TGS 2022

Bryan, TX | The Stella Hotel

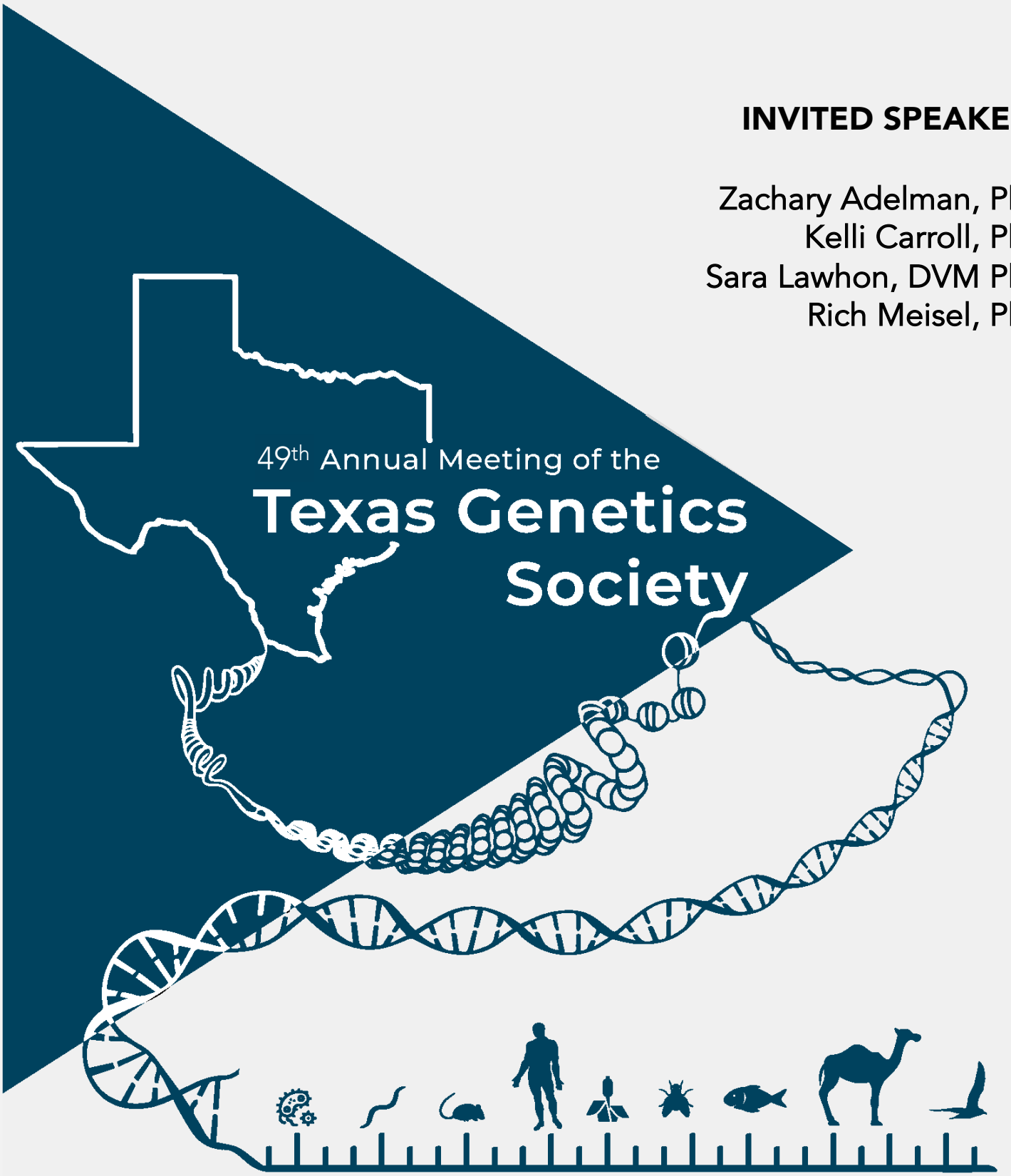
March 31–April 2, 2022

INVITED SPEAKERS

Zachary Adelman, PhD
Kelli Carroll, PhD
Sara Lawhon, DVM PhD
Rich Meisel, PhD

49th Annual Meeting of the

Texas Genetics Society



For more information see http://www.texasgeneticssociety.org/

Zachary Adelman, PhD, Texas A&M University

"Engineering and un-engineering the genome of the disease vector mosquito *Aedes aegypti*"

I am a Professor in the Department of Entomology and member of the Interdisciplinary program in Genetics and Genomics at Texas A&M University. After earning my undergraduate degree in Biochemistry from Ithaca College, I moved on to the world of disease vector mosquitoes and have never looked back. During my PhD research at Colorado State University, I worked on engineering recombinant viruses to block the replication of important human pathogens such as dengue. During my post-doctoral work at the University of California-Irvine I learned how to modify the mosquito genome itself, in the lab Anthony James where the technique was first developed. After starting my lab in 2005 at Virginia Tech, I moved to Texas A&M in 2016, where the major focus of my research remains on the development of novel gene editing/gene replacement approaches for disease vector mosquitoes as well as robust safeguards for their potential use. My research program has been continually funded by NIH/NIAID since 2007, with additional funding from NIFA and the State of Texas.

Kelli Carroll, PhD, Austin College

"Identification of Novel Regulators of Embryonic Development"

Dr. Kelli Carroll attended Davidson College in Davidson, NC where she obtained her bachelor's degree in Biology with a concentration in Neuroscience. She subsequently attended Harvard University where she received a PhD in Developmental and Regenerative Biology. Her PhD thesis in the lab of Dr. Trista North focused on the role of estrogen signaling in hematopoietic stem cell development and regeneration. She then moved to Dallas where she did a postdoc with Dr. Eric Olson in the molecular biology department at the University of Texas Southwestern Medical Center. Her postdoc research focused on skeletal and cardiac muscle development and function as well as applications of new genome editing technologies in the heart. In 2019, Kelli moved to Austin College in Sherman where she is an Assistant Professor of Biology. Her lab focuses on the identification of both genetic and environmental regulators of zebrafish development.

Sara Lawhon DVM, PhD, Texas A&M University

“Small Talk and Sequencing: *Staphylococcus pseudintermedius* Quorum-Sensing and Virulence in Dogs and Humans”

Dr. Sara D. Lawhon received her DVM from Texas A&M University in 1997 and her PhD from North Carolina State University in 2003 after completing an Infectious Disease Residency at North Carolina State University in 2001. She joined Texas A&M University as a faculty member in 2008. Her research focuses on bacterial pathogenesis and antimicrobial resistance in *Salmonella enterica* and *Staphylococcus pseudintermedius*. Her work has been funded by the FDA, CDC, the Morris Animal Foundation, and others. Her teaching centers on helping others understand bacterial diseases in animals and humans and to apply this knowledge for diagnosis, treatment, and prevention of infectious diseases in veterinary patients with an emphasis on antimicrobial stewardship and One Health. For this effort, she received a Zoetis Distinguished Veterinary Teacher Award in 2019 and the Student American Veterinary Medical Association (SAVMA) Teaching Excellence Award in 2020.

Rich Meisel, PhD, University of Houston

“House Fly Polymorphic Y chromosomes affect Myriad Ecologically Relevant Phenotypes”

I use genetic and genomic approaches to study evolutionary biology. I am interested in how genetic variation, inter-sexual differences, and environmental heterogeneity affect the evolution of phenotypes within populations and across species. I earned my BA in Biology from Cornell University, and my PhD in Genetics from Penn State University, where I studied the evolution of gene duplication and genome rearrangements in Drosophila. I was a postdoc at Cornell University, working with Andy Clark on sexually dimorphic gene expression and sex chromosomes in flies. I am currently an Associate Professor at the University of Houston, where my lab studies the evolution of sex chromosomes, sex determination, sexual dimorphism, and animal-microbe interactions.

Heath Blackmon, PhD, Texas A&M University

R Workshop director

Dr. Heath Blackmon is an Assistant Professor who joined the Biology Department at TAMU in 2017. He earned his BS in Environmental Science at Oregon State University, Summa Cum Laude, in 2010. He earned his PhD in Quantitative Biology at the University of Texas at Arlington in 2015. His research is in genome evolution, specifically sex chromosome and structural evolution. To do so, his group develops methods and databases that accelerate the analysis of data within quantitative genetic and phylogenetic frameworks. He is a member of the Genetics Society of America, Society for the Study of Evolution, American Genetics Association, The Coleopterists Society, American Society of Naturalists, and the Texas Genetics Society.

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Texas Genetics Society Meetings, 1974–2022

No.	Year	Location	Organizer	President	TGS Distinguished Geneticist Award	TGS Service Award
1	1974	Galveston	Barbara Bowman			
2	1975	Houston	Margery Shaw, Tom Caskey			
3	1976	Austin	Eldon Sutton			
4	1977	San Antonio	John Prince			
5	1978	Dallas	Raymond Lewandowski			
6	1979	Galveston	Lillian Lockhart			
7	1980	Houston		Eldon Sutton	--	--
8	1981	College Station		Barbara Bowman	--	--
9	1982	San Antonio		Robert Ferrell	C.P. Oliver	--
10	1983	Austin		Bob Sanders	Meta S. Brown	--
11	1984	Dallas		Lillian Lockhart	Bob Wagner	--
12	1985	Galveston		Arthur Beaudet	Rose Schneider	--
13	1986	Houston		Margery Shaw	T.C. Hsu	--
14	1987	College Station		Don Barnett	Margery Shaw	--
15	1988	Denton		Satish Srivastava	Eldon Sutton	--
16	1989	San Antonio		Frank Greenberg	Lillian Lockhart	--
17	1990	Austin		James Womack	Barbara Bowman	--
18	1991	Dallas		Charleen Moore	Dorothea Bennett	--
19	1992	College Station		Stephen Daiger	Bill Stone	--
20	1993	Galveston		Olivia White	Mike J. Siciliano	--
21	1994	Houston		John VandeBerg	Jack Schull	--
22	1995	San Antonio		Mary Jo Harrod	Frank Greenberg	--
23	1996	Austin		Fred Elder	James Womack	--
24	1997	Dallas		Bill Stone	Louise Strong	Don Barnett
25	1998	Austin		Sue Naylor	Tom Caskey	Eldon Sutton
26	1999	Austin		Ann Killary	Arthur Beaudet	Olivia White
27	2000	Houston		Mike Siciliano	Robert Ferrell	Fred Elder
28	2001	San Antonio		Paul Samollow	Sue Naylor	Charleen Moore
29	2002	South Padre		Ronald Walter	Alfred Knudson, Jr.	Andrew Dewees
30	2003	Austin		Jim Derr	Masatoshi Nei	Sue Ann Berend
31	2004	South Padre		Robert Baker	James Lupski	Sue Naylor
32	2005	Dallas		Christi Walter	Robert Baker	Paul Samollow
33	2006	Galveston		Rodney Nairn	Bert O'Malley	James Womack
34	2007	San Antonio		Sue Ann Berend	Jacqueline Hecht	Robert Baker
35	2008	College Station		Carol Wise	Larry Thompson	Christi Walters
36	2009	Austin		Laura Cox	Richard Gibbs	Michael J. Sicilliano
37	2010	Houston		Loren Skow	David Nelson	Rodney Nairn
38	2011	Dallas		Bhanu Chowdhary	David Russell	Carol Wise
39	2012	San Antonio		Ralf Krahe	Sen Pathak	Ann M. Killary
40	2013	College Station		Heather Conrad-Webb	Stephen Daiger	Joe Angel
41	2014	Waco		Penny Riggs	Gigi Lozano	Loren Skow
42	2015	Dallas		John (Trey) Fondon	Jonathan Cohen	Heather Conrad-Webb
43	2016	Houston		Clare Gill	Ralf Krahe	Stephen Daiger
44	2017	College Station		Erika Abel	Ann Killary	Penny Riggs
45	2018	College Station		Sarah Canterberry	David Threadgill	Erika Abel
46	2019	College Station		Jonathan Rios	Brendan Lee	David Nelson
47	2020	cancelled		Caleb Phillips	--	--
48	2021	virtual		David Aiello	Mark Kirkpatrick	Tina L. Gumienny
49	2022	College Station		Deborah Threadgill	--	

Texas Genetics Society 49th Annual Meeting
March 31–April 2, 2022
The Stella Hotel
4100 Lake Atlas Drive
Bryan, TX 77807

Thursday, March 31st

Aurora Room

2:00–5:00pm* **Pre-meeting R workshop**
Heath Blackmon, PhD

Celeste Pre-Function Area (hallway outside of Celeste Ballroom)

1:00–5:00pm **Late registration**
name tags, banquet tickets, reception drink tickets handed out

Orion Room

5:00–6:30pm TGS Board Meeting

5:00–6:30 pm **Vendor Exhibition—open to all participants**

Celeste Ballroom

6:30–7:30pm **Welcome and announcements**
Debbie Threadgill, TGS President 2022

***Opening Reception**

***Food and beverage provided during these sessions. Two drink tickets for beer or wine for either the reception or banquet.**

7:30–8:30pm **Opening keynote: Zachary Adelman, PhD**
"Engineering and un-engineering the genome of the disease vector mosquito *Aedes aegypti*"

8:30–10:00pm **Poster boards will be available for hanging up posters in the Aurora Room. Morning session posters must be hung up this evening, but all posters can be hung at this time.**
TGS members are free to retire to the Stella bar or head home.

Friday, April 1st

Celeste Ballroom

8:20–8:30am **Welcome and announcements**
Dr. Debbie Threadgill, 2022 TGS President

8:30–9:30am **Morning Keynote: Kelli Carroll, PhD**
"Identification of Novel Regulators of Embryonic Development."

9:30–10:00am **Contributed Papers Session: Model Organisms/Translation to Human Health**
session moderator TBA

9:30–9:45am **Investigating the regulators of microexon alternative-splicing in *C. elegans* using UNC-13 microexon model (F1)**
Bikash Choudhary, postdoctoral fellow, SMU

9:45–10:00am **Sex, strain, and diet dependent modulation of gut microbiota (F2)**
Anna Salvador, postdoctoral fellow, TAMU COM

Aurora Room

10:00–11:00am **Poster Session #1, even poster presentations**
(see end of program for assignments)
***Refreshment break**

Celeste Ballroom

11:00–12:00pm **Contributed Papers Session: Model Organisms/Translation to Human Health, continued**

11:00–11:15am **Spaceflight and microgravity response of plant telomeres and telomerase (F3)**
Borja Barbero Barcenilla, graduate, TAMU COALS

11:15–11:30am **FOXO1 inhibits the expression of canonical WNT target genes in a set of basal-like breast and glioblastoma multiforme cancer cell lines (F4)**
Shania Pintor, graduate student, UTRGV, Dept. of Biology

11:30–11:45am **ERBB4 mediates IL10-induced growth of EGFR–independent colon tumors (F5)**
Michael McGill, graduate student, TAMU IDP Graduate Program in Genetics and Genomics, COM

11:45–12:00pm **Negative feedback regulation in *Drosophila* dorsal-ventral patterning (F6)**
Allison Schloop, graduate student, NCSU/TAMU

Celeste Ballroom

12:00–1:15pm *Vendor workshops and lunch sponsored by 10X Genomics and Qiagen. **Lunch pick-up in the Celeste Pre-Function Area. Return to Celeste Ballroom for vendor workshops.**

Celeste Ballroom

1:15–2:15pm **Afternoon Keynote: Sara Lawhon DVM, PhD**
"Small Talk and Sequencing: *Staphylococcus pseudintermedius* Quorum-Sensing and Virulence in Dogs and Humans"

2:15–3:00pm **Contributed Papers Session: Microbial Genomics/Genetics**
session moderator: Kelli Carroll

2:15–2:30pm **Sheep in wolves' clothing: Temperate T7-like bacteriophages and the origins of the *Autographiviridae* (F7)**
Justin Boeckman, postdoc, TAMU Center for Phage Technology, COALS

2:30–2:45pm **Utilizing Mitochondrial Dysfunction in Disease to Uncover Mitochondrial Maintenance Mechanisms (F8)**
Armando Moreno, graduate student, Rice

2:45–3:00pm **Role of Host Genetics in Methicillin-Resistant Staphylococcus aureus (MRSA) infection (F9)**
Aravindh Nagarajan, graduate student, TAMU Interdisciplinary Graduate Program in Genetics and Genomics, COM

Aurora Room

3:00–4:00pm **Poster Session #2, poster presentations**
(see end of program for assignments)
***Refreshment Break**

Celeste Ballroom

4:00–5:15pm **Contributed Papers Session: Microbial Genomics/Genetics, continued**
session moderator: Kelli Carroll

4:00–4:15pm **Analyzing *Salmonella* serovar dynamics in beef cattle and the feedlot environment using whole genome (F10) sequencing and phylogenetics,**
Colette Nickodem, graduate student, TAMU CVM

4:15–4:30pm **Comparative Genomics of *Campylobacter rectus*, an "Emerging *Campylobacter* Species" (F11)**
Casey Hughes Lago, graduate student, TAMU Interdisciplinary Graduate Program in Genetics, COM

4:30–4:45pm **Investigating the downstream effect of the HOG and CWI MAPK pathways on gene expression changes observed in the *Saccharomyces cerevisiae* pgm2Δ mutant (F12)**
Madelyn Oliver, Austin College undergraduate

4:45–5:00pm **Investigating the role of RNA polymerase II stalling in spt4Δ-mediated rescue of *Saccharomyces cerevisiae* mutants lacking PGM2 (F13)**
Ruthann Schmiege, Austin College undergraduate

5:00–5:15pm **Identification and Characterization of TANGO6 in Zebrafish Development (F14)**
Hannah Herron, Austin College undergraduate

5:15–6:30pm Take down posters. Judges finalize scoring sheets.
Judges Meeting

Celeste Pre-Function Area

5:30–6:30pm **Visit vendor displays, network**

Celeste Ballroom

6:30–8:00pm **Banquet and Service Award Presentation, Acknowledgement of Sponsors, 1st Time Attendees/1st Time Presenters**

8:00–10:00pm TGS members are free to retire to the Stella bar or head home.

Saturday, April 2nd

Celeste Ballroom

8:20–8:30am **Session introduction**
Tina Gumienny, 2023 TGS President

8:30–9:30am **Morning Keynote: Rich Meisel, PhD**
House Fly Polymorphic Y chromosomes affect Myriad Ecologically Relevant Phenotypes

9:30–10:15am **Contributed Papers: Ecological Genetics, Genomics/ Evolutionary Genetics/Genomics**
session moderator: Megan Keniry

9:30–9:45am **Karyotypic stasis and swarming influenced the evolution of viral tolerance in a large bat radiation (S1)**
Nicole Foley, postdoc, TAMU CVM

9:45–10:00am **Testing for Signatures of Coevolutionary Local Adaptation and Congruent Gene Flow in a Co-Diversifying Ant-Endosymbiont Mutualism (S2)**
Brandon Meadows, graduate student, Texas Tech University

10:00–10:15am **Tree House Explorer: A Novel Genome Browser for Phylogenomics and Phylogeography (S3)**
Andrew Harris, graduate student, TAMU Interdisciplinary Graduate Program in Genetics, CVM

Celeste Pre-Function Area

10:15–10:35am ***Coffee Break, vendors breakdown exhibits**

Celeste Ballroom

10:35–11:35am **Contributed Papers: Ecological Genetics, Genomics/ Evolutionary Genetics/Genomics, continued**
session moderator: Megan Keniry

10:35–10:50am **Genomic Signatures of Cattle Introgression in Historical and Modern North American Bison (S4)**
Sam Stroupe, graduate student, TAMU CVM

10:50–11:05am **Genomic phylogeography of the Grace's Warbler (Setophaga graciae): evidence of in situ diversification and recent population expansion across pine-oak ecosystems (S5)**
Jack P. Hruska, graduate student, Texas Tech

11:05–11:20am **The evolution of four chromosomal inversions underlying ecological adaptation in Atlantic herring using long–read sequencing (S6)**
Minal Jamsandekar, graduate student, TAMU CVM, TGS student representative

11:20–11:35am **The Role of Centromeres in Chromosome Number Evolution (S7)**
Michelle Jonika, graduate student, TAMU Interdisciplinary Graduate Program in Genetics, COS, TGS student representative

11:35–12:00pm **Judges finalize scoring sheets from morning session**

12:00–1:00pm **TGS business meeting and awards presentations**

1:00pm **pick up box lunch and depart meeting**

Poster assignments: all even numbered posters are in the morning session and all odd numbered posters are in the afternoon session. Poster sessions are in the Aurora Room.

Poster session #1: Friday April 1st, 10:00–11:00am

P2. Coa4 acts upstream of Cox11 in the mitochondrial copper delivery pathway to Cox1 subunit of cytochrome c oxidase, Abhinav B. Swaminathan, graduate student presenter, TAMU COALS

P4. Sensory neuron transcriptomes reveal complex neuron-specific function and regulation of mec-2/Stomatin splicing, Canyon Calovich-Benne, graduate student presenter, SMU

P6. RNA binding proteins coordinately control lifespan in *C. elegans*, Rebekah Napier-Jameson, graduate student presenter, SMU

P8. Dissecting interactions across gene regulatory layers: Tdp-1 and Fust-1 coordinate with transcription factor Ceh-14 to affect reproduction in *C. elegans*, Morgan Taylor, graduate student presenter, SMU

P10. Characterizing the genetic and physical interaction of the DBL-1/BMP signaling pathway with BLMP-1/BLIMP1 transcription regulator in *Caenorhabditis elegans*, Mohammed Farhan Lakdawala, graduate student presenter, TWU

P12. Gene Regulatory Networks in Development: Genetic Variation and Robustness of Anterior-Posterior (AP) Axis Formation in *Drosophila*, Lossie ("Elle") Rooney, graduate student presenter, NCSU

P14. Analysis of pMad and Medea Expression in BMP Pathway in Drosophila with Multiple Fluorescent Proteins, Hung-Yuan (Zeke) Chen, graduate student presenter, TAMU Engineering

P16. Understanding DNA double-strand break (DSB) repair in *Aedes aegypti*, Joseph S. Romanowski, graduate student presenter, TAMU IDP Graduate Program in Genetics and Genomics, TAMU COALS

P18. Using natural gene drives and genetic engineering tools for population control of invasive mice on islands, Ana M. Velasquez Escobar, graduate student presenter, TAMU IDP Graduate Program in Genetics and Genomics, TAMU COM

P20. Theiler's Virus Induced Neuroinflammation of LRRK2 G2019S Transgenic Mice, Tae Wook Kang, graduate student presenter, TAMU CVM

P22. Identification of dysregulated small RNA in Angelman syndrome pig extracellular vesicles, Livia Schuller, graduate student presenter, TAMU IDP Graduate Program in Genetics and Genomics, TAMU CVM

P24. A Genomics Approach to Characterize White Coat Color Genes in American Bison, Bison bison. Carly Martone, graduate student presenter, TAMU CVM

P26. Genomic identification of the most diverged avian hybrid, James M. Alfieri, graduate student presenter, IDP in Ecology and Evolutionary Biology, TAMU

P28. The perils and promise of models of chromosome evolution, Terrence Sylvester, graduate student presenter, TAMU COS

P30. Cannabidiol (CBD) Signaling in Human Neuroblastoma, Claire Alexander, graduate student presenter, Lamar Univ, Biol.

P32. Evolution of Oxidative Stress Response Regulatory Function in Telomere-Associated Protein POT1b, David Curtis, technician presenter, TAMU COALS

P34. Testing in vitro toxicity using an organotypic culture model based on a novel mouse genetic reference population, Krishna N. Patel, technician presenter, TAMU COM

Poster session #2: Friday April 1st, 3:30–4:30pm

P1. Glyphosate's Effects on the Development of Zebrafish (*Danio rerio*), Mia Hibner, undergraduate presenter, Austin College

P3. A Characterization of the Role of the MRTF/SRF Pathway in Zebrafish Development, Taylor Dornseifer, undergraduate presenter, Austin College

P5. Characterization of the novel DUF4585 gene family in zebrafish, Yasmine Bukhari, undergraduate presenter, Austin College

P7. Exploring the effects of Methylglyoxal on cytosolic Ca2+ levels in the absence of HACS and intracellular Ca2+ efflux channels, Harsha Tamtam, undergraduate presenter, Austin College

P9. Examining growth phenotypes of the pgm2Δ mutation in *Saccharomyces cerevisiae* lacking or overexpressing TPS1, NTH1, and ATH1, Shruti Veera Raghavan, undergraduate presenter, Austin College

P11. Studying the effects of a primary microcephaly-associated mutation in *Caenorhabditis elegans*, Ramon Duran, undergraduate presenter, Univ. of Tulsa

P13. Transcriptional Regulation as a Conserved Function of BRCA1/BARD1 in *Caenorhabditis elegans*, Thu Uyen Nguyen, undergraduate presenter, TCU

P15. Genetic regulation of diet-induced thermogenesis in mice, Emanuele Baldassarri, undergraduate presenter, TAMU

P17. Accumulation of fat prior to dietary intervention may reduce efficacy of personalized dietary guidance in mice, Riley K. Watson, undergraduate presenter, TAMU

P19. The immune landscape of murine colorectal tumors, Matthew Crespo, Sophia Ferrer, Meghan Si, Holly Thill, Megan Thomas, Daniela Wong, undergraduate presenters, TAMU

P21. NF-κB-Inducing Kinase (NIK) Mediates Neuronal Function and Glioblastoma Tumor Microenvironment, Parker Smith, undergraduate presenter, TAMU

P23. Inequality of Sex Chromosome to Autosome Fusions, Kayla Wilholt, undergraduate presenter, TAMU

P25. Sequence and lineage characterization of major histocompatibility complex class I genes in Atlantic herring using comparative genomic approach. Mary Smith, undergraduate presenter, TAMU

P27. Reprogramming Collaborative Cross mouse embryonic fibroblast cells into induced pluripotent stem cells using the Sendai virus, Demi K. Waworuntu and Alex H. Phan, undergraduate presenters, TAMU

P29. CaveCrawler: An interactive analysis suite for cavefish bioinformatics, Annabel Perry, undergraduate presenter, TAMU

Postdoc presenters:

P31. Systems biology approaches to build a predictive model of Dorsal/NF-κB signaling network in the *Drosophila* embryo, Etika Goyal, postdoc presenter, TAMU Engineering

P33. FDX1 is required for copper release from elesclomol-copper complex in the mitochondria, Mohammad Zulkifli, postdoc presenter, TAMU COALS

P35. PROTECTION OF TELOMERES 1 regulates oxidative stress response and genome integrity in *Arabidopsis*, Ji-Hee Min, postdoc presenter, TAMU COALS

Platform presentation abstracts

F1. Investigating the regulators of microexon alternative-splicing in *C. elegans* using UNC-13 microexon model

B C Choudhary, Rebekah N Jameson, A D Norris

Southern Methodist University

Alternative splicing (AS) is one of the phenomena in higher eukaryotes to generate proteomic diversity in the cellular milieu. Exons with a size ≤30-50 nucleotides are classified as microexons (µexons). Microexons are shown to be enriched in the nervous system of higher organisms and altered splicing leads to autism-related neurological disorders. Using *C. elegans* as a genetic model, we found prp-40, a spliceosomal component, and a set of RNA-binding proteins (RBPs) as some of the candidates regulating AS of µexons in the nervous system. We modeled one of the alternatively spliced µexon of UNC-13 (a synaptic protein) to understand the splicing regulators and assess the physiological consequences of altered splicing of UNC-13 µexon on the animal. We found that the alternatively spliced form of UNC-13 µexon is tightly regulated in the nervous system. Two neuronally expressed RBPs, exc-7 and mbl-1 affected the UNC-13 µexon splicing at various levels. Animals with altered expression of UNC-13 isoforms showed various behavioral deficits. These behavioral deficits were directly associated with the release of synaptic vesicles (SVs) indicating various UNC-13 isoforms based on µexon "inclusion" or "exclusion" have different capabilities for the release of SVs at synapses. In conclusion, we found few regulatory candidates of µexon-splicing and functional consequences of altered splicing using UNC-13 µexon as an example.

Bikash C Choudhary

bchoudhary@smu.edu

Postdoc

F2. Sex, strain, and diet dependent modulation of gut microbiota

Anna C. Salvador1,2, Nazmul M. Huda3, Danny Arends4, Ahmed M. Elsaadi1, Anthony C. Gacasan1, Gudrun A. Brockmann4, Brian J. Bennett3,5, David W. Threadgill1,2,6

1 Department of Molecular and Cellular Medicine, Texas A&M Health Science Center, College Station, TX, 77843, USA 2 Department of Nutrition, Texas A&M University, College Station, TX, 77843, USA 3 Department of Nutrition, University of California Davis, Sacramento, CA, 95616, USA4Obesity and Metabolism Unit, Western Human Nutrition Research Center, USDA-ARS, Davis, CA, 956165 Züchtungsbiologie und Molekulare Genetik, Albrecht Daniel Thaer-Institut, Berlin, 10115, Germany 6 Department of Biochemistry & Biophysics, Texas A&M University, College Station, TX, 77843, USA

The gut microbiome has emerged as a key component underlying the application of precision nutrition and individualized dietary response. The microbiome is modulated by a combination of host genetics, diet, and sex effects. The magnitude of these effects and interactions among them is important to understanding inter-individual variability in gut microbiota. In a previous study, mouse strain-specific responses to American and ketogenic diets were observed along with several QTL for metabolic traits. In the current study, we searched for genetic variants underlying differences in the gut microbiome in response to American and ketogenic diets between C57BL/6J (B6) and FVB/NJ (FVB) mouse strains.

B6 females were crossed with FVB males to generate F1 mice and subsequently intercrossed to generate an F2 population. F2s were screened for their response to American (35% of energy from fat, 50% from carbohydrates) and ketogenic (84% of energy from fat, 0% from carbohydrates) diets during a 3-month feeding trial. Half of the F2 mice were placed on American diet (102 males, 122 females) and half on ketogenic diet (126 males, 119 females). Stool microbiota was analyzed by 16S rRNA V4 sequencing methodology. Sequences were de-multiplexed and amplicon sequence variance (ASV) was determined using the open-source software QIIME2-DADA2 pipeline. Taxonomy was assigned using the SILVA 132 reference database customized for 16s V4 (515F/806R) region of sequences at the threshold of 99% pairwise identity. α-diversity and β-diversity were calculated from the unfiltered ASV table. Any ASV not seen more than 5 times in at least 5% of the samples were removed for calculating differential bacteria abundance. For genetic mapping of microbiota traits, a core measurable microbiota was defined as those traits present in at least 20% of the individuals at the genus and species level of taxonomy.

Genetic mapping of microbial traits revealed 19 loci that were genotype specific, 13 loci that were genotype and diet specific, and 1 locus that was genotype and sex specific. For many microbial traits, irrespective to which quantitative trait loci model was used, diet or the interaction between diet and a genotype were the strongest predictors of the abundance of each microbial trait. Interestingly, multiple traits map to the distal part of Chr1 including metabolic and microbial traits as well as the eigenvectors extracted from principal coordinate analysis for measures of β-diversity. Conditioned linkage analysis suggests that there is a possible causal relationship between microbial diversity and abundances of ASV associated with the Rikenella, Ruminiclostridium and Bilophila taxa that is driven by genetic variation at the distal part of Chr1 (160.6 – 185.1 Mb).

Irrespective to genetic background, diet has a profound ability to modulate gut microbiota. Sex, while important to the analyses, was not as strong of a predictor for microbial abundances. These results demonstrate the importance of characterizing the magnitude of the effects that sex, diet, and genetic background have on inter-individual differences in gut microbiota. Precision nutrition will be advanced through integration of genetic variation, microbiota variation, and sex in response to diets varied in carbohydrate composition.

Anna C. Salvador

annacsalvador@tamu.edu

Postdoc

F3. Spaceflight and microgravity response of plant telomeres and telomerase

Borja Barbero Barcenilla, Alexander Meyer, Claudia Castillo-Gonzalez, Imara Perera, Roberto Aquilano, Sarah Wyatt, Dorothy Shippen

Texas A&M University, Ohio University, Texas A&M University, North Carolina State University, Universidad Nacional de Rosario, Ohio University, Texas A&M University

To realize NASA's goal of human colonization of Mars and the Moon by 2050, plants will be required for food production, carbon dioxide removal, oxygen production and water purification. Understanding plant adaptation to spaceflight is therefore essential for human space expansion. While little is known about plant responses to spaceflight, transcriptomic data showed the upregulation of multiple stress response pathways, including genomic and oxidative stress. Telomeres are essential structures that safeguard genome stability and are an important biological marker of survivability. Prior studies revealed that astronauts aboard the International Space Station (ISS) experienced increased telomere length and oxidative damage to their genomes during spaceflight. Here we set out to investigate telomere length homeostasis in relationship with cellular stress in Arabidopsis thaliana seedlings grown for 12 days either in orbit aboard the ISS, or under simulated microgravity conditions produced by a Random Positioning Machine. We report a substantial increase in telomerase enzyme activity in seedlings grown under spaceflight conditions as compared to both 1g ground controls and simulated microgravity. Despite the dramatic increase in telomerase activity we did not detect a significant change in telomere length. However, we found elevated levels of 8-oxoguanine in the DNA of seedlings grown aboard the ISS, as well as increased mitochondrial DNA, consistent with oxidative damage. These findings support previous omics analyses predicting spaceflight-induced oxidative stress in Arabidopsis. We postulate that increased telomerase activity in space-flown Arabidopsis is a response to excess ROS generated from the ionizing radiation environment of low Earth orbit, and may reflect a broader role for telomerase in the stress response. Altogether, our data indicate that plants have a robust mechanism of telomere maintenance, resulting in negligible telomere length fluctuations during spaceflight and microgravity conditions. These observations suggest that plants may be well-equipped to survive the stresses imposed by interstellar colonization.

Borja Barbero Barcenilla

bbarbero@tamu.edu

Graduate Student

F4. FOXO1 inhibits the expression of canonical WNT target genes in a set of basal-like breast and glioblastoma multiforme cancer cell lines

Shania Pintor, David Flores, Brianda Lozoya, Bipul Soti, Alma Lopez, Rishi Pokhrel, Joaquin Negrete, Michael Persans, Robert Gilkerson, Bonnie Gunn, and Megan Keniry

Departments of Biology (all authors), Clinical Laboratory Sciences (Robert Gilkerson)

FOXO transcription factors promote stem gene expression in poor prognosis basal-like breast cancer (BBC) and glioblastoma multiforme (GBM). To gain insight into the impact of FOXO1 in BBC, we treated BT549 cells with the FOXO1 inhibitor AS1842856 and identified differentially expressed genes. Gene Set Enrichment Analysis (GSEA) with RNA Seq data indicated that canonical WNT target genes including AXIN2, LEF1, and TCF7 were robustly induced upon FOXO1 inhibition. These genes were induced in GBM cell lines U87MG, LN18, LN229, A172, and DBTRG upon FOXO1 inhibition. FOXO1 RNAi or 5-AZA induced AXIN2, LEF1, and TCF7 in BT549 cells. This work is the first to report that FOXO1 restrains the expression of canonical WNT target genes in BBC and GBM cells.

Shania Pintor

shania.pintor01@utrgv.edu

Graduate Student

F5. ERBB4 mediates IL10-induced growth of EGFR-independent colon tumors

Michael P. McGill, Carolina Mantilla-Rojas, David W. Threadgill

Interdisciplinary Graduate Program in Genetics and Genomics, Department of Molecular and Cellular Medicine, Texas A&M University, College Station, TX 77843, USA

ERBB4 is commonly over-expressed in human colorectal cancer (CRC), however the utility of ERBB4 as a target for CRC therapeutics is largely unexplored. Our group recently identified a molecular subtype of CRC that arises independent of EGFR and displays a more aggressive growth phenotype than those dependent on EGFR. The robust growth phenotype of EGFR-independent tumors can be in part attributed to upregulation of IL10 signaling. In addition, EGFR-independent tumors display a significant upregulation of Erbb2 and Erbb4 transcripts in both spontaneous and sporadic CRC mouse models, perhaps compensating for the loss of EGFR. To investigate the importance of other ERBB receptors, we ablated Erbb4 to interrogate its influence on tumor development in vivo using a conditional allele of Erbb4tm1Fej (Erbb4f). ERBB4-deficient ApcMin/+ mice (ApcMin/+, ErbB4f/f, Tg(Vil1-Cre)) were established and used to show that ERBB4 ablation in the intestinal epithelia results in a significant decrease in the number of intestinal and colon tumors. Polyps lacking ERBB4 were also significantly reduced in size, contrary to what is observed with loss of EGFR. We also recently developed ERBB2-deficient ApcMin/+ mice, and preliminary results suggest that Erbb2 ablation also results in a decrease in intestinal and colon tumor number and size. Consistent with data from EGFR-independent tumors, transcriptomic analysis of ERBB4-deficient intestinal tumors predicted down-regulation of IL10 signaling, which was validated through Il10 and Socs3 qPCR. To complement our findings, the observed down-regulation of Il10 and Socs3 at the transcript level corresponded with a significant decrease in IL10 levels in the serum of mice harboring ERBB4 deficient tumors when compared to mice without tumors. Furthermore, we found that transcript levels of Erbb4 significantly decreased after anti-IL10 treatment of EGFR-independent tumors in vivo. This illustrates a possible negative feedback loop whereby neutralizing IL10 also leads to a reduction of Erbb4 expression, further reducing IL10 signaling. Taken together, the data suggest that the absence of EGFR triggers Erbb4 upregulation, implicating an important role for ERBB4 in EGFR-independent colon tumor growth. These results suggest that therapeutic targeting of ERBB4 may lead to a reduction in IL10 signaling and reduced intestinal polyp multiplicity and size in EGFR-independent tumors and inform the development of novel approaches to treat CRC that exhibit aberrant expression of EGFR and ERBB4.

Michael McGill

mpmcgill@tamu.edu

Graduate Student

F6. Negative feedback regulation in *Drosophila* dorsal-ventral patterning

Allison Schloop, Dr. Gregory Reeves

North Carolina State University, Texas A&M University

Development of an organism is dependent upon proper regulation of gene expression. Initiation of gene expression often relies on long-range signals referred to as morphogens; these morphogens form concentration gradients that aid in specific activation of genes responsible for proper body patterning. In Drosophila, one such morphogen is Dorsal (Dl), a transcription factor that helps with patterning of the dorsal-ventral (DV) axis in the early embryo. The impact of Dl is further refined by gene regulatory loops that help to control the dynamics of the Dl gradient. One regulatory loop of interest is the negative feedback loop with Cactus (Cact). Cact is initially bound to Dl, sequestering it to the cytoplasm, but Toll signaling on the ventral side of the cell degrades Cact and allows Dl to enter the nucleus. There, Dl can activate target genes, one of which is Cact, suggesting that Dl may regulate its own inhibition.

Our work currently focuses on establishing a system through which Cact can be examined in live embryos. Protein expression and use during development is very rapid; the turnover of Cact happens too quickly for standard live imaging techniques, like fluorescent protein fusions. Fluorescent proteins like GFP do not have enough time to mature and fluoresce before the associated protein is degraded. To work around this, we have utilized LlamaTags (Bothma et al. 2018) to image the dynamics of Cactus. We show that Cactus, while predominantly cytoplasmic, is also in the nucleus and shows a recoverable pattern after photobleaching. This provides initial evidence for an identifiable role of nuclear Cactus.

Allison Schloop

aeschloo@ncsu.edu

Graduate Student

F7. Sheep in wolves' clothing: Temperate T7-like bacteriophages and the origins of the Autographiviridae

Justin Boeckman, Abby Korn, Guichun Yao, Aravind Ravindran, Carlos Gonzalez, Jason Gill

Center for Phage Technology - Texas A&M University, Department of Plant Pathology and Microbiology - Texas A&M University, Department of Plant Pathology and Microbiology - Texas A&M University, Department of Plant Pathology and Microbiology - Texas A&M University, Department of Plant Pathology and Microbiology - Texas A&M University, Department of Animal Science - Texas A&M University

Bacteriophage T7 is an extensively studied virulent phage, and its taxonomic family, the Autographiviridae, is broadly synonymous with a strictly virulent lifestyle. It is difficult to imagine how a T7-like phage could function in a "domesticated" temperate lifestyle, in which it is incorporated into the host's genome. Here we describe two newly discovered temperate T7-like bacteriophages: ProddE, a Desulfovibrio phage, and Pasto, an Agrobacterium phage. Each contains recognizable T7-like proteins in the canonical T7-like gene order, but with the addition of lysogeny gene modules. Using ProddE and Pasto as templates, we identify similar T7-like prophage elements in a wide variety of Gram-negative bacterial genomes and a small number of Gram-positive genomes. These T7-like temperate elements are potential sources of novel lysis/lysogeny genetic switches for the maintenance of phage lysogeny. ProddE contains a phage-like repressor, while Pasto lysogeny appears to be controlled by a novel MarR-like transcriptional regulator. Both strategies seemingly rely on repression of the phage encoded RNA polymerase gene. In addition, identification of these elements in diverse bacterial species raises interesting evolutionary questions about the origins of T7-like phages and which lifestyle, temperate or virulent, is the ancestral form of the famously virulent Autographiviridae family.

Justin Boeckman, PhD

justin.boeckman@ag.tamu.edu

Postdoc

F8. Utilizing Mitochondrial Dysfunction in Disease to Uncover Mitochondrial Maintenance Mechanisms

Armando Moreno, Allison, Taffet, Natalia V. Kirienko

Rice University

Mitochondria are a critical component for cellular health, and a key determinant of the ability of apoptosis to limit the proliferation of cancer cells. Most commonly known as the “powerhouse of the cell”, mitochondria are much more than just a site for energy production; they participate in a myriad of functions, including several cell death pathways, homeostatic regulation of calcium and iron, coordinating the production of reactive oxygen species (ROS), and providing essential intermediates and regulation of cholesterol biosynthesis. Several critical pathways for maintaining mitochondrial homeostasis, including surveillance, repair, and recycling, have been identified within the past few decades, and often transcend this function to support general cellular homeostasis as well. For example, recent work from our lab has shown that a mitochondrial surveillance pathway called the ESRE network is activated by an increase in ROS is crucial for both mitochondrial and cellular homeostasis. Despite these discoveries leading to a greater understanding of mitochondrial maintenance, gaps remain in our understanding of how cellular aging affects mitochondrial function.

Cancer provides a powerful model to study the effects of mutations on mitochondrial function. There are many mutations associated with cancer that are related to a lack of cellular quality control. Databases such as COSMIC and CCLE, track mutations in various cancer cell lines, and with the help of these databases, we have compiled a list of genes commonly mutated in cancer. This set included both cancer driver and passenger mutations. Using the model organism Caenorhabditis elegans, we have knocked down orthologous genes using RNAi and performed a series of orthogonal assays to evaluate whether disrupting these genes affected sensitivity to mitochondrial damage. This high-throughput screen of about 600 genes left us with 50 genes that exhibited higher sensitivity to mitochondrial damage. Using these 50 genes as a seed set and WormNet to identify additional tightly associated genes for further validation, we obtained another list of 400 genes to screen. From this expansion screen, we obtained 89 genes to add to the original 50. With our assays we were able to develop a gene network of 139 genes that has a significant number of connections among network members.

Preliminary analysis has shown an enrichment of the network with genes related to cellular processes such as cell division, cell development, and cell fate. Functional validation of the genes in the network is underway, and preliminary data indicated that most of the genes, when mutated, exhibit mitochondrial dysfunction in various forms such as abnormal ATP levels, increased NADH, increased ROS, abnormal oxygen consumption, and a fragmented mitochondrial network. Not only do we see an effect on mitochondrial function, we also see an effect on alpha-synuclein aggregation (a hallmark of Parkinson’s disease) in a *C. elegans* Parkinson’s disease model. The overall goal of this project is to uncover novel mitochondria-related pathways and mechanisms that govern mitochondrial maintenance. With the completion of this network, we will have a powerful tool to understand mitochondrial regulation in disease.

Armando Moreno

am161@rice.edu

Graduate Student

F9. Role of Host Genetics in Methicillin-Resistant Staphylococcus aureus (MRSA) infection

Aravindh Nagarajan1,3, Kristin Scoggin1,3, David Threadgill1,2,4,5, Helene Andrews-Polymenis 1, 3 *

1Interdisciplinary Program in Genetics, Texas A&M University, College Station, Texas, United States of America
2Department of Molecular and Cellular Medicine, Texas A&M University, College Station, Texas, United States of America
3Department of Microbial Pathogenesis and Immunology, Texas A&M University, College Station, Texas, United States of America
4Texas A&M Institute for Genome Sciences and Society, Texas A&M University, College Station, Texas, United States of America
5Department of Biochemistry & Biophysics and Department of Nutrition, Texas A&M University, College Station, Texas, United States of America
*Corresponding author

Host-pathogen interaction is a complex phenomenon controlled both by the host and the pathogen, and leading to a variety of disease outcomes. Interactions between a host and pathogen can result in no disease (Resistant), a disease where the host is colonized but can 'tolerate' colonization (Tolerant) or severe disease (Susceptible). Staphylococcus aureus, a gram-positive bacterium, colonizes 50-60% of the human population intermittently or permanently as a commensal. However, S. aureus is also an opportunistic pathogen that causes skin, soft tissue, and bloodstream infections leading to abscess formation, endocarditis, and sepsis . We hypothesize that the host response to Methicillin-Resistant Staphylococcus aureus (MRSA) infection is influenced by the genetics of the host animal.

We model host genetic diversity using the Collaborative Cross (CC), a panel of recombinant mouse lines derived from eight founder strains representing high genetic variation across lines. This inbred panel has more than 40 million single nucleotide polymorphisms evenly dispersed across the genome and eight functional allele variants at any given locus. We surgically implanted telemetry devices in mice to monitor their core body temperature and activity, collected complete blood count, cytokines and chemokines, microbiome, and tissue samples before and after retro-orbital MRSA infection.

In our preliminary 7-day survival screen, we were classified CC lines into tolerant, resistant, and susceptible phenotypes based on survival and bacterial burden. We also observed sex differences in survival in some lines, where males appeared more susceptible to lethal infection than females. QTL analysis using bacterial burden, histopathology, and immune profile along with gene expression and microbiome difference should provide a basis to understand how the genetics of the host contribute to the outcome of infection. The data will help us understand the variation in infectious disease outcomes in the human population.

Aravindh Nagarajan

aravindh@tamu.edu

Graduate Student

F10. Analyzing Salmonella serovar dynamics in beef cattle and the feedlot environment using whole genome sequencing and phylogenetics

Colette Nickodem[1], Ashley Arnold[2], Kerri Gehring[2], Jason Gill[2 3], John Richeson[4], H.M. Scott[5], Jason Smith[6], Matthew Taylor[2], Javier Vinasco[5], Keri Norman[1]

[1]Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, Texas, [2]Department of Animal Science, Texas A&M University, College Station, Texas, [3]Center for Phage Technology, Texas A&M University, College Station, Texas, [4]Texas A&M AgriLife Research, Texas A&M University System, Amarillo, Texas, [5]Department of Veterinary Pathobiology, Texas A&M University, College Station, Texas, [6]Texas A&M AgriLife Research, Department of Animal Science, Texas A&M University, Amarillo, Texas

Salmonella can be harbored in beef cattle lymph nodes which are commonly incorporated into ground beef products making it a food safety concern. There is little understanding of Salmonella interactions between the feedlot environment and beef cattle. Our study aims to address this by assessing the relatedness of Salmonella serovars and antimicrobial resistance (AMR) genes between isolates from the feedlot environment, cattle feces and lymph nodes. Results will provide insight on Salmonella dynamics and the effectiveness of environmental feedlot interventions to mitigate Salmonella in beef cattle and therefore beef products. Beef cattle (n=360) and feedlot pens (n=30) were sampled on a monthly basis from June-December 2019 at the West Texas A&M University Research Feedlot in Canyon, TX. Longitudinal samples of freshly voided beef cattle feces, feedlot pen composite manure pack, feedlot pen composite dry, water, feed and cattle subiliac lymph nodes were collected and selectively cultured for Salmonella. All Salmonella isolates from pen composite manure pack (n=162), water (n=34), feed (n=13) and subiliac lymph node (n=96) samples and one randomly selected fecal Salmonella isolate per pen per month (n=189) were selected for whole genome sequencing on an Illumina MiSeq platform. A bioinformatics pipeline was used to determine serovar, sequence type, and resistance genes. Phylogenetic trees were developed to visualize isolate relatedness by feedlot pen, sample type and collection month. Eight Salmonella serovars (Kentucky (30.4%, n=150), Montevideo (27.9%, n=138), Anatum (20.2%, n=100), Lubbock (11.7%, n=58), Cerro (8.5%, n=42), Virginia (0.8%, n=4), Derby (0.2%, n=1), and Senftenberg (0.2%, n=1)) were identified with consistent sequence types within each serovar. All Kentucky isolates had a point mutation in the parC gene for quinolone resistance; however, phenotypic resistance and reduced susceptibility has not been tested. All other isolates were pan-susceptible except for one Senftenberg isolate which harbored AMR genes for aminoglycosides, ß-lactams, sulfonamides, macrolides, tetracycline and, chloramphenicol. Salmonella serovar composition by sample type showed a decrease in Montevideo proportion from pen environment (35.8%, n=58) to cattle fecal (26.5%, n=50) and lymph node (15.6%, n=15) isolates. There was an increase in proportion for both Lubbock and Anatum from pen environment (9.9%, n=16;14.8%, n=24) to cattle fecal (13.2%, n=25; 23.3%, n=44) and lymph node (17.7%, n=17; 30.2%, n=29) isolates. These trends suggest that the ability of Salmonella to migrate from the feedlot pen environment to the host is serovar specific. Phylogenetic trees clearly highlight Salmonella serovar trends by season, sample type and clustering among samples collected from pens close in geographic feedlot location. Observing these Salmonella dynamics between cattle and the feedlot environment will help identify targeted environmental treatments necessary to reduce or shift Salmonella from AMR to pan-susceptible serovars.

Colette Nickodem

cnickodem@tamu.edu

Graduate Student

F11. Comparative Genomics of Campylobacter rectus, an "Emerging Campylobacter Species"

Casey Hughes Lago, Deborah S. Threadgill

Texas A&M University
Molecular and Cellular Medicine Department

Campylobacter rectus is a gram-negative, anaerobic bacterium strongly associated with periodontitis. It also causes various extraoral infections and has been linked to adverse pregnancy outcomes, including low birth weight and pre-term labor in humans and murine models. C. rectus and related oral Campylobacters including C. showae, C. concisus, C. gracilis and others have been termed "emerging Campylobacter species" because infections by these organisms are likely underreported. Currently, there are only three publicly available genome sequences for C. rectus. This dearth of genomic information prevents the exploration of intraspecific genetic variability and genome evolution and limits our ability to study pathogenesis. We sequenced eight new C. rectus strains using Illumina MiSeq and used comparative methods to identify regions of interest. Secretion systems such as the type III flagellar secretion system (T3SS), type IV secretion system (T4SS), and type VI secretion system (T6SS) were identified and examined, since these are important for pathogenesis in other Campylobacter species. RAST, PATRIC, PHASTER, IslandViewer4 and other bioinformatics tools were used to assemble, annotate, and compare these regions in the genomes. QUAST was used to estimate completeness and showed high contiguity, and low error for the new genome assemblies. Each assembly had 62 contigs or less. N50 scores ranged from 107,141 to 368,575, while GC content ranged between 44.78 to 45.14%. The pan-genome of C. rectus, including the eight new and three old isolates, consists of 2670 genes with core and accessory genomes of 1429 and 1241 genes, respectively. All isolates have flagellar T3SS and T6SS hallmark proteins, while five of the isolates are missing a T4SS system. 21 prophage clusters were identified across the panel of isolates, including four that appear intact. Significant genomic islands were also found, suggesting regions in the genomes experienced horizontal gene transfer. Utilizing the data obtained from these genomic comparisons will allow us to exploit functional genomics to understand C. rectus secretion systems, the effect of these systems on pathogenesis, and implications to human health.

Casey Hughes Lago

caseyannehughes@tamu.edu

Graduate Student

F12. Investigating the downstream effect of the HOG and CWI MAPK pathways on gene expression changes observed in the Saccharomyces cerevisiae pgm2∆ mutant

Madelyn G. Oliver, Mandy R. Eckhardt, Keara D. Malone, Spencer L. Nystrom*, Rachel V. Jimenez, Courtney D. Goldstein, David P. Aiello

Department of Biology, Austin College, Sherman, TX, *Curriculum in Genetics and Molecular Biology, University of North Carolina at Chapel Hill

In Saccharomyces cerevisiae, the enzyme phosphoglucomutase (PGM) catalyzes the interconversion of glucose-1-phosphate (Glc-1-P) and glucose-6-phosphate (Glc-6-P). Previous research has shown that the loss of PGM2, the major isoform of PGM, in the context of galactose-grown cells results in a slow growth phenotype and altered ratio of Glc-1-P to Glc-6-P. Interestingly, the pgm2∆ mutant also exhibits defects in calcium homeostasis, including altered calcium uptake and accumulation and sensitivity to the calcineurin inhibitor, cyclosporin A. One area of interest in understanding the defects which occur due to loss of PGM2 is to investigate the changes in gene expression which occur in the pgm2∆ mutant relative to the wt strain. Previous research using RNA Seq and DESEQ-2 analysis identified that there is differential expression between strains. Further analysis using K-means clustering and DREME analysis suggested that these changes might be coordinately regulated by specific transcription factors. The current working model of the lab suggests that these changes in gene expression are mediated through hyperactivation of stress responses. This study seeks to characterize the role of the HOG (high osmolarity glycerol) and CWI (cell wall integrity) MAPK cascades in mediating the defects observed in the pgm2∆ mutant, specifically by observing the role of downstream targets from both of these pathways on gene expression changes within the mutant cell.

Madelyn Grace Oliver

moliver18@austincollege.edu

Undergraduate Student

F13. Investigating the role of RNA polymerase II stalling in spt4Δ-mediated rescue of Saccharomyces cerevisiae mutants lacking PGM2

Ruthann H. Schmiege, Keara D. Malone, Spencer L. Nystrom*, Rachel V. Jimenez, Courtney D. Goldstein, David P. Aiello

Austin College, Biology Department, Sherman, TX; *Curriculum in Genetics and Molecular Biology, University of North Carolina at Chapel Hill

In Saccharomyces cerevisiae, the enzyme phosphoglucomutase (PGM) allows the cell to interconvert glucose-1-phosphate (G1P) and glucose-6-phosphate (G6P). Loss of the gene encoding for the major isoform of PGM, PGM2, causes a slow growth phenotype and an increased ratio of G1P to G6P when cells utilize galactose as their primary carbon source. In addition, the pgm2Δ strain displays calcium homeostasis defects, including sensitivity to cyclosporin A and increased calcium uptake and accumulation. Previous research in the Aiello lab has found that loss of SPT4¸the nonessential component of the DSIF complex, rescues many of the pgm2Δ mutant growth defects, but the altered ratio of G1P to G6P is unaffected. DSIF is known to play an important role in promoting transcription elongation in S. cerevisiae, but evidence also suggests that Spt4 may play a role in negatively regulating transcription of certain genes. Previous research indicates that the loss of SPT4 may relieve transcriptional pausing or stalling at certain gene loci, resulting in an increase in gene expression. This study aims to investigate whether Spt4 mediates increased RNA polymerase II stalling in the pgm2Δ mutant, as well as whether select genes that show higher expression in the pgm2Δspt4Δ strain play a role in the spt4Δ-mediated rescue of pgm2Δ phenotypes.

Ruthann Helen Schmiege

rschmiege18@austincollege.edu

Undergraduate Student

F14. Identification and Characterization of TANGO6 in Zebrafish Development

Hannah Herron, Sydney Versen, Kelli Carroll

Austin College Biology Department

The Undiagnosed Disease Network (UDN) is a collection of clinicians and researchers that utilize modern technology to help diagnose individuals with rare or previously uncharacterized diseases. One of the genes that the UDN predicted as causal in developmental disease was Tango6, as a UDN participant with multiple point mutations in Tango6 presented with heart and brain abnormalities including atrial and ventricular septal defects, microcephaly, hydrocephalus, and agenesis of the corpus callosum. Tango6 was originally discovered in Drosophila, where it was predicted to play a role in Golgi body organization; it is also required in murine development. Single cell sequencing data on murine neuronal cell populations also predicted that Tango6 may be enriched in ependymal cells. In order to understand the role that Tango6 plays in development, we utilized embryonic zebrafish to analyze the quantitative and spatial expression of Tango6. In zebrafish, Tango6 is expressed from low to moderate levels between 24 and 120 hours post fertilization (hpf) with a small decrease in expression around 96 hpf. In situ hybridization demonstrated that Tango6 is generally present in the head around the midbrain-hindbrain boundary and is specifically expressed in a bilateral tube in the hindbrain beginning at 48 hpf through 120 hpf. Additionally, it is present in the developing esophagus and the gastrointestinal system from 96 through 120 hpf. Preliminary data of mosaically edited Tango6 knockouts generated using CRISPR have found an accumulation of blood in the gut by 96 hpf, suggesting defects in gut morphogenesis or function. Further analysis of the developing gut in the embryos at 96 hpf has shown cellular delocalization in the gut, which may be leading to the bloody gut phenotype. Based on the expression of Tango6 in the head around the midbrain-hindbrain boundary and the hydrocephalus of the UDN participant, we suspect that it is expressed in the ependymal cells of the choroid plexus. Furthermore, from the expression in the gut and bloody gut phenotype of the mosaics, we hypothesize that Tanog6 is present in the enterocytes, or the epithelial lining of the gut. In total, these data suggest that Tango6 is involved in brain and gut development, and further analysis of knockouts and spatial expression patterns is underway to determine the precise role of Tango6 in development and disease.

Hannah Herron

hherron20@austincollege.edu

Undergraduate Student

S1. Karyotypic stasis and swarming influenced the evolution of viral tolerance in a large bat radiation

Nicole M Foley1, Andrew J Harris1,2, Kevin R Bredemeyer1,2, Manuel Ruedi3, Sebastien J Puechmaille4, Emma C Teeling5, William J Murphy1,2

1Texas A&M University, Veterinary Integrative Biosciences, College Station, TX, 2Texas A&M University, Interdisciplinary Graduate Program in Genetics, College Station, TX, 3Natural History Museum of Geneva, Department of Mammalogy and Ornithology, Geneva, Switzerland, 4 University of Montpellier, Institut des Sciences de l'Évolution, Montpellier, France, 5University College Dublin, School of Biology and Environmental Science, Dublin, Ireland

The emergence of COVID-19, Ebola and SARS has urgently placed understanding bats' status as viral reservoirs as a major focus of global public health initiatives. The coevolution of bats and viruses make resolved phylogenies essential for predicting future disease emergence. Myotis bats are the second most speciose genus of mammals and have a near global distribution. Coronaviruses are most geographically widespread in these and other related bat species. However, the phylogeny of Myotis bats is poorly documented. Their conserved karyotype (2n=44) and swarming behavior, where multi-species male-biased assemblages form for mating, is thought to promote interspecific hybridization. Hybridization overwrite the species tree and confound standard phylogenomic analyses. To address this, we sequenced 58 Old World Myotis genomes and aligned them to an improved Myotis myotis reference genome where we assembled ~78Mb of additional contigs, including critical loci like the MHC, immunoglobin, and interleukin gene clusters. In the presence of hybridization the distribution of phylogenomic signal is non-random and predicted by recombination rate. To this end, we used a novel machine learning approach to infer a recombination map for M. myotis, the first for any bat species. Recombination rates, divergence time estimates, and tests of introgression were combined with recently developed locus-tree methods to sample local phylogenomic signal on a genomic scale to infer the species tree. Our results show widespread introgression across the majority of bat chromosome arms, while the species tree was limited to as little as 5-7% of the genome, notably near chromosome centers. Relationships recovered in standard coalescent and concatenation whole genome phylogenies are most consistent with the dominant signal of introgression. Across all clades, innate immunity genes were commonly found within the most significantly introgressed (top 0.05%) genomic regions, consistent with ancient and ongoing admixture across clades spanning the phylogeny. Together, our results suggest that the conserved chromosomal architecture and swarming behavior were both key to the success of this mammalian radiation and that viral tolerance may be an outcome of an excess of historical gene flow that maintained high genomic diversity, particularly at immunity loci. A deeper understanding of the evolutionary and genomic context within which these unique traits evolved may provide key insights into the biomedical mechanisms that underpin differential disease susceptibility across species.

Nicole Foley

nfoley@cvm.tamu.edu

Postdoc

S2. Testing for Signatures of Coevolutionary Local Adaptation and Congruent Gene Flow in a Co-Diversifying Ant-Endosymbiont Mutualism

Brandon A. Meadows, Joseph D. Manthey

Texas Tech University, Lubbock, Tx

Co-diversification is the result of shared evolutionary history between organisms, culminating in a pattern of congruent phylogenies. In contrast, coevolution occurs when intimately associated partners are subjected to similar selective pressures. However, a pattern of co-diversification does not necessarily indicate coevolution is occurring. All ants in the genus Camponotus feature a co-diversifying relationship with the obligate intracellular endosymbiont, Blochmannia. However, it is unknown to what extent, if any, the local environment affects coevolution between co-diversifying hosts and obligate endosymbionts. Here, we performed whole-genome resequencing of the western carpenter ant, Camponotus modoc, and their endosymbiont, Blochmannia throughout their range in the U.S. Rocky Mountains. We are using landscape genomics to test for patterns of coevolving local adaptation and landscape genetic methods to characterize migration surfaces and historical barriers to gene flow in the two partners. We have identified single nucleotide polymorphisms (SNPs) undergoing local adaptation in the ant host with two genotype-environment association analyses (LFMM2 and Redundancy analysis) and we will compare these to the SNPs undergoing local adaptation in Blochmannia to see if coevolving local adaptation is occurring. Additionally, we will perform Fast Estimation of Effective Migration Surfaces (FEEMS) on both Camponotus and Blochmannia to identify if historical migration surfaces are congruent between the two partners. To date, tests for local adaptation in co-diversifying systems have generally been limited to host-parasite relationships. These analyses will enable us to identify to the extent that coevolutionary local adaptation occurs and if the landscape facilitates similar patterns of historical gene flow between hosts and obligate endosymbionts.

Brandon A. Meadows

Brandon.Meadows@ttu.edu

Graduate Student

S3. Tree House Explorer: A Novel Genome Browser for Phylogenomics and Phylogeography

Andrew J. Harris (1, 2), Nicole M. Foley (1), Tiffani L. Williams (3), William J. Murphy (1, 2)

(1) Veterinary Integrative Biosciences, Texas A&M University, College Station, TX 77843
(2) Interdisciplinary Program in Genetics and Genomics, Texas A&M University, College Station, TX 77843
(3) Department of Computer Science, University of Illinois at Urbana-Champaign, Urbana, IL 61801

Genomes are mosaics of evolutionary histories that reflect ancient signatures of true species relationships, as well as incomplete lineage sorting (ILS) or gene flow. Understanding how and why phylogenetic and phylogeographic signal varies across different genomes can yield powerful insights into evolutionary history and adaptive evolution. One of the greatest challenges faced with interpreting variation in evolutionary signal is the highly fragmented nature of the visualization and comparison of diverse data types collected throughout analyses. Tree House Explorer (THEx) is a novel genome browser that fills this gap and integrates phylogenomic signal with genomic annotations into a single interactive platform. This allows users to visualize genome-wide variation in evolutionary histories as well as genetic divergence on a chromosome-by-chromosome basis, with continuous sliding window comparisons to gene annotations, recombination rates, and other user-specified, highly customizable genome feature annotations. We provide several illustrations of THEx's capabilities to easily combine diverse data types. First, we examine genome-wide phylogenomic signal based on the Zoonomia Project's 242 mammal genome alignment, including evidence of X-autosome discordance throughout the placental mammal radiations. Second, we apply THEx to several dozen cat genomes to identify putative genomic regions with signatures of adaptive introgression, including post-speciation gene flow between the Canada Lynx and Bobcat that potentially document historical adaptations of the Bobcat to colder northern climates inhabited by Canada lynx. THEx exemplifies a new era of interactive data visualization for population genomics and phylogenomics, providing a novel approach to analyze and interpret the diverse evolutionary histories woven throughout genomes.

Andrew J. Harris

ajharris@cvm.tamu.edu

Graduate Student

S4. Genomic Signatures of Cattle Introgression in Historical and Modern North American Bison

Sam Stroupe 1, David Forgacs 1*, Andrew Harris 2, James N. Derr 1, Brian W. Davis 2

1 Department of Veterinary Pathobiology, Texas A&M University College of Veterinary Medicine and Biomedical Science, College Station, TX
2 Department of Veterinary Integrative Biosciences, Texas A&M University College of Veterinary Medicine and Biomedical Science, College Station, TX
*Current address: Center for Vaccines and Immunology, University of Georgia, Athens, GA

American Bison experienced a significant population bottleneck in the 19th century due to indiscriminate killing, loss of access to suitable habitat, and disease. As a result, the population size decreased by over 99% leaving only two wild populations, a small number of plains bison in Yellowstone National Park, USA and a few wood bison in Wood Buffalo National Park, Canada. In addition, a few bison were maintained by cattle ranchers in private herds, many of whom successfully hybridized bison with various breeds of domestic cattle. These introgression events left a lasting legacy that have been identified using mitochondrial DNA and limited nuclear microsatellite analyses. However, no genome-wide assessment has been performed, and some herds were believed to be free of introgression based on current genetic testing strategies. Our study includes whole genome sequencing from nineteen modern and six historical bison of variable genome coverages that represent the genetic diversity of modern bison. Multiple approaches were utilized to identify putative cattle haplotypes in each bison genome. Evidence of recent hybridization with domestic cattle was detected in every bison, including those from herds previously thought to be free of introgression. Detected genomic signatures of domestic cattle introgression vary greatly in size and frequency by sample and herd, suggesting multiple historical hybridization events with subsequent genetic recombination over the last 200 years. Our results demonstrate that the only sufficient approach to accurately quantitate cattle introgression is through multiple methods using whole genome sequencing data.

Sam Stroupe

samstroupe@tamu.edu

Graduate Student

S5. Genomic phylogeography of the Grace's Warbler (Setophaga graciae): evidence of in situ diversification and recent population expansion across pine-oak ecosystems

Jack P. Hruska, Garth M. Spellman, John Klicka, Joseph D. Manthey.

Texas Tech University Department of Biological Sciences, Denver Museum of Nature and Science, University of Washington Burke Museum of Natural History and Culture and Department of Biology, Texas Tech University Department of Biological Sciences.

The fragmentation and expansion of habitat in response to Pleistocene glacial cycles is often cited as a driver of genetic differentiation. Under this model, it is assumed that biodiversity largely evolves in situ, and that genetic patterns are a consequence of populations tracking the contraction and expansion of a preferred habitat. Patterns of genetic diversity across birds inhabiting North and Middle American pine-oak ecosystems have often been explained by this paradigm. Several studies have demonstrated a latitudinal pattern of genetic differentiation, wherein more temperate pine-oak populations show evidence of low differentiation relative to higher differentiation in more tropical populations. Here, we examine whether this latitudinal pattern of differentiation is recovered in a pine-oak specialist, the Grace's Warbler (Setophaga graciae), that inhabits pine-oak ecosystems from Nevada to Nicaragua. We analyzed thousands of single nucleotide polymorphisms (SNPs) from 53 individuals to recover the expected latitudinal pattern of diversification, wherein more tropical populations are characterized by greater population structure, as recovered by ADMIXTURE, FST, and principal components (PCA) analyses. In addition, tropical populations show a greater impact of genetic drift, as demonstrated by TreeMix, and have reduced levels of heterozygosity, suggesting these populations have been subject to longer-term isolation and/or reduced effective population sizes. In contrast, temperate populations exhibit a reduced signature of population structure and greater levels of heterozygosity, indicating that these populations have either recently expanded or have been subject to ongoing gene flow. We hypothesize these patterns of differentiation are driven by differing regional responses of pine-oak forests to Pleistocene glacial cycles, when tropical forests expanded during cooler periods and temperate forests contracted.

Jack P. Hruska

jackphruska@gmail.com

Graduate Student

S6. The evolution of four chromosomal inversions underlying ecological adaptation in Atlantic herring using long-read sequencing

Minal Jamsandekar1, Mafalda Ferreira2, Mats Pettersson2, Brian Davis1, Leif Andersson1,2

1: Texas A&M University, Veterinary Integrative Biosciences, College Station, TX
2: Uppsala University, Department of Medical Biochemistry and Microbiology, Uppsala, Sweden

Chromosomal inversions suppress recombination and can be maintained for millions of years as balanced polymorphisms. But they are difficult to study due to complex genomic structure. We report a detailed characterization of four large inversions in the Atlantic herring genome, present on chromosomes 6, 12, 17, and 23, with corresponding sizes of 2.7, 7.8, 2.2, and 1.2 Mb, respectively, which show strong clinal gradients in their frequencies from south to north part of the Atlantic Ocean correlated with water temperature at spawning. We therefore named inversion haplotypes as ‘S’ (Southern) and ‘N’ (Northern). Atlantic herring is a pelagic fish and one of the most abundant vertebrates in the world with an effective population size (Ne) over a billion. We used pangenome and multi-genome alignment approach using PacBio HiFi and optical BioNano data from 12 individuals carrying S and N types and one outgroup species (European sprat) to accurately determine ancestral state, inversion breakpoints, and to study the structural variations surrounding breakpoints. We found extreme sequence variation and structural polymorphism near the breakpoints, mainly dominated by inverted duplications and complex repeats. To further study evolution of these inversions, we estimated dN/dS and diversity statistics (pi and dxy) using short-read data for 35 individuals, homozygotes for each S and N types. Established theories on inversions suggests that as inversion accumulates deleterious mutations over time leading to high mutation load. Unexpected, none of the S or N homozygotes supported this theory suggesting that purifying selection might be effective in removing deleterious mutations inside inversions. Moreover, nucleotide diversity values for S and N types were similar to each other and to the rest of the genome. This shows that these inversion polymorphisms have been maintained over a considerable time, hundreds of thousands of years and that the large Ne of Atlantic herring allows efficient purifying selection of both alleles at each locus. Overall, studying large inversions in Atlantic herring has led us to gain novel insights into the evolution of inversions.

Minal Jamsandekar

minal03@tamu.edu

Graduate Student

S7. The Role of Centromeres in Chromosome Number Evolution

Michelle Jonika (1,3), Sarah Ruckman (1,2), Claudio Casola (2,3,4), Heath Blackmon (1,2,3)

1 Texas A&M University, Department of Biology, College Station, TX, USA
2 Texas A&M University, Ecology and Evolutionary Biology Interdisciplinary Program, College Station, TX, USA
3 Texas A&M University, Genetics Interdisciplinary Program, College Station, TX, USA
4 Texas A&M University, Department of Ecology and Conservation Biology, College Station, TX, USA

Despite the fundamental role of centromeres, two different types are observed across plants and animals. Monocentric chromosomes possess a single region that functions as the centromere, while in holocentric chromosomes, centromere activity is spread across the entire chromosome. Proper segregation may fail in species with monocentric chromosomes after a fusion or fission, leading to chromosomes with no centromere or multiple centromeres. In contrast, species with holocentric chromosomes should still safely segregate chromosomes after fusion or fission. This, along with the observation of high chromosome numbers in some holocentric clades, has led to the hypothesis that holocentricity leads to higher rates of chromosome number evolution. To test for differences in rates of chromosome number evolution between these systems, we analyzed data from 4,393 species of insects in a phylogenetic framework. We found that insect orders exhibit striking differences in fissions, fusions, and polyploidy rates. However, we found no evidence across all insects that holocentric clades have higher rates of fissions, fusions, or polyploidy than monocentric clades. Our results suggest that holocentricity alone does not lead to higher rates of chromosome number changes. Instead, we suggest that other co-evolving traits must explain striking differences between clades.

Michelle Jonika

Michelle19@tamu.edu

Graduate Student

Poster presentation abstracts

P1. Glyphosate's Effects on the Development of Zebrafish (*Danio rerio*)

Mia Hibner

Austin College Biology Department

Glyphosate is a nonselective herbicide and one of the most commonly used pesticides in the United States. Glyphosate, the active ingredient in a popular herbicide commonly known as Roundup, kills plants by targeting a plant-specific enzyme in the Shikimate pathway. However, even though animals do not have a Shikimate pathway, Roundup has deleterious effects on humans and other vertebrates, including the development of non-Hodgkin's lymphoma. Despite its widespread use, glyphosate's mechanism of toxicity in humans is unknown. Previous research has shown that glyphosate results in morphological and behavioral abnormalities in embryonic zebrafish (*Danio rerio*), including decreased body length and spinal curvature. To assess specific organ abnormalities due to glyphosate exposure, zebrafish exposed to glyphosate were immunostained at 48 hours post-fertilization (hpf) to visualize motor neurons, which revealed less intense staining along the central nervous system and somites of the exposed embryos, though no change in overall motor neuron number was observed. The precise genes necessary important in neural development that are affected by glyphosate have not been poorly characterized. We have picked six genes, pax2a, pax8, otx2b, pax6a, hoxb1a, and egr2b, which are all involved in the development of the central nervous system for initial study. We will assess their expression and localization at 48 and 96 hours post-fertilization (hpf) following glyphosate exposure. Along with the central nervous system, we hope to study organogenesis of the kidney, liver, and heart to determine if other organs are affected by glyphosate exposure. In total, a more in-depth analysis of the effects of glyphosate on zebrafish development may aid in identifying this pesticide's mechanism of action in humans and other vertebrates.

Mia Jin Hibner

mhibner19@austincollege.edu

Undergraduate Student

P2. Coa4 acts upstream of Cox11 in the mitochondrial copper delivery pathway to Cox1 subunit of cytochrome c oxidase

Abhinav B. Swaminathan, Shivatheja Soma, Alison C. Vicary, Mohammad Zulkifli, Vishal M. Gohil

Department of Biochemistry and Biophysics, MS 3474, Texas A&M University, College Station, TX, USA

Cytochrome c oxidase (CcO) is a multimeric copper-containing enzyme of the mitochondrial respiratory chain that powers cellular energy production. The delivery of copper to Cox1 and Cox2, the two copper-containing subunits of CcO, is a complex process requiring multiple proteins that constitute the mitochondrial copper delivery pathway. Currently, the identity of all the members of the pathway is not known, though several evolutionarily conserved coiled-coil-helix-coiled-coil-helix (CHCH) domain-containing proteins have been implicated in this process. Here, we utilized a targeted yeast genetic epistasis screen that placed Coa4, a CHCH-domain containing protein, in the copper delivery pathway to the Cox1 subunit of CcO. Specifically, we show that overexpression of Cox11, a metallochaperone that inserts Cu into Cox1, can restore Cox1 levels, CcO assembly, and mitochondrial respiration in coa4Δ cells, implying that Coa4 acts upstream of Cox11 in the copper delivery pathway. Consistently, the abundance of Coa4 and Cox11 in mitochondria is reciprocally regulated. Additionally, we report that coa4Δ has reduced copper levels and exogenous copper supplementation can partially alleviate its phenotype, a finding that further links Coa4 to copper biology. Finally, we demonstrate that human Coa4 can replace the function of yeast Coa4 indicating its evolutionarily conserved role. Together, our work provides genetic and biochemical evidence for the role of Coa4 in the copper delivery pathway to the Cox1 subunit of CcO.

Abhinav B Swaminathan

abhinav22@tamu.edu

Graduate Student

P3. A Characterization of the Role of the MRTF/SRF Pathway in Zebrafish Development

Taylor Dornseifer, Biol 324, Kelli Carroll

Austin College Biology Department

Many studies have been performed to understand the function and mechanism of the myocardin-related transcription factors (MRTFs) in mice and human models. It is known that the MRTFs play a significant role in skeletal and cardiac muscle formation and contraction through regulation of actin polymerization and cytoskeletal dynamics. However, the function of the MRTFs in zebrafish has not been studied. This project attempts to determine whether the function of the MRTFs within the MRTF-SRF pathway is conserved in zebrafish. Due to a partial duplication of the zebrafish genome, zebrafish have four MRTF isoforms in contrast to the two isoforms present in mice and humans. However, this study only focuses on the two most highly expressed isoforms, MRTFs-Ab and Bb. Initial studies indicated that both MRTF-Ab and Bb were expressed robustly throughout the first 72 hours of embryonic development. Using pharmacological manipulation, we inhibited the MRTF-SRF pathway during the first 48 hours of zebrafish development. Morphological and heart rate analyses following pharmacological manipulation indicated stunted growth, cardiac edema, and decreased heartrate in a dose dependent manner. Additionally, embryos treated with higher doses did not respond to touch, indicating disrupted muscle contractility. These analyses suggest that MRTF inhibition causes abnormal cardiac and skeletal muscle morphology, suggesting that the function of the MRTF pathway in zebrafish is conserved. Interestingly, we also noticed inhibition of blood vessel formation after inhibition of MRTFs, suggesting that MRTFs in zebrafish may be highly involved in smooth muscle formation and function. Further, in situ hybridizations of 48 and 72 hpf embryos indicate that the MRTFs are expressed in the dorsal aorta and the intersomitic vessels. Therefore, this finding provides further evidence that the role and function of the MRTFs and the MRTF-SRF pathway is at least partially conserved in zebrafish.

Taylor Dornseifer

tsdornseifer@gmail.com

Undergraduate Student

P4. Sensory neuron transcriptomes reveal complex neuron-specific function and regulation of mec-2/Stomatin splicing

Xiaoyu Liang, Canyon Calovich-Benne, Adam Norris

Southern Methodist University

The function and identity of a cell is shaped by transcription factors controlling transcriptional networks, and further shaped by RNA binding proteins controlling post-transcriptional networks. To overcome limitations inherent to analysis of sparse single-cell post-transcriptional data, we leverage the invariant Caenorhabditis elegans cell lineage, isolating thousands of identical neuron types from thousands of isogenic individuals. The resulting deep transcriptomes facilitate splicing network analysis due to increased sequencing depth and uniformity. We focus on mechanosensory touch-neuron splicing regulated by MEC-8/RBPMS. We identify a small MEC-8-regulated network, where MEC-8 establishes touch-neuron isoforms differing from default isoforms found in other cells. MEC-8 establishes the canonical long mec-2/Stomatin isoform in touch neurons, but surprisingly the non-canonical short isoform predominates in other neurons, including olfactory neurons, and *mec-2* is required for olfaction. Forced endogenous isoform-specific expression reveals that the short isoform functions in olfaction but not mechanosensation. The long isoform is functional in both processes. Remarkably, restoring the long isoform completely rescues *mec-8* mutant mechanosensation, indicating a single MEC-8 touch-neuron target is phenotypically relevant. Within the long isoform we identify a cassette exon further diversifying *mec-2* into long/extra-long isoforms. Neither is sufficient for mechanosensation. Both are simultaneously required, likely functioning as heteromers to mediate mechanosensation.

Canyon Calovich-Benne

ccalovichbenne@smu.edu

Graduate Student

P5. Characterization of the novel DUF4585 gene family in zebrafish

Yasmine Bukhari, Douglas Anderson, Rhonda Bassel-Duby, Eric Olson, and Kelli J. Carroll

Austin College, Biology Department, Sherman, TX and Department of Molecular Biology, UT Southwestern, Dallas, TX

Skeletal muscle is one of the most significant tissues in the human body and plays an important role in functions including movement, maintenance of posture, and regulation of body temperature. Mutations in genes important for proper skeletal muscle development are responsible for hundreds of muscular diseases found in humans. However, the genetic cause of many muscle diseases is still unclear, making identification and characterization of novel genes important. We have identified a new family of three novel genes that share a common Domain of Unknown Function number 4585 (DUF4585). In embryonic and adult mice, these three genes are expressed in cardiac and skeletal muscle, and triple knockout mice exhibit defects in organelle positioning within skeletal muscle. In this study, we performed an in vivo investigation of two DUF4585 orthologs, orf71 and e22, in order to determine the expression patterns of these genes in zebrafish (*Danio rerio*). Expression pattern analysis by RT-qPCR shows that orf71 is the most highly expressed gene of the DUF4585 orthologs with particularly high expression in 72- to 120-hours post-fertilization (hpf) zebrafish. Whole mount in situ hybridization (WISH) shows that orf71 and e22 are highly expressed in the somites, or developing skeletal muscle, of zebrafish embryos. These results suggest that orf71 and e22 also play a role in the development of skeletal muscle during zebrafish development and that their function may be conserved across vertebrates. Future studies in the lab will aim to determine the role of orf71 in skeletal muscle development through the creation of knockouts (null mutants) using CRISPR.

Yasmine Bukhari

ybukhari18@austincollege.edu

Undergraduate Student

P6. RNA binding proteins coordinately control lifespan in *C. elegans*

Rebekah Napier-Jameson, Olivia Marx, Adam Norris

Southern Methodist University, Southern Methodist University and Penn State College of Medicine, Southern Methodist University

Regulation of gene expression affects lifespan in Caenorhabditis elegans. While transcription factors have been extensively studied for their role in aging, less is known about how RNA binding proteins may contribute to the aging process. We recently performed a CRISPR/Cas-9 based Synthetic Genetic Interaction (CRISPR-SGI) screen in *C. elegans* focused on conserved neuronally-expressed RNA binding proteins, and identified many double mutants with fitness defects. In one notable interaction between the ELAVL ortholog exc-7 and the MBNL1/2 ortholog mbl-1, double mutants displayed a severely shortened lifespan (~70%). exc-7 and mbl-1 single mutants have negligible effects on lifespan, demonstrating that the two RNA binding proteins coordinately control lifespan. Both genes are required for regulating hundreds of transcripts and isoforms. exc-7 and mbl-1 are both neuronally-enriched genes. mbl-1 tissue specific re-expression experiments have shown partial rescue of the lifespan phenotype with re-expression in the nervous or intestinal tissues of the double mutant but not muscle tissue. exc-7 re-expression experiments have shown partial rescue of the lifespan phenotype with re-expression in the nervous system but not any of the other tested tissues. We have used RNA seq data to investigate which RNAs may be uniquely dysregulated in the exc-7; mbl-1 double mutant. We identified eight uniquely dysregulated genes and have tested all these genes in order to investigate their effects within the double mutant. nhx-6 is a predicted Na/H exchanger which is expressed in the intestine. nhx-6 expression is up regulated in the double mutant. nhx-6 partially rescues the lifespan phenotype in exc-7; mbl-1 mutants. nhx-6 partially rescues several exc-7; mbl-1 healthspan phenotypes, including intestinal permeability, defecation cycle length, and pharyngeal pumping. We are currently investigating further genes of interest identified through our RNA seq analysis, and testing whether they modulate the lifespan phenotype of exc-7; mbl-1 mutants.

Rebekah Napier-Jameson

rnapierjameson@smu.edu

Graduate Student

P7. Exploring the effects of Methylglyoxal on cytosolic Ca2+ levels in the absence of HACS and intracellular Ca2+ efflux channels

Tamtam H., Selby MA., McBroom KE., Mpunga NP., Kannan A., Aiello DP.

Austin College, Sherman TX

The major isoform of phosphoglucomutase, PGM2, interconverts glucose-1-phosphate (G1P) and glucose-6-phosphate (G6P) in carbohydrate metabolism. Saccharomyces cerevisiae mutants lacking PGM2 exhibit altered G1P:G6P ratios due to an inability to interconvert the two. Additionally, the pgm2Δ mutant shows slow growth on galactose-containing media, cyclosporin-A sensitivity (CsA), greater induction of the unfolded protein response, and higher levels of intracellular Ca2+. Calcium influx across the plasma membrane is mediated by LACS (Low-Affinity Ca2+ Influx System), a protein encoded by FIG1, and HACS (High-Affinity Ca2+ Uptake System), an integral membrane protein complex encoded by MID1, CCH1, and ECM7. Loss of single HACS genes exacerbated the slow growth phenotype of pgm2Δ on galactose, and combinations of HACS gene deletions were near-fatal to the pgm2Δ strain. In lieu of observing the expected decrease in total cell Ca2+ in mid1Δ and cch1Δ mutants, we saw a rise in total cell Ca2+, further amplified in pgm2Δ strains. Previous work demonstrates that the addition of exogenous methylglyoxal (MG) rescues pgm2Δ growth defects, likely by increasing cytosolic Ca2+ levels through vacuole- and ER-independent mechanisms. MG addition rescued pgm2Δ HACS mutants' growth phenotypes. Current efforts are focused on the impact of MG on pgm2Δ mutants with various combinations of gene mutations preventing influx of calcium into the cytosol from either internal or external sources.

Harsha Tamtam

htamtam18@austincollege.edu

Undergraduate Student

P8. Dissecting interactions across gene regulatory layers: TDP-1 and FUST-1 coordinate with transcription factor CEH-14 to affect reproduction in *C. elegans*

Morgan Taylor, Olivia Marx, Angela Neunuebel, Adam Norris

Southern Methodist University

Gene expression is a multistep, carefully controlled process with distinct regulatory layers. Previous work in our lab suggested that crosstalk between these layers plays a significant role in coordinating gene expression. Recently, we embarked on a systematic reverse-genetic interaction screen in *C. elegans* with the goal of identifying functionally relevant coordination of gene expression across regulatory layers in the nervous system. We are particularly interested in crosstalk between transcription and RNA processing. We crossed previously-generated CRISPR-Cas9 RNA binding protein (RBP) deletions with existing transcription factor (TF) mutant strains, creating over a hundred RBP;TF double mutants. We screened these double mutants for unexpected phenotypes not seen in either of the constituent single mutants. A novel phenotype in the double mutant indicates a genetic interaction between the corresponding RBP and TF. The strongest double mutant phenotypes were further investigated to characterize underlying mechanisms that contribute to the phenotype. We have identified several strong genetic interactions by studying double mutants with a variety of unexpected phenotypes. Here, we present evidence that two ALS-related RBPs, FUST-1 and TDP-1, have a similar interaction with the transcription factor CEH-14. The loss of any one of these three genes alone has no significant effect on the overall health of the organism. However, fust-1; ceh-14 and tdp-1; ceh-14 double mutants both exhibit strong temperature-sensitive reproductive defects. Both double mutants, when grown at 25° C, exhibit deformed gonads, resulting in significantly reduced egg production. Our results implicate both defective sperm and oocyte function leading to this decline in fertility. RNA-seq results suggest that fust-1; ceh-14 and tdp-1; ceh-14 undergo similar gene dysregulation that cannot simply be explained by their shared ceh-14 mutation. The similarity of the double mutant phenotypes suggests that these three genes are involved in the same process. Additionally, the lack of a similar phenotype in a fust-1 tdp-1 double mutant implies that FUST-1 and TDP-1 interact with CEH-14, but not with each other. Our findings implicate an important role for CEH-14, FUST-1, and TDP-1 in facilitating reproduction in *C. elegans*. The physiological roles of FUST-1 and TDP-1, as well as their human homologs FUS and TDP43, have not yet been fully characterized. We hope that our findings will shed light on a fundamental role that these RNA binding proteins share.

Morgan Taylor

thompsonma@smu.edu

Graduate Student

P9. Examining growth phenotypes of the pgm2Δ mutation in *Saccharomyces cerevisiae* lacking or overexpressing TPS1, NTH1, and ATH1

Shruti V. Raghavan, Lara I. Shehadeh, Zoya Waheed, Katherine McBroom, Shreya Uppala, Sarah Smith, Akshaya Selvamani, Rebecca McDonald, Pranavya Manickavelu, Krishna Patel, Katrina Ngo, Ashley Charales, Vana Bahram, David P. Aiello

Austin College Sherman Texas

Phosphoglucomutase (PGM) is the enzyme responsible for interconverting glucose-1-phosphate (G1P) and glucose-6-phosphate (G6P) in *Saccharomyces cerevisiae* carbohydrate metabolism. Yeast lacking PGM2 (pgm2Δ), the major isoform of PGM, exhibit slow growth, calcium homeostasis defects, and an accumulation of glycogen when metabolizing galactose as a carbon source. The overexpression of GPH1, a glycogen breakdown gene, partially rescues pgm2Δ mutant defects. We hypothesized that the partial rescue was due to the protective effect of the increased trehalose levels, a carbohydrate source often produced in the absence of glucose. Overexpression of trehalose-6-phosphate synthase 1 (TPS1) successfully rescues pgm2Δ growth sensitivities, while tps1Δ mutation exacerbates pgm2Δ mutant phenotypes, revealing a potential link between trehalose synthesis and glycogen accumulation. To further examine this link and relationship with calcium homeostasis, we knocked out and overexpressed the genes encoding for two enzymes that hydrolyze trehalose to free glucose: an acid vacuolar trehalase encoded by ATH1 and a neutral cytosolic trehalase encoded by NTH1. Preliminary data exhibits an exacerbation of pgm2Δ growth defects upon ATH1 overexpression and a partial rescue of pgm2Δ associated with the ATH1 knockout, suggesting that vacuolar trehalose stores may be more relevant to pgm2Δ mutant defects than cytosolic stores.

Shruti Veera Raghavan

sraghavan19@austincollege.edu

Undergraduate Student

P10. Characterizing the genetic and physical interaction of the DBL-1/BMP signaling pathway with BLMP-1/BLIMP1 transcription regulator in *Caenorhabditis elegans*

Mohammed Farhan Lakdawala, Tina L. Gumienny

Division of Biology, School of the Sciences, Texas Woman's University, Denton, TX

Animals use multiple signaling pathways for cell-to-cell communication for proper development. One signaling pathway is defined by its ligand family of bone morphogenetic proteins (BMP). In the roundworm *C. elegans*, BMP member DBL-1 has a well-defined, conserved pathway. The DBL-1 signaling pathway is involved in a spectrum of traits, including body size, brood size, and others. How does this BMP pathway control target gene expression? We are using *C. elegans* to address this question. Previous studies in *C. elegans* show that transcriptional regulator BLMP-1 affects a similar array of traits as DBL-1. However, the relationship between DBL-1 and BLMP-1 is not studied. We discovered that DBL-1 and DBL-1 signaling are affected by loss of BLMP-1. We also found that DBL-1 negatively regulates blmp-1 expression. Additionally, ChIP-seq and RNA-seq data analyses suggest that DBL-1 pathway and BLMP-1 control expression of some common target genes, and act together.

Mohammed Farhan Lakdawala

mlakdawala@twu.edu

Graduate Student

P11. Studying the effects of a primary microcephaly-associated mutation in *Caenorhabditis elegans*

Amy Smith*, Mary Bergwell*, Ramon Duran#, Ellie Smith#, Carter Dierlam#, Jyoti Iyer

Department of Chemistry and Biochemistry, University of Tulsa, Tulsa, OK, 74104

Autosomal recessive primary microcephaly (MCPH) is a debilitating disorder which impedes the development of the brain due to a characteristic smaller head circumference in affected individuals. Previous research has identified and associated various genes and loci to MCPH, yet the disorder remains without treatment options or a cure. A study of a consanguineous Pakistani family identified a shared single point mutation in the HsSAS-6 gene (*sas-6(L69T)* in *C. elegans*) as a potential cause of MCPH in this family. The SAS-6 protein is an essential player in the centrosome duplication and ciliogenesis pathways. Centrosomes are organelles that are comprised of two centrioles and associated pericentriolar material. Centrosomes play a critical role in ensuring proper spindle assembly and ciliogenesis. Centrosome number is tightly controlled through the process of centrosome duplication during the S- phase in which exactly one daughter centriole is assembled orthogonally to the mother centriole. The mother centriole functions as a basal body on top of which the axoneme of the cilium is built. Since the *sas-6* gene is conserved between humans and *C. elegans*, we decided to create the human MCPH-associated *sas-6(L69T)* mutation in *C. elegans* using CRISPR in order to further investigate the effects of the mutation on development and other molecular pathways.

Interestingly, we found that brood size and embryonic viability were unaffected in *sas-6(L69T)* mutant *C. elegans*. These data indicate that the *sas-6(L69T)* mutation mildly inhibits SAS-6 function in regulating centrosome duplication. Therefore, to uncover subtle effects of the *sas-6(L69T)* mutation, genetic crossing was performed to introduce this mutation into a sensitized *zyg-1(it25)* background. Intriguingly, introduction of the *sas-6(L69T)* mutation into *zyg-1(it25)* greatly enhanced the embryonic lethality and centrosome duplication failures of the *zyg-1(it25)* worms. These data indicate that the *sas-6(L69T)* mutation inhibits SAS-6 function, which results in a failure of proper centrosome duplication. As the centrosomes fail to duplicate, embryonic lethality ensues in worms harboring the *sas-6(L69T)* mutation. Western blot analysis revealed that SAS-6 protein levels were reduced by 27% in the presence of the *sas-6(L69T)* mutation.

Since ciliogenesis defects have also been attributed to MCPH, we next questioned whether the *sas-6(L69T)* mutant worms exhibit any ciliogenesis defects. To examine ciliogenesis defects in these worms, we created an *osm-6p::gfp; sas-6(L69T)* strain by genetic crossing. This strain is marks all the ciliated sensory neurons. Spinning-disk confocal imaging of control and *osm-6p::gfp; sas-6(L69T)* strains revealed that the *osm-6p::gfp; sas-6(L69T)* worms had a shorter phasmid ciliary length than the control strain. Specifically, cilia length measurements indicated the overall, phasmid cilia length was reduced by over 2 µm in the *sas-6(L69T)* mutant worms ($p<0.0001$). These data indicate that the *sas-6(L69T)* mutation severely perturbs ciliogenesis.

Thus, through our studies, we find that the MCPH-associated *sas-6(L69T)* mutation mildly inhibits centrosome duplication and severely perturbs ciliogenesis in worms carrying this mutation. Future studies will involve determining whether the phasmid cilia defects in the *sas-6(L69T)* worms produce phasmid cilia-associated behavioral defects in these worms.

Ramon Duran

rad0065@utulsa.edu

Undergraduate Student

P12. Gene Regulatory Networks in Development: Genetic Variation and Robustness of Anterior-Posterior (AP) Axis Formation in Drosophila

Lossie (“Elle”) Rooney, Prasad Bandodkar, Cranos Williams, Gregory T. Reeves

NC State University Graduate Genetics Program, Texas A&M University Artie McFerrin Department of Chemical Engineering, NC State University Department of Electrical & Computer Engineering, Texas A&M University Artie McFerrin Department of Chemical Engineering

Body plan patterning is a critical step in embryonic development that has health and viability consequences across the life of the organism. Anterior-posterior (AP) axis formation is an early event in body plan patterning and establishes the head-to-tail orientation for determining cell and tissue fates. In Drosophila melanogaster, Bicoid is a well-studied transcription factor that acts as a morphogen in AP axis patterning by influencing expression of the Gap genes in a concentration-dependent manner to create distinct expression profiles. The Gap genes influence additional target genes that also show distinct expression profiles. Though this system has been studied extensively and many of the relevant genes have been identified, the mechanisms that allow robustness of AP axis formation across genetic backgrounds are not well-characterized. We address this gap using the natural variation of the Drosophila melanogaster Genetic Reference Panel (DGRP). By quantifying spatial expression patterns of AP genes across lines of the DGRP, we can identify genetic backgrounds that show significant changes in expression. We expect to identify genomic regions (QTLs) associated with these changes in expression, which we will interrogate for potential causal elements such as enhancers of AP genes. We will discuss current imaging results using ~70 lines and QTLs under investigation.

Lossie (“Elle”) Rooney

llrooney@ncsu.edu

Graduate Student

P13. Transcriptional Regulation as a Conserved Function of BRCA1/BARD1 in *Caenorhabditis elegans*

Uyen Nguyen, Ishor Thapa, Marlo Jeffries, Mikaela Stewart

Texas Christian University

Cells use diverse mechanisms to prevent DNA damage and tumor formation. Two tumor suppressors employed in this effort are the focus of our study: breast cancer type 1 susceptibility protein (BRCA1) and BRCA-1-associated RING Domain protein 1 (BARD1). These two proteins form a complex that suppresses the generation of estrogen-derived free radicals. Inherited mutations in BRCA1 or BARD1 are associated with an increased risk of developing breast or ovarian cancer in humans. The model organism Caenorhabditis elegans possesses the orthologs BRC-1 and BRD-1 which can be readily mutated, offering an attractive model to study biochemical functions. However, it is unknown if BRC-1/BRD-1 also regulates the transcription of estrogen metabolism (cyp) genes to control the production of free radicals as noted for the human homologs. Utilizing gene expression analysis and estrogen exposure assays, this study demonstrates that BRC-1/BRD-1 has a conserved function of regulating cyp genes in *C. elegans*. However, our data also shows that BRC-1 and BRD-1 do not necessarily protect DNA from free radical damage upon estrogen exposure, despite its proven inhibition of *cyp* genes expression. Further investigation is required to determine the function of these *cyp* gene homologs in *C. elegans*. Our findings of this additional conserved function of the BRCA1/BARD1 homologs in *C. elegans* further validate its use as a model organism to better understand the myriad ways BRCA1/BARD1 protects the genome.

Thu Uyen Nguyen

uyen.thu.nguyen@tcu.edu

Undergraduate Student

P14. Analysis of pMad and Medea Expression in BMP Pathway in Drosophila with Multiple Fluorescent Proteins

Hung-Yuan (Zeke) Chen, Gregory T. Reeves

The Artie McFerrin Department of Chemical Engineering, Texas A&M University, TX 77840, US

Morphogen gradients are important in early Drosophila embryo development. One such gradient, the BMP/Dpp gradient, patterns the dorsal region of the embryo, which induces a series of protein interactions. After BMP-like morphogen Dpp transports to the dorsal region and binds to type I receptors Thickveins (Tkv), Tkv is activated by type II receptor Punt and then phosphorylates Mothers against Dpp (Mad). The phosphorylated Mad (pMad) and Smad4 homolog Medea translocate together to the nucleus to regulate the target gene. Compared to the Dpp gradient, pMad and Medea are procedurally closer to gene regulation. However, the transport and expression of pMad and Medea are rarely discussed. Their expression depends on the morphogen concentration which is determined by the cell location. In this work, we tag eGFP and mScarlet I to Mad and Medea and mtagBFP to Histone 2A for locating the nuclei using Crispr-Cas9 techniques and analyze the embryo images after injection into flies and crossing. Finally, we then do image analysis of 14-cycle embryos to see the expression of these proteins.

Hung-Yuan Chen

hyst.chen@tamu.edu

Graduate Student

P15. Genetic regulation of diet-induced thermogenesis in mice

Emanuele Baldassarri1,2, Anna C. Salvador1,3, Alexandra Naron1,4, Thomas V. Wong1, Ryan McGovern1, Aaron Van Wettering1, Ahmed Elsaadi1, David W. Threadgill1,3,4

1 Department of Molecular and Cellular Medicine, Texas A&M University Health Science Center
2 School of Biosciences and Medicine, University of Surrey
3 Department of Nutrition, Texas A&M University
4 Interdisciplinary Department of Genetics, Texas A&M University

By better understanding the interpersonal differences in genetic background which may be responsible for variation in rates of thermogenesis in unrelated individuals, there would be an opportunity in developing precision dietetics to better address the obesity epidemic and other metabolic disorders. The ability to identify individuals that would respond best to a carbohydrate restricted diet would improve our ability to develop individualised treatments. This would improve efficacy of treatment and reduce economic and social strain on healthcare systems caused by the obesity epidemic.

We have previously demonstrated that A/J (AJ), C57BL/6J (B6), NOD/ShiLtJ (NOD), and FVB/NJ (FVB) mice had different metabolic responses when exposed to a ketogenic diet (high fat, no carbohydrate). While a significant increase in heat expenditure was observed across the 4 strains, the magnitude of this response varied between strains. The AJ mice had the steepest increase in heat expenditure whereas the B6 showed the most modest response to the ketogenic diet. The differences in metabolic rate could not be attributed to rates of activity or food consumption. To further investigate the genetic regulation of thermogenesis, an F2 population ((B6 x A) x (B6 x A)) was generated and exposed to the ketogenic diet for 3 months. The F2s were genotyped at 7854 markers on the Mouse Universal Genotyping Array (MUGA).

We performed linkage analysis using both an additive and interactive model to identify Quantitative Trait Loci (QTL). In the additive model the QTL is identified by summing the effects of sex and genotype alone while in the interactive model, the QTL is identified by summing the effects of sex, genotype and the interaction between sex and genotype. The additive model revealed a single QTL for body fat gain on Chr7 at 54.65 Mb ($\alpha = 0.05$). The interactive model revealed the same QTL for both body fat gain and interestingly, heat expenditure on Chr7 at 54.65 Mb($\alpha = 0.05$). Additional QTLs for body fat gain were observed on Chr3 at 58.37 Mb ($\alpha = 0.05$) and on Chr 11 at 72.26 Mb ($\alpha = 0.05$) as well as activity on Chr1 at 80.20 Mb ($\alpha = 0.05$) in the interactive model.

Two independent consomic lines were obtained to validate the effects of the AJ Chr1 (CSS1) and AJ Chr7 (CSS7) on the B6 background. CSS1 and CSS7 were backcrossed with B6, generating 4 distinct F1 populations: (B6 x CSS1), (CSS1 x B6), (B6 x CSS7) and (CSS7 x B6). The F1s were crossed to generate 4 distinct F2 populations: ((B6 x CSS1) x (B6 x CSS1)), ((CSS1 x B6) x (CSS1 x B6)), ((B6 x CSS7) x (B6 x CSS7)), and ((CSS7 x B6) x (CSS7 x B6)) F2s. Within each F2 population, some animals will inherit the AJ haplotype for the QTL regions identified on Chr1 and Chr7 while others will serve as littermate controls. Ultimately, we aim to further elucidate candidate genes responsible for variation in rates of thermogenesis in response to carbohydrate restriction to contribute to the advancement of precision dietetics.

Emanuele Baldassarri

emanueleb@tamu.edu

Undergraduate Student

P16. Understanding DNA double-strand break (DSB) repair in *Aedes aegypti*

Joseph S. Romanowski, Zach N. Adelman

Interdisciplinary Graduate Program in Genetics and Genomics, Department of Entomology

Gene drive is a highly efficient, species-specific method of genetic control that enables the spread of alleles in a super-Mendelian fashion to modify or suppress mosquito vector populations. By applying gene drive systems to Aedes aegypti, the primary vector of dengue, yellow fever, chikungunya, and Zika, it is possible to control Aedes populations and decrease the transmission of diseases they spread. While gene drive systems have shown promise in confined lab settings, lack of gene drive control mechanisms prevent them from being tested in field trials and thus our understanding of their effectiveness in natural environments. One way to overcome this obstacle is by engineering a self-eliminating gene drive that is able to revert gene drive mosquitoes to wild type over time by way of the single-strand annealing (SSA) double-strand break repair (DSB) pathway. By inducing DSBs in between transgenes flanked by identical sequences, transgenic cargo can be deleted through the single-strand annealing SSA repair pathway to shift gene drive populations back to wild-type. Although DSB repair and SSA is well understood in humans, mice, and yeast, less is known about the factors that regulate DSB repair in mosquitoes. By investigating the factors that influence DSB in mosquitoes, we can design a safer, biodegradable gene drive system to combat tropical diseases.

Joseph S. Romanowski

joeromanowski@tamu.edu

Graduate Student

P17. Accumulation of fat prior to dietary intervention may reduce efficacy of personalized dietary guidance in mice

Riley K. Watson1, Anna C. Salvador1,2 and David W. Threadgill1,2

1Department of Nutrition, Texas A&M University, College Station, TX 77843
2Department of Molecular and Cellular Medicine, Texas A&M University Health Science Center, College Station, TX 77843

Efforts to implement precision nutrition as well as predicting dietary response based on genetic information continue to proliferate. Previous studies have shown differential responses to American and ketogenic diets in C57BL/6J (B6) mice while FVB/NJ (FVB) mice were seen to have similar responses between the two diets. Additionally, prior data showed that B6 males who were exposed to an American diet (35% of energy from fat, 50% from carbohydrate) had higher amounts of fat mass in comparison to B6 males exposed a ketogenic diet (84% of energy from fat, 0% from carbohydrate). B6 females along with FVB males and females did not show diet-dependent differences of body fat. This preliminary data suggests that both sex and genetic background play a role in the response to carbohydrate restriction.

In the most recent study, a ketogenic diet was utilized as a dietary intervention for three months in both B6 and FVB mice after 3 months of exposure to the American diet. By the end of the study, it was found that B6 females who received the intervention gained less fat mass compared to B6 females who remained on the American diet (B6 female American: 15.94g, +/- 5.00g; B6 female Reversal: 9.67g, +/- 3.98g; $p = 0.007$). Surprisingly, B6 males who were exposed to the intervention diet gained more fat mass than B6 males who remained on the American diet (B6 male American: 19.69g, +/- 1.42g; B6 male Reversal: 23.86g, +/- 1.28g; $p < 0.001$) even though the prior data suggested that B6 males would likely respond best to the dietary intervention. As expected, FVB males and females did not show different responses to the American or dietary intervention diet (FVB male American: 11.74g, +/- 0.872g, FVB male Reversal 10.32g, +/- 3.60g; $p = 0.280$; FVB female American: 5.97g, +/- 2.59g, FVB female Reversal: 6.91g, +/- 2.27g; $p = 0.424$). Of note, B6 males gained significantly more fat mass prior to the dietary intervention in comparison to B6 females and FVB males or females (B6 male American: 42%, +/- 2%; B6 male Reversal: 48%, +/- 1%; $p < 0.001$).

The amount of fat mass that was gained on the American diet before the intervention was highly correlated to the amount of fat mass gained at the end of the study ($r = 0.878$, $p < 0.001$). This suggests that there are mechanisms contributing to obesity that are not attenuated by dietary intervention alone. We concluded that the effects of the amount of fat accumulation prior to intervention should be further studied to better understand the implications for the amount of fat mass present at the end of the study. Studies are underway to examine the effect of various time frames of exposure to an American diet before the introduction of a dietary intervention as well as surgical removal of adipose tissue at the time of the intervention to evaluate the implications for reversing obese phenotypes.

Riley K. Watson

rileywatsonnn@tamu.edu

Undergraduate Student

P18. Using natural gene drives and genetic engineering tools for population control of invasive mice on islands

Ana M. Velasquez Escobar, David W. Threadgill

Texas A&M University Interdisciplinary Program of Genetics and Genomics
Texas A&M University Department of Molecular and Cellular Medicine

Invasive mouse populations on islands are a threat to global biodiversity. Current population control methods rely on anticoagulant bait and trapping, which have the potential to harm off-target, potentially endangered, species as well as livestock. The need for species-specific population control increases as the size of the target area and human population increase. This project aims to use the mouse t-haplotype, a naturally occurring meiotic driver in mice, to engineer a mouse that can only have male progeny. Release of these mice in target areas where invasive mice reside could be an alternative and more humane method for species-specific eradication.

Ana M Velasquez Escobar

avelasquez1086@tamu.edu

Graduate Student

P19. The immune landscape of murine colorectal tumors

Matthew Crespo [1], Sophia Ferrer [1], Meghan Si [1], Holly Thill [1], Megan Thomas [1], Daniela Wong [1], Michael McGill [1,2], David Threadgill [1,2]

1. Department of Molecular and Cellular Medicine, Texas A&M Health Science Center
2. Interdisciplinary Graduate Program in Genetics and Genomics, Texas A&M University

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in men and women in the United States. ERBB4 is a transmembrane growth factor receptor that is commonly upregulated in human CRC yet remains relatively understudied. We are studying the role of ERBB4 in CRC progression and its possible utility as a target for precise CRC therapeutics using innovative preclinical mouse models. Our lab previously discovered that tumors developing in the absence of EGFR exhibit upregulation of ERBB4 and a more aggressive growth phenotype, at least in part due to an increase in the expression of an immunosuppressive cytokine, IL10. Interestingly, in tumors that develop in the presence of EGFR but the absence of ERBB4, IL10 signaling is significantly reduced, and the tumors that develop are significantly smaller. We hypothesize that in tumors that develop in the absence of ERBB4 there will be an increased presence of immune cells infiltrating the tumor, since IL10 levels are reduced, contributing to the observed reduction in the size of polyps. We are partially investigating this hypothesis by utilizing immunohistochemical (IHC) staining of tumors that developed with or without ERBB4 using antibodies that detect the presence of infiltrating immune cells. Specifically, we are staining for total macrophages (F4/80) and T-cells (CD3). Unfortunately, when IHC staining was initially applied to the samples, we observed high background staining and positively stained epithelial cells, indicating non-specific binding had occurred. Therefore, we conclude that in order to optimize visualization of the immune landscape of these tumors, proper fixation and preparation of our samples is imperative. In the future, we will attempt IHC staining again with increased antigen retrieval to further define the immune landscape of these tumors and elucidate the role of IL10 in the development of these tumors. Additionally, we will investigate the potential role of JAK/STAT signaling in the protection conferred by ERBB4 ablation. When we attempt IHC staining again, if we do not observe a significant difference in the immune landscape between colon tumors developing in the presence or absence of ERBB4, then the observed tumor growth is not the result of decreased immune activity conferred by IL10, but instead may stem for a more cell-directed effect. Since the IL10 cytokine functions to both suppress the immune system and increase JAK/STAT signaling, we will investigate the potential role of JAK/STAT signaling in the progression of these tumors.

Matthew Crespo, Sophia Ferrer, Meghan Si, Holly Thill, Megan Thomas, Daniela Wong

mpmcgill@tamu.edu

Undergraduate Student

P20. Theiler's Virus Induced Neuroinflammation of LRRK2 G2019S Transgenic Mice

Tae Wook Kang1, Sathvik Patchametla1, Prathmica Chandramohan1, Samera Mulatu1, Clifford Moshay1, Koedi Lawley1, Katia Amstalden1, Raquel Rech2, Chi G. Weindel3, Robert O. Watson3, Colin R. Young1, Candice Brinkmeyer-Langford1,4, C. Jane Welsh1,2,4

1Department of Veterinary Integrative Biosciences, 2Department of Veterinary Pathobiology, 3Department of Microbial Pathogenesis and Immunology, 4Texas A&M Institute for Neuroscience, Texas A&M University

The G2019S mutation in the multifunctional kinase LRRK2 is a common genetic determinant associated with Parkinson's disease. Previous studies have shown that underlying mitochondrial dysfunction in LRRK2 G2019S transgenic (Tg) mice ultimately causes induction of inflammatory cell death. This mutation results in hyperinflammation during infection. Theiler's murine encephalomyelitis virus (TMEV) is a natural pathogen of mice which causes encephalitis, epilepsy, and immune mediated demyelinating disease in genetically susceptible strains of mice. In this study we infected LRRK2 G2019S Tg mice derived from the C57BL6/J strain to observe effects on neuroinflammation. Wild type (WT) C57BL6/J mice were used as a comparative group. The results revealed that seizures were more prevalent and more severe in male Tg mice compared to WT mice. TMEV infected Tg mice also showed less body weight gain compared to WT mice with the effect being more exaggerated in males. Thymus weight was reduced in Tg males but not in females. Spleen weight was reduced in Tg mice compared to WT mice. Histological evaluation of the brain revealed that inflammatory lesions were evident in the hippocampus for both strains and sexes. Rostral lesions, meningitis and lesions around lateral ventricles were more pronounced in the Tg mice. Prominent gliosis, necrosis, and increased glial cell activation were also observed. Overall, these findings revealed that Tg mice were more prone to neuroinflammation than WT mice. Since this was a pilot study, a larger scale follow-up study is planned to further evaluate the results with an emphasis on investigating specific cell types in the brain related to neuroinflammation.

Tae Wook Kang

tkang@cvm.tamu.edu

Graduate Student

P21. NF-κB-Inducing Kinase (NIK) Mediates Neuronal Function and Glioblastoma Tumor Microenvironment

Parker Smith, Dong Lee, Raquel Sitcheran, Gerard Toussaint

Texas A&M Molecular and Cellular Medicine Department, Texas A&M University College of Medicine, Texas Brain and Spine Institute

Glioblastoma multiforme (GBM) is the deadliest form of primary brain cancer. Our lab has previously established that NF-κB-Inducing Kinase (NIK), a mitogen-activated protein kinase that is required for the activation of the noncanonical NF-κB pathway, promotes GBM invasion and tumor growth. Additionally, we have observed NIK-dependent dysregulation of metabolic pathways in several cancer cells and tissues. Neurons in the tumor microenvironment were recently shown to form functional synapses with GBM cells, promoting tumor progression and invasion through release of the presynaptic protein Neuroligin-3 (NLGN3), which activates the Phosphoinositide 3-kinase Mammalian Target of Rapamycin (PI3K-mTOR) pathway. To evaluate whether NIK impacts neuronal function to promote GBM progression and invasion, we generated NIK knockout (NIKKO) Human Cortical Neuron 2 (HCN-2). Western blot and immunofluorescence showed that, compared to WT cells, differentiated HCN-2 NIKKO cells expressed higher levels of differentiation markers in addition to higher levels of NLGN3. Seahorse assays revealed that HCN-2 NIKKO cells exhibited increased glycolytic activity as well as increased ATP levels. These results suggest that neuronal NIK may play tumor-suppressing roles in the GBM tumor microenvironment, which may counteract efforts to use NIK inhibitors as a therapeutic approach for this deadly cancer. Additional studies will examine whether NIK controls NLGN3 expression though the PI3K-mTOR pathway and examine the role of NIK in regulating functional interactions between neurons and GBM cells.

Parker Smith

pdsmith00@gmail.com

Undergraduate Student

P22. Identification of dysregulated small RNA in Angelman syndrome pig extracellular vesicles

Livia Schuller, Scott Dindot

Texas A&M University Department of Veterinary Pathobiology

Angelman syndrome arises from the loss of maternal UBE3A in central nervous system neurons and this cell-type specificity has made evaluating the efficacy of potential therapies challenging. The identification of a biomarker is an important step in evaluating therapies in development and accelerating them into clinical settings. Extracellular vesicles contain bioactive molecules and are prime candidates for biomarkers of neurological disorders because they express cell-type specific markers and can cross the blood brain barrier. MicroRNAs (miRNAs), which regulate the expression of mRNAs and are abundant in extracellular vesicles, have not been extensively studied in Angelman syndrome. We investigated the small RNA contents of extracellular vesicles isolated from pig serum and cerebrospinal fluid to identify dysregulated pathways involved in Angelman syndrome. Following the guidelines established by the International Society for Extracellular Vesicles, we demonstrated successful isolation of pig extracellular vesicles using a precipitation-based method. Small RNA sequencing results suggested that miRNAs were the most abundant biotype of RNA within extracellular vesicles. Three of these miRNAs: miR-1224, miR-132, and miR-181c, were downregulated in the serum of Angelman syndrome pigs. Interestingly, miR-132 is also involved in Rett Syndrome and MeCP2 duplication syndrome which have similar symptoms to Angelman syndrome. Gene Ontology analysis revealed that the contents of serum and cerebrospinal fluid extracellular vesicles are involved in neurological disease pathways, including seizures. There were 19 upregulated seizure-related miRNAs in the serum of Angelman syndrome pigs and 16 upregulated seizure-related miRNAs in the cerebrospinal fluid. Seizures are observed in over 80% of patients with Angelman syndrome and can be challenging to manage. Further investigation of the identified seizure-related pathways may lead to the identification of a potential efficacy biomarker for therapeutics contained within extracellular vesicles. Additionally, continued investigation of the role of miR-132 may identify pathways underlying the shared phenotypes between Angelman syndrome and Rett syndrome. A better understanding of the pathways affected by maternal UBE3A loss will not only highlight potential biomarker candidates, but also enhance our knowledge of Angelman syndrome in a way that is beneficial for continued therapeutic development.

Livia Schuller

laschuller@tamu.edu

Graduate Student

P23. Inequality of Sex Chromosome to Autosome Fusions

Kayla Wilhoit, Heath Blackmon

College of Veterinary Medicine and Biomedical Sciences, Department of Biology, Texas A&M University, College Station, TX, USA

Chromosomal fusions play an integral role in the remodeling of genomes and in karyotype evolution. Fusions that join a sex chromosome to an autosome are particularly abundant across the tree of life, but previous models on the establishment of such fusions have not accounted for the physical structure of the chromosomes. We have produced a forward time population genetic simulation to explore the outcomes of fusions to both the pseudoautosomal region (PAR) and non-recombining regions of sex chromosomes. The model can simulate the fusion of an autosome containing a sexually antagonistic locus to either the PAR or non-PAR end of a sex chromosome. The model is diploid, two-locus and biallelic, and is able to run thousands of simulations under a variety of conditions. Our results demonstrate that autosomal fusions to the PAR of a sex chromosome will not remain stable, and the fusion will switch from the X to the Y chromosome each generation due to recombination. As a result, beneficial linkage of sexually antagonistic alleles cannot have a fitness effect for more than one generation, and increasing selective pressure on the sexually antagonistic locus leads to decreased fused genotype frequency. In addition, our model demonstrates that autosomal fusions to the non-PAR of a Y chromosome lead to overall higher establishment rates of the fused genotype when compared to fusions to the non-PAR of the X chromosome.

Kayla Wilhoit

ktwilhoit@tamu.edu

Undergraduate Student

P24. A Genomics Approach to Characterize White Coat Color Genes in American Bison, Bison bison

Carly Martone (1), Sam Stroupe (1), Brian Davis (2), and James Derr (1)

(1) Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX
(2) Veterinary Integrated Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX

The American bison (Bison bison) is one of the most unique species on the planet considering its status as 1) an important wildlife species in National and State Parks; 2) an economically viable livestock species; 3) and a powerful religious symbol for many Native American tribes. Bison exhibiting a white coat color are particularly sought after due to their economic, aesthetic, and spiritual value. While multiple scientific investigations of this species have included complete genome sequencing, the bison genome has yet to be fully annotated as has been completed with domestic cattle (Bos taurus). The aim of this study is to provide proof-of-concept for a concurrent annotation project via white coat color gene identification including those conferring albinism, leucism, dilute color, or other coat color related phenotypes. Genes including PMEL, TYR, KITLG, MITF, SLC45A, MLPH, and MC1R were identified as primary candidate genes as they have been found to cause a white coat color phenotype in various other mammals. For this study, we developed high quality genome sequences from white bison that were suspected albinos (extreme lack of melanin) and compared their nucleotide sequences at these genes to multiple bison with wild-type coat color. We identified a homozygous missense mutation in exon 3 of the TYR gene on bison autosome 29 (c.1114C>gt;T) that tracks exclusively with this bison albino phenotype. This recessive mutation is at the same location resulting in the same protein substitution as a well characterized albino mutation in humans, leading us to propose that this is the causative mutation for at least one type of naturally occurring albinism in bison. Overall, identification of the causal allele conferring albinism in American bison is significant in its application to conservation management, livestock production, and the relationship between bison and Native American people with an immediate benefit of the project to provide proof-of-concept for the concurrent bison genome annotation.

Carly Martone

camartone@cvm.tamu.edu

Graduate Student

P25. Sequence and lineage characterization of major histocompatibility complex class I genes in Atlantic herring using comparative genomic approach

Mary Smith 1, Minal Jamsandekar 2, MiOk Lee 3, Leif Andersson 2,4,5

1 Department of Biology, Texas A&M University, College Station, TX 77843, 2 Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, TX 77843, 3 Department of Biochemistry and Biophysics, Texas A&M University, College Station, TX 77843, 4 Science for Life, Laboratory, Department of Medical Biochemistry and Microbiology, Uppsala University, 752 36 Uppsala, Sweden, 5 Department of Animal Breeding and Genetics, Swedish University of Agricultural Sciences, 750 07 Uppsala, Sweden

Major histocompatibility complex (MHC) are the most polymorphism genes in the vertebrate genome and are an integral part of an adaptive immune system. They are responsible for presenting antigenic peptides to T cells. MHC genes are classified into two major types, class I and class II. Class I genes presents endogenous antigens to cytotoxic T cells that are present on the surface of all nucleated cells, while MHC class II genes present exogenous antigens helper T cells that are present on antigen presenting cells. Class I genes in teleost fish are categorized into five lineages, U, Z, S, L, and P. In this study, we determined MHC class I genes, haplotypes, and lineages in Atlantic herring. Atlantic herring is the most abundant vertebrate in the world with an effective population size over one million. Studying MHC genes in such a species will broaden our understanding of nucleotide diversity of MHC genes in a large population where effects of genetic drift are minimal. We obtained MHC class I gene sequences in Atlantic herring using ENSEMBL annotation for the reference genome and found 19 genes, distributed across chromosomes 4, 5, 7, 9, and 19. Sequence alignment showed that class I genes are highly polymorphic with respect to SNPs, indels, and CNVs. To categorize sequences into their respective lineages, we constructed a phylogenetic tree comprising of class I sequences from Atlantic herring and from other fish species for which the lineages are already known. Once we obtain better understanding of MHC class I in the Atlantic herring reference genome, we aim to expand our analysis to 24 more genomes constructed using PacBio HiFi data.

Mary Katherine Smith

mksmith00@tamu.edu

Undergraduate Student

P26. Genomic identification of the most diverged avian hybrid

James M. Alfieri

Interdisciplinary Program in Ecology and Evolutionary Biology, Texas A&M University, College Station, TX, USA

Hybridization between diverged species is an important evolutionary event that shapes genomes, phenotypes, and species trajectories, yet most hybridization events are based on morphological and behavioral observations which are controversial. One specific hybridization record is particularly germane to both the ongoing discussion of the validity of phenotypic observations by non-experts and the general understanding of divergent hybridization because it was identified by experts using phenotypic observations and potentially represents the most diverged avian hybrid. Using genomic tools, we revisit a 64-year-old avian hybrid specimen, which was putatively identified as an F1 hybrid between the Rusty-margined Guan (*Penelope superciliaris*) and Helmeted Guineafowl (*Numida meleagris*) which diverged 65 MYA. Using aDNA extraction techniques, we obtained ~ 800 million 150 bp reads, leading to an expected coverage of 30X. We performed local BLAST searches containing 17 Galliformes and 1 Anseriformes species. To control for differences in genome contiguity, we partitioned the query sequences resulting in 1 million 100-bp fragments per species (~ 10% of the nuclear genome). We also performed BLAST searches for the mitochondrial genome, using a BLAST database containing 28 Galliformes species and 1 Anseriformes species. Finally, we constructed separate phylogenies for 8063 avian orthologs, and parsed the trees, extracting and counting the sister species of the hybrid species. We found that the nuclear BLAST hits were overwhelmingly concentrated in two species, N. meleagris (20% of hits), and the domestic chicken, *Gallus gallus* (20% of hits). The mitochondrial BLAST revealed that the maternal parent was N. meleagris. Of the 8063 ortholog phylogenies, 5910 had a species sister to the hybrid. 45% of the trees placed Gallus gallus sister to the hybrid, while 34% of the trees placed *N. meleagris* sister to the hybrid. These results question the veracity of hybrid identifications based on phenotypic observations because even with the specimen in hand and accompanied with detailed behavioral observations and provenance, expertly trained ornithologists were unable to confirm the identity of this F1 hybrid.

James M Alfieri

j.alfieri@tamu.edu

Graduate Student

P27. Reprogramming Collaborative Cross mouse embryonic fibroblast cells into induced pluripotent stem cells using the Sendai virus

Demi K. Waworuntu, Alex H. Phan, Krishna N. Patel, David W. Threadgill

(Demi) College of Agriculture and Life Sciences, (Alex) College of Veterinary Medicine and Biomedical Science, (Krishna) TAMU College of Medicine, (David) TAMU College of Medicine

According to the Center for Disease Control and Prevention, cardiovascular disease is the leading cause of death in the United States and although pharmaceutical drugs are carefully screened for potential cardiotoxicity, environmental chemicals are not. Recent research has shown that not only do environmental chemicals possess cardiotoxic effects, but they also affect human cardiomyocytes differently due to the large genetic diversity within humans. Our project is designed to program induced pluripotent stem cells (iPSCs) – which share similar characteristics with embryonic stem cells (ESC) – from mouse embryonic fibroblast (MEF) cells; iPSCs can eventually be differentiated into beating cardiomyocytes in the context of an embryoid body (EB). To better model the genetic diversity within the human population, a novel mouse genetic reference population, called the Collaborative Cross (CC), was used to compare adverse cardiotoxic effects induced by environmental chemicals both in vitro and in vivo. It was hypothesized that if the in vitro response proved to be correlative to the in vivo response, the human response could prove the same outcome. To begin, MEF cells were obtained by harvesting embryos from a CC mouse and culturing the cells in MEF media. The MEF cells were then reprogrammed using the Sendai Virus, an RNA virus that induces the expression of genes that force the MEF cells to return to its pluripotent state. Eight days after the transduction, the cells were cultured in ESC media in combination with several inhibitors meant to keep the cells in their pluripotent-like state. In the weeks following the transduction, cells were visually monitored for emerging iPSC colonies. Single colony subcloning was then performed to isolate the iPSCs from the MEFs that were not successfully transduced. After subcloning iPSCs for at least 5 passages, RT-PCR was performed in order to verify whether the cells had taken up and eventually cleared the virus. Overall, our data indicates that the Sendai virus can successfully reprogram MEF cells to iPSCs, however genetic background has been shown to affect iPSC generation of CC lines differently. Thus far, we have successfully transduced three CC lines and plan to do the same with five additional CC lines. In the future, the CC iPSCs will be used to generate beating cardiomyocytes in the context of an embryoid body for in vitro analysis of cardiotoxicity in response to environmental chemical exposure.

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Demi K. Waworuntu and Alex H. Phan

demiwaworuntu@tamu.edu

Undergraduate Student

P28. The perils and promise of models of chromosome evolution

Terrence Sylvester, Heath Blackmon

Department of Biology Texas A&M University College Station Texas 77840 USA, Department of Biology Texas A&M University College Station Texas 77840 USA

A surge of new and more complex models is allowing the rapid testing of evolutionary hypotheses. However, new approaches are often only tested on simulated data that fit the inference model's assumptions. However, biological datasets often violate model assumptions in unexpected ways. This has led to a cyclic pattern where a new model is developed and widely applied, and only after it is in widespread use, we realize that biological datasets may often suffer from inflated false-positive rates. We have discovered just such an issue in a chromosome evolution model that our lab has developed. This model allows rates of chromosome number evolution to vary depending on the state of a binary trait. In an analysis of the rates of chromosome number evolution in Lepidoptera, we used the larval feeding patterns as a binary trait and applied a biologically realistic model to infer the impact of this binary trait on the rates of chromosome number evolution. We find that the rates of chromosome number evolution are highly impacted by the binary trait in question. We then simulated a neutrally evolving binary trait and used the same model to test the significance of our results. We find that neutrally evolving simulated traits will be inferred to impact chromosome evolution rates 98% of the time. We show how to use simulated datasets like these to provide a valid p-value for the impact of empirical traits that will have a false positive rate of approximately 5%. Finally, these results suggest that the results that we obtained using the empirical data could be due to the presence of few rapidly evolving regions in Lepidoptera phylogeny and highlights the importance of assessing the models for inflated false-positive rates.

Terrence Sylvester

terrence@tamu.edu

Graduate Student

P29. CaveCrawler: An interactive analysis suite for cavefish bioinformatics

Annabel Perry, Suzanne E. McGaugh, Alex C. Keene, Heath Blackmon

Department of Biology at Texas A&M University (College Station, TX), Ecology, Evolution, and Behavior at University of Minnesota (Saint Paul, MN), Department of Biology at Texas A&M University (College Station, TX), Department of Biology at Texas A&M University (College Station, TX)

In recent years, non-traditional model organisms have become increasingly important for health and evolutionary research. These model organisms are necessary for some forms of research, as some diseases and evolutionary mechanisms can be studied only in specific species. The Mexican tetra is one such non-traditional model organism. This species consists of two morphs, a surface-dwelling and a cave-dwelling morph, which differ in key phenotypic features such as sleep, metabolism, and anxiety. Due to the homology between human and Mexican tetra genomes, these morphs are naturally occurring control and experimental groups with which to study the genetic basis of human disorders of sleep, metabolism, anxiety, and much more. Though Mexican tetra genetics research has proliferated in recent years, this surplus of data presents a challenge for researchers. There currently exists no central location in which to access Mexican tetra genetics data and no easy way to compare data from across studies and experimental contexts. To address this need, we created CaveCrawler, a web-based genetics inference tool which combines Mexican tetra genetics data from many studies to enable cross-study comparisons and identification of yet-to-be-answered research questions. In addition to advancing research in the Mexican tetra, CaveCrawler's open-source code can be adapted to incorporate data from other species, enabling researchers to create web-based genetics inference tools for their own non-traditional model organisms.

Annabel Perry

annabelperry@tamu.edu

Undergraduate Student

P30. Cannabidiol (CBD) Signaling in Human Neuroblastoma

Claire Alexander, Arizbeth Lopez Garcia, Maryam Vasefi*

Department of Biology, Lamar University, Beaumont, TX
*Assistant Professor, Department of Biology, Lamar University, Beaumont, TX

Cannabidiol (CBD) is a phytocannabinoid boasting neuroprotective, anxiolytic, antidepressant, and anti-inflammatory properties. Thus, CBD has the potential to treat psychiatric and neurodegenerative diseases via multiple targets, including 5-HT1A receptors, endocannabinoid mediators, and the intracellular ERK1/2 signaling pathway. Recent studies have suggested that chronic intra-DRN administration of CBD induces desensitization of 5-HT1A receptors and is associated with anxiolytic effects in rodents, though this effect has not been confirmed in human neurons. Likewise, the antidepressant effect of SSRIs is associated with 5-HT1A receptor desensitization, though these drugs may have unpleasant side effects. Moreover, studies suggesting neuroprotective effects of CBD support its candidacy for the treatment of neurodegenerative diseases, such as Alzheimer's Disease (AD), for which few treatments are available. Crucially, several studies have also suggested that CBD possesses similar mechanisms to SSRIs due to its 5-HT modulating effects and potential pro-neuroplastic effects. Given the intriguing association between psychiatric disorders and AD, in addition to the shared mechanisms of CBD and classic SSRIs, we investigate the potential mechanisms of CBD in the treatment of psychiatric disorders. Specifically, the objective of the project is to provide evidence of CBD-mediated desensitization of 5-HT1A receptors in human neurons. SH-SY5Y neuroblastoma cells will be dose-and time-dependently treated with CBD, then western blot and RT-PCR will be utilized to evidence the molecular pathway underlying this unique mechanism. Finally, agonist-antagonist studies will be used to confirm the involvement of 5-HT1AR in these CBD-ERK1/2 effects. Based on early evidence, CBD induces a dose-dependent response via ERK1/2 signaling. We also study the neuroprotective effect of CBD against amyloid-beta (Aβ). SH-SY5Y cells are cultured in 96-well plates and exposed to amyloid-beta (Aβ) prior to CBD treatment. Evidence of CBD's protective effects will be deduced by the application of MTT assay. Our results suggest that CBD potentiates the proliferation of healthy neurons compared to control. Interestingly, CBD treatment minimally preserves neuronal proliferation following Aβ treatment, compared to Aβ-treated control. This project will support other studies revealing CBD-mediated enhanced cell survival in SH-SY5Y cells, while also providing evidence of CBD's anti-amyloidogenic mechanism. This study will support the utility of CBD in the treatment of multiple neurological disorders via receptor desensitization and enhanced cell viability.

Claire Alexander

ealexander5@lamar.edu

Graduate Student

P31. Systems biology approaches to build a predictive model of Dorsal/NF-κB signaling network in the Drosophila embryo

Etika Goyal 1, Sadia Siddika Dima1, Sharva Vijayakumar Hiremath 2, Gregory T Reeves 1

1, Texas A&M University, College Station, Texas
2, North Carolina State University, Raleigh, NC

Systems biology faces a conundrum in the realm of computational modeling. On the one hand, models are necessary to integrate all of the experimental data into one explanatory system. On the other, the large number of unknown parameters limits the utility of systems biology models. To overcome this difficulty, we have performed two types of measurements. First, we have measured the whole system, which allows for the full systems biology model to be fit to the data. Second, we have performed localized experiments, which isolate only 1-2 parameters for estimation. As a model system, we have focused on the Dorsal gradient, which patterns the dorsal-ventral (DV) axis of the early embryo.

Dorsal (Dl), which is ubiquitously expressed and is one of three Drosophila homologs of NFkB, is translated in the early embryo from maternally deposited dl mRNA. Dl protein binds to the IkB homolog Cactus (Cact), which helps in retaining it in the cytoplasm, and hence, blocks it from entering the nuclei to regulate its target genes. Our aim is to perform detailed measurements of individual biophysical parameters and global morphogen gradient properties in the early Drosophila embryo. As an example, we quantitatively measured the nuclear import and export rates of Dl and Dl/Cact complex through a fluorescence recovery after photobleaching (FRAP) assay in which we bleached single nuclei (ventral and dorsal side). These and other localized experiments that provide estimates of isolated parameters allow us to build predictive systems biology models, which will help us to understand the general knowledge of the NF-κB signaling module found in animals from Cnidarians to humans.

Etika Goyal

egoyalg@tamu.edu

Postdoc

P32. Evolution of Oxidative Stress Response Regulatory Function in Telomere-Associated Protein POT1b

Ji-Hee Min, Claudia Castillo-González, Borja Barbero Barcenilla, David Curtis and Dorothy E. Shippen

All are affiliated with Texas A&M University

Protection of Telomeres 1 (POT1) is the most conserved member of the shelterin complex, which is a group of telomere-binding proteins that assist with telomere maintenance and genome stability. The flowering plant Arabidopsis thaliana contains a unique gene duplication for the POT1 gene, encoding two divergent POT1 paralogs termed AtPOT1a and AtPOT1b. AtPOT1a functions in the positive regulation of telomerase, the enzyme responsible for maintaining G-rich repeats on 3' telomeric ends. Little is known about the function of AtPOT1b, but it does not play a conventional role in telomere biology. Recent unpublished data in Shippen lab indicate that Catalase 2 (CAT2), an ROS scavenging enzyme, interacts with AtPOT1b in a yeast two hybrid screen. In addition, AtPOT1b regulates catalase activity and ROS accumulation as demonstrated through the reduced catalase activity of pot1b mutants, indicating AtPOT1b involvement in the oxidative stress response. Here, we map the interaction domain between CAT2 and AtPot1b, AtPot1a, and two other ancestral copies of POT1, Carica papaya (Papaya POT1) Physcomitrella patens (Phsyco POT1) using yeast two hybrid assays. We identify the OB1 domain of AtPOT1b and the C-terminal domain of AtPOT1a, Papaya POT1, and Physco POT1 as responsible for the CAT2 interactions. Furthermore, using genetic, biochemical and cell biology techniques, we show the oxidative stress management function of ATPOT1b is present in ancestral POT1 proteins. Recent studies implicate telomere proteins and telomerase in the response to oxidative stress. Our findings support this conclusion and suggest that the oxidative regulatory function of POT1 is ancestral and pre-dates the duplication of the Arabidopsis POT1a and POT1b genes.

David Curtis

david_curtis17@tamu.edu

Technician

P33. FDX1 is required for copper release from elesclomol-copper complex in the mitochondria

Mohammad Zulkifli, Shivatheja Soma & Vishal M. Gohil

Department of Biochemistry & Biophysics, Texas A&M University, College Station, TX

Copper (Cu) is an essential micronutrient that is required for the structure and function of a number of cuproenzymes including the mitochondrial cytochrome c oxidase. Genetic mutations that prevent Cu absorption or transport to cuproenzymes result in lethal human disorders such as Menkes disease and a subset of mitochondrial disorders. Currently, no effective therapy exists for these disorders. This is because the direct administration of Cu salts is ineffective in delivering Cu across cellular membranes to the cuproenzymes present in different subcellular compartments. To identify compounds that can transport Cu across biological membranes, we performed a targeted small molecule screen in yeast cells and identified an investigational anticancer drug, elesclomol (ES), as the most potent Cu-transporting molecule. ES rescued Cu-deficient phenotypes in different genetic models of copper deficiency including yeast, mammalian cells, zebrafish, and mouse by delivering Cu to the mitochondria and restoring cytochrome c oxidase activity. Translating these exciting new findings into the development of ES as a therapeutic agent for Cu deficiency disorders requires understanding its mechanism of Cu-release inside the cells. Towards this end, we show that the mechanism by which Cu is released from ES inside the cells is distinct from other Cu-transporting pharmacological agents and requires the presence of the mitochondrial protein FDX1. Our study offers ES as a promising therapeutic agent for the treatment of Menkes and associated disorders of hereditary Cu deficiency.

Mohammad Zulkifli

mohammad.zulkifli@agnet.tamu.edu

Postdoc

P34. Testing in vitro toxicity using an organotypic culture model based on a novel mouse genetic reference population

Krishna N. Patel, David W. Threadgill
Department of Molecular and Cellular Medicine, Texas A&M Health Science Center College of Medicine, College Station, TX

Cardiovascular disease (CVD) is the leading cause of death worldwide and environmental exposures contribute significantly to CVD morbidity. However, the potential cardiac related toxicologic effects of environmental chemicals is largely unknown. Compared to pharmaceuticals, relatively few environmental chemicals have been tested for cardiotoxicity due to the lack of accessible cardiac safety models and models accurately evaluating *in vitro*-to-*in vivo* translation. Additionally, extrapolating *in vivo* risk and hazard prediction based on current *in vitro* models is challenging due to the lack of genetic diversity represented in these models. Advances in stem cell research have shown that somatic cells of various genetic backgrounds can successfully be reprogrammed to generate induced pluripotent stem cells (iPSCs), which exhibit a pluripotent stem cell-like state similar to that of embryonic stem cells (ESCs). We have generated iPSCs from mouse embryonic fibroblasts (MEFs) of individuals from a novel mouse genetic reference population, called the Collaborative Cross (CC). These iPSCs can be differentiated into beating cardiomyocytes in the context of an embryoid body organotypic culture model (EB-OCM), providing an *in vitro* model for cardiotoxicity testing of environmental chemicals. Currently, we are focused on generating iPSC-derived cardiomyocytes from eight CC lines and performing *in vitro* chemical toxicity screening. Results from the *in vivo* portion of this study have shown that there is inter- and intra-strain variability in response to chemical exposures, highlighting the significance of using a genetically diverse model and supporting our hypothesis that genetic variation influences response. Utilizing genetically-matched CC iPSC-derived cardiomyocytes and mice allows us to model the genetic diversity present in the human population, and thereby accurately translate *in vitro* cardiotoxicity related responses to potential *in vivo* cardiotoxicity risk and hazard of environmental chemicals.

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Krishna N. Patel
technician

P35. PROTECTION OF TELOMERES 1 regulates oxidative stress response and genome integrity in Arabidopsis

Ji-Hee Min, Claudia Castillo-González, Borja Barbero Barcenilla, David Curtis and Dorothy E. Shippen

Department of Biochemistry and Biophysics, Texas A&M University, College Station, Texas USA

Telomeres solve the end-replication problem and protect the ends of eukaryotic chromosomes. These functions are mediated by the telomerase reverse transcriptase and the shelterin complex. Recent studies suggest that telomere-associated factors also play important roles in response to extrinsic and intrinsic stress, especially oxidative stress, but such mechanisms are not well understood. The most conserved component within shelterin is Protection of Telomeres 1 (POT1). POT1 functions in telomere replication and chromosome end protection, and it is encoded by a single-copy gene in most organisms, including humans. However, in the Brassicaceae family, which includes Arabidopsis thaliana, POT1 gene duplication gave rise to two functional POT1 paralogs, AtPOT1a and AtPOT1b. We previously reported that AtPOT1a associates with the telomerase RNP and positively regulates the enzyme activity. Here we show that AtPOT1b is not required for canonical telomere-related functions and instead modulates the response to oxidative stress. Loss of AtPOT1b results in ROS accumulation, chromatin relaxation, and decreased genome-wide DNA methylation. AtPOT1b is enriched at telomeres when plants are grown without the natural anti-oxidant, sucrose. Loss of AtPOT1b also results in higher 8-oxoG content at telomeres, implying that AtPOT1b binding to telomeres mitigates DNA oxidation. Furthermore, AtPOT1b interacts with Catalase 2 (CAT2) and regulates catalase activity. Notably, while ancestral single copy POT1 genes are unable to rescue the telomeric phenotype of an AtPOT1a deficiency, they rescue the ROS phenotype of null AtPOT1b mutants. These findings suggest that the Arabidopsis POT1 proteins may a play direct role in regulating redox homeostasis, and further that this function predates the POT1 duplication in Brassicaceae. Altogether, these results shed new light on the non-canonical functions of telomere-associated proteins and the interplay between the genome and the stress response.

Ji-Hee Min

minjihee15@tamu.edu

Postdoc