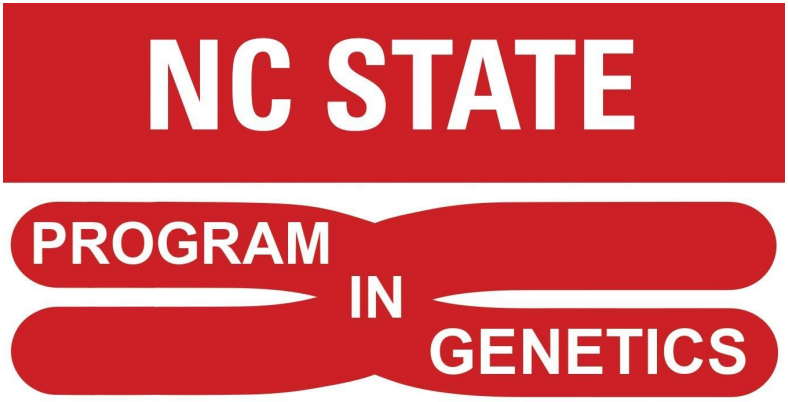

PROGRAM IN GENETICS

7th ANNUAL FALL RETREAT

Friday, August 12, 2016

The State Club at

North Carolina State University

The Program in Genetics welcomes you to The 7th Annual Genetics Fall Retreat!

Say hello to some of our new faces!

2016 – 2017

New Graduate Students for the Program in Genetics

Aldo Carmona Baez

Khushi Goda

Anna Rogers

Lindsay Simmons

Allison Schloop

Program in Genetics Fall Retreat Schedule

1st Floor Foyer

8:30 AM	Registration check-in
	Poster Presentation set-up in PENC Room 120 (Presenters - Please note that poster boards are labeled even/odd numbers for convenience during the poster presentation sessions)
	Breakfast buffet

Great Reception Ballroom (Room 122)

9:00 AM	Opening remarks by Dr. Trudy Mackay Director of the Program in Genetics

Faculty Vignettes - Great Reception Ballroom (Room 122)

9:20 AM	Dr. Yi-Hui Zhou
9:30 AM	Dr. Jose Alonso
9:40 AM	Dr. Fred Gould
9:50 AM	Dr. Johanna Elfenbein
10:00 AM	Dr. Reade Roberts
10:10 AM	Dr. Christian Maltecca
10:20 AM	Dr. Gregory Reeves

1st Floor Foyer

10:30 AM Coffee Break – All day beverage service provided.

Fall Retreat Group Photo – Grand staircase in the 1st Floor Foyer

Postdoctoral Blitz - Great Reception Ballroom (Room 122)

11:00 AM Dr. Wen Huang

11:10 AM Dr. Kaj Hulthen

11:20 AM Dr. Nathaniel Grubbs

11:30 AM Dr. Marine Baptissart

11:40 AM Dr. Horiyuki Mochizuki

11:50 AM Dr. Marcelo Mollinari

Lunch - Great Reception Ballroom (Room 122)

12:00 PM Lunch – Catered Deli Sandwiches

Teaching Genetics Education - Great Reception Ballroom (Room 122)

1:00 pm Dr. Betty Gardner

1:10 pm Dr. Chris Halweg

1:20 pm Dr. Whitney Jones

Social Activity on Paved Lawn Outside of the State Club

1:30 PM Social Activity – Photo Scavenger Hunt!
Leaders/Creators: Grace Parker and Brandon Baker

How to Play:

- Divide into teams of 6 people (maximum).
- For team photos (except first two), one person on your team can take the photo, but everyone else must be in the photo.
- Teammate photos only require one person on your team to be in the photo.
- You may only take pictures using one cell phone/camera.
- Each picture can only count for one item.
- Number the items in the order that the photos were taken.
- Don't do anything illegal, dangerous, or damaging to property!
- The team with the most points wins! (See separate handout for photo scavenger hunt list)

New Genetics Graduate Student Orientation - Conference Room 118

2:30 PM	New students meet with Dr. Trudy Mackay and Melissa Robbins

Poster Presentations - PENC Room 120

Enjoy Coffee! – All day beverage service provided in 1st Floor Foyer

2:30 PM	Poster Presentations (Even Numbers)
3:15 PM	Poster Presentations (Odd Numbers)

Student Achievements - Great Reception Ballroom (Room 122)

4:00 PM	Tiffany Garbutt
4:10 PM	Joel Johnstun
4:20 PM	Megan Williamson
4:30 PM	Farida Akhtari
4:40 PM	Fabio Morgante
4:50 PM	Megan Serr
5:00 PM	ADJOURN. Thank you for joining us! We hope to see you next year!
5:15 – 5:30 PM	Take down posters and clean up!

Faculty Vignettes

Grand Ballroom

9:20 AM – 10:30 AM

Pathway analysis for RNA-Seq data using a score-based approach

Yi-Hui Zhou

A variety of pathway/gene-set approaches have been proposed to provide evidence of higher-level biological phenomena in the association of expression with experimental condition or clinical outcome. Among these approaches, it has been repeatedly shown that resampling methods are far preferable to approaches that implicitly assume independence of genes. However, few approaches have been optimized for the specific characteristics of RNA-Seq transcriptional data, in which mapped tags produce discrete counts with varying library sizes, and with potential outliers or skewness patterns that violate parametric assumptions. We describe transformations to RNA-Seq data to improve power for linear associations with outcome and flexibly handle normalization factors. Using these transformations or alternate transformations, we apply recently developed null approximations to quadratic form statistics for both self-contained and competitive pathway testing.

The approach provides a convenient integrated platform for RNA-Seq pathway testing. We demonstrate that the approach provides appropriate type I error control without actual permutation and is powerful under many settings in comparison to competing approaches. Pathway analysis of data from a study of F344 vs. HIV1Tg rats, and of sex differences in lymphoblastoid cell lines from humans, strongly supports the biological interpretability of the findings.

Translational regulation of plant hormone responses

Jose M. Alonso, Javier Brumos, Catharina Merchante, Jeonga Yun, Serina Mazzoni, Anna N. Stepanova

Survival of plants greatly depends on the ability of these sessile organisms to tune their hardwired developmental programs to the constant changes in their environment. Although it is clear that plant hormones play a central role in this signal integration process, the exact molecular mechanisms involved are still largely unknown. Until recently, most studies have approached this question by examining the effects of different plant hormone regimens on transcript levels. Our recent work has taken advantage of the development of genome-wide translation profiling (the Ribo-seq) to uncover a novel level of regulation in the plant response to the hormone ethylene. Specifically, we have found that the signaling molecule EIN2 and the nonsense-mediated decay proteins UPFs play a central role in a previously uncharacterized ethylene-induced translational response. Currently, we are investigating the role of other plant hormones in gene-specific translational regulation. Our studies are uncovering new nodes of interaction between hormones, as well as the role of 3'UTRs and 5'uORFs in the regulation of plant responses to these key growth regulators.

Governance of engineered crops and gene drive systems

Fred Gould

The Genetic Engineering and Society Center at NCSU has been very active at the local, national, and international level in helping to develop governance systems for genetically engineered organisms. Three members of the Center have or are serving on National Academy of Sciences (NASEM) studies examining potential future products of genetic engineering. I will discuss the process and findings of one study on engineered crops and another on the use of synthetic gene drive systems for altering populations of pests and disease vectors.

Multicopy single-stranded DNA regulates translation and metabolism in Salmonella

Johanna Elfenbein, EJ Fritch, P Desai, HM Brewer, ES Nakayasu, C Ansong, JN Adkins, M McClelland, HL Andrews-Polymenis

Non-typhoidal Salmonella replicates within the low-oxygen conditions in the intestinal lumen during enteritis. STM3846, a reverse transcriptase, produces a single stranded DNA-RNA hybrid called multicopy single-stranded DNA (msDNA). msDNA is important during growth of Salmonella in the intestine and is critical for its growth in anaerobic conditions in vitro. We hypothesize that msDNA is a regulator of gene expression.

To determine what proteins and transcripts were altered in abundance in msDNA mutants during anaerobic growth, we used both proteomic and transcriptomic approaches. We compared protein abundance during aerobic and anaerobic growth between mutants deficient in msDNA and the isogenic wild-type. We also compared transcript abundance after shift from aerobic to anaerobic conditions.

Pathways important for anaerobic growth and virulence, including anaerobic carbon metabolism and utilization of anaerobic electron acceptors were among the proteins of altered abundance in msDNA mutants. We found 36 genes with altered expression in msDNA-deficient mutants. Functional predictions for these genes revealed that 25% have putative functions in transport and metabolism and 17% are involved in translation. One of the msDNA-repressed genes alters translation of a transcriptional regulator in the aerobic regulatory pathway of a global regulator of metabolism and virulence. Together these results suggest that msDNA regulates the anaerobic expression of genes that function in metabolism, transport, and translation. Our data suggest that msDNA regulates expression of genes with both clear and unclear requirements during anaerobic growth. Further characterization of the regulatory targets of msDNA should improve our understanding of how Salmonella thrives in anaerobic conditions.

Evolution of the gut across trophic levels

Kaitlin P. Coyle, Amanda N. Cass, Natalie B. Roberts, Patrick J. Ciccotto, Ashley Elias, Kaitlyn Stanley**, Reade B. Roberts**

Diet-related disease outcomes stemming from both undernourishment and overconsumption represent evolutionary discordance: the human genome has been unable to evolve to match rapid dietary changes brought on by overpopulation and the agricultural and industrial revolutions. If we reveal pathways of genetic evolution taken by other vertebrates as they adapted to diverse diets, we should identify pathways for therapeutic intervention for pathological conflicts in humans brought on by maladaptive diets. East African cichlid fish species recently evolved diverse dietary adaptations, providing powerful strategies to understand the genetic basis of dietary response. Comparison of species across trophic levels (herbivore, omnivore, and carnivore) reveals species-specific differences in gross gut morphology, epithelial architecture, and the gut microbiota; transcriptional comparisons suggest genes and genetic networks that may underlie these differences. Comparisons of whole genome sequence of dozens of species identify genes that have diverged consistently by trophic level, including complex evolution at a candidate gene producing three alleles that correspond to the three trophic levels. On-going work includes functional analyses of genes identified above, and continued exploration of the genomic architecture of dietary adaptation via quantitative trait loci mapping in an inter-species omnivore-by-carnivore cross.

Breeding for healthier livestock

Christian Maltecca, J. Howard, F. Tiezzi

Managing inbreeding and genomic diversity is an often forgotten path to ensure healthy livestock. Management of diversity rests on three pillars. Understanding the basis and consequences of genetic diversity. Controlling the population effective size. Optimize genetic variability deployed through mating plans. Inbreeding management often rely on the implicit assumption that individuals with the same inbreeding share the same genomic load. Marker information allows instead for regions-specific homozygosity causing inbreeding depression to be identified. Yet, these regions are expected to be at a low frequency so that traditional association methods based on estimating dominance effects lack statistical power. Methods that exploit the fact that longs runs of homozygosity
(ROH) are enriched with deleterious variants can have greater power in identifying haplotypes linked to inbreeding depression. We have employed a combined coalescence and forward-in-time simulator to investigate the use of alternative similarity metrics in identifying and curtail the propagation of deleterious haplotypes in selected cattle populations. As the genomic load is spread over variants of increasingly small effect, measures that aggregate the overall effect of a region become more effective than estimating dominance effects or the use of overall genomic similarity in curtailing the accumulation of inbreeding. Using the same principle we employed an heuristic method to identify haplotypes with negative effect for variants of small effect. When employed in simulated data the heuristic is better able to detect regions of the genome associated with inbreeding depression regardless of the effect size of the single mutations. This might have implications both in reducing and managing the genomic load of breeding populations, as well as providing a basis for the dissection of complex traits related to fitness and/or disease resistance.

Formation and Interpretation of Morphogen Gradients

Greg Reeves

The morphogen gradient is the prevalent model for spatial control of cellular differentiation in developing tissues. As a model system, we study patterning networks in the early fruit fly embryo. This model system is extraordinarily tractable and amenable to live and fixed imaging, genetic manipulations, and transgenesis. Here we will discuss the formation and interpretation of the Dorsal/NF-κB gradient, which patterns the embryos' dorsal-ventral (DV) axis. Dorsal, a transcription factor, is retained in the cytoplasm through binding to the inhibitor, Cactus/IκB. Toll signaling on the ventral side of the embryo results in the degradation of Cactus (Cact) and the import of Dorsal into the nucleus. Recent measurements of the Dorsal (dl) gradient have shown that it is highly dynamic and too narrow to pattern the entire DV axis.

Our modeling work shows that dl/Cact complex in the nucleus contributes to some of the fluorescence measurements of the dl gradient, resulting in a difference between the presumed (measured) dl gradient and the true dl activity gradient. Subtracting the inactive dl/Cact complex from the dl fluorescence measurements results in a dl activity gradient with an extended dynamic range, which carries sufficient positional information to pattern the entire DV axis. Further model analysis on the dynamics of dl gradient formation shows that the dynamics are the result of slow accumulation of total dl on the ventral side of the embryo. We present experimental and modeling results that uncover the mechanism behind this overall accumulation.

Postdoctoral Blitz

Great Reception Ballroom (Room 122)

11:00 AM – 12:00 PM

Spontaneous mutations and the origin and maintenance of quantitative genetic variation

Wen Huang (equal contribution), Richard F Lyman (equal contribution), Rachel A Lyman, Mary Anna Carbone, Susan T Harbison, Michael M Magwire, Trudy FC Mackay

Mutation and natural selection shape the genetic variation in natural populations. Here, we directly estimated the spontaneous mutation rate by sequencing new *Drosophila* mutation accumulation lines maintained with minimal natural selection. We inferred strong stabilizing natural selection on quantitative traits because genetic variation among wild-derived inbred lines was much lower than predicted from a neutral model and the mutational effects were much larger than allelic effects of standing polymorphisms. Stabilizing selection could act directly on the traits, or indirectly from pleiotropic effects on fitness. However, our data are not consistent with simple models of mutation-stabilizing selection balance; therefore, further empirical work is needed to assess the balance of evolutionary forces responsible for quantitative genetic variation.

Living in a risky world: Antipredator adaptations and phenotypic integration

Kaj Hulthén and Brian Langerhans

In this talk, I will give a brief introduction to my doctoral studies and also introduce my postdoctoral project at NC State. During my PhD, I studied anti-predator adaptations and particularly partial migration, which is characterised by within-population variation in migratory tendency such that just a fraction of the population migrates. I documented links between single traits (e.g. behaviour and morphology) and migratory life-history, defence adaptations and survival but generally without an explicit consideration of the phenotype as an integrated whole. As my thesis focussed primarily on migration as an anti-predator strategy, I became fascinated with understanding how environmental variation and predation can influence the evolution of phenotypic integration, i.e. correlated networks of phenotypic traits, which is the focus of my postdoc project.

Genetic Pest Management: Progress on Multiple Fronts

Nathaniel Grubbs, Fu-Chyun Chu, and Dr. Marce Lorenzen

Agricultural pests cost farmers billions of dollars a year in control expenses and production losses. Meanwhile, concerns about chemicals drive consumers increasingly away from conventionally-grown produce. Genetic Pest Management practices seek to address both of these concerns through highly-specific targeting of pest genomes with tools like gene drive and CRISPR/Cas9 genome editing. Our lab works with several pest species, including the western corn rootworm, *Diabrotica virgifera virgifera*, and the red flour beetle, Tribolium castaneum, in the hopes of developing novel methods of genetic control. We are the first to have successfully transformed Diabrotica, and are now working on using transformed beetles to study resistance development. We are also working on improving usability of the CRISPR/Cas9 system in this beetle, with the goal of eventually building a gene-drive system for control of this pest However, synthetic gene drives are susceptible to breakdowns due to mutation or recombination. The Medea element, found in Tribolium is a natural gene drive system, and appears to resist such instabilities. By elucidating Medea's mode of action, we hope to provide the pest control community with an alternative system, one that may be more stable and reliable gene drive tool. In addition, we are working on determining the feasibility of a control method employing oral RNAi to control this pest in less developed nations. Our current progress towards developing these novel tools for Genetic Pest Management will be presented.

Developmental Programming in Response to Maternal Overnutrition

Marine Baptissart, Christine Bradish, David Reif and Michael Cowley

Perinatal environmental exposure can permanently impact offspring health; a process called developmental programming. In particular, maternal high-fat-diet (mHFD) predisposes offspring to adult metabolic disorders including obesity and excess hepatic lipid storage (steatosis). Molecular mechanisms leading to steatosis include enhanced fatty-acid uptake, increased triglyceride synthesis and decreased beta-oxidation. However, how mHFD exposure during prenatal or early postnatal development differentially impacts these pathways remains unclear. Evidence suggests that epigenetic modifications are likely to be crucial for developmental programming by modulating transcriptional network activity. In this context, our study aims to 1) discriminate the molecular changes induced by prenatal and postnatal mHFD exposure, and; 2) test whether epigenetic mechanisms underlie the relative contributions of these distinct time-windows to steatosis in later life. Using a cross-fostering strategy, C57Bl/6 mice were exposed to mHFD (45% fat), or corresponding control diet, during prenatal and/or postnatal development. At birth, weaning and adulthood, we performed metabolic tests and characterized histological and molecular changes in the liver. At weaning, mice exposed to postnatal but not prenatal mHFD exhibit abnormal white adipose tissue accumulation and hepatic steatosis. This is associated with hepatic transcriptional changes including an increase in expression of the transcription factor Zac1. Zac1 controls a coordinately expressed Imprinted Gene Network (IGN) shown to regulate lipid storage in vitro. However, the function of Zac1 and the IGN in the liver is unknown. We hypothesize that this network contributes to hepatic lipid storage during development, and that Zac1 constitutes an epigenetic mediator between mHFD and steatosis in later life.

Urine BRAF Mutation as a Molecular Marker for Canine Bladder and Prostate Cancers

Hiroyuki Mochizuki, Susan G. Shapiro, and Matthew Breen

Bladder and prostate cancers are aggressive genitourinary cancers in dogs, characterized by invasion to surrounding tissues and high metastatic potential. Current diagnosis of canine bladder and prostate cancers requires histopathological examination of a biopsy. Such specimens require specialized medical equipment and invasive procedures, limiting the availability of diagnosis by histopathology for many canine patients. Access to a non-invasive means to confirm diagnosis is currently an unmet need. Recently, the canine BRAF V595E mutation was detected in ~80% of canine bladder and prostate cancers, suggesting that the mutation may serve as a molecular marker for these canine cancers.

In this study, we developed a droplet digital PCR (ddPCR) assay for detection of the canine BRAF V595E mutation. The assay was evaluated in DNA samples prepared from urine specimens obtained from 26 canine cancer patients (23 bladder and 3 prostate cancers), as well as from 37 control dogs (27 healthy and 10 cystitis). The sensitivity to detect the mutant allele was compared with conventional Sanger sequencing.

ddPCR had superior sensitivity for detection of the V595E mutation over Sanger sequencing, with a detection limit as low as just 1 mutant in 10,000 wild-type alleles (~0.01%). The ddPCR assay identified the mutation in urine samples from 85% (22/26) of canine bladder and prostate cancer patients, while the mutation was absent in control dog specimens. We have shown that ddPCR is a sensitive molecular technique with the potential to facilitate accurate and non-invasive means of canine bladder and prostate cancers.

Genetic Mapping in Complex Autopolyploids

Marcelo Mollinari, Guilherme Pereira da Silva, Antonio Augusto F. Garcia and ZhaoBang Zeng

Autopolyploid species play a fundamental role in agriculture. They are formed by multiple sets of chromosomes derived from the same species. This special condition imposes challenges to the construction of genetic linkage maps. Despite advances in genetic mapping in autotetraploids, there is a lack of methods to construct genetic maps in organisms with ploidy levels greater than four, such as sweet potato, sugarcane, strawberry, some ornamental flowers and forage crops. The construction of these maps is a key step for genetic studies, including QTL analysis, assembly of genomes, and study of evolutionary process. In this work, we present a method and software to construct genetic linkage maps using multidose markers autopolyploids. The method combines exact multipoint based models and two-point heuristics. Currently, the method is implemented for any even ploidy level up to 12 and the software is under development. To evaluate the method we conducted a simulation study considering three ploidy levels (4, 6 and 8). Also, we analyzed a full-sib tetraploid potato population dataset comprising 156 individuals and 5732 SNP markers. The results showed that in both scenarios the method perform reliably. In the vast majority of the simulations the linkage phase configuration of the markers was estimated correctly. Also, the recombination fraction matrices obtained with the analysis of the potato dataset was highly monotonic, indicating a good estimation of the genetic map. Moreover, the multipoint method was very important in complex scenarios where the two-point approach could not estimate the correct linkage phase.

Teaching Genetics Education

Great Reception Ballroom (Room 122)

1:00 PM – 1:30 PM

Re - TH!NKing Genetics

Marian (Betty) Gardner

As part of the accreditation process, NC State developed a focused five-year plan to enhance student learning called TH!NK. The plan was designed to foster students' critical and creative thinking in their courses and to encourage the use of those approaches as they solve real-world problems. Instructors are trained in TH!NK pedagogical strategies that provide opportunities for students to practice and enhance their critical thinking abilities. Until now, the TH!NK classes were introductory classes that primarily served freshmen. This fall, I will be incorporating some TH!NK strategies into the Principles of Genetics (GN 311) class as part of the new vertical integration program. Becoming more intentional about encouraging critical thinking processes in our classes, providing students with opportunities to reflect upon their work, and consistently using the TH!NK vocabulary should help the students mature in their critical and creative thinking abilities as they expand their knowledge of genetics.

Cheating Made Easy: Online Crowd-Sourced Exams and Homework Banks

Chris Halweg

Believe it or not, your homework and test question answers have created a global economy. Students are willing to 'sell' them and pay money for access to these crowd-sourced materials. Not only that, students can ask online 'experts' the answers to your homework questions. These grade-enhancement services could be inflating your course grades. A brief overview of these services will be provided as well as a discussion on course design aspects and possible counter measures given the prolific uses of these services by students.

Online Assessment for Principles of Genetics

Whitney M. Jones

In the Principles of Genetics course, GN312, we have begun using Moodle for online assessments. These exams, administered at the testing center, will allow us to better monitor our learning outcomes and evaluate student understanding across sections and semesters.

Poster Presentations
PENC Room 120

2:30 PM - 3:15 PM

Poster Presentations (Even Numbers)

3:15 PM - 4:00 PM

Poster Presentations (Odd Numbers)

(Poster 1)

Quantification of behavioral and heritability correlates in prairie voles, a socially monogamous rodent

Andrea Vogel and Lisa McGraw

Prairie voles (*Microtus ochrogaster*) are among the rare mammal species that have monogamous relationships and have become a model system for understanding the neurogenetic basis of social behaviors such as biparental care of young and pair bonding. Studying the strength of the pair-bond can inform researchers about complex mental health disorders with social components, such as autism, schizophrenia, depression, and anxiety. Although many prairie voles are monogamous, others will engage in extra-pair copulations, and many never form pair bonds at all. To begin to gain an understanding of the genetic basis for behavioral variation in this species, we examined socially-relevant behaviors including anxiety, alloparental care, and aggression against same-sex intruders. Furthermore, pair-bonding is hypothesized to create behavioral changes in the animals, so we examined these behaviors both before and after mating. We have determined that the related behaviors are not correlated with the amount of time spent with a partner, nor are any of the behaviors highly heritable. This experiment establishes the scope of individual variation of pair-bonding, which will be explored in more depth using neurobiology and genetic techniques.

(Poster 2)

Understanding the mechanisms in the Bone morphogenetic proteins (BMP) signaling network

Aydin Beseli and Greg Reeves

The BMP signaling network controls a diversity of cellular responses in most animals including flies and humans. The concentration gradient of BMP signaling in nuclear cycle (nc) 14 in Drosophila melanogaster embryogenesis determines dorsal-ventral patterning by setting at least three distinct spatial domains. Starting with early nc 14, low levels of BMP signaling on the dorsal half of the embryo lead to the differentiation of this region into dorsal epidermis by activating Type I genes. In later nc 14, BMP signaling sharpens and intensifies on the dorsal side of the embryo and activates Type II genes and Type III genes in the dorsal-most 12% and 5% of the embryo, respectively, leading the development of these cells into the amnioserosa. Under a simple affinity threshold model, where the activation of target genes depends on the concentration threshold of the signal, the Type I genes would turn off in the cells where the BMP signal is lost. However Type I genes remain activated after BMP signaling is lost. The lateral shoulder hypothesis explains the persistence of Type I and II genes in the cells after BMP signaling is lost by claiming that a low, undetectable level of BMP signal remains over the threshold. As an alternative hypothesis, there might be memory transducers activated by the same broad transient of BMP signaling in the early nc 14 that keep Type I, and possibly Type II BMP target genes active even after BMP signal would be lost. To test this hypothesis, we will monitor the BMP signaling in live embryos to determine whether or not there is a difficult-to-detect shoulder of BMP signaling throughout nc 14. Also we will determine whether Type I enhancers remain transcriptionally active after BMP signaling refinement. These results would help us understand the mechanisms overlying the patterning and development in animals.

(Poster 3)

Transcriptional regulatory logic of valve margin development

Bhupinder Sehra, Robert Franks, Veronica Gregis

In flowering plants the gynoecium (seedpod) is critical for reproductive success. The mature seedpod serves as protection during seed maturation until dehiscence (pod shatter) occurs allowing for seed dispersal. The valve margin (VM), longitudinal furrows in the walls of the seedpod made of a lignified and cell separation layer, is required for pod shatter.

The transcription factor, SHATTERPROOF2 (SHP2) is important for VM development; plants with mutations in the paralogs SHATTERPROOF 1 (SHP1) and SHP2 lack a VM and are indehiscent. Regions of high sequence similarity have been identified phylogenetically in the promoter/enhancer regions of SHP2. Subsequent functional analyses have highlighted a 1kb region that is capable of giving late SHP2 expression primarily in the VM.

A region of high sequence similarity with several binding sites specific to MADS domain proteins, transcription factors that help to specify organ identity during plant development, has been found within the 1kb fragment. Functional analysis shows that proximal consensus sequences for BASIC PENTATCYSTEINE (BPC) proteins that have been shown to interact with MADS proteins to repress transcription may regulate SHP2 through this region. Mutagenesis of specific MADS protein binding sites, potentially including AGAMOUS-LIKE 15 and AGAMOUS-LIKE 18, also suggests and a role in SHP2 regulation during late seedpod patterning.

(Poster 4)

Quantitative analysis of ethylene response in *Arabidopsis thaliana* using infrared imaging

David A. Bullock, Jose Alonso, and Anna Stepanova

Ethylene is a gaseous phytohormone involved in multiple aspects of plant growth, development, senescence, stress response, and is known to modify gene expression on the transcriptional and translational level. When seedlings are germinated in the dark in the presence of ethylene, they undergo the triple response, which involves growth inhibition and radial expansion of hypocotyls and roots, and exaggeration of the apical hook curvature. This unique phenotype is linked to changes in gene expression. The role of ethylene in the regulation of transcription is well characterized, but little was known about this hormone's involvement in translation. Through ribosomal footprinting, a mechanism for ethylene-mediated translational regulation was recently established and a set of genes repressed by ethylene at the translational level was identified. We will test the role of these genes in the ethylene response by characterizing T-DNA knockout mutants in the classical triple response assay, as well as in the state-of-the-art growth-response kinetic assays by employing an infrared live imaging system to monitor subtle changes in the rates of elongation in hypocotyls and roots of dark-grown seedlings upon ethylene treatment and withdrawal. In addition, we will explore the role of another plant hormone, auxin, which is known to interact with ethylene, in the kinetic assays by examining the ethylene response kinetics in a series of previously characterized auxin mutants. This project will expand our limited knowledge of ethylene-triggered translational regulation and the role of auxin in the response to ethylene.

(Poster 5)

Drosophila Lifespan: Effects of RNA Interference (RNAi)-Suppression

Desiree Unselt, T. G. Campbell, K. Ward, A. Weitzel, R. R.H. Anholt, and T. F.C. Mackay

Understanding the genetic mechanisms affecting variation in lifespan in natural populations is crucial for understanding the genetic basis of age-related diseases. Lifespan is known to vary in natural populations due to the segregation of multiple genetic factors as well as to exposure to different environmental conditions with a heritability of approximately 10-30%. Further, many pathways associated with lifespan, such as the insulin or insulin-like signaling pathway, are evolutionarily conserved between humans and model organisms. *Drosophila melanogaster* is a powerful model for assessing naturally occurring genetic variation in lifespan because of the ability to perform genomic analyses on a large scale while effectively monitoring genetic backgrounds and controlling environmental conditions. The *D. melanogaster* Genetic Reference Panel (DGRP), which consists of 205 sequenced inbred lines, allows for the investigation of natural genetic variation on phenotypically variable traits. To identify polymorphisms associated with variation in aging, a genome wide association (GWA) study utilizing the DGRP was conducted. This resulted in the identification of 28 genes significantly associated with lifespan. To validate their effects on lifespan, we knocked down the expression of these genes using RNA interference (RNAi) and a ubiquitous driver. This revealed several significant results associated with lifespan in the RNAi knockdown genotypes relative to their controls. Specifically, 13 genes (48%) had an effect in at least one sex, demonstrating sex-specific genetic architecture of lifespan. Additionally, 8 of the most significant genes (p-value < 0.01) increased lifespan when knocked down, providing evidence that lifespan is regulated at the transcriptional level. In the future, we plan to further functionally validate the role of these genes in the genetic control of lifespan using an overexpression assay. These experiments will contribute to our overall goal in establishing novel genetic networks associated with variation in aging. Since basic biological processes, such as aging, are evolutionarily conserved, these studies will also provide candidate genes for investigation in other species, including humans.

(Poster 6)

Genetic variation at a CNE contributes to microhabitat-associated behavioral differentiation in Malawi African cichlid fishes

Emily C. Moore, Lynea I. Bull, and Reade B. Roberts

The adaptive radiation of East African cichlid fishes has resulted in a species-rich flock that displays astounding trophic, morphological, and nuptial diversity. Within genera, fine-scale niche partitioning has resulted in sympatric sister species that inhabit definable microhabitats with distinct selection pressures. Previous investigations of cichlid adaptation to microhabitat have focused on morphological and physiological adaptation to factors such as diet (ie. jaw morphology) and depth (ie. photopigment), with little work focused on mechanisms of behavioral adaptation to environment. To identify behavioral divergence occurring during microhabitat differentiation, we tested species of Malawi cichlids found in either the sediment-free, rocky reefs or the sand-rock interface for a variety of environment-usage phenotypes in a controlled laboratory setting. Computer-aided analysis of fish response to new objects, new environments, and home-tank grooming behavior reveals distinct behavioral patterns between rock and interface species. Investigation of population genomic data has resulted in the identification of a candidate locus that segregates with behavioral type in the wild, and controlled breeding experiments have allowed for the interrogation of the locus in the lab. Individuals with the ‘sand’ genotype at a conserved non-coding element (CNE) spend more time in the center of an open arena, compared to full sibs with the ‘rock’ genotype. Gene expression studies have confirmed expression of candidate genes in brain tissue, and show allelic bias in levels of candidate gene expression, which is associated with CNE genotype.

(Poster 7)

Polygenic Sex Determination in *Astatotilapia burtoni*

Erin Peterson and Reade Roberts

Across different animal groups, there are multiple mechanisms for sex determination, such as genetic or environmental factors. African cichlid fishes are an extremely diverse group that has undergone an explosive radiation of speciation. This radiation has produced a good model for the exploration of different traits, including different genetic sex determination systems and their role in speciation. In some fish and other animals, polygenic sex determination (PSD) is one of these systems employed and in a specific species of cichlids, *Astatotilapia burtoni*, it is believed that PSD is at work. Three possible sex-determining alleles have been mapped through linkage mapping. The loci appear to be working in both ZZ/ZW and XX/XY patterns on linkage groups 13 and 5-14. Following the determination of the sex-determining alleles, epistatic interactions will be determined through selective breeding. The understanding of gonadal maturation is of interest as gonadal sex may drive secondary sexual characteristics. It is believed that premature gonads are bi-potential but that these sex-determining alleles work to push the gonad to either fate, male or female. The time point at which this male/female decision occurs is not known and with histological examination and other techniques, such as RNA-seq, will be determined. Overall, we hope to gain a better understanding of the evolution of gene regulatory networks associated with PSD systems, and the role of PSD in rapid speciation.

(Poster 8)

Genomic regulation of limited lifespan and reproductive senescence

Grace A. Parker and Trudy F. C. Mackay

Limited lifespan and senescence are near-universal phenomena. These quantitative traits exhibit variation in natural populations due to the segregation of many interacting loci and from environmental effects. Due to the complexity of the genetic control of lifespan and senescence, our understanding of the genetic basis of variation in these traits is incomplete. Our goal is to identify causal genes associated with increased lifespan and postponed reproductive senescence in *Drosophila melanogaster* by functional analyses of genetically divergent genes between five long-lived (O) lines selected for postponed reproductive senescence and five unselected (B) lines. Preliminary data assessing productivity of the reciprocal crosses of the O and B lines suggest that genes influencing reproductive senescence are maternally-controlled. Therefore, all of the candidate genes tested are expressed in the ovaries of females. To determine which of these candidate genes exhibit a quantitative change in lifespan or reproductive productivity, I have assessed lifetime reproduction of candidate genes from the Vienna collection of RNAi lines in which gene expression is knocked down in ovaries. Identifying specific genes affecting increased lifespan and delayed reproductive senescence will increase our knowledge of the evolutionary role of naturally segregating populations on overall fitness and may provide potential targets for therapeutic intervention to delay senescence in populations with increasing lifespans.

(Poster 9)

Phenotypic Variation in Olfactory Behavior in a Population of Inbred Wild-Derived Lines of *Drosophila simulans*

Huriyyah Chaudhry, **Mahesh Pinapaka**, Lavanya Turlapati, Gunjan Arya, Richard F. Lyman, Trudy F.C. Mackay, and Robert R. H. Anholt

For most animals, the response to odorants is critical in mediating interactions with their environments. The ability to respond to chemical signals is essential for survival and reproduction. Previous genome-wide association studies on the *Drosophila melanogaster* Genetic Reference Panel (DGRP), a population of 205 inbred wild-derived lines with fully sequenced genomes, identified polymorphisms and genetic networks associated with natural variation in olfactory behavior. Here, we studied variation in olfactory response to the odorant benzaldehyde in a closely related sympatric population of inbred wild-derived lines of *Drosophila simulans*. As in the DGRP, there is minimal genetic variation within these lines, but genetic variation among the lines reflects that of the population from which they were derived. We used the classical "dipstick" assay with the isogenic Canton S (B) reference strain to measure dose-response curves, which established 0.3% (v/v) as an optimally discriminating concentration to detect phenotypic variation in response to benzaldehyde. Response scores ranged from about 1.60 to 4.96, showing substantial phenotypic variation. Analysis of variance showed significant Line and Line x Sex terms with a broad sense heritability H2=0.50, indicating a substantial genetic component to the observed phenotypic variation, which presents a favorable scenario for future genome-wide association analyses.

(Poster 10)

Subfunctionalization and Neofunctionalization of *Drosophila* Odorant Binding Proteins

Joel A. Johnstun, Frances S. Haire, Trudy F. C. Mackay, and Robert R. H. Anholt

The functions of most *Drosophila* odorant binding proteins (Obps) remain unexplored, and many exist in tandem arrays throughout the genome. As these genes most likely arose through recent duplication, genes within a cluster likely have partially redundant or pleiotropic functions. Here, we used the CRISPR-Cas9 system to generate two knock-out lines, the first lacking the four paralogs of the Obp56a-d cluster, and the second lacking the single Obp56h gene, another possible paralog of the Obp56 cluster. Various phenotypic tests on these knockout lines demonstrate significant functional overlap and novel pleiotropic functions. Both lines shared decreased viability in early development, development time, and copulation latency, while the Obp56a-d KO line uniquely showed decreased height of pupation. The Obp56h KO line showed increased copulation duration and decreased aversion to 2-heptanone. Reinserting the Obp56a-d genes one-by-one and in various combinations in a PhiC31 integration site engineered in their original location during CRISPR-Cas9 excision will enable reconstruction of their functional evolutionary history. Supported by NIH grant GM059469.

(Poster 11)

Functional Characterization of Multiple Promoter Alleles of the bellwether gene in *Drosophila melanogaster*

Júlia Frankenberg Garcia, Mary Anna Carbone, Trudy F. C. Mackay and Robert R. H. Anholt

Lifespan varies among individuals, but the genetic factors that contribute to variation in lifespan are not completely understood. *Drosophila melanogaster* presents a powerful genetic model system to explore the genetic underpinnings of longevity, since its lifespan is limited and both the genetic background and environment can be controlled precisely. A previous study identified sequence variants associated with differences in lifespan between five long-lived lines originally selected for delayed reproduction (O lines) and their five unselected controls (B lines). Two single nucleotide polymorphisms in the promoter of the bellwether (blw) gene (A>G and G>T) were associated with differences in lifespan between the O and B lines. To assess whether associated polymorphisms in the blw promoter may contribute to differences in lifespan by modulating gene expression, we amplified 500 bp upstream promoter sequences containing all four possible haplotypes (AG, AT, GG, GT) and assessed promoter activity in an in vitro luciferase reporter system. Our results show that the AG haplotype characteristic of the B lines showed ~18% greater expression of luciferase than the GT haplotype, which is associated with the long-lived O lines. Current experiments are designed to assess to what extent alternative blw alleles modulate lifespan in a common genetic background. The blw gene codes for the alpha subunit of the mitochondrial ATP synthase, and thus may represent a possible molecular link between metabolic rate and lifespan.

(Poster 12)

Dynamic changes in vaginal microbiota accompany first estrus and copulation in the prairie vole

Nishi Shah, **Kaitlyn Stanley**, Andrea Vogel, Kaitlin Coyle, Caitlin Clement, Natalie Roberts, Lisa A. McGraw and Reade B. Roberts

Vaginal microbiota form a mutualistic relationship with their host and often act as the first line of defense in the female reproductive tract. Despite its importance, the vaginal microbiota is poorly studied, and little is known about the compositional changes during an individual's lifespan (for example, changes from birth to copulation to pregnancy, and its effect on overall host health). Prairie voles (*Microtus ocrogaster*) are a monogamous species, making them an interesting model to characterize the vaginal microbiota and the subsequent changes during such transitional stages. This characterization is the overall objective of our research; additionally, we asked research questions such as what are the effects of estrogen priming on vaginal microbiota, what are the effects of copulation on vaginal microbiota, and how comparable is the vole vaginal microbiome to the human vaginal microbiome. By utilizing a 16S rDNA library prep run on the Illumina MiSeq, we were able to answer these research questions. We found that the microbiota exhibit differences in composition by location, sex, pre- and post-estrogen injections, and pre- and post- copulation. Estrogen priming of female voles before copulation appears to cause fluctuations in not only vaginal microbial composition, but also male microbial composition. Copulation can cause various changes in vaginal microbial composition, most notably the transfer of male microbes. Unfortunately, vole vaginal microbiota contains relatively low quantities of Lactobacillus, the dominating microbiota in humans, thus rendering the prairie vole an unlikely model for human reproductive microbiota studies.

(Poster 13)

Transgenerational Effects of Parental Age on Complex Traits in *Drosophila melanogaster*

Kyle Kapur, Shanshan Zhou, Trudy F. C. Mackay and Robert R. H. Anholt

Epigenetic modifications modify DNA structure and regulate gene expression. They are environmentally plastic and can change dynamically during senescence. Incomplete reprogramming of epigenetic state during gametogenesis and early embryogenesis can result in inheritance of epigenetic marks in the next generation offspring and affect offspring phenotypes. To understand how and to what extent epigenetic state is passed down to subsequent generations, we examined several quantitative traits in the first and second-generation offspring from 3-5 day-old and 4 week-old *Drosophila melanogaster* parents in two different inbred backgrounds. We tested startle-induced locomotion, chill coma recovery time, starvation stress resistance, alcohol sensitivity, and fecundity of males and females for both parents and offspring from the two generations. We found significant differences between offspring from young and old parents for alcohol sensitivity and chill coma recovery time for the first-generation offspring, and for all the traits for the second-generation offspring. The phenotypic transgenerational effects were replicated in both genetic backgrounds, but the effects were in opposite directions for some traits. Future ChIP-Seq, miRNA-Seq and whole genome transcriptional profiling on both parental and offspring flies from two generations will identify epigenetic factors that contribute to the phenotypic differences between offspring from young and old parents.

(Poster 14)

Cardiac Expression Patterns Associated with Feline Cardiomyopathy Mutations

Mary Anna Carbone, **Joshua David Slaydon,** Kathryn Meurs and Trudy F. C. Mackay

Hypertrophic Cardiomyopathy (HCM) is an inherited disease characterized by thickening of the left ventricular myocardium. Mutations in the gene MyBPC3 have been associated with HCM in people. The disease commonly affects young athletes and often goes unnoticed because its first symptom is usually congestive heart failure. In addition to affecting humans, HCM is the most common form of heart disease in cats. Two separate mutations in feline MyBPC3, A31P and R820W, have been identified in the Main Coon and Ragdoll breeds respectively. While HCM is a fairly common genetic disease it is difficult to obtain a large sample size of either cats or humans with this condition. A possible solution to this problem is to use Drosophila melanogaster as a model to study HCM. In this study, we have PCR-amplified the MyBPC3 coding sequence from feline cardiac tissue and will clone the gene into the pUASt-attb expression vector. Using site-directed mutagenesis we will generate the A31P and R820W mutated variants. Transgenic flies will be produced that overexpress the MyBPC3 genes using PhiC31 transformation. The cardiac tubes and heart-rates of flies that express the MyBPC3 gene and its variants will be compared. RNA-sequencing will be conducted to reveal expression patterns of transcripts affected by the overexpression of MyBPC3. Regulatory pathways that are uncovered by this study can serve as a translational model for studies of therapeutics in human and feline clinical trials.

(Poster 15)

Molecular Genetics of Glaucoma in a Canine Model

Mary Anna Carbone, Leslie Shannon, Gunjan Arya, Hans Westermeyer, Kathryn Meurs, and Robert R. H. Anholt.

Glaucoma is a leading cause of vision loss. It is an optic neuropathy characterized by progressive loss of retinal ganglion cells, degeneration of the optic nerve and visual field defects. The most common type of glaucoma is primary open-angle glaucoma (POAG), but angle-closure glaucoma (PACG) is common in Asian populations. Canines can serve as a model for glaucoma, since their eye morphology is similar to that of people, and as companion animals they share common environments. PACG is the most common form of glaucoma in canines and is typically caused by the collapse of the iridocorneal angle (the angle between the iris and the trabecular meshwork) resulting in blockage of fluid outflow and elevated intraocular pressure (IOP). Identification of candidate risk loci for PACG could allow early diagnosis and disease prevention. We propose to identify risk alleles using whole-genome DNA sequencing from canine blood samples. Regulatory pathways involved in the disease process will be assessed using RNA sequencing from trabecular meshwork samples. Myocilin, the first gene product associated with congenital glaucoma in humans, is often correlated with severity of disease or elevated IOP. We have quantified myocilin protein levels in the aqueous humor of affected and unaffected canines as a potential indicator of early diagnosis. Polymorphisms and regulatory pathways that will be uncovered by this study in canines can serve as a translational model for studies of therapeutics in human clinical trials.

(Poster 16)

Epigenetic regulation of aging in *Drosophila melanogaster*

Q. Brent Chen & Trudy F. C. Mackay

As the average lifespan of the world population continues to increase, deciphering the biological underpinnings of natural variation in aging and lifespan are becoming critical to managing aging-related diseases. Currently, age-related diseases, such as cancer, cardiovascular diseases, neurodegenerative diseases, and type II diabetes, are the largest impact ailments affecting the healthspan of the elderly population. While the genetic and environmental influences governing lifespan have been extensively studied, the epigenetic factors underlying aging remain largely unexplored. Chromatin structure and epigenetic regulation can integrate genetic and environmental signals through histone modifications and DNA methylation. Here, we utilize *Drosophila melanogaster* to identify changes in chromatin structure and histone modifications that accompany aging. Developing chromatin state profiles and tracking histone modification changes over time can lead to a fuller understanding of the epigenetic factors associated with aging.

(Poster 17)

Understanding sexual fertility in *Aspergillus flavus* through analysis of F1 progeny

Richard M. Gell and Ignazio Carbone

Aspergillus flavus produces aflatoxin, which is a constant threat and economic burden to corn and oilseed crops worldwide. In order to manage this problem more cost effectively, a greater understanding of A. flavus biology and genetics is required. One important question is how genetic information moves between strains. A. flavus, previously thought of as only asexual, has recently been found to undergo sexual reproduction both in laboratory crosses and in the field. During the mating process, the sclerotium, a survival structure, of one strain acts as the female parent providing both the mitochondria and a matrix for the ascocarps and progeny to grow, while a spore or propagule from a second strain fertilizes as the male. The fertility of mating pairs is highly variable and influenced by the directionality of the cross. We are examining crosses that exhibit high fertility with one direction, but low fertility when male and female parents are reversed. Genome wide polymorphism screening using double digest Restriction Associated DNA sequencing (ddRADseq) was performed for 36 progeny from each direction of two biased crosses. These data are being used to provide an understanding of genetic inheritance and recombination in A. flavus and serve as genetic markers for mapping genomic regions that may bias fertility. By understanding these aspects of A. flavus genetics, we create opportunities to utilize strain fertility in the selection of biological control agents.

(Poster 18)

Predictable and Tunable Control of Gene Expression in Multicellular Organisms

Thomas Jacobsen, Ashley Jermusyk, Chase Beisel, Gregory Reeves

Tools for regulating gene expression have been widely developed for single-celled organisms, such as bacteria and yeast. However, these genetic tools are currently limited or have yet to be established in more complex organisms. Here we describe self-cleaving hammerhead ribozymes; catalytic RNA constructs that can undergo a phosphodiester cleavage reaction, resulting in mRNA cleavage and degradation, thus inhibiting gene expression. To implement fine-tuning capabilities for this genetic tool, various “competing sequences” can be cloned upstream of the ribozyme. Depending on thermodynamics, these “competing sequences” can interact with a major stem of the ribozyme through Watson-Crick base pairing, thus allowing for various conformational changes of the ribozyme structure. Since the cleavage activity of the ribozyme is largely dependent on the kinetics of the cleavage reaction, as well as the thermodynamics of the “competing sequences”, the level of gene expression can be predicted and tuned using various sequences.

Multiple ribozyme constructs were cloned either upstream or downstream of gfp, which was under the control of a constitutive promoter. These constructs were transiently transfected into HEK293T cells. The addition of different “competing strands” resulted in variable expression of GFP, but also appeared to interfere with its translational activity. Future work will be conducted to analyze the thermodynamics of the “competing sequences”, as well as to incorporate these tools in a synthetic network in the model organism, *Drosophila melanogaster*.

Student Achievements

Great Reception Ballroom (Room 122)

4:00 PM – 5:00 PM

Genetic Background Influences Stem Cell Derivation

Tiffany A. Garbutt, David L. Aylor, & David W. Threadgill

Induced pluripotent stem cells (iPSCs) are differentiated cells that have been reprogrammed back into an undifferentiated embryonic stem cell like state with the ability to differentiate into any cell type of the adult organism. Induced pluripotent stem cells offer a potentially unlimited source of patient specific embryonic stem cell like (ESC-like) cells that could be used for both research and therapeutics. However, research into the effect of genetic background on the ability derive iPSCs has been limited, despite knowledge that genetic background influences ESC derivation and pluripotency. We tested the ability of eight genetically diverse inbred mouse strains to derive iPSCs and find that six strains are permissive to ESC-like iPSC derivation, whereas two strains, the NOD/LtJ and WSB/EiJ strains are non-permissive to ESC-like iPSC derivation. Treatment with GSK3 β and MEK inhibitors allow for the derivation of transcriptionally homogenous ESCs from both permissive and nonpermissive strains, but the use of GSK3 β and MEK inhibitors during the reprogramming of differentiated fibroblasts has been unsuccessful. Here, we use the GSK3 β and MEK inhibitors in a new treatment, termed 2iS that can be used during reprogramming to derive ESC-like iPSCs from non-permissive strains. Subsequent iPSCs were RNA sequenced and analyzed for similarity to the ESC cell state.

Subfunctionalization and Neofunctionalization of *Drosophila* Odorant Binding Proteins

Joel A. Johnstun, Frances S. Haire, Trudy F. C. Mackay, Robert R. H. Anholt

The functions of most *Drosophila* odorant binding proteins (Obps) remain unexplored, and many exist in tandem arrays throughout the genome. As these genes most likely arose through recent duplication, genes within a cluster likely have partially redundant or pleiotropic functions. Here, we used the CRISPR-Cas9 system to generate two knock-out lines, the first lacking the four paralogs of the Obp56a-d cluster, and the second lacking the single Obp56h gene, another possible paralog of the Obp56 cluster. Various phenotypic tests on these knockout lines demonstrate significant functional overlap and novel pleiotropic functions. Both lines shared decreased viability in early development, development time, and copulation latency, while the Obp56a-d KO line uniquely showed decreased height of pupation. The Obp56h KO line showed increased copulation duration and decreased aversion to 2-heptanone. Reinserting the Obp56a-d genes one-by-one and in various combinations in a PhiC31 integration site engineered in their original location during CRISPR-Cas9 excision will enable reconstruction of their functional evolutionary history. Supported by NIH grant GM059469.

Genetic approaches to produce male only strains of the insect pests using Lucilia cuprina

Megan Williamson

The Australian sheep blowfly, Lucilia cuprina, is a major agricultural pest in Australia and New Zealand. Genetic approaches, such as the sterile insect technique (SIT), have been considered for use for control in Lucilia cuprina. For over 60 years, SIT has been used successfully to control the New World screwworm (NWS) but more efficient genetic systems would facilitate control of NWS in areas where it is endemic. In SIT programs, females cost money to rear and can hinder the effectiveness of the program by outcompeting with wildtype females to mate with the sterile males. For this reason, transgenic sexing systems have been developed that produce only males when fed a diet lacking tetracycline. Our lab has developed a two component transgenic sexing system in Lucilia cuprina that consists of a driver containing an early cellularization gene promoter and a tetracycline transactivator, and an effector, containing tetO binding sites and a proapoptotic gene separated by a female specific intron. This work created male-only lines but had an issue with leaky expression- some males were dying along with the females. My work has been focusing on the use of different early cellularization gene promoters and proapoptotic gene combinations in the aim of identifying a less leaky combination. Preliminary data has showed some promising combinations of driver and effector lines. These transgenic sexing systems combined with an SIT program could lead to more efficient systems for genetic control of Lucilia cuprina and NWS.

The influence of Neandertal alleles on cytotoxic response

Farida S. Akhtari and Alison Motsinger-Reif

It is now established through various studies that people of Eurasian origin contain traces of DNA inherited from interbreeding with Neandertals. Recent studies have shown that these Neandertal variants influence a range of clinically important traits and diseases. Understanding the genetic factors responsible for the variability in individual response to drug or chemical exposure is a key goal of pharmacogenomics and toxicogenomics, as dose responses are clinically and epidemiologically important traits. It is well established that ethnic and racial differences are important in dose response traits, but to our knowledge the influence of Neanderthal ancestry on dose response is unknown. Towards this aim, we examined if Neandertal ancestry plays a role in cytotoxic response to anti-cancer drugs and toxic environmental chemicals. We identified common Neandertal variants in lymphoblastoid cell lines (LCLs) derived from the globally diverse 1000 Genomes Project and Caucasian cell lines from the Children's Hospital of Oakland Research Institute. We analyzed the effects of these Neandertal alleles on cytotoxic response to 29 anti-cancer drugs and 179 environmental chemicals at varying concentrations using genome-wide data. We identified & replicated regional genes from these association results, including a single nucleotide polymorphism in the SNORD-113 cluster. Our results also show that the Neandertal alleles cumulatively lead to increased sensitivity to both the anti-cancer drugs and the environmental chemicals. Our results demonstrate the influence of Neandertal ancestry-informative markers on cytotoxic response. These results could be important in identifying biomarkers for personalized medicine or dissect the underlying etiology of dose response traits.

Effect of Genetic Architecture and Sample Size on the Accuracy of Genomic Prediction of Complex Traits

Fabio Morgante, Wen Huang, Christian Maltecca, and Trudy Mackay

Understanding the genetic architecture of complex traits is a fundamental aim of many branches of genetics. Genome wide association studies (GWAS) have been successful at identifying loci affecting complex traits. However, those loci account for just a very small proportion of the total genetic variation ("missing heritability") and prediction of phenotypes based on the loci uncovered by GWAS has had low accuracy. Regressing phenotypes on genome-wide markers concurrently (whole genome regression, WGR,) may capture a conspicuous amount of the genetic variation of complex traits and, thereby, increase predictive ability. However, most WGR methods assume strict additive and infinitesimal architecture; failure of any of these assumptions may lead to low predictive ability. Here, we investigated the effect of genetic architecture and sample size on the accuracy of prediction of complex traits. We used G-BLUP methodology and the unique resource of the Drosophila Genetic Reference Panel (DGRP), a collection of 205 fully sequenced inbred lines as well as simulated data. The results show that accuracy of prediction increases as sample size increases, conditional on the trait genetic architecture being taken into account in the statistical model. In particular, strict additive models may fail completely if epistasis contributes to the genetic architecture of the trait. However, when an epistatic model is fitted, the accuracy of prediction rises, even with small sample size. In summary, this study shows the importance of accounting for genetic architecture to increase the accuracy of genomic prediction of complex traits.

Towards a genetic pest management approach for invasive mice: Assessing reproductive competitiveness of male laboratory mice

Megan Serr, Caroline Leitschuh, Nicole Heard, John Godwin

House mice are significant and invasive pests, particularly on islands. Genetic engineering could pose an alternative to the traditional method of toxicants as a means of rodent eradication on islands. Ongoing research efforts are aimed at creating a strain of mice genetically engineered to produce offspring that are heavily male-biased with the goal of suppressing invasive mouse populations on islands. Successful implementation of this approach depends on engineered hybrid males mating successfully in complex environments. This project explores the genetic and behavioral differences between Mus musculus strains in terms of mating and fecundity using wild house mice derived from an invasive population on the Farallon islands (MmF) and a laboratory strain (tw2). Mice with the 't allele' (tw2) have a naturally occurring meiotic drive system. To assess fertility in hybrid crosses, tw2 males were paired with wild-derived females from the Farallon islands (MmF). Results of these matings indicate a significant difference in litter size with hybrid litters having fewer offspring (MmF [7.8] > MmF x tw2 [5.4]). Next, we used larger (3 meter2) enclosures with enrichment to increase environmental complexity. We introduced both a MmF and a tw2 male to four MmF females to assess female mate choice. Initially the tw2 males were dominant but none of the offspring carried the t-allele. The goal is to continue to backcross lab into wild strains and assess breeding and reproductive success in environments that more realistically represent those of an island where this approach would be implemented.

Have a question concerning the Program in Genetics?
Contact one of us below!

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Thanks for attending the 7th Annual Program in Genetics Fall Retreat 2016!

Join us again next year!