Agenda: ISG Networking Event
September 26, 2024

Much appreciation for your patience if the timing on our agenda becomes slightly off.

Presenter abstracts follow the agenda.

9:00AM	Welcome **Rachel O'Neill, PhD, Director, Institute for Systems Genomics, UConn**
9:10	*Future-proofing the Anthropocene using museomics - Koalas, cockatoos, and dark data* **Rebecca N Johnson, CW Whitney Chief Scientist and Associate Director for Science, Smithsonian National Museum of Natural History**
10:10	Coffee Break Poster Sessions: Ganesh, Gupta, Riccard, Vuruputoor, Webser, Weiner
10:55	Welcome Back
11:00	*Estimating co-evolutionary and co-introgression networks from publicly available data* **Andrius J. Dagilis, PhD, Assistant Professor, Department of Ecology and Evolutionary Biology, UConn**
11:20	*The Effect of Metformin on Influenza Vaccine Responses in Nondiabetic Older Adults* **Jenna M. Bartley, PhD, Assistant Professor, Department of Immunology, UConn Health**
11:40	*Engineering Tools to Interrogate The Host Immunity, Microbiome, and Their Interactions* **Sasan Jalili, PhD, Assistant Professor, JAX-GM, Department of Immunology, UConn Health, Biomedical Engineering Department, UConn**
12:00	*Natural Killer Immune cells in Health and Disease* **Silke Paust, PhD, Professor, JAX-GM**
12:20	Lunch Break Poster Sessions: Fleck, Lin Lab, Myles, Standish, Struba, Wang

1:20 Welcome Back

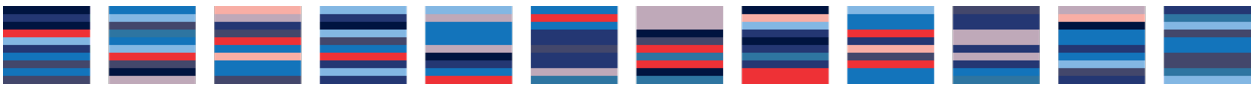
1:25 *The role of methane-producing anaerobes in One Health*
Michel Geovanni Santiago-Martínez, PhD, Assistant Professor, Department of Molecular and Cell Biology, UConn

1:45 *Using genomics to understand plant metabolic diversity*
Karolina Heyduk, PhD, Assistant Professor, Department of Ecology and Evolutionary Biology, UConn

2:05 *Identification of cell-free circulating nuclear DNA in older adults with depression*
Breno Diniz, MD, PhD, Associate Professor, UConn Center on Aging Department of Psychiatry, UConn Health

2:25 *Who Understands Scientific Knowledge Better: Judges or Scientists?*
Robert Bird, M.B.A., J.D., Professor of Business Law, School of Business, UConn

2:45 Closing Remarks & Poster Awards Announcement
Brenton Graveley, PhD, Associate Director, Institute for System Genomics,UConn Health



Abstracts:

Future-proofing the Anthropocene using museomics - Koalas, cockatoos, and dark data

Rebecca N Johnson, CW Whitney Chief Scientist and Associate Director for Science, Smithsonian National Museum of Natural History

Some biologists estimate that up to 35% of animals and plants could become extinct in the wild by 2050 due to global climate change. This alarming reality highlights the urgent need for innovative solutions to understand and conserve biodiversity. Fortunately, a hidden tool lies within the walls of natural history museums – vast collections of biological specimens. These collections are not just a static record of the past, but rather a trove of data waiting to be unlocked.

The Smithsonian's National Museum of Natural History (NMNH) houses the world's largest collection of biological specimens. These collections hold a wealth of information about past ecosystems and can offer crucial insights into how species have adapted and changed over time. However, much of this data remains inaccessible, locked away as "dark data."

At the NMNH, we are committed to unlocking this hidden potential. By utilizing new technologies, we are transforming museum collections into powerful tools for

conservation. I will give some examples from wildlife genomics, from cockatoos to koalas, which explore the rich source of data in museum collections and how it can be translated into actionable conservation information.

The Effect of Metformin on Influenza Vaccine Responses in Nondiabetic Older Adults

Jenna M. Bartley, PhD, Assistant Professor, Center on Aging and Department of Immunology, University of Connecticut Health Center

Aging is associated with progressive declines in immune responses leading to increased risk of severe infection and diminished vaccination responses. Influenza (flu) is a leading killer of older adults despite availability of seasonal vaccines. Geroscience-guided interventions targeting biological aging could offer transformational approaches to reverse broad declines in immune responses with aging. Here, we evaluated effects of metformin, an FDA approved diabetes drug and candidate anti-aging drug, on flu vaccination responses and markers of immunological resilience in a double-blinded placebo-controlled study. Healthy older adults (non-diabetic/non-prediabetic) were randomized to metformin or placebo treatment for 20 weeks and were vaccinated with high-dose flu vaccine after 10 weeks of treatment. Peripheral blood mononuclear cells (PBMCs), serum, and plasma were collected prior to treatment, immediately prior to vaccination, and 1, 5, and 10 weeks post vaccination. Increased serum antibody titers were observed post vaccination with no significant differences between groups. Metformin treatment led to trending increases in circulating T follicular helper cells post-vaccination. Furthermore, 20 weeks of metformin treatment reduced expression of exhaustion marker CD57 in circulating CD4 T cells. Pre-vaccination metformin treatment improved some components of flu vaccine responses and reduced some markers of T cell exhaustion without serious adverse events in nondiabetic older adults. Thus, our findings highlight the potential utility of metformin to improve flu vaccine responses and reduce age-related immune exhaustion in older adults, providing improved immunological resilience in nondiabetic older adults.

Who Understands Scientific Knowledge Better: Judges or Scientists?

Robert Bird, M.B.A., J.D., Professor of Business Law, School of Business, University of Connecticut

Scientific knowledge has influenced the law and legal decisions for centuries. But what role should modern science play in courts today? This presentation explores a recent legal change that fundamentally shifts the influence of the role of experts in rulemaking. This presentation will also highlight the implications of that decision, how judges today perceive genetic and genomic research, and opportunities for science to play its essential role in a democratic society.

Estimating co-evolutionary and co-introgression networks from publicly available data

Andrius J. Dagilis, PhD, Assistant Professor, Department of Ecology and Evolutionary Biology, University of Connecticut

The abundance of available genetic resources has enabled long existing methods to be applied to rich new data-sets. Co-evolutionary networks, estimating which genes have co-evolved across a broad set of species, can be constructed using orthologous gene data. Similarly, existing data allows us to estimate which genes co-introgress across species boundaries in different systems. By comparing the two, we can ask if two genes that co-evolve are also more likely to co-introgress, or if introgression is unable to bring such pairs of genes along. The latter case may help explain why introgressed alleles are often deleterious, as they potentially lack crucial evolutionary partners that allow them to function in the original population.

Identification of cell-free circulating nuclear DNA in older adults with depression

Breno Diniz, MD, PhD, Associate Professor, UConn Center on Aging, Department of Psychiatry, University of Connecticut Health Center

Background: Circulating cell-free DNA (ccfDNA) are small fragments (~166bp) of DNA that circulate freely in various biofluids and at low concentrations (~1-20ng/mL) in healthy individuals. It can be released through multiple mechanisms (apoptosis, necrosis, NETosis, active secretion) and can offer a “snapshot” of different cellular physiological and pathological processesStudies evaluating ccfDNA as a biomarker of depression have primarily focused on ccfDNA of mitochondrial origin (ccf-mtDNA), with inconsistent findings across studies, but there is limited information about ccf-DNA from nuclear origin (ccf-nDNA) in this condition. This study aims to evaluate if changes in ccf-nDNA in older adults with major depression, by analyzing its concentration and size distribution in plasma.

Methods: This pilot study included 24 older individuals, comprising individuals with LLD (n=13) and healthy controls (n=11). The two groups were matched for age and sex. We extracted ccf-nDNA from archived plasma samples and performed a next generation, paired-end short-read sequencing. The nuclear-mapped reads were quantified, and the size distribution of ccfDNA fragments was assessed.

Results: Older adults with major depression had significantly higher levels of mapped ccf-nDNA reads compared to healthy controls ($p < 0.05$). Additionally, there was a trend toward a higher level of fragments between 167-177 bp sizes ($p=0.06$) in the major depression group, indicating an evidence that cellular apoptosis is a possible mechanism of release of ccf-nDNA in this sample.

Conclusion: Our findings indicate that nuclear ccfDNA levels are elevated in individuals with LLD. The observed trends in ccfDNA fragment size distribution warrant further investigation with a larger sample size to determine the diagnostic utility of ccfDNA. In future studies, we aim to perform a more detailed examination of ccfDNA fragmentation patterns to gain deeper insights into the mechanisms underlying ccfDNA release in depression.

Using genomics to understand plant metabolic diversity

Karolina Heyduk, PhD, Assistant Professor, Department of Ecology and Evolutionary Biology, University of Connecticut

Plants adapt to stressful environments in diverse ways, including through changes to core metabolic pathways like photosynthesis. To understand how these adaptation evolve, we turn to plant lineages that inhabit extreme habitats like deserts, and using comparative genomics to determine how gene expression regulation, metabolic fluxes, and genomic architecture contribute to the genomic underpinnings of plant metabolic novelty.

Engineering Tools to Interrogate The Host Immunity, Microbiome, and Their Interactions

Sasan Jalili, PhD, Assistant Professor, The Jackson Laboratory for Genomic Medicine, Department of Immunology, UConn Health, Biomedical Engineering Department, UConn

The interplay between commensal microbiota and the mammalian immune system involves complex interactions in both homeostasis and disease, but many unknowns and challenges remain in understanding microbiome-immunity dynamics. While animal models have been extensively used to study host−microbiome interactions, there are limited bioengineered systems that can fully recapitulate human organs and their immune-microbiome interactions. Recent advances in tissue engineering, microfabrication, and stem cell biology have led to the development of sophisticated organoid cultures and organ-on-chip models that closely mimic the human cellular environment. Our lab has developed a human organ on a chip systems that maintain a stable community of living human microorganisms in direct contact with human cells. Additionally, our microneedle skin patch platform allows for noninvasive, longitudinal immune monitoring. These advanced tools help uncover immune-microbiome interactions in human conditions such as infectious diseases, autoimmunity, and cancer, offering novel ways to simulate and study complex host-microbiome dynamics.

Natural Killer Immune cells in Health and Disease

Silke Paust, PhD, Professor, The Jackson Laboratory for Genomic Medicine

Pancreatic Cancer (PC) is a highly metastatic cancer and a leading cause of cancer deaths in the US, with a 5-year survival rate of 10%. Chemotherapy and radiation are the main treatments, but response rates are low. Although immunotherapy has shown success in many cancers, PC is resistant due to poor immune cell infiltration, exhaustion, and a hostile tumor microenvironment. There is an urgent need for effective PC treatments. We examined freshly excised PC tissues from treatment naïve and chemotherapy/radiation treated patients to identify tumor fighting immune cells capable of infiltrating PC. We found a robust presence of Natural Killer (NK) cells, a type of immune cell known to robustly kill tumors. However, while abundant, PC-resident NK cells were exhausted and had stopped killing the tumor. Thus, we infused activated NK cells from healthy donors into immune-compromised mice with surgically implanted human PC. Notably, therapeutically infused NK cells robustly infiltrated pancreatic tumors to eradicate or shrink tumors and reduce metastatic occurrences. Importantly, tumors did not recur, nor did metastases develop in “complete responder” mice after therapy was stopped for six months – the equivalent of ~ 20 human years. By developing a successful immunotherapy for PC, our proposal has the clinical and immunologic depth to be highly significant and impactful: it will shape the future of solid

tumor immunotherapy and offer novel and effective treatment options for difficult-to-treat solid tumors with high metastatic potential.

The role of methane-producing anaerobes in One Health

Michel Geovanni Santiago-Martínez, PhD., Assistant Professor, Department of Molecular and Cell Biology, University of Connecticut

Oxygen-sensitive microorganisms (anaerobes) participate in nutrient cycling using diverse energy sources but growing without respiring oxygen. Methane-producing anaerobes from Domain Archaea (methanogenic archaea) are crucial in nutrient cycling because methane is the end-product of microbial decomposition of organic matter in the absence of oxygen, but also because methane is a potent greenhouse gas and balances the Earth's climate. Methanogenic archaea are free-living organisms that typically live in sediments and soils, but few species have been also found in host-associated microbiomes, including the gastrointestinal tract, respiratory tract, skin and mouth of humans and other animals. *Why do methanogenic archaea live in such diverse environments? How do methanogenic archaea survive under oxygen-induced stress?* These are the main biological questions that we are currently addressing in our projects using diverse experimental approaches. The long-term goals of our research are to understand the mechanisms that regulate metabolic pathways in methanogenic archaea, their interactions with other members of microbial communities, and their impact on the health of people, animals, and the environment.

Posters:

NaP-TRAP: A tool to identify *cis*-elements regulating mRNA translation

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

Novel gene evolution and 3D chromatin 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 the organization of chromatin 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 significance of human genes, grouped by their evolutionary age, within the 3D organization of the genome. We reveal that genes of different evolutionary origin have distinct positioning

relationships with both domains and loop anchors, and remarkably consistent associations with boundaries across cell types. While the functional associations of each group of genes are primarily cell type-specific, the associations of recently evolved genes are sensitive to 3D genome architecture. Moreover, the sensitivity of recent genes to disease 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, the distinct relationships of gene evolutionary age, function, and positioning within 3D genomic features contribute to tissue-specific gene regulation in development and disease.

Unraveling the Dinoflagellate Genome

Presenter name: Alex Francoeur, Yifan Gu, Jackson Sanders, PhD Candidates
Affiliated Lab: Lin Lab, Department of Marine Sciences, UConn

CartograPlant: Integration of FAIR Data Stewardship, Analytics, and Georeferenced Plant Populations for a Changing World

Presenter name: Meghan Myles, PhD Candidate
Affiliated Lab: Wegrzyn Lab, Department of Ecology and Evolutionary Biology, UConn
Abstract: CartograPlant (https://cartograplant.org/) is a novel web-based application that connects analytic workflows to georeferenced plant populations and their associated genotypic and phenotypic datasets. CartograPlant provides an accessible and extensive data repository, offering representation for both model and non-model plant species from around the world. To date, CartograPlant hosts genetic and/or phenotypic data from 801 different plant species across 321 genera. It also offers 988 regional and global environmental layers with which users can interact. The centralization of this genotypic, phenotypic, and environmental data allows for the possibility of meta-analysis across studies. Users can select from thousands of plants based on individual interests (traits, region, species, marker types). This meta-analysis was developed using the Galaxy framework and supports diversity estimation, calculations of population structure, and performance of association mapping and landscape genomics.

Genotypic and phenotypic data are collected both through direct author submission of studies to the TreeGenes database (https://treegenesdb.org/) and through biocuration efforts of published studies (via supplemental datasets) as well as those affiliated with Dryad. With the relatively recent advent of technologies such as high-throughput sequencing, more biological data is available now than ever before. It is important to store these data in standardized formats and with descriptive metadata so that they are machine-readable for proper representation in analytic pipelines. Our goal is to follow the FAIR principles of data storage: we ensure that data is Findable, Accessible, Interoperable, and Reusable.

Intron classes within 3D genome landscape in development and disease

Presenter name: Sean Riccard, PhD Candidate
Affiliated Lab: Erceg Lab, Department of Molecular and Cell Biology, UConn

Chromosomal changes in single-nuclei of developing *Drosophila* embryos

Presenter name: Akshada Shankar Ganesh, PSM Candidate
Affiliated Lab: Erceg Lab, Department of Molecular and Cell Biology, UConn

Transcriptomic analysis of the fire blight pathogen *Erwinia amylovora* on leaf surface structures identified genes important for host entry

Presenter name: James Standish, Graduate Research Assistant
Affiliated Lab: Quan Zeng, The Connecticut Agricultural Experiment Station, UConn
Abstract: The plant epidermis, a cuticle barrier covering plant surface, serves as the first layer of defense against plant pathogens. Unlike the fungal pathogens, bacterial pathogens do not contain penetration structures therefore have to enter plants through natural openings or wounds. In a previous research, we found *Erwinia amylovora*, the causal agent of fire blight, colonize on leaf surface structures glandular trichomes (GT) and nonglandular trichomes (NT) epiphytically, before entering hosts through wounds created during abscission of these surface structures. However, genes of *E. amylovora* important for the colonization of GT and NT is unknown. In this study, we inoculated leaves with *E. amylovora,* harvested GTs and NTs from leaves, and performed a transcriptomic analysis to identify key genes involved in the colonization of GTs and NTs. On GTs, 1,099 DEGs were identified, Kegg pathways of bacterial motility, DNA repair/recombination, and transporters were found to be upregulated and prokaryotic defense, enzymes with EC numbers, and unknown protein functions were downregulated. Importantly, virulence genes such as genes encoding the type III secretion system and amylovoran biosynthesis were found to be upregulated on GTs. Using mutagenesis and GUS labeling we validated their functions as critical for successful colonization of GTs. This study not only highlights an underexplored infection pathway but also emphasizes the importance of specific gene functions in enabling bacterial entry and colonization through naturally occurring wounds.

Interrogating 3'UTR-mediated translational control during early vertebrate embryogenesis

Presenter name: Anna Struba, PhD Candidate
Affiliated Lab: Beaudoin Lab, Department of Genetics and Genome Sciences, UConn Health
Abstract: The plant epidermis, a cuticle barrier covering plant surface, serves as the first layer of defense against plant pathogens. Unlike the fungal pathogens, bacterial pathogens do not contain penetration structures therefore have to enter plants through natural openings or wounds. In a previous research, we found *Erwinia amylovora*, the causal agent of fire blight, colonize on leaf surface structures glandular trichomes (GT) and nonglandular trichomes (NT) epiphytically, before entering hosts through wounds created during abscission of these surface structures. However, genes of *E. amylovora* important for the colonization of GT and NT is unknown. In this study, we inoculated leaves with *E. amylovora,* harvested GTs and NTs from leaves, and performed a transcriptomic analysis to identify key genes involved in the colonization of GTs and NTs. On GTs, 1,099 DEGs were identified, Kegg pathways of bacterial motility, DNA repair/recombination, and transporters were found to be upregulated and prokaryotic defense, enzymes with EC numbers, and unknown protein functions were downregulated. Importantly, virulence genes such as genes encoding the type III secretion system and amylovoran biosynthesis were found to be upregulated on GTs.

Using mutagenesis and GUS labeling we validated their functions as critical for successful colonization of GTs. This study not only highlights an underexplored infection pathway but also emphasizes the importance of specific gene functions in enabling bacterial entry and colonization through naturally occurring wounds.

From needles to reads: Utilizing 'omics' technologies to inform conservation of the eastern hemlock

Presenter name: Vidya S Vuruputoor, PhD Candidate
Affiliated Lab: Wegrzyn Lab, Department of Ecology and Evolutionary Biology, UConn

Investigating the Role of eIF4A2 in Early Vertebrate Development

Presenter name: Xiaonan (Nina) Wang, PhD Candidate
Affiliated Lab: Beaudoin Lab, Department of Genetics and Genome Sciences, UConn Health

EASEL (Efficient, Accurate, Scalable Eukaryotic modeLs), a tool for the improvement of eukaryotic structural and functional genome annotation

Presenter name: Cynthia N. Webster, PhD Candidate
Affiliated Lab: Wegrzyn Lab, Department of Ecology and Evolutionary Biology, UConn

Simulation of metastatic spread under cancer type-specific patterns

Presenter name: Samson Weiner, PhD Candidate
Affiliated Lab: Bansal Lab, Department of Computer Science & Engineering, UConn