Agenda: June 22 ISG Networking Event

Much appreciation for your patience if the timing on our agenda becomes slightly off.
Presenter abstracts start on Page 2.

9:00AM	Welcome Rachel O'Neill, PhD, Director, Institute for Systems Genomics, UConn
9:10	*Expanding our knowledge of genome activation through epigenomics and expansion microscopy* **Antonio Giraldez, PhD, Fergus F. Wallace Professor of Genetics Chair, Genetics, Yale School of Medicine**
10:10	Coffee Break Poster Sessions: *Denegre, Fleck, Gilmore, Gupta, Ivanova, Phoenix, Tocco, Weiner, Zhai/Woodruff*
10:55	Welcome Back
11:00	*Applications of Deep Learning in Translational Oncology* **Jill Rubinstein, PhD, The Jackson Laboratory for Genomic Medicine and Hartford Healthcare**
11:20	*Splicing-associated mechanisms in AML drug resistance* **Eric Wang, PhD, Assistant Professor, The Jackson Laboratory for Genomic Medicine**
11:40	*Janus Base Nanopiece: A Novel Delivery Technology for Gene Editing* **Yupeng Chen, PhD, Associate Professor, Biomedical Engineering, UConn**
12:00	Lunch Break Poster Sessions: *Akella, Child, Ferraj, Khouri-Farah, Francoeur, Jin, Wanner, Yuan*
1:00	Welcome Back
1:05	*Regulation of lipid absorption by intestinal lymphatics* **Georgia Zarkada, MD, PhD, Assistant Professor, Department of Physiology and Neurobiology, UConn**
1:25	*Altered Anti-Viral Immune Responses in Monocytes in Overweight Heavy Drinkers* **Adam Kim, PhD, Assistant Professor of Medicine, UConn Health**
1:45	*Kinetic networks identify key regulatory nodes and transcription factors in differentiation cascades* **Michael Guertin, PhD, Associate Professor, Genetics and Genome Sciences, UConn Health**
2:05	Closing Remarks & Poster Awards Announcement Brenton Graveley, PhD, Associate Director, Institute for System Genomics,UConn Health

Abstracts:

Janus Base Nanopiece: A Novel Delivery Technology for Gene Editing

Yupeng Chen, PhD, Associate Professor, Biomedical Engineering, UConn

The emerging DNA nanotechnology has made a remarkable impact on intracellular delivery of nucleic acids. Janus base nanomaterials (JBNs), designed and developed by my lab, are a new family of materials self-assembled from small-molecule units mimicking DNA base pairs. Unlike conventional DNA nanomaterials, JBNs are not restricted by the natural DNA structures, so they have great versatility to be engineered into different nanostructures for a broad range of applications. Here, we will demonstrate to use the JBNs to form rod-shaped nanoparticles, named Janus base nanopieces, which were specifically designed for the intracellular delivery of large mRNA such as the Cas9 mRNA for gene editing. Therefore, the Janus base nanopiece is a powerful tool for gene engineering in vitro and in vivo.

Expanding our knowledge of genome activation through epigenomics and expansion microscopy

Antonio Giraldez, PhD, Fergus F. Wallace Professor of Genetics
Chair, Genetics, Yale School of Medicine

Development begins with a single-cell zygote, the product of the union of sperm and oocyte. Upon fertilization, the zygotic genome undergoes extensive developmental reprogramming during the Maternal-to-Zygotic transition (MZT), which confers a totipotent state upon the zygote. This universal step in animal development results in the activation of the zygotic genome, the reprogramming of maternally inherited regulators, and the initiation of embryonic development. My laboratory investigates the mechanisms that regulate the activation of the genome and the post-transcriptional regulation of the maternal mRNAs with the goal of drawing common principles in biology.

In this seminar I will present our recent research on the mechanisms that control genome activation and the sequence of events that dictate chromatin reprogramming to stablish developmental competency during genome activation. I will further discuss our recent work on using imaging and expansion microscopy to directly visualize the interplay between changes in chromatin structure and transcriptional activation during cellular reprogramming. We have developed a super-resolution imaging method termed Chromatin Expansion Microscopy (ChromExM) that is capable of resolving individual nucleosomes with multimodal labelling capabilities in developing embryos, approaching ~3nm resolution. Using this method we have visualized the interaction between transcription factors and nucleosomes, the recruitment of RNA Pol II to specific genes by TFs, and transcribing RNA Poll II in string-like nanostructures associated with nascent RNAs. I will discuss how these methods have provided a new model for transcriptional activation and how ChromExM is a broadly applicable method to uncover principles of transcriptional organization and enhancer-promoter interactions during genome activation.

Kinetic networks identify key regulatory nodes and transcription factors in differentiation cascades

Michael Guertin, PhD, Associate Professor, Genetics and Genome Sciences, UConn Health

Adipocytes contribute to metabolic disorders such as obesity, diabetes, and atherosclerosis. Prior characterizations of the transcriptional network driving adipogenesis overlook transiently acting transcription factors (TFs), genes, and regulatory elements that are essential for proper differentiation. Moreover, traditional gene regulatory networks provide neither mechanistic details about individual RE-gene relationships nor temporal information needed to define a regulatory hierarchy that prioritizes key regulatory factors. To address these shortcomings, we integrate kinetic chromatin accessibility (ATAC-seq) and nascent transcription (PRO-seq) data to generate temporally resolved networks that describe TF binding events and resultant effects on target gene expression. We identify Twist2 as a previously unappreciated effector of adipocyte differentiation. We find that TWIST2 acts as a negative regulator of 3T3-L1 and primary preadipocyte differentiation. We confirm that Twist2 knockout mice have compromised lipid storage within subcutaneous and brown adipose tissue. This network inference framework is a powerful and general approach for interpreting complex biological phenomena and can be applied to a wide range of cellular processes.

Altered Anti-Viral Immune Responses in Monocytes in Overweight Heavy Drinkers

Adam Kim, PhD, Assistant Professor of Medicine, UConn Health

Alcohol abuse causes increased susceptibility to respiratory syndromes like bacterial pneumonia and viral infections like SARS-CoV-2. Heavy drinkers (HD) are at higher risk of severe COVID-19 if they are also overweight, yet the molecular mechanisms are unexplored. Single-cell RNA-seq (scRNA-seq) was performed on peripheral blood mononuclear cells from lean or overweight HD and healthy controls (HC) after challenge with a dsRNA homopolymer (PolyI:C) to mimic a viral infection and/or with lipopolysaccharide (LPS). All monocyte populations responded to both PolyI:C and LPS with pro-inflammatory gene expression. However, expression of interferon stimulated genes, essential for inhibiting viral pathogenesis, was greatly reduced in overweight patients. Interestingly, the number of upregulated genes in response to PolyI:C challenge was far greater in monocytes from HD compared to HC, including much stronger pro-inflammatory cytokine and interferon-γ signaling responses. These results suggest increased body weight reduced anti-viral responses while heavy drinking increased pro-inflammatory cytokines.

Applications of Deep Learning in Translational Oncology

Jill Rubinstein, PhD, The Jackson Laboratory for Genomic Medicine and Hartford Healthcare

An overview of multiple computational oncology studies that integrate clinical, genomic, and imaging data to explore the dynamics of tumor heterogeneity and evolution in response to treatment. I will present brief summaries of several research avenues ranging from digital pathology projects using publicly available molecular and imaging datasets to longitudinal studies of BRAF-mutant PDX mouse models undergoing targeted treatment. The underlying theme is the integration of diverse, high-dimensional data types to drive the development of tools with translational applicability, while improving our understanding of tumors' evolutionary dynamics.

Splicing-associated mechanisms in AML drug resistance

Eric Wang, PhD, Assistant Professor, The Jackson Laboratory for Genomic Medicine

Acute myeloid leukemia (AML) is the most common type of acute leukemia in adults and continues to have a dismal prognosis (~25% five-year overall survival)[1]. Approximately 50% of AML patients will undergo disease relapse due to intrinsic or acquired resistance to standard AML therapies. The presence of low tumor mutational burden in relapsed AML patients suggests that non-genetic mechanisms that contribute to drug resistance. We have recently uncovered RNA splicing factor vulnerabilities in acute leukemias[2,3], underlining the importance of the splicing machinery to support tumor maintenance. However, splicing -associated mechanisms that promote the transition to a treatment-resistant state in AML remain poorly understood. Here we have performed CRISPR/Cas9 screens and identified splicing factors that modulated AML responsiveness to venetoclax therapy through mis-splicing of anti-apoptotic proteins. Moreover, analysis of patients that relapsed from chemotherapy identified that the long isoform of RUNX1 (RUNX1C) is critical for driving chemoresistance in AML. Altogether these findings implicate the importance of splicing alterations that influence drug response in AML patients as well as therapeutic strategies to overcome resistance.

Regulation of lipid absorption by intestinal lymphatics

Georgia Zarkada, MD/PhD, Assistant Professor, Department of Physiology and Neurobiology, UConn

Lymphatic vessels are responsible for tissue drainage, and their malfunction is associated with chronic diseases. Lymph uptake occurs via specialized open cell-cell junctions between capillary lymphatic endothelial cells (LECs), while closed junctions in collecting LECs prevent lymph leakage. LEC junctions are known to dynamically remodel in development and disease, but how lymphatic permeability is regulated remains poorly understood. By studying the permeability of intestinal lymphatic capillaries to lipoprotein particles known as chylomicrons, we uncover Rho-associated kinase (ROCK)-dependent cytoskeletal contractility as a fundamental mechanism of LEC permeability regulation. Antagonistic inputs into ROCK-dependent cytoskeleton contractions balance the interconversion of lymphatic junctions in the intestine and regulate chylomicron absorption in response to dietary lipid ingestion.

Posters:

The First Genome Reference for the Tropical Legume, *Inga vera*, and Comparative Analysis of Genes Involved in Nitrogen Fixation Among the *Fabaceae*

Presenter name: Harshita Akella, Undergraduate
Affiliated Lab: Wegrzyn Lab, Department of Ecology and Evolutionary Biology, UConn

Abstract: *Inga vera*, a tropical plant native to South America, is a lesser-known legume of the Mimosoid clade under the subfamily Caesalpinioideae in *Fabaceae*. *I. vera* has local importance, including being used as shade plants for coffee and cocoa plantations. The legume *I. vera* fixes nitrogen (N), which is an ecologically important trait that converts atmospheric N2 to NH3 (ammonia), making N accessible for plant development and growth. The Nodule Inception (NIN) genes and NLPs (NIN-like Proteins) are involved in N fixation in legumes by regulating root nodule formation through nitrate signaling. Previous comparative genomic analyses in the *Fabaceae*, in particular, the subfamilies *Caesalpinioideae* and *Papilionoideae*, focused on *Glycine max* (Soybean), *Lotus japonicus*, *Phaseolus vulgaris* (Green beans), and *Medicago truncatula* and identified NINs and NLPs as important regulators of root nodule formation. However, the focus largely remained within *Papilionoideae*, which is the 'pea-

flowering' legume sub-family containing well-known crop species with economic benefits.

Due to the lack of genomic data for *Caesalpinioideae*, especially the Mimosoid clade, a genome of *I. vera* would be an important resource to enable analyses of gene family homologs for NINs and NLPs involved in N fixation and root nodule symbioses (RNS) with a well-represented group of species within *Fabaceae*. *I. vera* would also be the first member of the *Inga* genus to have its genome sequenced.

Understanding Splicing Regulation during Human Heart Organogenesis

Presenter name: Kevin Child, Postdoctoral Fellow
Affiliated Lab: Cotney Lab, Department of Genetics and Genome Sciences, UConn Health
Abstract: Congenital Heart Defects (CHDs) are the most common congenital abnormality worldwide, affecting approximately 1% of all births. Controlled gene expression during cardiac development, particularly through organogenesis, is crucial for normal development. Our lab has directly examined both chromatin state and composite level gene expression ranging from Carnegie stages (CS) 13 to 23 (4 to 8 post-conception weeks). We identified a module of genes with dynamic expression through this period that significantly enriched for genes involved in RNA splicing and processing. Given the dynamic nature of splicing at later timepoints and the module of genes related to regulation of splicing, we sought to investigate splicing in the organogenesis phase. When we compared alternative splicing (AS) between our 8 CS timepoints, we find 3,749 genes with AS events within this period. These are distinct from our previously reported differentially expressed genes but also enriched for genes related to cardiac development. We also found evidence for splicing events which result in previously unannotated transcripts. To confirm these results, we performed Nanopore long-read sequencing of cDNA libraries from our samples. Using a combination of long- and short-read data we generated a comprehensive, novel cardiac-centric gene annotation. From this analysis we identified 13,137 novel transcripts including several variants of well-known cardiac genes. One example is TBX5, a gene which mutations have been implicated in Holt-Oram Syndrome, that contains a novel TSS with high conservation and constraint in humans. Understanding transcript utilization and AS will lead to better screening for CHDs clarifying the unexplained CHD cases.

Blame Grandpa: Transgenerational Effects on Mouse Behavior Due to X chromosome Epimutation

Presenter name: Katelyn Denegre, PhD Candidate
Affiliated Lab: M. O'Neill Lab, Department of Molecular and Cell Biology, UConn

Structural Variation Leads to Transcript Diversity in Mice

Presenter name: Ardian Ferraj, PhD Candidate

Affiliated Lab: Beck Lab, The Jackson Laboratory for Genomic Medicine and UConn Health
Abstract: Structural variants (SVs) are differences in DNA ≥ 50 nucleotides. Although SVs occur less frequently when compared to single nucleotide variants and small insertions and deletions, nucleotide changes caused by SV vastly outnumber other variant types in diverse mammalian populations. Recent advances in long-read DNA sequencing technology allow for more complete resolution of SV. Although SVs have been extensively characterized in diverse human and mouse genomes, their effect on

host transcription genome-wide is largely unknown. We recently conducted long-read sequencing to characterize SVs in a cohort of genetically diverse inbred mouse genomes. Here, we utilize these assemblies in conjunction with long-read RNA sequencing on 10 mouse embryonic stem cell (mESCs) lines derived from unique strains to resolve transcript variation due to SV. By aligning RNA long reads to assemblies of the individual animals, we have characterized mESC transcripts that are directly tied to SVs. We find over 3,738 transcripts which contain SV sequences, arising from 1,729 unique SVs. By comparing our isoform libraries to the Gencode reference, we find that 34% (1,282) of SV-containing isoforms are novel, with 20% (740) containing novel exons and splice donor and/or acceptor sites. Lastly, we performed differential isoform expression analysis to find rare instances of SV-containing isoforms that are differentially expressed when compared to canonical isoforms found in Gencode. These data indicate that SV sequences are present in novel transcripts and that SVs contribute to transcriptomic diversity in diverse mouse populations.

Novel gene evolution and 3D genome organization

Presenter name: Katherine Fleck, PhD Candidate
Affiliated Lab: Erceg Lab, Department of Molecular and Cell Biology, UConn
Abstract: Genome organization may be intricately tied to regulating genes and associated cell fate decisions. Recent technological advances in mapping of chromosomal interactions and single-cell imaging have provided insights into chromatin organization at various levels including domains, loops, and boundaries. However, how the placements of genes of different evolutionary age in the 3D genome landscape relate to their biological role remains unclear. In this study, we examine the positioning and functional associations of human genes, grouped by their evolutionary age, within the 3D genomeorganization. We reveal that genes of different evolutionary origin have variable positioning relationships with both domains and loop anchors, but remarkably consistent associations with boundaries across cell types. The functional associations of each grouping of genes are primarily cell type-specific, however, those with recently evolved genes are sensitive to 3D genome architecture. Moreover, the sensitivity of such recent genes in diseased state is more pronounced in loop anchors compared to domains. We complement these findings with analysis of the expression from genes of differing evolutionary ages across cell types. Altogether, these distinct relationships between gene evolutionary age, their function, and positioning within 3D genomic features may contribute to understanding tissue-specific gene regulation in development and disease.

Segmental duplication-mediated variation across diverse mouse genomes

Presenter name: Eden Francoeur, PhD Candidate
Affiliated Lab: Beck Lab, Biomedical Science, UConn Health and The Jackson Laboratory for Genomic Medicine
Abstract: Segmental duplications (SDs) are amongst the most rapidly evolving regions of mammalian genomes and are a major source of variation within a species. SDs are large (>1kb), highly homologous DNA sequences (>90%) that constitute >5% of the mouse genome. The homology between SDs and the orientation of the repeats—direct or indirect—can lead to ectopic rearrangements resulting in large structural variants (SVs), specifically deletions, duplications, and inversions. Previous studies have identified SD-mediated rearrangements responsible for reproductive, immune, and behavior related differences between mouse strains. While these SVs have been identified at targeted loci, the extent of SD recombination resulting in SVs between diverse subspecies of mice is unknown. Using parameters from the literature, we have determined that ~22% of direct and ~24% of indirect SDs present in the mouse genome

are potential candidates for recombination. To test our hypothesized regions for SD-mediated variation in mice, we used our orthogonal datasets of short-read sequencing, long-read sequencing, and optical mapping from 10 diverse strains and identify 9 inversions, 155 duplications, and 321 deletions with support from at least two of the three orthogonal methods. Many of these SVs lead to copy number variation of genes, including olfactory receptor genes. We further examined the breakpoints of SDs to give insights into SD origin in the mouse genome, and found a significant enrichment for LINE transposons flanking SDs. With our SD-mediated variation predictions, callset, and breakpoint enrichment analysis, we are investigating how transposons and SDs act as drivers of genomic and transcriptomic evolution.

Identifying key underlying regulatory networks and predicting targets of orphan box C/D SNORD116 snoRNAs in Prader-Willi Syndrome

Presenter name: Rachel Gilmore, PhD Candidate
Affiliated Lab: Cotney Lab, Department of Genetics and Genome Sciences, UConn Health
Abstract: Prader-Willi Syndrome (PWS) is a neurodevelopmental disorder caused by loss of paternal expression of an imprinted region on chromosome 15. PWS is characterized by initial hypotonia and failure-to-thrive, followed by hyperphagia and obesity. Therapeutic intervention is focused on ameliorating symptoms as there is no cure. Most PWS cases exhibit megabase-scale deletions encompassing the imprinted chr15q11-q13 locus. Recently, several PWS patients have been identified harboring a much smaller deletion encompassing primarily the *SNORD116* gene cluster, composed of 30 copies of individual *SNORD116* box C/D snoRNAs. This finding suggests *SNORD116* is a direct driver of PWS phenotypes. However, *SNORD116* snoRNAs are termed ‘orphans’ because no verified targets have been identified. It is crucial to identify the targets and functions of *SNORD116* snoRNAs because all reported PWS cases lack their expression.

To begin addressing this, we engineered two different deletions modelling PWS in two distinct hESC lines to control for genetic background. We also utilized an inducible Neurogenin-2 expression system to enable quick, reproducible differentiation of these lines into neurons. Performing bulk RNA-sequencing on resulting neurons allowed us to identify a novel list of ~40 genes transcriptionally dysregulated in our PWS-like systems. Importantly, our results showed it is critical to use multiple isogenic cell line pairs as this eliminated many spuriously differentially expressed genes. Employing the recently described computational tool snoGloBe, we discovered these dysregulated genes are significantly enriched for predicted *SNORD116* targeting versus control analyses. Our results indicate a novel gene regulatory network controlled by *SNORD116* is likely perturbed in PWS patients.

Ampyra (drug used to alleviate motor symptoms of multiple sclerosis) Potently Modulates Ethanol-Induced Effects on the Neuronal Spontaneous Electrical Activity

Presenter name: Violetta Ivanova, Postdoctoral Fellowtoral Fellow
Affiliated Lab: Antic Lab, Department of Neuroscience, UConn Health
Abstract: Significant research effort is invested in finding additional chronic pharmacotherapy that would promote reductions in alcohol (Ethanol) intake. However, a pharmacotherapy for treating acutely intoxicated patients (for example, young people after party) and saving their lives in the emergency room is currently missing. Keeping such patients awake, agile and respiratory-compensated with a help of adjuvant drugs may be useful. We found an alcohol-induced depression of synaptically evoked

population voltage (network) responses in all layers of the mouse frontal and parietal cerebral cortex; this depression can be reversed by application of 4-aminopyridine aka dalfampridine (Ampyra™). Ampyra is a "*neuron excitability booster*" used to improve walking in patients with multiple sclerosis. In our hands, in brain slices pretreated with debilitating concentrations of Ethanol (20 mM), bath application of Ampyra restores the amplitude and propagation of evoked synaptic depolarizations. The aforementioned experiments have addressed the synaptic transmission specifically, because our population voltage signals are dominated by EPSPs occurring in massive dendritic trees of cortical pyramidal neurons, while the neuronal action potentials (spikes) are filtered out (do not contribute to the optical signals significantly). To address neuronal spiking specifically, we investigated the effects of Ethanol and Ampyra on cultured mouse neurons. We found that at a concentration of 20 mM, Ethanol caused a significant increase in the amount of spontaneous neuronal activity (spiking), while at a higher concentration of 40 mM, it actually decreased the number of spikes in the neuronal culture. Interestingly, in the presence of either 20 mM or 40 mM of Ethanol, bath application of Ampyra was able to increase the spiking frequency of the cultured cortical neurons. Our findings suggest that Ampyra is a potent modulator of Ethanol-induced changes in the cerebral cortex. Even in the presence of Ethanol-induced increase in spontaneous spiking, Ampyra was able to further increase the spiking frequencies of the neurons. Notably, at 20 mM concentration, Ethanol decreases the amplitude of EPSPs in brain slice preparations but increases the spiking of neurons in cell culture. Overall, our results indicate that Ampyra could be a promising treatment for acute alcohol intoxication, as it may help alleviate the suppressive effect of alcohol on neuronal functions (EPSPs and spiking).

NaP-TRAP-Seq: An approach to study the role of mRNA *cis*-elements in translational regulation

Presenter name: Amit Gupta, Postdoctoral Fellow
Affiliated Lab: Beaudoin Lab, Department of Genetics and Genome Sciences, UConn Health

Identification and Functional Characterization of Alternative Transcripts of LncRNA HNF1A-AS1 and Their Impacts on Drug Metabolism

Presenter name: Jing Jin, PhD Candidate
Affiliated Lab: X. Zhong Lab, Department Pharmaceutical Sciences, UConn

Foxp1 and Foxp2 regulate cerebellar hemisphere formation by controlling the diversification of Purkinje cells

Presenter name: Nagham Khouri-Farah, PhD Candidate
Affiliated Lab: Li and Cotney Labs, Department of Genetics and Genome Sciences, UConn Health
Abstract: Purkinje cells (PC) are the sole output neurons of the cerebellar cortex and play a pivotal role in cerebellum functioning. Furthermore, PC are presumed to orchestrate cerebellar development by regulating the differentiation of other cerebellar cell types. In the mammalian cerebellum, PC display transient molecular heterogeneity during development. However, the underpinnings of PC heterogeneity remain poorly understood due to the lack of entry to assess individual PC subtypes. Through single-cell RNA sequencing, we identified 11 molecularly distinct PC subtypes in the embryonic mouse cerebellum. Using CyCIF, a highly multiplexed immunofluorescence imaging method, and light-sheet fluorescent microscopy (LSFM), we assigned PC subtypes to their positions and resolved their three-dimensional distribution in the

cerebellar cortex. Different subtypes of PCs form distinct cell clusters coinciding with the anteroposterior and mediolateral patterning of the developing cerebellum. Remarkably, PC subtypes display distinctive combinatorial expression patterns of *Foxp1* and *Foxp2*, which have been implicated in developmental speech and language disorders and Autism in humans. Through single-cell genomics and quantitative spatial transcriptomic analysis, we showed that cerebellum-specific deletion of *Foxp1* and *Foxp2* disrupted a subset of PC subtypes and the formation of the cerebellar hemisphere. Together, our findings demonstrate that *Foxp1* and *Foxp2* act in concert to govern the differentiation of PC subtypes and, subsequently, control the formation and expansion of the cerebellar hemispheres, which is an innovative feature of the mammalian cerebellum and is involved in higher cognitive functions.

Single Cell Transcriptomic Analysis of Breast Tumor Endothelial Cell Populations Reveal Distinct Phenotypes of Vascular Subpopulations

Presenter name: Kathryn Phoenix, PhD Candidate
Affiliated Lab: Claffey Lab, Department of Cell Biology, UConn Health

Spectrum of lesions associated with West Nile viral infections in 7 birds and 1 alpaca from southern New England

Presenter name: Natalie S. Tocco, DVM,MSC Candidate
Affiliated Lab: Connecticut Veterinary Medical Diagnostic Laboratory, UConn

Distance-Based Reconstruction of Single-Cell Tumor Phylogenies

Presenter name: Samson Weiner, PhD Candidate
Affiliated Lab: Bansal Lab, Department of Computer Science & Engineering, UConn
Abstract: Somatic copy number aberrations (sCNAs) are key drivers for cancer initiation and proliferation, and play an important role in shaping the heterogeneous genomic landscape within tumors. This makes them ideal phylogenetic markers for inferring evolutionary relationships among tumor cell subpopulations and characterizing intra-tumor heterogeneity. Furthermore, advances in single-cell DNA sequencing (scDNA-seq) technologies are making it possible to obtain sCNAs datasets of tumor populations at ever-larger scales. As a result, several sophisticated methods have been proposed to reconstruct phylogenies using sCNA data, including methods that explicitly model copy number evolution. However, such methods are often too slow for large datasets. Moreover, there is incomplete understanding of how the performance of such methods is affected by error and other features of the analyzed datasets. In this work, we propose two simple distance-based phylogeny reconstruction approaches based on single-cell copy number profiles. Using a wide range of realistically simulated datasets, we find that these two distanced-based approaches consistently outperform other, more sophisticated methods in terms of both scalability and, surprisingly, accuracy.

Utilizing Whole Exome Sequencing for the Assessment of Unclassified Glycogen Storage Diseases and Disorders of Energy Metabolism

Presenter name: Corbinian Wanner, MD/MPH Candidate
Affiliated Lab: GSD Laboratory/ Lee Lab, School of Medicine, UConn Health

The fungal microbiome of the upper airway is associated with future loss of asthma control and exacerbation among children with asthma

Presenter name: Hanshu Yuan, PhD Candidate
Affiliated Lab: Y. Zhou Lab, School of Medicine, UConn Health

Egg consumption alters T cell-related gene expression and the capacity of HDL to modulate $CD4^+$ T cell activation

Presenter names: Fangyi Zhai, MA Candidate, Rachael Woodruff, Undergraduate
Affiliated Lab: Anderson Lab, Department of Nutritional Sciences, UConn

Abstract: We investigated whether consuming egg whites vs. whole eggs impacts peripheral blood mononuclear cell (PBMC) gene expression and whether changes in PBMC gene expression correlate with HDL profiles. Moreover, we investigated whether HDL following egg intake could directly regulate T cell activation and whether T cell effects were associated with changes in HDL composition. Healthy men and women (n = 26) participated in a 16-week randomized, crossover intervention trial in which they followed a 4-week diet free of eggs, 3 whole eggs/day or 3 egg whites/day. We observed that consumption of whole eggs altered PBMC mRNA expression of T cell-related genes relative to other diet deriods, while increasing LPS-induced PBMC IL-1β secretion. Notably, changes in the expression of genes related to T cell activation, differentiation, chemotaxis, and survival were positively correlated with changes in serum concentrations of total and large HDL. Independent of egg intake, HDL dose-dependently increased T cell counts and IL-2 secretion, while decreasing lipid rafts. In evaluating diet effects, we observed that HDL following the whole egg and egg white diet periods significantly increased lipid raft formation relative to an egg-free diet, and that HDL following whole egg intake increased T cell receptor-mediated IL-2 secretion compared to HDL following the egg white diet. Moreover, egg-induced changes in HDL proteomic and lipidomic composition correlated with HDL-mediated regulation of activated Jurkat IL-2 secretion. Our findings suggest that changes in PBMC gene expression and CD4+ T cell activation following egg intake correlate with changes in HDL profiles.