes have been described for HAA patients undergoing embolization. Fortunately, our patient’s cholecystitis was managed successfully with percutaneous cholecystostomy tube placement. In conclusion, embolization is a reasonable treatment strategy for symptomatic HAA patients. However, providers must be vigilant for hepatobiliary complications.

Poster 20

Collective invasion is associated with liver metastasis in pancreatic ductal adenocarcinoma

Jennifer Eng, Carl Pelz, Koei Chin, Jason Link, Dove Keith, Rosalie Sears

Fifty percent of PDAC patients present with distant metastasis and face a dismal prognosis of 8 to 11 months. However, patients with lung metastases have better prognosis than patients with metastatic spread to other sites. In our PDAC metastasis cohort, patients with lung-only metastasis survived longer than patients with liver metastasis, despite sharing the same tumor subtype. To understand features of the primary tumor linked to metastatic site, we generated a novel gene signature for primary organotropism (pORG) that distinguishes primary tumors that developed liver metastasis from those that developed lung metastasis, independent of known tumor subtypes. We generated cyclic immunofluorescence multiplex imaging data from 34 primary tumors, 9 with radiographically documented liver metastasis and 4 with lung metastasis without liver metastasis. Intriguingly, malignant cells from high pORG, liver-tropic tumors had an increased fraction KRT19-high tumor cells relative to low pORG tumors and were distinctly epithelial in morphology, with increased tumor cell spatial contact in tissues. To reconcile the metastatic behavior of liver-tropic tumors with their apparent enrichment for epithelial-state cells, we hypothesized that liver-tropism was associated with a partial epithelial-to-mesenchymal transition (EMT) state and metastasis via collective invasion. Bulk transcriptional analysis of over 200 PDAC primary tumors revealed a distinct subset of high pORG tumors have increased expression of markers linked to partial EMT and collective invasion, including RAB11a, Rho-like GTPases, and proteases MMP7 and KLK7, supporting a model of E-cadherin internalization facilitating partial EMT and collective invasion. For validation, we characterized in-vitro migration modes of conventional and patient-derived PDAC cell lines. Collectively migrating cells had faster wound closure than those migrating as single cells, and similar to liver-tropic tissues, had high KRT19 expression and increased tumor cell spatial contact. Our work shows similarities between in-vitro collective migration phenotypes and in-vivo liver-tropic phenotypes in PDAC.

Poster 21

Recovered Parental Acute Kidney Injury Results In Dysfunctional Pregnancy and Offspring Programming

Jessica F. Hebert, Jacqueline Emathinger, Nicole Andeen, Susan Gurley, Michael P. Hutchens

Background: Rhabdomolysis-induced acute kidney injury (RIAKI) follows muscular trauma and is observed in people of childbearing age. Although apparent recovery is common, prior AKI increases the risk of renal and reproductive disease. We hypothesized that recovered AKI induces pregnancy complications and developmentally programs offspring disease.
Methods: Procedures were approved by institutional IACUC. Rhabdomyolysis in 8-12 week old C57BL/6J mice was induced via intramuscular injection of 50% glycerol (8 mL/kg); shams were untreated. AKI was assessed 24 hours later via glomerular filtration rate (GFR; uL/min/100g body weight) and repeated 2 weeks post-recovery to establish functional recovery, followed by 1) timed sham/sham and RIAKI/RIAKI matings for pregnancy (gestational day (GD) 16.5) and 2) adult offspring (12 weeks, 6 months) effects. Urine was collected 24 hours before GFR and tissue harvest for later analysis. Statistics were assessed by t-test for 2 group analyses, and two-way ANOVA with posthoc tests for analyses by sex.
Results: 1) Despite normal GFR pre-pregnancy, recovered RIAKI dams had lower GFR than shams at GD 16.5 (p<0.01). Fetoplacental ratio was lower in RIAKI offspring (p<0.01) with no difference in litter number, but 3x greater perinatal death. Albuminuria (p<0.01) and low molecular weight proteinuria were observed in RIAKI dams. RIAKI dams had less megalin (p<0.05) and more angiotensin II (AngII) in the proximal tubule brush border than shams, with evidence of subcapsular fibrosis. 2) Offspring of recovered RIAKI parents have sexually dimorphic responses related to renal function. GFR was reduced in offspring of both sexes by 6 months (males: p<0.05, females: p<0.01). Circulating AngII levels were decreased in plasma from only female RIAKI offspring compared to shams (p<0.05); however, adult males from RIAKI pairings gained more weight than sham males between young and middle adulthood (p<0.05).
Conclusions: RIAKI poses gestational risk long after initial apparent recovery, likely due to new proximal tubule dysfunction in the setting of pregnancy after RIAKI. Renal function in pregnancy, particularly essential function of the proximal tubule via megalin and AngII, is altered by prior RIAKI. Developmental programming results in adults with reduced GFR, and older male offspring with increased weight gain.

Poster 22

Cryo-EM study of glycosome isolated from Leishmania tarentolae

Jianhao Cao, Liman Zhang

Trypanosomatida contains a group of kinetoplastid unicellular eukaryotes having a well-defined nucleus and other cell organelles including glycosome, kinetoplasts and flagella. Some species have life-cycles involveing both human and other vertebrate or invertebrate hosts. Various species of Leishmania in the Trypanosomatida genus typically transmitted by sandflies and cause series of clinical manifestations named Leishmaniasis. The glycosome is a featured membrane-enclosed organelle in the body of Leishmania. It is known to harbor most peroxisomal enzymes and 9 glycolytic enzymes for energy metabolism. In the present study, we isolate glycosome from Leishmania tarentolae and use both negative-stain and cryo-EM to confirm the pure glycosome fraction and identify the glycosome fraction with featured protein arginase (ARG). In future work, we can use both single particle analysis and tomography to study the architecture of both the glycosome organelle and proteins/complexes which helps to explore new drug targets.

Poster 23

Effect of selection for ethanol preference on the transcriptome in the central nucleus of the amygdala of HS-CC mice

JQ Anderson, P Darakjian, TJ Phillips, RJ Hitzemann, AR Ozburn

Alcohol use disorder (AUD) is a complex, polygenic disease that has a heritability of about 0.5 for risk. Dysregulation of the transcriptome which precedes exposure to alcohol may contribute to risk for AUD. In this work, we leveraged the genetically diverse HS-CC (heterogeneous stock – collaborative cross) mouse population to perform short term selective breeding for high vs. low ethanol preference, in a two-bottle choice paradigm, to detect changes in the transcriptome associated with ethanol preference. RNA-seq data for the central nucleus of the amygdala for 200 ethanol naïve mice (50/sex/genotype) from selection generation five were used to study differentially expressed genes (DEGs: 2996 genes, FDR < 0.05), differentially variable genes (DVs: 845 genes, FDR < 0.1), differentially wired genes (DWs: 1402 genes, FDR < 0.1), and to construct gene co-expression networks. High-preference network modules enriched in DEGs, DVs, DWs or in highly connected genes not found in the low-preference network were tested for gene ontology enrichment and observed to reproduce data from an earlier set of high and low ethanol preference lines. Ontologies significantly (FDR < 0.05) associated with risk for ethanol preference include: (1) Inflammatory response (Il34, Il17ra, Trl1, Trl6, Trl13, Dusp1), (2) Glutamatergic and GABAergic synapse (Dlg2, Dlg3, Dlg4, Dlgap2, Dlgap3, Gria3, Grin2b, Gabre, Gabrg1, Gabrq), (3) Cilia motility (Dynah6, Dynah7, Dynah10, Dynah11), and (4) Translation and Respiration (Rps*, Rpl*, Mrps*, Mrpl*, Ndufa3, Ndufa5, Ndufa10, Nduga13). These results nominate targets to be considered for manipulation to determine their impact on the development and persistence of alcohol drinking.

Poster 24

Inter-host social interactions and physical contact promote microbiota transmission

Laura Desban, Brynn Smith, Raghuveer Parthasarathy, Judith Eisen, Karen Guillemin

Sociality and group living confer many benefits, from the societal to the microbial. Recent studies in humans and non-human primates suggest that social networks can promote inter-individual transmission of beneficial microbes. However, microbial transmission has largely been investigated in the context of infectious diseases. In this project, we have characterized animal and microbial behaviors that mediate inter-host microbiota dispersal. We take advantage of the zebrafish model to carry out fine manipulations of social behaviors and microbial associations. We have uncovered novel patterns of social interactions associated with non-reciprocal microbiota transmission. We demonstrate that close physical contact facilitates direct transmission of zebrafish-associated bacteria, with variation between bacteria from different body sites. Finally, we show that specific microbial traits, such as high motility, can overcome host social isolation to promote dispersal. Together, our observations shed light onto mechanisms underlying social transmission of animal microbiomes.

Poster 25

Uncovering Genotype-Phenotype Relationships Across the Tbr1 Allelic Spectrum

Marissa Co, Cierra LeBlanc, Andrew Nishida, Kevin M. Wright, Brian J. O'Roak

De novo mutations in TBR1 (T-Box Brain Transcription Factor 1) confer increased likelihood of autism and other neurodevelopmental conditions. Clinical genetic data reveals a variety of TBR1 mutational subtypes and emerging genotype-phenotype correlations. To improve in vivo modeling of this allelic spectrum compared to multi-exon knockout mice, we generated mice carrying clinically relevant point mutations in Tbr1. Early-truncating mutations (p.A136fs, p.G346fs) abolish TBR1 protein, while a T-Box missense mutation (p.K228E) upregulates a hypofunctional protein. Despite their opposing effects on TBR1 levels, all mutations disrupt the anterior commissure axon tract, recapitulating a frequent MRI finding in human TBR1 patients. RNA-seq suggests dysregulation of extracellular matrix genes during cortical development, which could underlie dendritic and axonal defects found in Tbr1 mutants. Finally, in vitro analyses show differential impacts of p.K228E and C-terminal truncation (p.T532fs) on TBR1 protein functions, reflecting differences in clinical phenotypes between C-terminal variant carriers and other TBR1 variant carriers. Future studies will further decode TBR1-dependent molecular networks orchestrating cortical development and enhance our understanding of the neurobiology of autism.

Poster 26

Hepatic STAT3 signaling impairs ketogenesis and drives early pancreatic cancer cachexia

Paige C. Arneson-Wissink, Heike Mendez, Katherine Pelz, Jessica Dickie, Daniel L. Marks, Aaron J. Grossberg

Cancer cachexia is highly prevalent in pancreatic ductal adenocarcinoma (PDAC) patients and results in a decreased quality of life. Current literature lacks a complete understanding of the events that occur early in cachexia development, which limits our ability to identify therapeutic prevention strategies for cachexia. To better characterize early-stage cachexia, we evaluated a murine model of PDAC at 7-10 days after adult mice received orthotopic injections of the PDAC cell line KrasG12D; p53R172H/+; Pdx1-cre (KPC). We documented that mice early in PDAC development have increased muscle vulnerability to wasting after caloric deprivation. This early sign of cachexia was associated with impaired hepatic ketogenesis. Hepatic ketogenesis normally supplies energy-rich ketone bodies to fuel the brain, heart, and skeletal muscle when glucose is limited. Our work suggests that metabolic adaptation to nutritional stress is impaired in patients and mice with PDAC. PDAC mice had suppressed fasting blood ketone levels and octanoate challenge revealed impaired ketogenic potential in PDAC mice. This associated with decreased expression of genes regulating beta oxidation and ketogenesis in the liver (Ppara, Acox1, Acadm, Hmgcs2, Ehhadh, Acaa2, Bdh1). We hypothesized that inflammatory signaling in the liver through signal transducer and activator of transcription 3 (STAT3) leads to metabolic changes associated with impaired adaptive response to undernutrition during early-stage PDAC cachexia. Genetic ablation of interleukin 6 (IL-6) or STAT3 reversed metabolic deficits and prevented skeletal muscle loss. This led us to conclude that IL-6 signaling via STAT3 in hepatocytes impairs adaptive metabolism, makes PDAC mice vulnerable to nutritional stress, and promotes muscle wasting. Maintaining PDAC mice on a ketogenic diet recapitulated this effect, independently of proteolysis. This work expands on prior knowledge of IL-6 in cancer cachexia, implicates impaired hepatic metabolism as an early event in cachexia progression, and highlights the liver as a target for potential cachexia prevention strategies.

Poster 27

Role of peripheral inflammation in driving central nervous system inflammatory signature in pathogenesis of alzheimer's disease

Paula Sanchez-Molina, Alina Bogachuk, Carlos M Soto-Faguás, Randy L Woltjer, Sally A Cowley, Joseph F Quinn, Bahareh Ajami

Alzheimer's disease (AD) impacts an estimated 6.5 million people in the United States, but it cannot yet be prevented or halted. AD animal models are based on human mutations that cause amyloid-β (Aβ) pathological accumulation. However, the failure of the majority of Aβ-related clinical trials, has begged the necessity of an alternative approach to address AD therapies. Interestingly, most of the genetic and non-genetic risk factors for developing sporadic AD are associated with inflammation. It is known that microglia, the immune cells of the central nervous system, play a key role in the pathogenesis of AD. Moreover, people with systemic inflammatory diseases have a higher incidence of developing AD. In this context, we hypothesize that a specific subset of cells in peripheral blood contributes to AD development through its communication with microglial cells in the brain parenchyma.
To address this hypothesis, we have analyzed peripheral blood mononuclear cells (PBMCs) from sex- and age-matched healthy and AD subjects using CyTOF and CITE-seq technologies. Moreover, we used in vitro and histological approaches to study interactions between PBMCs and human microglial cells.
Our preliminary data show that blood from AD patients present a specific inflammatory subset of immune cells characterized by the upregulation of pro-inflammatory signaling pathways and cytokines. In addition, healthy PBMCs developed an inflammatory phenotype after stimulation with AD plasma. Histological analysis revealed the presence of T cells in contact with microglia in the parenchyma of AD brains, suggesting a drive of microglial cells towards an inflammatory phenotype that could contribute to AD pathology. Importantly, we demonstrated that microglia change their transcriptome after stimulation with PBMCs from AD donors.
Together, our data demonstrate the contribution of peripheral immune cells in AD and reinforce that studying AD as a multifactorial disease could be key to its prevention and treatment.

Poster 28

Simulation of 24-2 Visual Field Tests Using Nerve Fiber Layer Measurements from Disc Scans on Structural OCT and OCT Angiography

Po-Han Yeh, Ou Tan, Aiyin Chen, Eliesa Ing, Jie Wang, Yali Jia, David Huang

Background:
The relationship between nerve fiber layer thickness (NFLT) obtained from structural OCT and nerve fiber layer plexus capillary density (NFLP-CD) from OCT angiography and mean deviation on visual field tests is not linear. To address this issue, we aimed to develop new metrics, namely, nerve fiber layer mean deviation (NFL-MD) and nerve fiber layer plexus mean deviation (NFLP-MD), to enhance the correlation with visual field outcomes.
Method:
Our study included glaucoma patients exhibiting disc rim thinning or retinal nerve bundle defects, as well as healthy control participants. Disc scans were conducted using Solix, a spectral-domain OCT system (Visionix/Optovue, CA). The NFLT and NFLP-CD measurements were divided into eight sectors based on a modified Garway-Heath scheme. Each sector was further divided into four evenly tracks, resulting in a total of 32 tracks per scan. These track values were converted into a logarithmic dB scale and used to simulate sector visual field (VF) deviation through quadratic regression. The sector-simulated values were weighted and summed to calculate NFL-MD and NFLP-MD. Pearson correlations were employed to assess the relationship between NFL-MD, NFLP-MD, and VF-MD. A five-fold cross-validation approach was used to prevent overfitting. The diagnostic performance was evaluated using the area under the receiver operating characteristics curve (AROC).
Result
Our study enrolled 132 eyes from 132 participants, comprising 51 with perimetric glaucoma, 40 with pre-perimetric glaucoma, and 41 with control eyes. The Pearson correlation between NFL-MD and VF-MD was notably high at 0.773 (0.694-0.834), surpassing the correlation between NFL thickness and VF-MD, which was 0.589 (0.465-0.690). Similarly, the correlation between NFLP-MD and VF-MD was substantial at 0.793 (0.722-0.849), exceeding the correlation between NFLP-CD and VF-MD, which was 0.643 (0.535-0.734).
Conclusion
The simulated visual field tests based on OCT and OCT angiography demonstrated improved agreement with actual 24-2 visual field tests compared to the original NFL thickness and NFLP-CD. NFL-MD and NFLP-MD exhibited better diagnostic accuracy and reproducibility than actual VF-MD. Given their enhanced correlation with disease severity and reproducibility, these metrics may hold promise for improving glaucoma monitoring.

Poster 29

Targeted delivery of magnetic nanoparticles with ultrahigh heating efficiency for systemic hyperthermia

Prem Singh, Ananiya A. Demessie, Youngrong Park, Abraham S. Moses, Tetiana Korzun, Fahad Y. Sabei, Hassan Albarqi, Leonardo Campos, Cory R. Wyatt, Khashayar Farsad, Pallavi Dhagat, Conroy Sun, Olena Taratula, Oleh Taratula

Introduction: Magnetic fluid hyperthermia is an experimental cancer therapy that utilizes the capacity of magnetic nanoparticles to elevate intratumoral temperature upon exposure to an external AMF. According to prior preclinical and clinical research, an intratumoral temperature > 44 0C is typically needed to halt tumor growth. Low intratumoral heating efficiency of the currently available magnetic nanoparticles at clinical dosage of 10 mg kg-1 restrict the translation of magnetic hyperthermia from bench to bedside.

Methods: We have developed an advanced thermal decomposition method for the synthesis of novel cobalt-doped core (magnetite) – shell (maghemite) iron oxide nanoparticles (Co-Fe3O4/γ-Fe2O3). To achieve efficient delivery, their surface was modified with both PEG molecule and a peptide as a targeting moiety to LHRH receptors overexpressed ovarian carcinoma cells.

Results: Our data reveal that the low nitrogen flow rate during the thermal decomposition reaction results in cobalt-doped iron oxide nanoparticles with a magnetite (Fe3O4) core and a maghemite (γ-Fe2O3) shell with an ultrahigh ILP of 48.0 nH m2 kg-1. Our in vivo research shows that these nanoparticles containing a cancer-targeting peptide are biocompatible after being administered systemically at a concentration of 4 mg kg-1. When exposed to an external AMF (420 kHz, 26.9 kA m-1), the delivered nanoparticles elevate temperature in both subcutaneous and metastatic cancer tumors to 50 0C.

Conclusion: We have developed magnetic nanoparticles with an extremely high heating capacity by using an advanced thermal decomposition method. Our results suggest that low nitrogen flow rates during the synthetic procedure led to the production of nanoparticles with a magnetite core and maghemite shell.

Poster 30

Harnessing tissue specific immune memory for cancer early detection

Rashi Yadav, Joshua Moreau

Tissue-resident memory lymphocytes (Trms) are heterogenous T cell population with both effector and memory function. It has been established that these are long term resident that usually don't recirculate and are phenotypically and morphologically highly specialized for their local microenvironment. Trms have a guarding function as they provide first line of defense against reoccurring insults. In addition to immunosurveillance, they play an important role in maintaining homeostasis in the tissue of residence. On contrary to establishing a residence, there are few evidences where Trms re-enter the circulatory system. In our study, we are aiming to elucidate if Trms exit their tissue of residence in early melanoma patient and if they can be used as a biomarker for early detection of cancer. Here, we use matched tumor, healthy skin and blood samples to find if Trms can be detected and profile them using flow cytometry, single cell RNA seq and spatial transcriptomics.

Poster 31

Peripheral Nerve Interfaces and a Tool to Predict Stimulation-Induced Neural Tissue Damage

Rebecca A. Frederick

Electrical stimulation of peripheral nerves is used to restore motor function, supplement sensory feedback, and enhance neural plasticity. The desire to develop wireless neural stimulation devices presents unique technical challenges to achieving effective and beneficial neuromodulation. In this work, we present the results of a 9.5-month rodent study evaluating the performance of a novel wireless microelectrode array for neural stimulation. Additionally, this work presents a model for predicting the likelihood of stimulation-induced tissue damage from stimulation waveform parameters. A 16-electrode wireless device was implanted in the left sciatic nerve of n=6 female Sprague Dawley rats. Multiple assessments of both nerve function and device function were recorded at least every two weeks throughout the study. Data pulled from literature sources reporting both tissue outcomes and electrical stimulation parameters were used to develop the predictive model. The model uses a random forest algorithm and 12 different stimulation waveform parameters to predict if the stimulation is likely to damage neural tissue. Results of the 9.5-month study showed that implantation of the wireless interface did not cause significant functional deficit, and that the device could consistently control hindlimb motor function with current thresholds remaining stable across all 96 implanted electrodes. Our model was able to predict parameter classification as damaging or non-damaging with 88.3% accuracy, compared to the 63.9% accuracy of the most used model in the field (Shannon equation), when tested on the same dataset. This work provides new tools for advancing the development of safe and effective neuromodulation technology.

Poster 32

Disabling COX-2 S-Nitrosylation by CRISPR-Induced Mutation in Breast Cancer to Clarify the Role of COX2 in Disease Progression

Reuben Hoffmann, AeSoon Bensen, Elise De Wilde, Zheng Xia, Pepper Schedin

Post-partum breast cancer (diagnosed within ten years of childbirth) has poor outcomes. Breast involution, the process by which breast tissue returns to normal after lactation, is an inflammatory process that is thought to contribute to these poor outcomes. COX-2 (PTGS2) is a known regulator of breast involution and its associated inflammation and the primary target of Non-Steroid Anti-Inflammatory Drugs (NSAIDs). In many solid cancers, COX2 is involved in tumor progression and is an oncogene in various murine models, yet both its correlation to cancer progression as well as attempts to target it therapeutically have given mixed results. These incongruities may be due to post-translational modification; COX-2 undergoes S-nitrosylation, and the modified form (SNO-COX-2) correlated with epithelial to mesenchymal transition (EMT) in tumor cells in 3D culture, whereas non-nitrosylated COX2 did not correlate with EMT. To study the possible effect of COX-2 nitrosylation on tumor formation and progression, we aimed to develop a COX2 mutant breast cancer cell line, in which COX2 cannot be nitrosylated. MCF10ADCIS, an early-stage human breast cancer cell line, was transformed using CRISPR with a single disabling missense mutation at the nitrosylation site. Following transformation, 59 individual clones were isolated, and the site of mutation was sequenced. We identified 10 heterozygotic clones with the desired mutation, including one clone that also retained the WT allele as a classical heterozygote. Current studies are performing a second round of CRISPR to produce a homozygote COX2 loss-of-function cell line as well as validation of the mutant protein. The resulting cell lines, once validated, will be a model for the loss of nitrosylation while retaining otherwise-functional COX-2 in breast cancer cells. Our CRISPR approach will also be used to induce the same mutation in non-cancerous cell types in order to explore for tumor-intrinsic and -extrinsic roles of SNO-COX-2 in cancer progression.

Poster 33

Vitamin D metabolism is suppressed postpartum: implications for targeting the postpartum window for cancer prevention

Sarah Bernhardt, Pepper Schedin

Postpartum mammary gland involution is a physiologic inflammatory process that associates with increased risk of postpartum breast cancer (PPBC). In rodents, involution promotes breast cancer progression, and treatment with anti-inflammatory agents slows tumor growth. These data provide rationale for targeting the pro-tumor window of involution with anti-inflammatory agents for PPBC prevention. Here, we assessed the potential of vitamin D (VitD), an anti-inflammatory agent, for PPBC prevention.

To model VitD deficiency and supplementation, mice were fed diets deficient or supplemented with VitD for 4 weeks. Blood was collected from nulliparous (never-pregnant) and 2 days post-wean (involution) mice, and serum VitD (i.e., 25(OH)D) measured. Nulliparous mice supplemented with VitD showed a >2-fold increase in serum 25(OH)D (67.4±8.1nmol/L) compared to mice fed a deficient diet (28.7±11.7nmol/L, p<0.01). In contrast, supplementation of involution mice did not increase serum 25(OH)D (supplemented=46.6±8.7nmol/L, deficient=33.7±8.5nmol/L, p>0.05).

Activation of dietary VitD requires hydroxylation in the liver, producing circulating (25(OH)D) and active (1,25(OH)2D3) forms. Thus, reduced serum 25(OH)D during involution could be due to impaired VitD hydroxylation in the post-wean liver. RNAseq analysis of livers showed reduced expression of genes involved in vitamin D hydroxylation (Cyp2r1, Cyp27a1) during involution. Further, liver concentrations of 25(OH)D (1.3±0.6ng/g) and 1,25(OH)2D3 (0.3±0.2ng/g) were reduced in involution mice, compared to nulliparous mice (25(OH)D=2.0±0.4ng/g, 1,25(OH)2D3=0.9±0.4ng/g, p<0.05).

To understand how suppressed VitD metabolism affects the anti-cancer activity of dietary VitD, mammary cancer cells (D2A1, 2×104 cells) were injected into mammary fatpads of mice. In nulliparous mice, VitD supplementation associated with a 3-fold reduction in tumor growth (p=0.03); whereas no anti-cancer effects were observed in involution mice. These findings suggest the anti-cancer effects of VitD are blocked postpartum, due to suppression of VitD metabolism in the liver. To improve treatment outcomes for young mothers, an understanding of how the post-wean liver metabolizes various therapies is required.

Poster 34

Partial MHC Class II construct protects white matter function in EAE mouse model

Sarah Zerimech, Hung Nguyen, Halina Offner, Selva Baltan

Multiple Sclerosis (MS) is a chronic demyelinating disease with prominent axon dysfunction. Experimental autoimmune encephalomyelitis (EAE) is the most common animal model for MS study. DRα1-MOG-35-55 (DRhQ) is a partial major histocompatibility complex (MHC) Class II construct that promotes remyelination and axonal recovery, and limits EAE progression. However, no direct assessment of axonal function has been performed. In this study, we characterized axonal conduction properties in EAE using electrophysiology on corpus callosum (CC) slices obtained from EAE mice.

Male C57BL6 mice (8-12 weeks) were immunized with subcutaneous (s.c) injection of an emulsion of immunogenic peptide and complete Freund's adjuvant, and scored for signs of EAE until the day of experiment. DRhQ was injected s.c daily (5 days) beginning on day mice started displaying EAE signs (score=2). EAE score of control mice was between 4-5, while treated mice score was of 1. Extracellular compound action potentials (CAPs) were evoked across the CC on acute slices obtained from control and treated mice. CAPs displayed a typical 2-peak shape, representing fast (myelinated) and slow (unmyelinated) conducting axons. The functional integrity of CC axons was monitored by quantifying the CAP area. Excitability of CC axons was tested by evoking CAP at various stimulation intensities. Under baseline conditions, axon conduction properties remained similar between the groups, while axon excitability was lower in treated mice. Moreover, when we challenged the axon function with an ischemic episode, CAPs recovered better in treated mice compared to control. In addition, DRhQ treatment drastically preserved microglia, astrocytes, axons, and myelin against EAE induced injury.

Our results show that DRhQ effectively preserves white matter integrity and function after EAE, and support its therapeutic potential for clinic application.

Poster 35

Large scale expression of human proteome antigen libraries in E. coli

Sayandeep Gupta, Natanya Villegas, Carmen Resnick, Keane Deas, Calin Plesa

Antibodies are a class of proteins produced by the immune system in response to foreign invaders such as bacteria, viruses, and cancer cells. These proteins have become essential tools in medicine, with applications ranging from diagnostics to disease treatments to autoimmune disorders. However, the production of antibodies is a costly and time-consuming process, as it is currently carried out against a single antigen target at a time, increasing development time. We aim to enable a multiplexed antibody generation method using scalable technologies for gene synthesis, library-on-library screening, antibody generation, and in vivo protein-protein interaction assays. We aim to create a heterologous expression system enabling the generation of antibodies against all potential antigen targets in a target proteome and subsequently conducting proteome-scale tests of cross-reactivity. The general schema for the initial phase of the project involves leveraging gene synthesis technologies to construct proteome-scale gene libraries comprising over 13,300 full-length human proteins and to assess their aggregation and toxicity profiles in a heterologous expression system. Subsequently, we will implement a large-scale library-on-library selection for antibody-antigen interactions in vivo, utilizing a multiplexed protein fragment complementation assay. The culmination of this research aims to identify antibody hits that exhibit specificity, sequence verification, and the ability to interact with all antigens, thereby significantly reducing the cost of antibody generation and antibody-based biotherapeutic production.

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Poster 37

The dual role of urea as a new motif for hydrogen bond enhanced halogen bonding in anion recognition

Shiva Moaven, Thaís de Faria, Hannah Bates, Jessica Lohrman, Douglas Banning, Michael Haley, Darren Johnson

This project is over synthesis and application of a family of hydrogen bond enhanced halogen bond (HBeXB) donor for anion binding. Amino and amide functional groups have previously shown that they can increase the strength of the σ-hole of a halogen atom to bind to anions and perform catalysis. In this study, we showed that a urea motif can increase the strength of σ-hole on the halogen atoms, and the second urea hydrogen atom can cooperatively bind to anions with the halogen bond donor. To ensure that the measured binding affinities (Ka) are the result of cooperative hydrogen and halogen bonding, due to the possibility of the formation of binding conformation, we prepared two control receptors one containing Br which will be a weaker halogen bond donor compared to the original compound, and the second one will be an all-hydrogen bond donor receptor. The measured binding affinities for the bromo receptor and all hydrogen bond donors were lower and higher than the original receptor. These results were also further supported with DFT calculations and QTAIM to show that the binding energy of the HBeXB donor receptors will be about 30 kJ/mol lower than the hydrogen bonding receptor.

Poster 38

Enhancing Urea-Formaldehyde Microcapsules Stability through Additive Modulation

Sivashankari Rajasekaran, Bao Huynh, Ana Paula Fugolin

Abstract
Objective: Urea-formaldehyde networks are widely utilized for encapsulating healing agents to repair microstructural cracks in dental restorative materials under thermal and masticatory stresses. While this approach holds promise for extending the clinical lifespan of dental restorations, it faces challenges related to physicochemical stability and potential formaldehyde cytotoxicity. In this study, we explore a novel approach by combining melamine and a high-toughness acrylamide additive, N, N-Dimethylacrylamide (DMAM), to enhance the thermo-mechanical stability of poly (urea-formaldehyde) microcapsules (PUF) shells.
Methods: PUF microcapsules were prepared by the double emulsion method using mechanical stirring as the method of emulsification. The urea-formaldehyde shell was modified with different concentrations of melamine (0, 2.5, 5, 7.5 and 10%), encapsulating two different compositions of healing agents such as 100% T (TEGDMA-Triethylene glycol dimethacrylate) and a combination of 80% T (TEGDMA) + 20%D (DMAM). Microcapsule morphology was observed by optical and scanning electron microscopy and the images were utilized to calculate the average diameter using the ImageJ software. The yield of microcapsules (%) was calculated after each reaction and the encapsulation efficiency (%) was calculated using acetone extraction method. The microcapsules were incubated in various organic solvents for 24 hours to study their stability with the addition of DMAM and melamine.
Results: The incorporation of melamine significantly impacted the shell's characteristics, making them rougher as the melamine concentration increased. This change was also reflected in an increase in brittleness. The reaction yield percentage ranged from 60 to 85%, and the capsule size from 80 to 150 µm. On placing the microcapsules between a glass slide and cover slip for 30 minutes, 100T microcapsules broke and released the healing agent except for 100T-5% melamine microcapsules. Whereas 80T/20D capsules were stable up to 7.5% of melamine. From these studies we concluded the most effective combination was achieved with the addition of both the high-toughness additive DMAM and 5% melamine.

Poster 39

Gene flow toward prokaryotes divergence

Sophia Lambert, Stilianos Louca

The process of speciation has long been studied in evolution in part to understand the immense diversity of living organisms that once inhabited the Earth. In the case of prokaryotic organisms, our understanding of the microevolutionary mechanisms leading to speciation events is still scarcely understood on a wide taxonomical scale. Specifically, their mode of reproduction challenges our comprehensive view of barriers to gene flow in sympatry - a prerequisite to speciation.
Two models have been proposed to describe modes of speciation in non-sexually reproducing organisms. The two models differ mainly by the assumed frequency of homologous recombination among closely related lineages. The first model, the Ecotype model, assumes that homologous recombination within an ecotype is rare. Thus speciation can occur if a new genotype, abled to colonize a new niche, escapes the periodic selection from its former ecotype. The second model, the Recombination model, assumes that homologous recombination is frequent among closely related populations. Under that scenario, speciation occurs when mutation or recombination with distantly related lineages is frequent enough that it can lead to population divergence before recombination create enough cohesion among lineages.
As recombination rate appears to be highly variable among prokaryotic organisms, we do not expect one mode of speciation to be universal in the prokaryotic realm. To thoroughly investigate the modes of speciation across a wide range of prokaryotic taxon, we analyzed the distribution of single-nucleotide polymorphisms across around 200,000 prokaryotic assembled and complete genomes. This enables us to identify species-like unit characterized by genomic-wide selective sweeps (supporting the Ecotype model) as opposed to genetic-specific sweeps (supporting the Recombination model).
We believe that characterizing the desperate modes of speciation in the prokaryotic realm will pave the way to prokaryotic comparative analyses of speciation process. Natural extensions of this work would be to integrate species traits to understand the disparity of speciation modes in prokaryotes and potentially improve diversification models with more realistic microevolutionary mechanisms.

Poster 40

Glial Glutamate Transporters are Essential for Auditory Coding in the Ventral Cochlear Nucleus

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Auditory signaling in the cochlear nucleus (CN) is mediated by the transmitter glutamate acting on fast-gating postsynaptic AMPA receptors. Following glutamate release, it rapidly diffuses away and is taken up by glial glutamate transporters (e.g., EAATs1-3). At many synapses, this uptake process is slow compared to the timescale of fast transmission. In this study, we explored how glutamate re-uptake mechanism affects signaling at auditory nerve fibers (ANF) synapses onto T-stellate cells. These cells encode signal intensity by integrating AN inputs that fire as sound level increases. As the number of active fibers and their firing frequency increases with sound intensity, we hypothesized that removal of glutamate transients must be robust to keep up with such activity. To test this, we recorded from T-stellate cells and used a selective blocker of glutamate transporters. In control solutions, each strong EPSP generated a single spike regardless of the stimulus rate, and spiking quickly terminated after stimulus. As more fibers were recruited, more spikes were obtained up to a saturating level. By contrast, at low stimulation rates, transporter blockade caused doubling of spikes upon each stimulus, while at high frequencies the neurons continued to fire for hundreds of milliseconds after the end of the stimulus. A linear relation between stimulus number and spike output was lost upon transporter blockade. Delayed firing was caused by a large buildup of glutamate, evidenced by a slow decay of synaptic current that was blocked by AMPAR blockers. Transporters rapidly clear glutamate at these synapses, effectively isolating transmitter from nearby synapses to prevent pooling and spillover. As a result, these neurons can respond to increases in the rate of presynaptic spikes and number of active synapses with parallel increases in postsynaptic spike output. Thus, the activity of glial cells is essential to fast coding of signals in CN.

Poster 41

Unraveling PP2A's post translation control of MYC in onset & progression of PDAC

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Introduction
Deregulation of MYC and inactivation of the serine/threonine protein phosphatase 2A (PP2A) is persistently found in patients with pancreatic ductal adenocarcinoma (PDAC). PP2A modulates MYC activity through its degradation; however, the precise mechanism remains unclear. Small molecule activators PP2A (SMAPs) regulate the holoenzyme assembly consisting of a scaffolding-A subunit and a catalytic-C subunit, and over 40 distinct substrate directing regulatory-B subunits. In this study, we investigate if deregulation of MYC through loss of methylation of PP2A-C subunit drives PDAC initiation and progression.

Methods
We investigated the influence of SMAPs on MYC's stability using clinical specimens, cellular, and mouse models. Clinical specimens consisted of tissue microarray (TMA) from patients with pancreatitis and PDAC. Cellular models involved ex-vivo acinar cell assays and proximity ligation assays. Mouse models included caerulein-induced pancreatitis, genetic mouse models like Ptf1a-Cre; LSL-KRASG12D (KC) and LSL-Kras G12D;P53 R172H/+;Pdx1-Cre (KPC), along with pharmacological inhibition studies with SMAPs.

Results and discussion
Our TMA demonstrates a loss of Methyl-PP2A-C (Methyl-C) along with an increase in the stable and active phosphoform of MYC (p62MYC) as PDAC progresses from acinar-to-ductal metaplasia (ADM)-PanINs-PDAC. In ex-vivo ADM assays, SMAPs (DT061) treatment significantly decreased the transformation of acinar cells to duct-like cells compared to untreated acinar cells from WT and KC mice, suggesting that PP2A modulates the early events that drive pancreatic lesions. Furthermore, SMAPs reduced caerulein-mediated inflammation in normal mice and suppressed pancreatic PanIN lesion development and collagen deposition in caerulein-treated KC mice. This phenotype of SMAPs was correlated with decreased p62MYC levels and increased Methyl-C staining in caerulein-treated WT and KC mice. Also, in KPC mice, we observed DT061 reduced PDAC tumor growth which was correlated with decreased levels of p62MYC.

Conclusion
Together, our results indicate SMAPs, via its ability to negatively regulate MYC, as a viable therapy for high-risk individuals with chronic pancreatitis to prevent the onset of PDAC.

Poster 42

Coordinated assembly of branched actin networks by Dip1, Wsp1, and Arp2/3

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Branched actin networks is critical for cellular forces involved in endocytosis and cell motility. The seven subunit Arp2/3 complex is an actin nucleator that produce branched actin network upon activation by WASP family proteins. WISH/DIP/SPIN (WDS) family proteins activate Arp2/3 on their own or via synergy with WASP to generate linear actin filaments that are used by WASP-bound Arp2/3 complex to propagate branch network assembly . In Schizosaccharomyces pombe, Dip1 (WDS) and Wsp1 (WASP) are both required for normal actin assembly at endocytic sites. However, how dip1, the initiator of branched actin networks, and wsp1, the propagator, coordinately regulate the assembly of force-producing actin networks is unknown. The N-terminus of the of dip1 is required to rescue normal actin assembly and for localization of dip1 to endocytic sites, but is not required for Arp2/3 complex activation in vitro. These data suggest that dip1 must be recruited to endocytic sites to initiate branched actin assembly. We verified the importance of direct recruitment of dip1 by engineering a GFP-GFP nanobody interaction to artificially recruit dip1ΔN to endocytic sites. We used reconstituted actin-based motility assays to better understand how dip1 and wsp1 coordinately regulate Arp2/3 complex. These assays revealed that sub-micromolar concentrations of soluble Dip1 accelerate motility of Wsp1-conjugated beads. Higher concentrations of soluble dip1 cause actin assembly away from the bead surface, thereby consuming Arp2/3 complex and actin to hinder motility. Our data show how two Arp2/3 complex activators with distinct biochemical properties coordinate to generate branched actin networks.

Poster 43

Heart specific LIM protein (CSRP3), as a novel cardio-renal connector in acute cardiorenal syndrome-related CKD progression

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Background: Cardiorenal syndrome type 1 (CRS1) is acute kidney injury (AKI) caused by acute cardiovascular disease. AKI subsequently causes chronic kidney disease (CKD). Our translational CRS1 model, cardiac arrest and cardiopulmonary resuscitation (CA/CPR) causes AKI-CKD transition characterized by reduced GFR, increased fibrosis, renovascular hypertrophy, and elevated blood pressure. Heart specific LIM protein (CSRP3) was secreted into bloodstream and taken up by proximal tubules in the kidney. We hypothesized that cardiac CSRP3 mediates CRS1-induced AKI-CKD.

Method: We generated inducible cardiac CSRP3 KO mice (iCSRP3KO, csrp3 flfl/myh6 cre-esr1). CA/CPR was performed to inducible proximal tubules specific megalin KO mice (iMegKO), and iCSRP3KO mice. Renal ischemia reperfusion injury (IRI) mice were injected 5ug recombinant human CSRP3 (rCSRP3) or PBS. In addition, CSRP3-treated IRI mice received cilastatin, a FDA-approved megalin inhibitor, or vehicle (PBS). 49 days after surgery, GFR, αSMA expression, and renovascular wall thickness were analyzed. For in vitro study, primary culture of human proximal tubular epithelial cell (hPTEC) was treated with rCSRP3 then subjected to bulk RNA sequence or immunofluorescence imaging.

Results: rCSRP3 was megalin-dependently taken up by proximal tubules in vivo (iMegKO mice or cilastatin-treated mice) and in vitro (LRP2 siRNA treated hPTEC). SnRNA sequencing of CA/CPR kidney and bulk RNA sequencing of CSRP3 treated PTEC demonstrated similar alteration of fibrosis- and myogenesis-related genes. CSRP3-treated IRI mice (CSRP3-IRI) demonstrated reduced GFR (p<0.05), increased fibrosis (p<0.05) and renovascular hypertrophy (p<0.01) compared with PBS-treated IRI mice. iCSRP3KO mice demonstrated less severe CKD compared with littermate control Finally, genetical megalin deletion (iMegKO-CA/CPR) or pharmacological megalin inhibition (cilastatin-CSRP3-IRI) demonstrated higher GFR (p<0.05), less fibrosis (p<0.05), and less renovascular hypertrophy (p<0.01) compared with controls.

Conclusion: We demonstrated a novel cardiorenal interaction in CRS1 which depends on injury-induced CSRP3 release from the heart and renal uptake through the megalin-mediated endocytic system.