NC STATE UNIVERSITY

Genetics and Genomics Initiative

3rd ANNUAL RETREAT

Saturday, August 29, 2020

Zoom Link:
https://ncsu.zoom.us/j/99544049614?pwd=NDBzUjFyME16ZTluTVUwYjZYa1JPQT09

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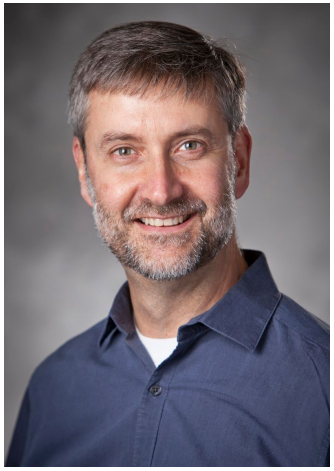
Keynote Speaker for the Genetics & Genomics Initiative 3rd Annual Retreat



Dr. Gregory A. Wray, Duke University
Professor of Biology
Director of the Duke Center for Genomics and Computational Biology (GCB)

Dr. Gregory Wray is Professor of Biology at Duke University. His research focuses on the evolution of gene regulation, primarily using sea urchins and great apes as models. He is especially interested in understanding the trait consequences of genetic variation in noncoding regions of genomes, how gene regulatory networks are shaped by natural selection, and which molecular mechanisms contribute to evolutionary changes in gene expression. Dr. Wray completed his undergraduate studies in biology at the College of William and Mary and his doctorate at Duke University before carrying out post-doctoral research at Indiana University and the University of Washington. He was an Assistant Professor at the State University of New York before moving back to Duke in 2000. Since 2014 he has directed Duke's Center for Genomic and Computational Biology.

Keynote Presentation

No Gene Is an Island: The Evolutionary Causes and Consequences of Gene Interactions

Both transmission genetics and population genetics were founded on considering the alleles of single genes in isolation. This monogenic approach cast a long and deeply influential shadow over the thoughts of evolutionary biologists during the 20th century. Today, of course, we "know" that genes interact extensively. But how much have we really learned about the role of gene interactions in shaping the organization of genomes, genetic variation within populations, and the genetic architecture of traits? In the lecture, I'll explore these questions from a first-person perspective. Along the way, I'll reveal why I've worked on so many different organisms during my career and make some irreverent predictions about the future of evolutionary biology.

The Genetics and Genomics Initiative (GGI) welcomes you to the 3rd Annual Retreat!

Schedule of Events

Welcome & Updates - Zoom Meeting Link

9:00 AM — Opening remarks by Dr. Fred Gould
Welcome from Dean Linton, Dean McGahan, and Associate Dean Meurs
Updates from the GGI Executive Committee
- Seminar Series
- GGI Contest Winners
- RIGs
- New Faculty
- GG Scholars Program (Cohort, Curriculum, & Recruiting)
- Director Search
- Discussion

BREAK & SPONSOR MEETINGS - HALF HOUR

10:30 AM — Attendees take a break, and individuals who signed up meet with sponsor representatives for 15 minute blocks. Retreat will reconvene at 11:00 AM

Breakout Room 1 - Agilent
Breakout Room 2 - PacBio
Breakout Room 3 - Qiagen

Keynote Speaker - Zoom Meeting Link

11:00 AM — **Dr. Gregory Wray**, Professor of Biology and Director of the Duke Center for Genomic and Computational Biology, Duke University
No Gene Is an Island: The Evolutionary Causes and Consequences of Gene Interactions

BREAK & SPONSOR MEETINGS - ONE HOUR

12:00 PM — Attendees break for lunch, and individuals who signed up meet with sponsor representatives for 15 minute blocks. Retreat will reconvene at 1:00 PM

Breakout Room 1 - Agilent
Breakout Room 2 - PacBio
Breakout Room 3 - Qiagen

External Sponsor Presentations - Zoom Meeting Link

1:00 PM — Presentations from PacBio, Agilent, and Qiagen

Science Talks: Session 1 - Zoom Meeting Link

1:15 PM — **Dr. Benjamin Callahan**, Assistant Professor of Microbiomes and Complex Microbial Communities, Population Health and Pathobiology, CVM
Amplicon sequencing in the era of highly-accurate long-reads

1:30 PM — **Kimberly N. D'Arcangelo**, PhD Student in Quesada Lab, Entomology and Plant Pathology, CALS
Population genetics and genomics strategies for biosurveillance and improved management of cucurbit downy mildew

1:45 PM — **Dr. Elizabeth Lucas**, Assistant Professor of Neurobiology, Molecular Biomedical Sciences, CVM
A sex-specific circuit for emotional memory

2:00 PM — **Dr. Christina Zakas**, Assistant Professor of Evolutionary Genetics, Biological Sciences, COS
Finding the Genetic Basis of Developmental Evolution using a Marine Model

2:15 PM — **Todd Kuiken, Ph.D**, Senior Research Scholar & GES Center Executive Committee Member, Genetic Engineering and Society Center
Biology in a World without Borders

BREAK & SPONSOR MEETINGS - 30 MINUTES

2:30 PM — Attendees take a break, and individuals who signed up meet with sponsor representatives for 15 minute blocks. Retreat will reconvene at 3:00 PM

Agilent - Not Available
Breakout Room 2 - PacBio
Breakout Room 3 - Qiagen

Internal Sponsor Presentations - Zoom Meeting Link

3:00 PM — Presentations from NC State Genomic Sciences Laboratory (GSL) and Cellular and Molecular Imaging Facility (CMIF)

Science Talks: Session 2 - Zoom Meeting Link

3:15 PM — **Dr. Caroline Laplante**, Assistant Professor of Quantitative and Computational Biology, Molecular Biomedical Sciences, CVM
Seeing is understanding: quantitative microscopy to uncover how proteins organize to drive cell shape changes

3:30 PM — **Dr. Rafael Guerrero**, Assistant Professor of Evolutionary Genetics, Biological Sciences, COS
Inferring patterns of sex-chromosome in dioecious nightshades

3:45 PM — **Dr. Anna Locke**, USDA Assistant Professor, Crop and Soil Sciences, CALS / Research Plant Physiologist, Soybean & Nitrogen Fixation Research Unit, USDA Agricultural Research Service
When genes aren't enough: the role of plant physiology in soybean breeding

4:00 PM — **Dr. Kelly Meiklejohn**, Assistant Professor of Forensic Science, Population Health and Pathobiology, CVM
Applications of next-generation sequencing to forensic science

GGI Paper of the Year Presentation - Zoom Meeting Link

4:15 PM **Dr. Michael McLaren,** Postdoctoral Research Scholar in Callahan Lab, Population Health and Pathobiology, CVM
Consistent and correctable bias in metagenomic sequencing experiments

Adjourn - Zoom Meeting Link

4:30 PM Closing remarks by Fred Gould

Thank you for joining us, we hope to see you next year! Abstracts for all talks are provided on the following pages.

Abstracts

Science Talks: Session 1

Dr. Benjamin Callahan, Assistant Professor of Microbiomes and Complex Microbial Communities, Population Health and Pathobiology, CVM

Amplicon sequencing in the era of highly-accurate long-reads

In recent years, long-read sequencing technologies have been developed that can produce sequencing reads that extend tens of kilobases in length, but that suffer from high (~10%) per-base error rates. Recently highly-accurate long-read sequencing technologies have been developed that can produce multi-kilobase reads with extremely high per-base accuracies (>99.9%). I will present and evaluate two such technologies, PacBio HiFi and LoopSeq SLR sequencing, and discuss potential applications of long-read amplicon sequencing using these high-fidelity technologies.

Kimberly N. D'Arcangelo, PhD Student in Quesada Lab, Entomology and Plant Pathology, CALS

Population genetics and genomics strategies for biosurveillance and improved management of cucurbit downy mildew

Pseudoperonospora cubensis is a broad host-range oomycete pathogen that infects many Cucurbitaceae crops. Following a population shift in 2004, cucurbit downy mildew (CDM) has become the most devastating disease of cucurbits in the Eastern United States (US) due to a failure of previously effective cucumber host resistance and reduced efficacy of some commercial fungicides. Population genetics analyses revealed two host-adapted clades in P. cubensis, Clade 1 and Clade 2. Using comparative genomics, species-specific and host-preference diagnostic markers were identified in the nuclear genome of P. cubensis and a qPCR assay for pathogen monitoring was developed. TaqMan® qPCR assays for detection of mutations known to confer resistance to FRAC 11 and FRAC 40 fungicides were also developed. Genotyping of isolates infecting cucurbits showed that mutations conferring resistance to FRAC 40 fungicides were more prevalent in Clade 2 isolates, and wild hosts were capable of harboring resistant P. cubensis isolates. To apply our findings for field disease management, the clade-distinguishing assay was implemented into a spore-trapping system for validation in sentinel plots at two locations over a two-year period. Sporangia-DNA was always detected before CDM symptoms were observed in hosts corresponding to each clade validating our biosurveillance system. Furthermore, pathogen monitoring revealed seasonality in host-adapted clades. Our findings are a significant step towards a P. cubensis biosurveillance system that can monitor inoculum levels, provide information about cucurbit infection risk based on clade, detect fungicide resistance in fields, and ultimately guide population-informed management practices.

Dr. Elizabeth Lucas, Assistant Professor of Neurobiology, Molecular Biomedical Sciences, CVM

A sex-specific circuit for emotional memory

Fear-based psychiatric conditions, such as post-traumatic stress and anxiety disorders, are the most prevalent mental illnesses worldwide, affecting 18% of the population annually. These illnesses are thought to arise from enhanced encoding of cues associated with aversive outcomes, leading to maladaptive fear responses that persist in the absence of threat. Women are twice as likely as men to be diagnosed with fear-based mental illness, suggesting that the mechanisms underlying associative fear memory differs between the sexes. One possibility is that females encode fear memories through different neural networks than males. To explore this possibility, we quantified expression of the neural activity marker c-fos throughout selected forebrain regions in auditory fear conditioned and naïve male and female littermates. While both sexes equally engaged canonical regions of cued fear circuit, such as basolateral and central amygdala, we found a robust female-specific increase of c-fos expression in the lateral septum (LS). We next used designer receptors exclusively activated by designer drugs (DREADDs) to determine if sex-specific LS activation is causally related to sex-specific memory encoding. We bilaterally infused adeno-associated viruses encoding hM3DGq (excitatory DREADD), hM4DGi (inhibitory DREADD), or eYFP (empty-vector control) into the LS of male and female mice, injected clozapine-N-oxide 30 minutes prior to auditory fear conditioning, and assessed fear memory encoding and persistence. LS activation enhanced fear memory in females but impaired memory formation in males. Conversely, LS inhibition enhanced fear memory in males but rendered female fear memory more pervious to degradation. To reveal the neurons of the LS memory ensemble, we employed a viral vector approach for permanent eYFP labeling of neurons active during fear memory acquisition. Consistent with our c-fos data, we observed more tagged neurons in fear-conditioned females than fear-conditioned males or naïve animals of either sex. Analyses of eYFP-positive terminals revealed that female LS ensemble neurons mainly project to the lateral hypothalamic area, periaqueductal gray, and ventral hippocampus. Taken together, these data suggest that sex-specific engagement of the lateral septum during associative fear learning enhances fear memory in females through canonical mediators of fear-evoked responses. This in turn might be a contributing factor for the increased prevalence of fear-based psychiatric disorders observed in women. Current studies seek to reveal the genetic identity of memory encoding LS neurons as well as their transcriptional responses during aversive learning.

Dr. Chrstina Zakas, Assistant Professor of Evolutionary Genetics, Biological Sciences, COS

Finding the Genetic Basis of Developmental Evolution using a Marine Model

Phenotypic evolution in animals is constrained by the mechanics of early development. Macroevolutionary changes are initially shaped by developmental constraints, where simple trade-offs can ultimately result in a vast spectrum of physiological, morphological, and ecological differences. How do these major transitions in development mode occur and what are their evolutionary consequences? A major goal of my research is characterizing the extent and distribution of genetic variation that contributes to early development. The polychaete Streblospio benedicti provides a unique opportunity to address this issue because it has two types of mothers who produce distinct offspring that differ in egg size, early development, and larval morphology. It is an ideal genetic model for understanding how transitions in developmental program evolve. Because early development is strongly influenced by maternal effects, we focus on finding the genetic contribution of maternal background to developmental phenotypes. We integrate aspects of population genetics, quantitative genetics, and developmental biology within a single species to identify how genomic variation influences life-history.

Todd Kuiken, Ph.D, Senior Research Scholar & GES Center Executive Committee Member, Genetic Engineering and Society Center

Biology in a World without Borders

Rapid advances in biological and information technologies has broken down the traditional "borders" of biology and changed how genetic technologies are taught, accessed, developed and perceived. Challenging society along with national and international governance systems with what were once clear boundaries between science, the public, the environment and "bio"security. This talk with examine the changing landscapes of biology in a world without borders.

Science Talks: Session 2

Dr. Caroline LaPlante, Assistant Professor of Quantitative and Computational Biology, Molecular Biomedical Sciences, CVM

Seeing is understanding: quantitative microscopy to uncover how proteins organize to drive cell shape changes

The mechanisms that govern cellular division are critical to both development and cancer progression. Our research combines quantitative microscopy techniques and genetics to determine how cells divide. This presentation will highlight our recent progress in elucidating the molecular architecture of the proteins inside the contractile ring of and how this organization generates the force to cleave a cell.

Dr. Rafael Guerrero, Assistant Professor of Evolutionary Genetics, Biological Sciences, COS

Inferring patterns of sex-chromosome in dioecious nightshades

Recent transitions to dioecy (i.e. separate female and male individuals) offer a unique perspective on the origin of sex, the dynamics of sex-linked genomic regions, and subsequent sex-chromosome divergence. With the goal of establishing a new system in which to test theoretical predictions about the mode and tempo of sex chromosome evolution, we generated the first genome sequence of a dioecious Solanum and use it to ascertain the genetic basis of sex determination in this species. We assembled and annotated the genome of S. appendiculatum (assembly size: ~750 Mb;scaffold N50: 0.92 Mb; ~35,000 genes) and identified sex-specific sequences and their locations in the genome. We also quantified sex-biased gene expression in floral tissues and analyzed gene-family evolution patterns specific to S. appendiculatum, which consistently implicate genes controlling pectin degradation and modification in the expression of sex. Our results also suggest that males in this species are the heterogametic sex, and provide the foundational resources for future studies on the independent evolution of dioecy in this speciose and agriculturally important clade.

Dr. Anna Locke, USDA Assistant Professor, Crop and Soil Sciences, CALS / Research Plant Physiologist, Soybean & Nitrogen Fixation Research Unit, USDA Agricultural Research Service

When genes aren't enough: the role of plant physiology in soybean breeding

Improving crop production is critical to feed the growing population in an increasingly challenging climate. Soybean breeders made huge gains in the 20th century, and the advent of genomics enabled the identification of genes controlling some key agronomic traits. However, agriculturally important phenotypes like seed composition and abiotic stress tolerance are genetically complex, often linked with yield penalties, and can be challenging to screen for in large populations. Our research aims to fill this gap with a better understanding of whole-plant genotype × environment responses. In one example, we are testing a whole-plant mechanistic drought tolerance hypothesis in the field and working with engineers to more efficiently screen germplasm for drought tolerance using computer vision and machine learning. In another project, we are identifying novel markers for heat stress tolerance through a mechanistic approach that integrates chamber-generated -omics data with agronomic outcomes in the field.

Dr. Kelly Meiklejohn, Assistant Professor of Forensic Science, Population Health and Pathobiology, CVM

Applications of next-generation sequencing to forensic science

DNA profiling is known as the gold standard for the analysis of forensic evidence. However, in many scenarios the quantity and quality of DNA can be suboptimal for processing using traditional methods. The introduction of next generation sequencing (NGS) nearly a decade ago revolutionized molecular biology, and recently forensic laboratories have been exploring whether this technology can be used to analyze challenging evidence samples. This presentation will explore current applications and research of NGS to the analysis of human and non-human DNA associated with forensic evidence.

GGI Paper of the Year Presentation

Dr. Michael McLaren, Postdoctoral Research Scholar in Callahan Lab, Population Health and Pathobiology, CVM

Consistent and correctable bias in metagenomic sequencing experiments

Marker-gene and metagenomic sequencing have profoundly expanded our ability to measure biological communities. But the measurements they provide differ from the truth, often dramatically, because these experiments are biased toward detecting some taxa over others. This experimental bias makes the taxon or gene abundances measured by different protocols quantitatively incomparable and can lead to spurious biological conclusions. We propose a mathematical model for how bias distorts community measurements based on the properties of real experiments. We validate this model with 16S rRNA gene and shotgun metagenomics data from defined bacterial communities. Our model better fits the experimental data despite being simpler than previous models. We illustrate how our model can be used to evaluate protocols, to understand the effect of bias on downstream statistical analyses, and to measure and correct bias given suitable calibration controls. These results illuminate new avenues toward truly quantitative and reproducible metagenomics measurements.

Thank you for attending the Genetics and Genomics Initiative 3rd Annual Retreat!

Have a question concerning the Genetics and Genomics Initiative?

Contact one of the Executive Committee members!

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