TGS 2023

Texas Genetics Society

50th Annual Meeting 2023

Austin, TX
Holiday Inn Austin Midtown
March 23 – 25, 2023

Barbara Bowman Distinguished Geneticist Award Keynote Speaker

Nancy Moran, PhD, UT Austin

Invited Speakers

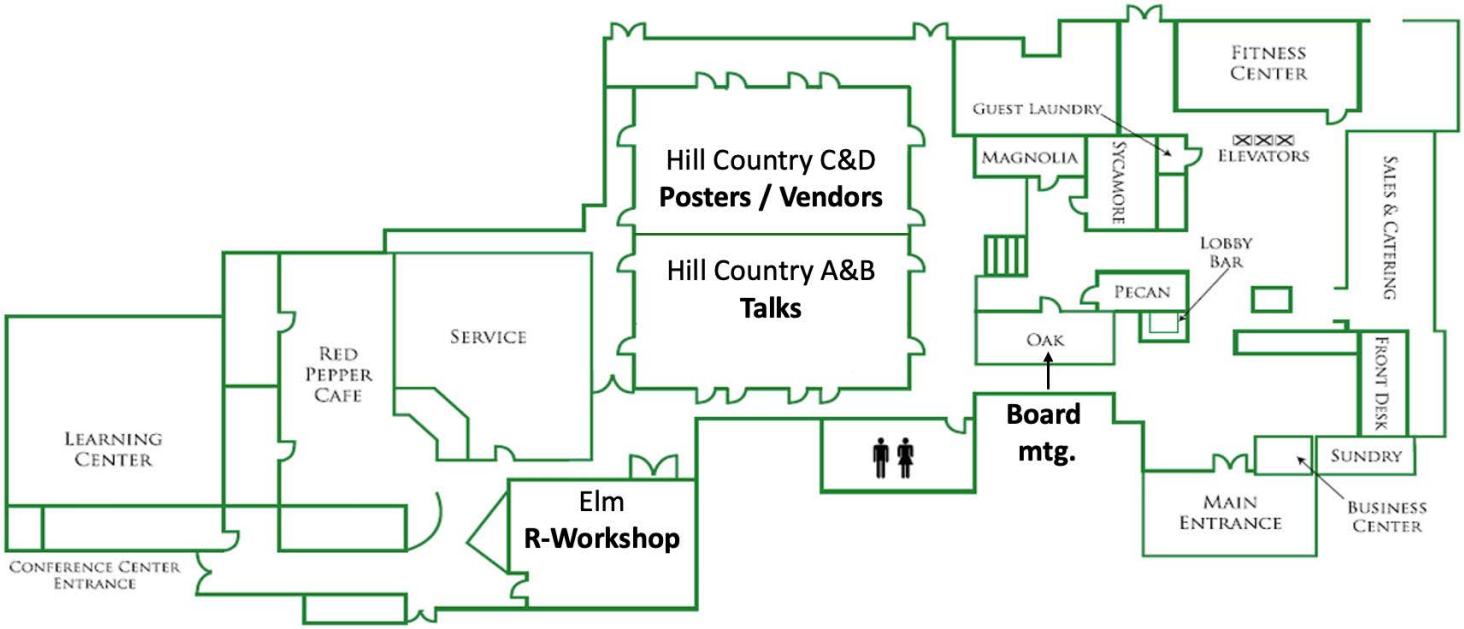
Kira Delmore, PhD, TAMU

Jacob Daane, PhD, U. Houston

Vanessa Macias, PhD, UNT

Natasha Kirienko, PhD, Rice U.

Meeting Room Information



Social Media

FaceBook: Texas Genetics Society
LinkedIn: Texas Genetics Society
Mastodon: @TxGS@mstdn.plus
Twitter: @TX_GeneticsSoc

Table of Contents

Welcome to the 50th Annual Meeting of the Texas Genetics Society!

On behalf of the Board of Directors, it is our pleasure to welcome you to the half-century celebration and meeting of the Texas Genetics Society! The TGS was formed in 1974 to celebrate the successes of researchers in Texas, facilitate collaboration, and to provide a forum for discussion of advances in genetics. We are proud to continue the tradition of encouraging undergraduate and graduate students, postdoctoral scientists, and staff scientists to present their research findings encompassing diverse areas of genetics, fostering the careers of Texas geneticists by increasing their visibility and regional service, and providing a welcoming, collegial scientific environment. Our membership includes geneticists from academic (undergraduate to R1), research, and clinical institutions across Texas.

We sincerely appreciate our **sponsors** who enrich this meeting with their contributions. Their sponsorship not only lets us see the latest goods and services available to genetics researchers, but also allows us to maintain relatively low registration fees for our annual meeting. Please visit our sponsors at breaks and during poster sessions to satisfy your curiosity and to say thank you for their sponsorship of this meeting! This meeting was partially supported by a Meetings Grant from the Society for Developmental Biology.

This year, we started the Presidents' Fund, the brainchild of **Dr. Jonathan Rios** (2018–2019 TGS President). Thank you to **Dr. Olivia Masih White** (1992–1993 TGS President), **Dr. David Aiello** (2020–2021 TGS President), and **Anonymous** for their support of this fund.

This event is possible because of the work of many people. Last year's **TGS members** voted to hold this meeting in Austin. This year's **board of directors** served as the nominating committee and provided input on key decisions. We are most appreciative of our **invited speakers**, **session moderators**, and **judges**. **Dr. Heath Blackmon**, TAMU Associate Professor of Biology and 2022–2023 TGS President-elect, not only led the R meeting workshop again this year with his group, but was instrumental in making this meeting happen. **Dr. Ryan Gray**, UT Austin Assistant Professor of Pediatrics, was the local organizing committee. Trainee board members **Minal Jamsandekar** and **Canyon Calovich-Benne** promoted the meeting on multiple social media platforms. **Dr. Penny Riggs**, TAMU Associate Vice President for Research and Associate Professor of Functional Genomics, printed awards. **Dr. Pat Howard-Peebles**, clinical cytogeneticist at Howard-Peebles Consulting and immediate past TGS historian, provided TGS documents displaying at this meeting. **Evan Hocker**, Registrar for Archives & Manuscripts at the Briscoe Center for American History at the University of Texas at Austin, processed the TGS papers they hold in their archives and gave us duplicates for sharing at this meeting. **Yvette Campbell, CMP**, Meetings Made Easy broker (https://www.meetingsme.com/), helped us find and secure the venue. **Angie Mitschke**, Holiday Inn Midtown Austin's Director of Sales, and **Mayra Lopez**, Banquet/ Catering Convention Services Manager, made our meeting needs and budget work. **Napu Baza** designed the flyers, program cover, and artwork. **Megan Fietz**, Visit Austin convention services coordinator (visitaustin.org), provided Austin brochures and recommendations. Our **speakers**, **poster presenters**, and **attendees** will provide engaging discussions at the sessions and social events, so **thank you** for joining us this year!

If you're interested in or curious about serving on the TGS board as a trainee member (a two-year position), at-large member (three-year position), secretary/treasurer (three-year position), historian, or president-elect (one year, with one year as president), please talk with a current board member! We'll be voting on nominees at the business meeting on Saturday.

We hope that you have an enjoyable and rewarding meeting!

Tina L. Gumienny, PhD, 2022–2023 TGS President

Texas Genetics Society
Board of Directors
2022–2023

President	Tina L. Gumienny Texas Woman's University	tgumienny@twu.edu
President-Elect	Heath Blackmon Texas A&M University	blackmon@tamu.edu
Secretary-Treasurer	Deborah Threadgill Texas A&M University	
Historian	Open	
Past President 2021–2022	Deborah Threadgill Texas A&M University	
Past-President 2020–2021	David Aiello Austin College	
Trainee Board Members	Minal Shrikant Jamsandekar TAMU (2021–2023)	Canyon Calovich-Benne SMU (2022–2024)
At-Large Board Members 2020–2023	Georgios Karras MD Anderson Cancer Center	Megan Keniry University of Texas Rio Grande Valley
At-Large Board Members 2021–2024	Penny Riggs Texas A&M University	Nicole Phillips UNTHSC
At-Large Board Members 2022–2025	Kelli Carroll Austin College	Joe Manthey Texas Tech University
Local Organizing Committee	Ryan Gray UT Austin	

Do you want to join the Board?
Questions?
Please talk to or email Tina L. Gumienny or Heath Blackmon.
We welcome self-nominations!

Nancy Moran, PhD, University of Texas at Austin
2023 TGS Barbara Bowman Distinguished Geneticist

The Bacterial Gut Symbionts of Bees: from Evolution to Engineering

Dr. Nancy Moran studies the biology of symbiosis, particularly that between multicellular hosts and microbes. Symbioses are central in the evolution of complexity, have evolved many times and are critical to the lifestyles of many animals and plants and also to whole ecosystems, in which symbiotic organisms are key players. The primary reason that symbiosis research is suddenly active, after decades at the margins of mainstream biology, is that DNA technology and genomics give us enormous new ability to discover symbiont diversity, and more significantly, to reveal how microbial metabolic capabilities contribute to the functioning of hosts and biological communities.

Heath Blackmon, PhD, Texas A&M University

R Workshop director

Dr. Heath Blackmon is an Associate Professor who joined the Biology Department at TAMU in 2017. His research is focused on evolutionary genetics and genomics often with a focus on understanding the role of epistasis in the evolution of genome structure. His group applies theoretical and empirical approaches and uses a broad range of model organisms including beetles, fish, birds, and plants.

Kira Delmore, PhD, Texas A&M University

Seasonal migration; its role in speciation and genetic basis

Dr. Delmore obtained her BSCH, MA and PhD at universities in Canada (Queen's University, and the Universities of Calgary and British Columbia, respectively) before spending 3 years as a Postdoc at the Max Planck Institute for Evolutionary Biology in northern Germany. Her research is motivated by understanding where diversity originated in the natural world and how it is maintained. She is inspired by the varied ways in which hybrid zones and young species complexes can be used to understand this topic. Most of her work focuses on songbirds and has started to move into the realm of conservation, using her results to inform data-drive management strategies for endangered populations.

Jacob Daane, PhD, University of Houston

Déjà vu: exploring 'replicate' radiations of perciform fishes to understand the genetic and developmental origins of key traits and adaptation to extreme environments

Dr. Jacob Daane attended the University of Wisconsin-Madison, where he obtained a bachelor's degree in Molecular Biology. He subsequently attended Harvard University, where he received his PhD in Biological and Biomedical Sciences. His dissertation work focused on genetic mechanisms of size regulation and proportional growth using the zebrafish fin as a model system. During his postdoctoral work at Northeastern University, he investigated the genetic basis of the adaptive radiation of Antarctic fishes, which have evolved numerous traits that, while adaptive in specific environmental contexts, would be considered pathological in humans. These traits include the complete loss of red blood cells, low skeletal density, and the loss of the glomerulus in the kidney. In 2022, Jake started his lab at the University of Houston. His lab investigates the evolutionary and developmental mechanisms underlying the evolution of new traits as species adapt to environmental extremes. His lab approaches these questions through a combination of comparative genomics in fishes and experimental work in the zebrafish.

Vanessa Macias, PhD, University of North Texas

Expanding molecular genetics for basic and applied studies in mosquito biology

Vanessa Macias is an Assistant Professor in the Department of Biological Sciences at the University of North Texas exploring the molecular genetics of mosquito biology. Vanessa hails from the great state of New Mexico where she studied microbiology and biochemistry at New Mexico State University earning a bachelor's and master's degrees. Her dissertation work at the University of California, Irvine was the beginning of her love of small RNAs and genetic engineering (GE). As a post-doctoral fellow at Penn State Vanessa applied genetic engineering tech in insects more broadly, including in bees and stink bugs. In her new laboratory at UNT, projects are geared toward both creating new GE technologies and in applying those technologies to understanding basic mosquito biology with a specific interest in the molecular mechanisms of the piRNA pathway and its roles in genetic communication between hosts, transgenes and viruses.

Natasha Kirienko, PhD, Rice University

Mitochondrial surveillance in health and disease

Dr. Kirienko received her BS in Biochemistry and MS in Biology from Southern Federal University (Russia). She performed her undergraduate and MS research at the Institute of Protein Research (Russian Academy of Sciences). Then she moved to the US, where she received her PhD from the University of Wyoming in the lab of Dr. David Fay, working on the model organism *Caenorhabditis elegans*. Her dissertation focused on the roles of Retinoblastoma ortholog in cancer and beyond. Dr. Kirienko moved to Boston, where she did her postdoctoral studies at Massachusetts General Hospital & Harvard Medical School under Fred Ausubel and Gary Ruvkun. During her postdoc, she studied host-pathogen interactions using *C. elegans*. She started her independent lab at Rice University in 2015. Dr. Kirienko's research focuses on the role of mitochondria in disease (including neurodegeneration and cancer) and during bacterial infections. During her time at Rice she has trained 9 graduate and over 50 undergraduate students in her lab.

Vendor Sponsors

bionano™

Miltenyi Biotec

PHCbi

TWIST BIOSCIENCE

ThermoFisher SCIENTIFIC
The world leader in serving science

Graduate Program Sponsors

TEXAS A&M UNIVERSITY Biology

TEXAS WOMAN'S UNIVERSITY

Meeting Grant Funding

DEV BIO SOCIETY FOR DEVELOPMENTAL BIOLOGY

Previous Texas Genetics Society Meetings, 1974-2022

No.	Year	Location	Organizer		
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		
			President	**TGS Distinguished Geneticist Award**	**TGS Service Award**
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	canceled	Caleb Phillips	--	--
48	2021	virtual	David Aiello	Mark Kirkpatrick	Tina L. Gumienny
49	2022	Bryan	Deborah Threadgill	--	Kelli Kochan

Texas Genetics Society 50th Annual Meeting
March 23–March 25, 2022
Holiday Inn Austin Midtown
6000 Middle Fiskville Rd
Austin, TX 78752

Thursday, March 23rd

Elm Room

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

Hill Country Ballroom Foyer

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

Sycamore Room

5:00–6:30 pm TGS Board Meeting

Hill Country C/D Ballroom

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

Hill Country A/B Ballroom

6:30–7:30 pm Welcome and announcements
Tina L. Gumienny, TGS President 2022–2023

*Opening Reception

*Light food and beverages are provided during these sessions.
Two drink tickets for beer, wine, or liquor are provided that can be used at the Thursday reception and Friday banquet.

7:30–8:30 pm Opening Keynote 1: Kira Delmore, PhD
Texas A&M University, College Station
Seasonal migration: its role in speciation and genetic basis

8:30–10:00 pm Hang up posters in the Hill Country C/D Ballroom.
Morning session posters must be hung up this evening, but all posters may be displayed at this time.
View posters and visit sponsor tables.
TGS members are free to converge at the Holiday Inn bar or other local venue (see back pages).

Friday, March 24th

Hill Country A/B Ballroom

7:30–8:20 am *Breakfast, networking, informal poster viewing

8:20–8:30 am Welcome and announcements
Dr. Tina L. Gumienny, 2022–2023 TGS President

8:30–9:30 am Morning Keynote 2: Vanessa Macias, PhD
University of North Texas, Denton
Expanding molecular genetics for basic and applied studies in mosquito biology

9:30–10:00 am Contributed Papers Session: Genetics Methods and CUREs
session moderator TBD

9:30–9:40 am Creation and optimization of a novel bioluminescent reporter tag for *C. elegans*
Liam Schuck, Undergraduate Student,
University of Texas at Austin

9:45–10:00 am Evaluating authenticity and visualization of *C. elegans* TAU with a split fluorophore
Gillian Witten, Undergraduate Student,
University of Texas at Austin

Hill Country C/D Ballroom

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

Hill Country A/B Ballroom

11:00–12:00 pm Contributed Papers Session: Genetics of Human Disorders
Session moderator Sarah Christian, Texas A&M University

11:00–11:10 am Heterozygosity for HOGA1 variants is associated with an increased risk for kidney stones
Sohum S. Purao, Graduate Student,
Texas A&M University

11:15–11:30 am Singleminded 2/Semaphorin 7a regulation of a PI3K subunit switch in ER+ breast cancer progression
Hannah Carter, Graduate Student,
Texas A&M University

11:30–11:40 am Altered neonatal development, reduced vocalizations, impaired brain growth, motor incoordination and abnormal EEG in a pig model of Angelman syndrome
Luke Samuel Myers, Graduate Student,
Texas A&M University

11:45–12:00 pm Missense variants in pericellular matrix components increase risk of adolescent idiopathic scoliosis
Anas M. Khanshour, Senior Scientist,
Texas Scottish Rite Hospital for Children

Hill Country A/B Ballroom

12:00–1:15 pm *Vendor workshops and lunch sponsored by Twist Biosciences and Bionano Genomics. Lunch pick-up in the Ballroom foyer. Return to Ballroom A/B for vendor workshops.

12:10–12:40 pm Raising the Bar in NGS with Twist Biosciences
Tim Farinholt, PhD, Twist Biosciences Field Application Scientist

12:40–1:10 pm Revealing Structural Variations that Matter with Optical Genome Mapping
Diana Marcela Rush, Bionano Genomics Technical Sales Specialist

Hill Country A/B Ballroom

1:15–2:15 pm Afternoon Keynote 3: Jacob Daane, PhD
U. Houston
Déjà vu: exploring 'replicate' radiations of perciform fishes to understand the genetic and developmental origins of key traits and adaptation to extreme environments

2:15–3:00 pm Contributed Papers Session: Genetics of Cell Biology
session moderator: Matthew Crook, PhD, TAMU San Antonio

2:15–2:30 pm Translationally controlled one-carbon metabolic enzymes contribute to cell cycle progression and metabolic output in *S. cerevisiae*
Staci Hammer, Graduate Student,
Texas A&M University

2:30–2:45 pm Haploinsufficiency of cytosolic ribosomal protein RPS-10 confers mitochondrial perturbations
Agustian Surya, Graduate Student,
University of Texas at Austin

2:45–3:00 pm Overactive EGF signaling in *Caenorhabditis elegans* reduces lipid levels by activating downstream Ras and inhibiting SREBP1
Matt Crook, Assistant Professor,
Texas A&M University-San Antonio

Hill Country C/D Ballroom

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

Hill Country A/B Ballroom

4:00–5:15 pm Contributed Papers Session: Evolutionary Genetics and Genomics
session moderator: Heath Blackmon

4:00–4:15 pm Long read based chromosome-level reference genome that encounters complex repetitive sequences in Alpaca (*Vicugna pacos*)
Mayra N. Mendoza Cerna, Graduate Student,
Texas A&M University

4:15–4:30 pm Ultracontinuous genomes elucidate complex speciation patterns within Panthera
Andrew J Harris, Graduate Student,
Texas A&M University

4:30–4:45 pm Re-assessment of Yellowstone National Park bison population subdivision with SNPs and microsatellites
Sam Stroupe, Graduate Student,
Texas A&M University

4:45–5:00 pm Worse than nothing at all: the inequality of sex chromosome to autosome fusions
Kayla Wilhoit, Undergraduate Student,
Texas A&M University

5:00–5:15 pm Characterization of haplotype structure and nucleotide diversity of MHC class II genes In Atlantic herring using long-read sequencing
Minal Jamsandekar, Graduate Student,
Texas A&M University

5:15–6:30 pm Judges Meeting. Judges finalize scoring sheets from Friday sessions.

Hill Country C/D Ballroom

5:30–6:30 pm Visit vendor displays, network, view posters

Hill Country A/B Ballroom

6:30–8:30 pm *Banquet and Service Award Presentation, Acknowledgement of Sponsors

Banquet table topics (12): academic careers at PUIs/LACs (undergrad/liberal arts), academic careers in research, all about graduate school, how to secure a postdoc position, equity in science, first gen. in higher ed/science, tenure-track success, post-tenure paths, industry careers, researching development, *C. elegans*/model system advances, teaching genetics

Barbara Bowman Award distinguished speaker: Nancy Moran, PhD, UT Austin

The Bacterial Gut Symbionts of Bees: from Evolution to Engineering

Social bees, including honey bees and bumble bees, harbor distinctive bacterial communities: a set of about 5 core lineages that have co-evolved with hosts for 80 million years. Largely due to their fastidious growth requirements, these communities were only recognized 15 years ago. Since then, all members have been cultured and genetically manipulated in the laboratory. Hosts can be inoculated with defined communities, making this an ideal system for exploring how host-restricted symbiont lineages affect host biology, by defending against pathogens, degrading toxic or nutritive components of food, and interacting with immune systems. also an ideal system for reconstructing how symbiont lineages have diversified within and between hosts, and how their genomes have evolved. Our investigations show that these bacterial symbionts form recombining species with extensive horizontal gene transfer. Symbiont speciation sometimes tracks that of hosts and sometimes occurs within a host species, through isolation linked to different ecological and spatial niches within the gut. Finally, by manipulating genomes of these symbionts, we can use them to trigger targeted RNAi responses in the host, which can serve as a tool for elucidating functions of host genes or for thwarting RNA viruses of bees.

8:30–10:00 pm TGS members are free to retire to the Holiday Inn bar or head home. Posters may be taken down.

Saturday, March 25th

Hill Country A/B Ballroom

7:30–8:20 am *Breakfast, networking, informal poster viewing

8:20–8:30 am Session introduction
Heath Blackmon, 2023–2024 TGS President

8:30–9:30 am Morning Keynote 4: Natasha Kirienko, PhD
Rice University
Mitochondrial surveillance in health and disease

9:30–10:10 am Contributed Papers: Genetics in Development and Disease
session moderator: Theodora Koromila, PhD, UT Arlington

9:30–9:40 am Changes in mitochondrial respiratory chain super complexes across functional mammary gland development
Ramsey Jenschke, Graduate Student,
Texas A&M University

9:45–10:00 am RNAi pathways prevent mis-regulation of the spermatogenesis developmental program during stress in *C. elegans*
Alicia K. Rogers, Assistant Professor,
University of Texas at Arlington

10:00–10:10 am Regulation of an effector triggered immune response in *C. elegans* against the mitis group streptococci
Anastasiia Ahmedaly, Technician,
The University of Texas HSC at Houston

Hill Country Foyer

10:15–10:30 am *Coffee Break, vendor exhibit breakdown

Hill Country A/B Ballroom

10:35–11:30 am Contributed Papers: Gene Regulation and Genomics
session moderator: Elif Sarinay Cenik, PhD, UT Austin

10:35–10:50 am Alternative-splicing regulators and functional relevance of microexons
Bikash C Choudhary, Postdoc,
Southern Methodist University

10:50–11:00 am Epidermal ribosome synthesis inhibition induces a nutrition-uncoupled organism-wide growth quiescence in *C. elegans*
Qiuxia Zhao, Postdoc,
University of Texas at Austin

11:05–11:20 am	Sensory neuron transcriptomes reveal complex neuron-specific function and regulation of *mec-2*/Stomatin splicing Canyon Calovich-Benne, Graduate Student, Southern Methodist University
11:30-12:00 pm	Panel Question and Answer with keynote speakers
11:30–12:00 pm	Judges finalize scoring sheets from Saturday sessions
12:00–1:00 pm	TGS business meeting and awards presentations
1:00 pm	Meeting adjourned

All poster sessions will be in the Hill Country C/D Ballroom. Posters presented by undergraduates are in Session #1. All other posters are in Session #2.

Poster session #1: Hill Country C/D Ballroom, Friday March 24, 10:00–11:00 am

P1 The mutation analysis of RGD (Arg-Gly-Asp) cell-binding motif in the basement membrane proteins of *Caenorhabditis elegans*
Jeancarlo Gutierrez, Jonathan Yeow, Undergraduate Student, Baylor University

P3 DEB-1/Vinculin proline-rich-linker (PRL) plays important roles in touch sensitivity and egg-laying of *Caenorhabditis elegans*
Lianzijun Wang, Undergraduate Student, Baylor University

P5 Investigating the role of Hsp90 in mutation accumulation in yeast
Morike Ayodeji, Undergraduate Student, The University of Texas MD Anderson Cancer Center

P7 Quantitative assessment of HSP90-stress-induced genome instability
Zoe Wang, Undergraduate Student, The University of Texas MD Anderson Cancer Center

P9 Examining trehalose accumulation in the *Saccharomyces cerevisiae* pgm2Δ mutant
Lara Shehadeh and Micaiah Wetzold, Undergraduate Students, Austin College

P11 Exploring sexual antagonism as a driver of sex chromosome – autosome fusions in mammals using stochastic mapping techniques
Max Chin, Undergraduate Student, Texas A&M University

P13 A characterization of mutating the NID-1 protein on the behavior of *C. elegans*
Garrick Owen, Undergraduate Student, Baylor University

P15 Characterizing the substrate target of BRCA1/BARD1 in *C. elegans*
Caitlin Lightle, Undergraduate Student, Texas Christian University

P17 Characterization of DUF4585 genes in zebrafish
Phoebe Nguyen and Jessilyn Tran, Undergraduate Student, Austin College

P19 Glyphosate's effects on the development of zebrafish (*Danio rerio*)
Cody Dean, Undergraduate Student, Austin College

P21 Identifying the role of SOX9 in neural crest EMT
Hannah Herron, Undergraduate Student, Austin College

P23 The effects of mutation in *mec-9* Kunitz domains on mechanosensation in *C. elegans*
Hunter Hennig, Undergraduate Student, Baylor University

P25 Investigating the effects of the HOG and CWI MAPK cascades on growth defects observed in the *Saccharomyces cerevisiae pgm2Δ* mutant
Wenqi Ding, Undergraduate Student, Austin College

P27 Modelling the *Caenorhabditis elegan*s gonad over developmental time using the Distal Tip Cell marker *lag-2p::gfp*
Elaine Tennyson, Undergraduate Student, Texas A&M University

P29 Possible roles of the proprotein convertase KPC-1/Furin and transcription factor EOR-1/PLZF in Compartmentalized Cell Elimination
Nathan Rather, Undergraduate Student, The University of Texas at Arlington

P31 Project Gen: Looking at cognitive function and memory
Shubhi Nanda, Undergraduate Student, University of Texas at Austin

P33 Exploring the diversity of soil microbiota in cadaver decay islands (CDI) located in central Texas
Katherine E. McBroom, Undergraduate Student, Austin College

P35 Yeast p24 family proteins and CSG2 in relation to *pgm2*Δ phenotypic defects in the secretory pathway
Shruti Veera Raghavan, Undergraduate Student, Austin College

P37 The role of RNA polymerase I in lifespan extension of *Caenorhabditis elegans*
Amanda Leonita, Undergraduate Student, University of Texas at Austin

P38 The membrane distal NPxY motif in β integrin cytoplasmic domain plays an important role in reproductive behavior
Arlyn Alcid, Undergraduate Student, Department of Biology, Baylor University

Poster session #2: Hill Country C/D Ballroom, Friday March 24, 3:00–4:00 pm

P2 Subtle sex-differences in learning for Nadk-knockout 5XFAD Alzheimer's Disease model mice
Sohum S. Purao, Graduate Student, Texas A&M University

P4 Small effective population size drives chromosome number evolution in carnivores
Michelle Jonika, Graduate Student, Texas A&M University

P6 Development of an inducible nano-luciferase spore tagging system for tracing the biodistribution of *Clostridioides difficile* spores in the GI tract during infection
Osiris K. Lopez-Garcia, Graduate Student, Texas A&M University

P8 Communication is key: Singleminded2s maintains the integrity of mitochondria associated membranes for proper differentiation
Lilia Sanchez, Graduate Student, Texas A&M University

P10 Wright was right: Over one thousand datasets support the critical role of epistasis in genetics and evolution
Jorja Elliott, Graduate Student, Texas A&M University

P12 The membrane distal NPxY in β integrin cytoplasmic domain plays an essential role in reproductive behavior
Josh Bumm, Graduate Student, Baylor University

P14 Impact of mitochondrial homeostasis on the immune response during mammary epithelial cell differentiation
Ramiah Vickers, Graduate Student, Texas A&M University

P16 Activation of CREB signaling controls a feedback loop required for the homeostasis of connective tissues of the spine
Valeria Aceves, Graduate Student, University of Texas at Austin Dell Medical School

P18 Fitness relationship between genome fragmentation and environmental stability
Andres Barboza Pereira, Graduate Student, Texas A&M University

P20 The tissue-specific role of SMN-1 in *C. elegans*
Anusha Iyengar, Graduate Student, Southern Methodist University

P22 Elucidating the evolution of the recombinational landscape of placental mammals using comparative genomics
Isabella R. Childers, Graduate Student, Texas A&M University

P24 Odd Pair (Opa) and Ocelliless (Oc) dynamics in Drosophila brain development
Shiva Abbasi, Graduate Student, University of Texas at Arlington

P26 The evolution of chromosome number and sex chromosome system in Odonata
Matthew Marano, Graduate Student, Texas A&M University

P28 Comparative genomics of *C. rectus*, an “emerging *Campylobacter* species”
Casey Hughes Lago, Graduate Student, Texas A&M University

P30 Utilizing a F2 population to investigate the genetic regulation of diet-induced thermogenesis in mice exposed to a ketogenic diet
Alexandra Naron, Graduate Student, Texas A&M University

P32 Using CRISPR Cas9 to investigate the role of an evolutionary conserved SNORD115 cluster in the regulation and expression of the paternally imprinted gene UBE3A
Alasdair J Taylor, Graduate Student, Texas A&M University

P34 Studying dysregulated gene expression in the frontal cortex of a pig model of Angelman syndrome using single-cell RNA sequencing
Ashley Coffell, Graduate Student, Texas A&M University

P36 Antisense oligonucleotide quantification via splint-ligation and PCR
Thomas Jepp, Graduate Student, Texas A&M University

P40 Transgenerational effects of a small RNA mediated feedback loop on the homeostasis of 22G-RNAs levels in *C. elegans*
Ha Meem, Graduate Student, University of Texas at Arlington

P42 Elucidating the mechanism of MUT-16-dependent regulation that fine tunes the ALG-3/4 pathway to maintain proper spermatogenesis in *C. elegans*
Triltoma Sen, Graduate Student, University of Texas at Arlington

P44 Mitochondrial transport, endoplasmic reticulum shape, and mitochondria-endoplasmic reticulum contacts regulate Compartmentalized Cell Elimination
Aladin Elkhalil, Graduate Student, University of Texas at Arlington

P46 Developing genetic biocontrol tools for suppression of invasive rodents
Ana Velasquez, Graduate Student, Texas A&M University

P47 A Novel PPARy-B-Catenin Signaling in Placenta Development, Regarding Preeclampsia
Yushu Qin, Graduate Student, Texas A&M University

P48 Winning Against Unbalanced Datasets In A Machine Learning De Novo Genes Prediction Algorithm In Angiosperms
Adekola Owoyemi, Graduate Student, Texas A&M University

P49 Identifying candidate genetic mechanisms and modifier genes underlying genetic context-dependent colorectal cancer progression in the absence of ERBB3
Kaitlyn Carter, Graduate Student, Texas A&M University

P39 In vivo genetic analysis of schizophrenia through a novel developmental cell death paradigm
Hannah Selvarathinam, Technician, The University of Texas at Arlington

P41 ER network stability promotes organized microtubule disassembly during Compartmentalized Cell Elimination
Karen Juanez, Technician, The University of Texas at Arlington

P43 The co-evolution of phylogenomic signal, gene linkage, and recombination rate in placental mammals
Nicole Foley, Postdoc, Texas A&M University

P45 Characterizing the genetic and physical interaction of the DBL-1/BMP signaling pathway with BLMP-1/BLIMP1 transcription regulator in *Caenorhabditis elegans*
Tina L. Gumienny, Faculty, Texas Woman's University

Platform Abstracts

in order of presentation

Creation and optimization of a novel bioluminescent reporter tag for *C. elegans*

Liam Schuck

University of Texas at Austin, Dr. Ryan Doonan, mentor

Fluorescent protein tagging is a powerful research tool that allows for the visualization of protein localization, expression, and function. That said, there are two pervasive issues with fluorescent imaging: 1) it requires expensive fluorescent microscopes, and 2) fluorescent light causes photobleaching of fluorophores over time, making the fluorescence of the protein disappear. I have designed a different type of protein tag derived from *Neonothopanus nambi* for use in *Caenorhabditis elegans* that would alleviate both of these issues.

Bioluminescence is the ability for an organism to produce light via the enzymatic reaction between a luciferin and a luciferase. While bioluminescent reporter systems have been designed before, they require an external substrate supply or are toxic to Eukaryotic life. Recently, the entire bioluminescence-producing pathway of *N. nambi* was elucidated. This enables the luciferin to be synthesized in vivo, unlike other luciferins. By fusing a modified luciferase gene of *N. nambi* to the N-terminal or C-terminal of a protein via Cas-9 and inserting the necessary genes for the synthesis of the luciferin substrate into the background of *C. elegans*, the luciferase tag should function similarly to fluorescent proteins without requiring a fluoroscope or any substrate input. This will create a low-cost and user-friendly protein tag that can be seen with both the naked eye and under simple compound microscopes.

Many modifications will be made to the proteins in the luciferase pathway to optimize for protein tagging. First, the majority of the substrate's biosynthetic pathway will be added to a plasmid (plasmid 1) via Gibson assembly. The proteins will either be fused to promote substrate shuttling or separated via 2a viral peptides. This plasmid will have the genes driven by a ubiquitously expressed promoter. This plasmid will then be injected into the *C. elegans* gonad. The resulting luminesce of the worms will be measured using a plate reader.

The H3H::Luz fusion will be iteratively truncated by the ITCHY protocol established by Patrick and Gerth (2014) and transformed into HT115 E. coli cells and treated with hispidin. The resulting colonies' luminescence will be measured with the plate reader and the colonies with the highest luminescence will be selected. This will reduce the size of the eventual protein tag encoding H3H and Luz, reducing steric hindrance on the tagged protein. The smallest and most functional gene sequence will be added to plasmid 1 and then will be amplified via error-prone PCR to induce random mutations. The mutagenized plasmids will be inserted into the *C. elegans* gonad and screened for highest luminescence.

Once all components are optimized, H3H::Luz will be fused to the C-terminal of *C. elegans* His-72 via Cas-9 insertion. The remaining genes in plasmid 1 will be inserted into a mosSCI site, allowing for the worms to luminesce on any medium. Multiple genes will then be tagged and compared to their fluorescent protein tagged version.

Liam Schuck

liamschuck@gmail.com

Undergraduate Student

Evaluating Authenticity and Visualization of *C. elegans* TAU with a Split Fluorophore

Gillian Witten, Ella Demott, Carrie Meng, and Ryan Doonan

Glow Worms Stream, Freshman Research Initiative, College of Natural Sciences, The University of Texas at Austin, Austin TX, USA; Department of Neuroscience, The University of Texas at Austin, Austin TX, USA ; Department of Molecular Biosciences, The University of Texas at Austin, Austin TX, USA

Alzheimer's disease is characterized by the hyperphosphorylation of the microtubule-associated protein Tau, resulting in the accumulation of insoluble neurofibrillary tangles that inhibit the transport of nutrients throughout the neuron, resulting in cell death. As such, it is of high interest to evaluate the microbiological mechanisms of this neurodegenerative process. Fluorescent tagging allows for the visualizations of protein expression in vivo. Multi-copy transgene arrays have been used in *C. elegans* to tag proteins but can cause abnormal expression. While CRISPR knock-ins of fluorescent tags at endogenous loci bypass this challenge, it has its limitations. For one, large proteins may still interfere with expression due to disruption at the site of chaperone proteins. This is especially a challenge for low molecular weight proteins that are a fraction of the size of a full-length fluorescent protein tag. Secondly, fluorescent transgenes may prove challenging to knock in. To address these two problems, split fluorophores may be used. These are fragments of a fluorescent protein that alone are not fluorescent, but rather fluoresce once they assemble in vivo. The smaller fragment serves as a "tiny tag" for the protein of interest, whereas the larger fragment is expressed separately. Importantly, because the protein only fluoresces in the subset of cells or tissues with both fragments, it becomes easy to visualize the subcellular expression of even ubiquitous protein in a combinatorial manner. We used this approach with a *C. elegans* optimized version of split fluorophore mScarlet, wrmScarlet, to study the expression of *C. elegans* ortholog of human TAU, known as protein tau-like 1 (PTL-1). The *ptl-1* gene encodes 6 isoforms of PTL-1. Based on unique gene structures, we were able to tiny tag PTL-1 in the following different ways: (1) isoform a only, (2) the N-terminus of isoforms a, b, and c, and (3) the C-terminus of all isoforms. Mutations in *ptl-1* can result in defects in touch sensation in certain genetic backgrounds due to abnormal microtubules in touch-sensitive neurons. To assess whether tiny tags affect PTL-1 function, we assayed anterior and posterior gentle touch. Touch sensation was indistinguishable between wild type and tagged worms, indicating that our PTL-1 tags demonstrate authentic expression, and interestingly, that there is either always some tagged TAU unbound, or that the assembly of the fluorescent composite structure is reversible. Despite verifying the authenticity of TAU's expression, we have so far been unable to visualize expression in the worms with the ubiquitous tag. This suggests that split fluorophore tags may not be effective endogenous reporters for low molecular weight proteins such as tau.

Gillian Witten

witteng1@utexas.edu

Undergraduate Student

Heterozygosity for HOGA1 variants is associated with an increased risk for kidney stones

Sohum Purao, Alexander Chang, Natasha Strande, Sarah H. Elsea

Texas A&M School of Medicine, Bryan, TX 77807 , Dept. of Nephrology, Geisinger Medical Center, Danville, PA 17822 , Dept. of Nephrology, Geisinger Medical Center, Danville, PA 17822, Dept. of Molecular & Human Genetics, Baylor College of Medicine, Houston, TX 77030

Primary hyperoxaluria (PH) is a rare autosomal recessive hereditary disorder of glyoxylate metabolism that is characterized by excessive endogenous oxalate production due to impaired oxalate catabolism. Excess oxalate is excreted through the kidneys and over time, typically results in nephrolithiasis, including calcium oxalate renal stone formation. Insufficient activity of any one of three primary enzymes involved in glyoxylate metabolism (AGT [PH1], GRHPR [PH2], or HOGA [PH3]) can result in similar clinical outcomes. PH3 is associated with bi-allelic variants in HOGA1, coding for 4-hydroxy-2-oxoglutarate aldolase. Pathogenic variants in HOGA1 cause abnormal urine oxalate levels, nephrolithiasis, and even end-stage renal disease. However, both the genetic and clinical heterogeneity of PH3 greatly contribute to the difficulties in diagnosis and further understanding this disease. Additionally, although the recessive form has been well-documented to lead to the many effects highlighted above, risk for kidney stone formation and kidney disease in individuals heterozygous for HOGA1 pathogenic variants has not been described. In this study, pathogenic and likely pathogenic variants in HOGA1 were curated from the literature, and variant prevalence assessed using the Genome Aggregation Database (gnomAD) to determine allelic frequencies across ethnic populations and estimate disease prevalence. Stringent ACMG pathogenicity guidelines were used to curate 72 reported disease-associated HOGA1 variants. Disease prevalence was estimated at ~1/70,000, or approximately 4,600 individuals in the U.S. of any age with potential to develop PH3. The heterozygous carrier frequency was estimated at ~1/130 individuals or approximately 2.4 million individuals nation-wide, with higher carrier frequencies observed in East Asian and Ashkenazi Jewish populations. Furthermore, while previous studies have shown intermittent levels of urine oxalate in some heterozygous individuals, few studies have broadly assessed the impact of carrier status in healthcare populations. Using exome sequencing and electronic health record data from the Geisinger MyCode DiscovEHR study, we investigated prevalence and phenotypic spectrum of kidney disease for pathogenic HOGA1 variants. Analysis revealed higher risk of nephrolithiasis in patients heterozygous for a P/LP HOGA1 variant compared to controls (7.9% vs. 5.8%), compared to patients without variants in PH-associated genes. In terms of the most common P/LP variants, c.700+5C>T (70/844; 8.3%; p=0.002), p.Glu315del (8/79; 10.1%;p=0.1), p.Ala36val (6/45; 13.3%; p=0.03), p.Pro190Leu (7/41; 17.1%; p=0.002), c.944_946del (8/79; 10.1%; p=0.1) all were associated with increased risk of nephrolithiasis. While no associations with glomerular filtration rate or end-stage renal disease were identified in HOGA1 carriers in this population, kidney stones pose a significant burden on quality of life. This preliminary analysis showed association between three heterozygous HOGA1 variants and a common characteristic of PH3; however, there is a strong likelihood that other pathogenic/likely pathogenic variants cause similar conditions. The adult-onset of nephrolithiasis in heterozygotes also supports the need for additional studies in healthcare populations to determine other associated factors leading to clinical presentation in carriers. Our analyses show that while the recessive form of PH3 is rare, it is likely underdiagnosed, and heterozygous individuals for pathogenic variants in HOGA1 may also show mild to severe phenotypic changes observed in PH3, which may be preventable through early identification and intervention.

Sohum S. Purao

sohumpurao@tamu.edu

Graduate Student

Singleminded 2/Semaphorin 7a regulation of a PI3K subunit switch in ER+ breast cancer progression

Hannah Carter, Garhett Wyatt, Rachel Steinmetz, Lyndsey Crump, Traci Lyons, and Weston Porter

Texas A&M University, Texas A&M University, University of Colorado Anschutz Medical Campus, University of Colorado Anschutz Medical Campus, University of Colorado Anschutz Medical Campus, Texas A&M University

Estrogen receptor positive (ER+) breast cancers (BC) comprise over 70% of breast cancers and are treated with a variety of targeted therapies. Despite this, most breast cancer-related deaths are attributed to recurrent ER+ breast cancer. Thus, there is an unmet need to identify novel targets for treating ER+ patients with metastasis. We have identified a tumor suppressor, Singleminded 2s (SIM2s), expressed in mammary epithelial cells that inhibits EMT and metastasis, and is downregulated in the progression of breast disease. Our previous studies found that loss of SIM2s expression results in downregulation of ESR1 and increased basal markers in the MCF7 (ER+ BC) cell line. Concurrent studies in the Lyons Lab at the University of Colorado identified a similar phenotype and expression with overexpression of Semaphorin 7a (SEMA7A) in the MCF7 cell line. Preliminary studies showed that overexpression of SEMA7A promotes resistance to ER and CDK4/6 targeted therapies. Further investigation of these phenotypical similarities shows a reciprocal relationship between SIM2 and SEMA7A at the protein and message level. Our preliminary data shows that loss of SIM2 confers an upregulation of SEMA7A, AKT signaling, EMT signatures and decreased ESR1, CDH1, and PTEN protein and mRNA expression. Moreover, we have found that loss of SIM2s and gain of SEMA7A leads to a PI3K subunit switch resulting in down-regulation of PIK3CA (p110α) at the protein level and up-regulation of PIK3CD (p100δ) gene expression. Our study suggests a SIM2s/SEMA7A switch which may confer therapeutic resistance in ER+ BC via upregulation of PIK3CD. Thus, a SIM2s/SEMA7A switch may act as a prognostic indicator to provide therapeutic advantages in resistant ER+ BC metastasis.

Hannah Carter

hcarter12@tamu.edu

Graduate Student

Altered neonatal development, reduced vocalizations, impaired brain growth, motor incoordination and abnormal EEG in a pig model of Angelman syndrome

Luke Myers1, Sarah G. Christian1, Sean Simpson2, Renan Sper2, Clint Taylor1, Annalise Schlafer1, Laura Montes1, Hillary Shaheen1, Ruth Robinson1,3, Bradley Revell1,3, Carol Knight1,3, Cristina Cordona1,3, Livia Schuler1, Thomas Jepp1,3, Daniela Ramos1, Desiree Slaughter1, Aubrey Rinderknecht1, Alasdair Taylor1,3, Charlie Collins1,3, Joseph Ready1,3, Kranti Konganti4, Jay Griffin5, Wade Friedeck5, Heather Born6, Chelsea Richardson7, Vidya Sridhar8, FIRE consortium#, William J. Murphy9, Jorge Piedrahita2, and Scott V. Dindot*1#

1. Department of Veterinary Pathobiology, College of Veterinary Medicine & Biomedical Sciences, Texas A&M University, College Station, TX, USA 2. Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC, USA 3. School of Biosciences and Medicine, University of Surrey, Guildford, UK 4. Texas A&M University Institute for Genome Sciences and Society, Texas A&M University, College Station, TX, USA 5. Veterinary Medical Teaching Hospital, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843, USA 6. Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA 7. emka Technologies Inc, Sterling, VA 20166, USA 8. Translational Imaging Center, Texas Institute for Preclinical Sciences, Texas A&M University, College Station, TX 77843, USA 9. Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA

#FIRE Consortium Members
Edwin Weeber - Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, USA; David Segal - MIND Institute, Genome Center, and Department of Biochemistry and Molecular; Medicine, University of California Davis, Davis, CA, USA
Anne Anderson - Department of Pediatrics and Neurology, Baylor College of Medicine, Houston, TX, USA; Kevin Nash - Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, USA; Jill Silverman - MIND Institute and Department of Psychiatry and Behavioral Sciences; University of California Davis School of Medicine, Sacramento, CA

Angelman syndrome is a severe neurodevelopmental disorder characterized by hypotonia, failure to thrive, developmental delay, intellectual disability, absent speech, motor incoordination, and epilepsy. It is caused by the loss of the maternally inherited allele of the imprinted ubiquitin-protein ligase E3A (UBE3A) gene. Rodent models of Angelman syndrome do not fully recapitulate all the symptoms associated with the condition, and there are limitations in performing studies on rodents, particularly newborn animals. Here, we developed a large animal model (pig, Sus scrofa) of Angelman syndrome using the CRISPR/Cas9 and cloning technologies. Our results show that pigs with a maternally derived deletion of UBE3A have altered neonatal development, reduced vocalizations, impaired brain growth, motor incoordination, ataxia, and abnormal electroencephalogram activity. Many of these phenotypes manifested in newborns and persisted throughout development. We anticipate that this pig model will advance our understanding of the pathophysiology of Angelman syndrome and be used as a preclinical large animal model for testing promising therapeutics.

Luke Samuel Myers

lukemyers@tamu.edu

Graduate Student

Missense variants in pericellular matrix components increase risk of adolescent idiopathic scoliosis

Anas M. Khanshour, Hao Yu, Aki Ushiki, Xiao-Yan Li, Nao Otomo, Yoshinao Koike, Elisabet Einarsdottir, Yanhui Fan, Lilian Antunes, Yared H. Kidane, Reuel Cornelia, Rory Sheng, Yichi Zhang, Jimin Pei, Nick V. Grishin, Bret M. Evers, Jason Pui Yin Cheung, John A. Herring, Chikashi Terao, You-Qiang Song, Christina A. Gurnett, Paul Gerdhem, Shiro Ikegawa, Jonathan J. Rios, Stephen J. Weiss, Nadav Ahituv, Carol A. Wise

Center for Pediatric Bone Biology and Translational Research Scottish Rite for Children Dallas TX USA; Department of Integrative Biomedical Sciences College of Veterinary Medicine Texas A&M University College Station TX USA; Department of Bioengineering and Therapeutic Sciences University of California San Francisco San Francisco CA USA; Institute for Human Genetics University of California San Francisco San Francisco CA USA; Division of Molecular Medicine and Genetics Department of Internal Medicine University of Michigan Ann Arbor MI USA; Life Sciences Institute University of Michigan Ann Arbor MI USA; Laboratory of Bone and Joint Diseases RIKEN Center for Integrative Medical Sciences Tokyo JP; Laboratory for Statistical and Translational Genetics RIKEN Center for Integrative Medical Sciences Yokohama JP; Science for Life Laboratory Department of Gene Technology KTH-Royal Institute of Technology Solna SE; School of Biomedical Sciences The University of Hong Kong Hong Kong SAR CN, Department of Neurology Washington University in St. Louis St. Louis MO USA; School of Pharmaceutical Sciences Tsinghua University Beijing CN; Department of Biophysics, University of Texas Southwestern Medical Center Dallas TX USA; Technology (CLINTEC) Karolinska Institutet Stockholm Uppsala University Uppsala SE; Department of Surgical Sciences Uppsala University & Department of Orthopaedics and Hand Surgery Uppsala University Hospital Uppsala SE; Eugene McDermott Center for Human Growth and Development University of Texas Southwestern Medical Center Dallas TX USA; Therapeutic Sciences University of California San Francisco San Francisco CA USA; Department of Orthopaedic Surgery University of Texas Southwestern Medical Center Dallas TX, USA; Eugene McDermott Center for Human Growth and Development University of Texas Southwestern Medical Center Dallas TX USA; Department of Pediatrics University of Texas Southwestern Medical Center Dallas TX USA

Adolescent idiopathic scoliosis (AIS) is a common and progressive spinal deformity that exhibits significant sexual dimorphism, with females having at least a five-fold greater risk of disease progression compared to males. Despite its medical significance, insights into the pathogenesis of AIS are just emerging. Prior population-based genetic association studies in multiple ancestral groups identified significant associations that implicate genes involved in cartilage and connective tissue development. Additional genetic studies in families and functional experiments using vertebrate model systems have highlighted components of the extracellular matrix (ECM), the so-called “matrisome”. We hypothesized that alterations in components of the ECM disrupt proper spinal alignment and contribute to AIS. Here to identify novel functional AIS risk loci, we tested the association of common protein-altering variants (MAF > 0.01) in ECM genes in a discovery cohort of 1,358 AIS cases and 12,507 controls, followed by meta-analysis of significant associations in additional cohorts from USA, Sweden-Denmark, Japan, and Hong Kong (total N=103,757 individuals). We identified significant associations with variants in two pericellular matrix genes, MMP14 (rs1042704 p.(Asp273Asn); OR=1.210 [95% CI=1.134-1.291], P=7.61E-9) and COL11A1 (rs3753841p.(Pro1335Leu); odds ratio (OR)=1.118 [95% CI=1.081-1.156], P=7.07E-11). By analysis of MT1-MMP+/lacz and MT1-MMPlacz/lacz mice, we show that Mmp14 is expressed in periosteum and developing vertebrae of mouse spine, whereas collagen XI alpha chain protein (a1(XI)), encoded by Col11a1, is abundant in mouse vertebral growth plates and intervertebral disc (IVD). In vitro, collagen-degrading activity of the AIS-associated MMP14 p.(Asp273Asn) variant protein is significantly reduced compared to the non-risk variant. Using siRNA-mediated knockdown experiments in cultured cartilage cells, we further find evidence of an Esr2-Col11a1-Mmp3 signaling axis. These studies support a new model wherein molecular variation in genes required for the development and maintenance of the pericellular matrix can increase AIS susceptibility.

Anas M. Khanshour

anas.khanshour@tsrh.org

Senior Scientist

Translationally controlled one-carbon metabolic enzymes contribute to cell cycle progression and metabolic output in *S. cerevisiae*

Staci Hammer and Michael Polymenis

Texas A&M University

One carbon (1C) metabolism encompasses the biosynthetic pathways generating precursor molecules for amino acid, lipid, and nucleotide synthesis. Ribosome profiling in budding yeast *S. cerevisiae* previously suggested some 1C enzymes are translationally controlled during the cell cycle. However, their protein levels and impact on cell cycle progression remained unknown. Using actively growing, synchronous yeast cell cultures, we identified two enzymes that dramatically change abundance after G1 phase: Ade17p (15-fold change) and Cho2p (4-fold change). Ade17p operates in the de novo purine synthesis pathway while Cho2p catalyzes the last methylation step in phosphatidylcholine (PC) synthesis. Individual knockout strains of these enzymes provided insight into their roles in cell cycle progression. Loss of Ade17p resulted in delayed budding (representing START), without lowering the overall growth rate, suggesting a specific role at that cell cycle transition. PC can be formed from the de novo or salvage pathways, utilizing Cho2p or choline respectively. Thus, we looked at loss of Cho2p in the presence and absence of exogenous choline to extrapolate the effects of each pathway. Regardless of choline addition, loss of Cho2p also resulted in START delay but unlike Ade17p, was accompanied by a slow growth rate. These results highlight the importance of the de novo PC synthesis pathway in cell cycle progression. Overall, our results provide new information of the effects of translationally controlled enzymes on the cell cycle and resulting changes to the metabolome. The next step is to understand how these enzymes are translationally controlled by identifying the elements acting at their respective mRNAs.

Staci Hammer

sehammer@tamu.edu

Graduate Student

Haploinsufficiency of cytosolic ribosomal protein RPS-10 confers mitochondrial perturbations

Agustian Surya and Elif Sarinay Cenik

Department of Molecular Biosciences, University of Texas Austin, Austin, TX, USA

Germline single loss of function mutations in ribosomal protein genes lead to ribosomopathy disorders, the most common being Diamond Blackfan Anemia (DBA). To understand the cellular and organismal consequences of deviations in translational machinery, we have generated *Caenorhabiditis elegans* strains with heterozygous loss of function mutations within different ribosomal protein (RP) genes (*rpl-5*, *rpl-33*, *rps-23*, and *rps-10*), 3 of which are associated with DBA. We find that these heterozygous mutants display delayed postembryonic development and increased oxidative stress resistance in a Nrf2 (*skn-1*) dependent fashion. Among these mutants, we found that *rps-10* haploinsufficient animals interestingly show unique defects in their overall energy levels, with significantly elevated ADP/ATP ratios. We tested the hypothesis of whether the mitochondrial activity is compromised in *rps-10* single copy loss of function mutants as the main source of cellular ATP is produced by mitochondrial respiration. We found that indeed *rps-10* heterozygous mutants displayed reduced mitochondrial activity, which can be rescued back by reverting the loss of function copy back to wild-type. Consistently, RNAi knockdown of rps-10 specifically reduces oxygen consumption in contrast to the knockdown of other ribosomal protein genes tested. In contrast, general mitochondria abundance is measured by the intensity of fluorescent-tagged inner membrane protein COX-4 and outer membrane protein TOMM-20, which levels are not suppressed. Taken together, mutation or knockdown of *rps-10* negatively impacts mitochondrial activity. Interestingly, the Pearson syndrome, caused by mitochondrial DNA deletions, manifests the same hematological defects and can be misdiagnosed as DBA. Thus, downstream molecular mechanism investigation of the heterozygous *rps-10* loss of function animals could give us significant insight into understanding tissue-specific downstream effects of human ribosomopathy disorders.

Agustian Surya

agustian_surya@utexas.edu

Graduate Student

Overactive EGF signaling in *Caenorhabditis elegans* reduces lipid levels by activating downstream Ras and inhibiting SREBP1

Lizzi Wong, Allison Bogasich, Elaine Tennyson, Zaynab Garbe, Michael Landez, William Benedict, Brenda Zarazua, and Matt Crook

Texas A&M University-San Antonio

Epidermal growth factor (EGF) signaling controls multiple processes in the nematode *Caenorhabditis elegans*, including vulval and excretory system development, quiescence and cell survival. We found that animals with a gain-of-function mutation in the EGF receptor, *let-23*, are also visibly paler than wild type animals. Using quick Oil Red O (qORO) staining, we found that *let-23gf* animals have ~10% less total lipids than wild-type, but reduced *let-23* signaling had no effect. LET-23 signals through two known pathways, the Ras-MAPK signaling cascade and the IP3/ *itr-1* pathway. We found that overactivation of Ras (*let-60*) decreased lipid staining to *let-23gf* levels, but lipid levels in *itr-1* overactivation animals were similar to wild type. Similarly reducing Ras signaling in a let-23gf background partially restored lipid levels to wild-type.

A key player in lipid homeostasis is SREBP1/ *sbp-1*, a transcription factor that is retained in the cytoplasm until activated. To investigate the effect of EGF signaling on SBP-1 activity we used a *sbp-1p::sbp-1::gfp* reporter to measure the ratio between active nuclear SBP-1 and inactive cytoplasmic SBP-1. We found that the SBP-1 nuclear:cytoplasmic ratio was lower in *let-23gf* and *let-60gf* animals relative to wild-type and *itr-1gf* animals, suggesting that EGF signaling via Ras suppresses SBP-1 activity and therefore lipid synthesis.

Given the role of SBP-1 as a lipid synthesis transcription factor, we hypothesised that lipid synthesis genes would be downregulated in *let-23gf* animals. To test our hypothesis we used RNAseq to compare the transcriptomes of wild type, *let-23gf* and *sbp-1rf* animals. Instead of a decrease in lipid synthesis gene expression in our two mutants we found a coordinated upregulation in the expression of genes involved in bacterial defense and innate immunity. We subsequently confirmed our top five upregulated genes by qPCR, not only in *let-23gf* and *sbp-1rf*, but also in *let-60gf*. These data suggest an updated model, where overactive EGF signaling promotes an increase in the innate immune response by inhibiting SBP-1, and that the metabolic demands of this increased immune response are responsible for the decrease in lipid levels seen. Future work will involve characterization of the role of the five upregulated genes in both the altered lipids levels of *let-23gf* mutants and the activation of the innate immune response in *C. elegans*.

Matt Crook

matthew.crook@tamusa.edu

Faculty

Long read based chromosome-level reference genome that encounters complex repetitive sequences in Alpaca (*Vicugna pacos*)

Mayra N. Mendoza, Kylie Munyard, Terje Raudsepp, Brian W. Davis

Department of Veterinary Integrative Biosciences, School of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA; Faculty of Health Sciences, Curtin Medical School, Curtin University, Perth, Australia; Department of Veterinary Integrative Biosciences, School of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA; Department of Veterinary Integrative Biosciences, School of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA/Department of Small Animal Clinical Sciences, School of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA

A reference genome is the most essential asset to contemporary genetics research and necessary to study the health and structure of populations, evolution, morphological variation, and heritable disease. It is also the reference to determine sequence-based genomic, epigenomic, and transcriptomic variation and identify variation associated with phenotypes and disease. As such, the utility of fragmented reference genomes containing non-chromosomally assigned contigs or scaffolds are limited. Here we combined PacBio long-read and high-fidelity circular consensus sequencing, Hi-C chromatin conformation capture, optical genome mapping (OGM), and manual curation to generate a chromosome-level alpaca reference VicPac4. Assignment of sequence scaffolds and super-scaffolds was supported by the alpaca cytogenetic map and the recently available alpaca 76K SNP chip data. The current assembly is 2,572 Mb, with 1200 contigs (N50 = 40.28 Mb) and 783 scaffolds (N50 = 67.53 Mb). Of the initial 790 scaffolds retrieved from OGM, 44 were manually assigned into 37 scaffolds that represent 36 autosomes pairs and the X chromosome, with lengths from 6.7 to 127.7 Mb; 746 scaffolds with a median size of 579 kb remained unassigned. We also corrected several chromosomal mis-assignments in the previous alpaca reference VicPac3.1 and evaluated the utility of the 76K SNP chip in the context of our highly accurate assembly. Likewise, we were able to locate complex repetitive sequences, such as telomeric TTAGGG repeats in the ends of at least 36 chromosome arms. Furthermore, the conserved sequences of 18S-5.8S-28S rDNA, also known as Nucleolar Organizer Regions (NOR), were found in several unassigned scaffolds, facilitating their assignment to the respective NOR chromosomes. The improved chromosome-level alpaca reference VicPac4 has considerably enhanced accuracy and contiguity and will be the basis for the first population-level alpaca genome variant database.

Mayra N. Mendoza Cerna

mmendoza@tamu.edu

Graduate Student

Ultracontinuous genomes elucidate complex speciation patterns within Panthera

Andrew J. Harris, Brian W. Davis, Klaus-Peter Koepfli, Eduardo Eizirik, and William J. Murphy

Veterinary Integrative Biosciences, Texas A&M University, College Station, TX 77843, Interdisciplinary Program in Genetics & Genomics, Texas A&M University, College Station, TX 77843; Smithsonian Conservation Biology Institute, Center for Species Survival, National Zoological Park, 3001 Connecticut Avenue NW, Washington, DC 20008, USA, Smithsonian-Mason School of Conservation, George Mason University, Front Royal, VA 22630, USA, School of Health and Life Sciences, Pontifical Catholic University of Rio Grande do Sul, Av. Ipiranga, 6681, prédio 12C, sala 134, Porto Alegre, Rio Grande do Sul 90619-900, Brazil,

Genomes are a mosaic of evolutionary histories that reflect ancient signatures of true species relationships and incomplete lineage sorting (ILS) or gene flow. Understanding how and why phylogenetic signal varies across species genomes can yield powerful insights into species' evolutionary histories and adaptive evolution. By integrating diverse data types with local genealogies, one can differentiate genetic variation consistent with the species tree from that stemming from natural selection, ILS, or gene flow. To better resolve the complex evolutionary history of the living cat species of the genus Panthera, we aligned PacBio HiFi genomes from the jaguar, leopard, snow leopard, lion, and Indochinese clouded leopard to a highly continuous single haplotype assembly from the tiger. We conducted a whole-genome sliding window phylogenomic analysis and used our novel phylogenomics browser Tree House Explorer (THEx) to visualize genome-wide variation in evolutionary histories and genetic divergence on a chromosome-by-chromosome basis in the context of recombination rates. We identified significant differences in the distribution of phylogenetic signal along the X chromosome, where low recombining regions harbor signal of the species tree. However, a subset of these regions contains signal of ancient introgression of the leopard with an extinct or unsampled species with an ancient origin. Whole genome evaluations of structural variation also indicate enrichment of structural rearrangements along the X chromosome, which likely played a role in the unique distribution of phylogenetic signal across the X chromosome and reproductive isolation.

Andrew J Harris

ajharris@cvm.tamu.edu

Graduate Student

Re-assessment of Yellowstone National Park bison population subdivision with SNPs and microsatellites

Sam Stroupe, Chris Geremia, Rick L. Wallen, James N. Derr

Texas A&M University School of Veterinary Medicine and Biomedical Sciences, Yellowstone National Park , Yellowstone National Park, Texas A&M University School of Veterinary Medicine and Biomedical Sciences

Yellowstone National Park is the home of the only plains bison population to have continually existed as wildlife, on the same landscape, through the population bottleneck of the late 19th century. Nevertheless, by the early 1900s, only 22 wild bison were known to have survived poaching. Salvation efforts included the addition of 18 females from Montana and 3 bulls from Texas to augment this population. A century later, nuclear microsatellite-based population level assessment revealed two genetically distinct bison sub-populations that potentially distinguish the native and introduced animals. However in 2016, an analysis of mitochondrial haplotypes failed to discriminate strong population subdivision in bison sampled throughout the Park, suggesting more recent admixture between the two historical sub-populations. This study is designed to delineate any current sub-structure in the Yellowstone bison population by strategically sampling the two major summer breeding populations and the two major winter ranges. Population level metrics will be derived using the same microsatellite loci as the original study along with a newly developed set of highly informative bison specific Single Nucleotide Polymorphisms (SNPs). Continued evidence of population sub-division (or the lack thereof) has significant implications for the long-term management and conservation of the historically important and iconic bison herd.

Sam Stroupe

samstroupe@tamu.edu

Graduate Student

Worse than nothing at all: the inequality of sex chromosome to autosome fusions

Kayla Wilhoit, Emmarie Alexander, and Heath Blackmon

Department of Biology, Interdisciplinary Program in Genetics and Genomics, Department of Biology, Texas A&M University, College Station, Texas

Chromosomal fusions play an integral role in genome remodeling and 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 predict that a fusion joining an autosome to the pseudoautosomal region (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. We have produced a forward time population genetic simulation to explore the outcomes of fusions to both the pseudoautosomal 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. Our model is diploid, two-locus and biallelic, and is able to run thousands of simulations under a variety of conditions. Our results show a clear pattern where fusions to the non-PAR are favored in the presence of sexual antagonism and fusions to the PAR are disfavored in the presence of sexual antagonism.

Kayla Wilhoit

ktwilhoit@tamu.edu

Undergraduate Student

Characterization of haplotype structure and nucleotide diversity of MHC class II genes in Atlantic herring using long-read sequencing

Minal S. Jamsandekar1, Fahime Mohamadnejad Sangdehi2, Brian Davis1, Mats E. Pettersson2, Leif Andersson1,2

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

Major histocompatibility complex (MHC) genes are some of the most polymorphic genes in vertebrate genomes with more than 1,000 alleles at some human MHC loci. They play an important role in adaptive immune system by presenting antigens to the T cells and thereby protecting the organism from infections and neoplasms. Classical MHC genes are often highly polymorphic in contrast to non-classical MHCs that show genome-average level of polymorphisms. We studied MHC class II genes in Atlantic herring, one of the most abundant vertebrates on earth. The aim of this study is to explore how polymorphic the most polymorphic genes in the vertebrate genome are in one of the most abundant vertebrates. We implemented PacBio HiFi long-read sequencing to shed light on this question. We sequenced 14 Atlantic herring individuals from three geographical locations to study 28 haplotypes per locus. We constructed two high quality haploid genome assemblies for each sample and annotated MHC II genes on each assembly and built a haplotype map. We found 5-8 loci for classical and up to 4 non-classical MHC loci per haplotype. This number is larger than that previously reported for any other vertebrate. The antigen peptide binding region of the classical MHCs showed high nucleotide diversity and signals of positive selection with high dN/dS ratio. The long-read sequencing approach allowed accurate estimates of the genetic diversity at highly polymorphic MHC loci, and provided new information how natural selection is shaping variation in MHC genes in the Atlantic herring.

Minal Jamsandekar

minal03@tamu.edu

Graduate Student

Changes in mitochondrial respiratory chain super complexes across functional mammary gland development

Ramsey M. Jenschke, Steven W. Wall, Jessica Epps, Lilia Sanchez, Monique Rijnkels, and Weston Porter

Texas A&M University College Station

Determining the energetics of normal mammary gland development is an essential step towards understanding breast cancer. The changes that occur to the mammary gland during pregnancy and lactation present a uniquely metabolically dynamic environment as the mitochondria rise to the challenge of increasing energetic demands and structural remodeling. While morphological differences in mitochondria across mammary gland development have been noted and we have previously dem onstrated that mitochondrial autophagy, termed mitophagy, is a necessary requirement for the lactogenic differentiation of mammary epithelial cells (MECs), the functional change within the mitochondria themselves has not been elucidated. By studying energetic changes in cancer cells via blue-native polyacrylamide electrophoresis (BNPAGE), we have found that bHLH/PAS family transcription factor Singleminded-2 (Sim2s) plays a role in the stabilization of mitochondrial respiratory chain super complexes (MRC SCs). Sim2s also plays an essential role in mitochondrial turnover during mammary gland development, prompting the investigation into a potential link between changes in the MRC and mitophagy in normal mammary gland development. Using HC11 cells, a mouse mammary epithelial cell line that undergoes functional differentiation analogous to the mammary gland in vivo, we show here that the MRC undergoes structural changes during differentiation. BNPAGE followed by western blot visualization showed that SCs are most stabilized at 24 hours differentiation, corresponding to the peak of functional differentiation in vivo. With the reduction of Sim2 via sh knockdown, we see that the differentiation associated changes in MRC are absent, indicating the additional role of Sim2 in regulating not only mitochondrial turnover, but also the functional difference of mitochondria caused by the increased mitophagy. Inhibition of autophagy, and its corresponding differentiation, with Bafilomycin A1 (Baf) showed the same lack of MRC reorganization, indicating that the shift in complex formation occurs through the formation of new mitochondria. To determine changes in mitophagy in vivo, we are using the Mitochondria Quality Control (MitoQC) mouse to fluorescently visualize mitochondrial turnover during the change from pregnancy through lactation to involution. Preliminary images show higher levels of turnover in lactation into involution, corresponding with the peak differentiation time points and their subsequent changes in MRC organization. Taken together, this data shows for the first time that mitophagy is necessary for mammary gland differentiation and is driven by the need for increased MRC super complex stability and activity to meet energy demands of a developed mammary gland.

Ramsey Jenschke

ramsey.jenschke@tamu.edu

Graduate Student

RNAi pathways prevent mis-regulation of the spermatogenesis developmental program during stress in *C. elegans*

Cara McCormick and Alicia K. Rogers

University of Texas at Arlington

The coordination of gene regulatory networks during development is necessary for maintaining fertility. In *C. elegans*, totipotent germ cells can develop into oocytes or sperm, thus inappropriate activation or silencing of genes responsible for promoting either fate can have detrimental effects on an organism's reproductive potential. Spermatogenesis and oogenesis are temporally separated within the germline tissue during the L4 and adult developmental stages, respectively. Yet, it remains unclear how these developmental programs are robustly executed, particularly during stressful conditions. Here we show RNA interference (RNAi) pathways act to restrict expression of spermatogenesis genes to the L4 developmental stage during heat stress. RNAi pathways use Argonaute proteins complexed with small RNAs to transcriptionally and post-transcriptionally regulate genes and plays key roles in development and fertility. We performed differential expression analysis of mRNA-seq and small RNA-seq libraries from L4 and adult-stage wild-type and *mut-16* mutants, which lack a critical RNAi pathway protein, grown at permissive (20ºC) and elevated temperature (25ºC). Our analyses revealed spermatogenesis-enriched gene expression is developmentally mis-regulated in a small RNA-dependent manner at elevated temperature. In heat stressed *mut-16* mutants, spermatogenesis genes are silenced during the L4 stage and then activated during the adult stage when oogenesis typically occurs. Previously, it was shown that the ALG-3/4 branch of the RNAi pathways regulates expression of spermatogenesis genes and is critical for thermotolerant male fertility. Disruption of the ALG-3/4 pathway at elevated temperature leads to failure of spermatids to activate into mature sperm during spermiogenesis. We found that the genomic loci of *alg-3* and *alg-4* are targeted by small RNAs, and that during heat stress, MUT-16-dependent small RNAs are required for L4 stage-specific expression of the Argonautes, ALG-3 and ALG-4. Moreover, a sperm activation assay revealed that, like ALG-3/4 pathway mutants, spermatids of heat stressed *mut-16* mutants fail to activate. These findings indicate that RNAi pathways are essential for properly coordinating the developmental program of spermatogenesis during heat stress. We propose that appropriate expression of spermatogenesis genes is achieved through small RNA-mediated genetic switches that regulate the expression of ALG-3 and ALG-4 to control ALG-3/4 pathway function throughout development. Moreover, this work provides key insights into the different molecular mechanisms that RNAi pathways employ to maintain both maternal and paternal germ cells' reproductive potential, and further highlights the complexities and importance of RNAi-mediated gene regulation in development.

Alicia K. Rogers

alicia.rogers@uta.edu

Faculty

Regulation of an effector triggered immune response in *C. elegans* against the mitis group streptococci

Anastasiia Ahmedaly, Ashley Persons, Lorraine Byrd, and Ransome van der Hoeven

Department of Diagnostic and Biomedical Sciences, The University of Texas Health Science Center at Houston, School of Dentistry.

Recent studies in plants and animals suggest that some effectors can illicit an immune response mainly by disrupting core host processes. This response known as Effector Triggered Immunity (ETI) becomes more relevant in cells lacking a complete range of pattern recognition receptors such as intestinal epithelial cells. In the worm, the BZIP transcription factors ZIP-2 and CEBP-2 mediate an ETI in the intestinal cells in response to Endotoxin A produced by Pseudomonas aeruginosa. Recently, we have shown ZIP-2 is activated in the worm in response to hydrogen peroxide (H2O2) produced by the mitis group streptococci. The mitis group streptococci are residents of the oral cavity and have shown to be opportunistic pathogens. These microorganisms produce H2O2 as a major virulence factor that contributes to their pathogenicity. Using *Streptococcus gordonii* as a representative of the group, we showed that *zip-2* is required for the survival of the worms and activates the expression of the *zip-2*-dependent gene *irg-1*. However, we did not observe a significant change in survival of cebp-2 mutant worms relative to the wild type worms on *S. gordonii*. This suggests CEBP-2 doesn't contribute to the worm's immune response against *S. gordonii*. Therefore, we investigated if ZIP-2 interacts with other proteins to elicit an ETI response against the mitis group. Using the WormBase interaction partners database, we identified potential candidates that interacted with ZIP-2. We knockdown these candidate genes in N2 worms and worms expressing *irg-1* fused to Green Fluorescent Protein (GFP) and observed the survival and the expression of GFP on *S. gordonii* respectively. Significant increase in survival of *attf-4*, *nhr-68* and *mdt-11* knockdown worms was observed relative to the vector control treated worms. Furthermore, a significant increase in the expression of *irg-1::GFP* was observed in *attf-4*, *nhr-68* and *mdt-11* knockdown worms relative to the vector control treated worms. We also observed *nhr-111* knockdown worms were more susceptible to the pathogen and the expression of *irg-1::GFP* was significantly lower compared to the vector control treated worms respectively. Future studies will focus on characterizing the roles of these proteins in regulating the ETI response to the mitis group streptococci.

Anastasiia Ahmedaly

anastasiia.ahmedaly@uth.tmc.edu

Technician

Alternative-splicing regulators and functional relevance of microexons

Bikash C Choudhary, Rebekah N Jameson, Adam D Norris

Southern Methodist University, Dallas, Texas, USA

Alternative splicing (AS) is one of the phenomena to generate transcriptomic and proteomic diversity in higher eukaryotes. Exons with a size ≤30-50 nucleotides are classified as microexons (μexons). μexons 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 are interested in finding the splicing regulators and function of μexons. We chose UNC-13 μexon as a model for the same. UNC-13/Munc-13 is a synaptic protein involved in synaptic vesicle (SV) exocytosis. We generated UNC-13 bicolor-splicing reporter transgenic animals and found AS of UNC-13 μexon is tightly regulated. Candidate gene studies resulted in two neuronally expressed RNA binding proteins (RBPs), *exc-7* and *mbl-1* affecting the UNC-13 μexon-splicing at various levels. To understand the physiological relevance of the two different isoforms, we misexpressed the two isoforms by using genome editing. Animals with the altered expression of UNC-13 isoforms showed various behavioral deficits, specifically in the release of synaptic vesicles (SVs), concluding μexon included and skipped UNC-13 isoforms may have different capabilities in the release of SVs at synapses. We also found other Munc-13 family μexons are affected by *exc-7* and *mbl-1* suggesting it as a common regulator for the Munc family

Bikash C Choudhary

bchoudhary@smu.edu

Postdoc

Epidermal ribosome synthesis inhibition induces a nutrition-uncoupled organism-wide growth quiescence in *C. elegans*

Qiuxia Zhao, Rekha Rangan, Shinuo Weng, Cem Özdemir, and Elif Sarinay Cenik

Department of Molecular Biosciences, University of Texas Austin, Austin, TX, USA

Inter-organ communication is a key aspect of multicellular organismal growth, development, and homeostasis. Importantly, cell- non-autonomous inhibitory cues that limit tissue specific growth alterations are poorly characterized due to limitations of cell ablation approaches. Here, we report a robust system to investigate nutrition-independent organism-wide growth coordination by modulating ribosome biogenesis at distinct steps in a tissue-specific and reversible fashion in *Caenorhabditis elegans*. We find an organism-wide growth quiescence response upon suppression of ribosome synthesis either by depletion of an RNA polymerase I (Pol I) subunit or either of two critical ribosome biogenesis factors, RRB-1 and TSR-2, which are the chaperone proteins required for assembly of ribosomal proteins, RPL-3 and RPS-26, respectively. The observed organism-wide growth checkpoint is independent of the nutrition-dependent insulin signaling pathways and is not rescued by daf-16(mu86), a bypass mutation that suppresses the starvation-induced quiescence response. Upon systematically exploring tissues involved in this process, we find that inhibition of epidermal ribosome synthesis is sufficient to trigger an organism-wide growth quiescence response and leads to organism-wide gene expression changes. At the RNA level, we observe over- and under-expression of several tissue-restricted genes in a wide range of cell types, including touch receptor neurons suggesting inter-organ communication upon epidermis driven ribosome inhibition. At the protein level, we observed over-expression of secreted proteins (CPR-4, TTR family proteins) as well as an organism-wide reduction both in cytosolic and mitochondrial ribosomal proteins in response to epidermis RNA Pol I depletion. Finally, we find that dense core vesicle secretion specifically from the epidermis tissue by the unc-31 gene plays a significant role in mediating the quiescence phenotype. Taken together, these results suggest the presence of a nutrition-independent multicellular growth coordination initiated from the epidermis tissue.

Qiuxia Zhao

qiuxia.zhao@utexas.edu

Postdoc

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

Canyon Calovich-Benne, Xiaoyu Liang, and 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

Poster Abstracts

P1. The mutation analysis of RGD (Arg-Gly-Asp) cell-binding motif in the basement membrane proteins of *Caenorhabditis elegans*

Jeancarlo Gutierrez and Jonathan Yeow

Baylor University, Myeongwoo Lee lab

The cell-matrix interaction is mediated by the communication between the integrin receptor and extracellular matrix (ECM) proteins. The mammalian cell culture system showed that RGD (Arg-Gly-Asp) motifs are the cell-binding sites of ECM proteins and are known to interact with cell surface receptors of the ECM, such as integrins. These RGD motifs have been shown to play essential roles in cell-matrix interaction, but the role of the RGD motifs beyond the mammalian system was poorly understood. The *Caenorhabditis elegans* genome contains approximately three thousand RGD motif-containing proteins, but of these proteins, ten were identified as containing RGD motifs in the basement membrane ECM. These ten genes are DIG-1, LON-2/glypican, B0393.5/SNED-1, CLE-1/COLXVIII, EMB-9/COLIV, HIM-4/hemicentin, LAM-3/laminin α, LET-2/COLIV, NID-1/nidogen, and UNC-52/perlecan. To study the role of the RGD motifs in the basement membrane proteins, we created mutations in the RGD motifs in these ten genes using the CRISPR-Cas9 system.
The effects of deleting the RGD motifs in *nid-1*/nidogen and *lam-3*/laminin α showed significant behavioral and reproductive defects. Compared to the double mutant of *lam-3/nid-1*, the double mutant was more phenotypically similar to *lam-3* ΔRGD than *nid-1* ΔRGD. The mutated alleles of (*unc-52 kq745* and *kq2023*)performed very poorly in all the assays when compared to N2. The RGD mutations in *him-4*/hemicentin and CLE-1/COLXVIII showed low levels of egg-laying. This suggests that the RGD motif in the ECM component plays a key role in reproductive behavior. A similar approach to the other genes mentioned above is underway. Through the study of RGD mutations in *C. elegans* ECM proteins, we hope to gain further insight of the key role of the cell-binding motif in *C. elegans* and other invertebrate species.

Jeancarlo Gutierrez, Jonathan Yeow

Jeancarlo_gutierrez1@baylor.edu

Undergraduate Student

P2. Subtle sex-differences in learning for Nad-knockout 5XFAD Alzheimer's Disease model mice

Anthony Allam, Sohum Purao, Sapan Hari, and Sarah H. Elsea

Baylor College of Medicine, Houston, TX 77030, Texas A&M School of Medicine, Bryan, TX 77807, Dept. of Molecular & Human Genetics, Baylor College of Medicine, Houston, TX 77030, Baylor Genetics, Houston, TX 77030, BCM-Human Genome Sequencing Center, Houston, TX 77030

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by marked deficits in memory, thinking, and behavior affecting over 6 million Americans aged 65 and older. The classical clinicopathological model of Alzheimer's implicates extracellular beta-amyloid plaques, intracellular tau tangles along with cortical and subcortical atrophy, particularly of the basal ganglia and global loss of synaptic connections as key drivers/features of the disease. In particular, degeneration of the basal forebrain, the major site of cholinergic output, has been shown to cause memory loss indicative of AD. Oxidative stress has been proposed in the pathogenesis of AD, as excessive reactive oxygen species have been shown to precipitate the formation of beta-amyloid plaques. Therefore, in our study, we investigated the effects of oxidative stress in cholinergic neurons and its implication in AD. We specifically targeted the enzyme NADK due to its key role in regulation of oxidative stress and previous research implicating its role in pancreatic cancer which has been shown to be ~6.7-old more prevalent in AD patients. In this study, we hope to understand the phenotypic effects of NADK depletion in cholinergic neurons during the pathogenesis of AD. In order to study these effects, we generated a conditional Nadk knockout in the 5xFAD transgenic Alzheimer's disease mouse model. The 5XFAD mouse was developed to express high levels of APP (amyloid precursor protein), correlating with increased accumulation of beta-amyloid peptide species and therefore, onset of AD. Behavioral and cognitive phenotypic effects in 5XFAD-Chatcre-*Nadk-/-* mice were measured at 12-16 weeks of age. Mice were taken through various behavioral tests: Morris water maze (MWM), fear conditioning (FC), open-field analysis (OFA), and catwalk XT gait analysis. From the behavioral assays conducted, several notable findings pointed towards an alternative theory behind the cognitive changes observed in this mouse model. For example, in the OFA assay, spatial learning in the mouse is measured by distance moved. When comparing female Nadk-knockouts to male in the OFA, females traversed significantly greater distance than their male counterparts ($p=0.005$), exhibiting signs of better spatial learning. Additionally in the same assay, we interestingly found a pattern of female Nadk-KO performing better in horizontal activity, total distance covered, and vertical activity than WT-5XFAD females. This improvement was significantly different from the decline in performance seen in males from WT-5XFAD to Nadk-KO in those same categories ($p=0.01$, $p=0.001$, $p=0.03$, respectively). This assay along with others highlight the presence of subtle sex-specific differences in associative and spatial learning, emotional and spatial memory, and motor ability associated with the knockout of Nadk in cholinergic neurons in the 5XFAD Alzheimer's disease model. Overall, compared to 5XFAD mice, female 5XFAD-Chatcre-*Nadk-/-* mice were less impaired and exhibited higher functioning compared to their male counterparts. These data suggest that depletion of NADK in cholinergic neurons represents a sex-specific effect on phenotypic severity of Alzheimer's disease, supporting alternative sex-dependent pathogenesis and progression of AD.

Sohum S. Purao

sohumpurao@tamu.edu

Graduate Student

P3. DEB-1/Vinculin proline-rich-linker (PRL) plays important roles in touch sensitivity and egg-laying of *Caenorhabditis elegans*

Lianzijun Wang, Jc Gutierez, Juliana Askren, Haiden Jordal, Jayson Partel, and Myeongwoo Lee

Department of Biology, Baylor University, Waco, TX 76798, United States

As a scaffolding cytoplasmic protein, vinculin comprises an N-terminal globular head and a C-terminal tail region, connected by a proline-rich-linker (PRL) domain. The Vinculin head is associated with the talin-integrin complex, while its tail binds to the actin filament. As part of the core focal adhesion molecules, vinculin plays a vital role in cell-matrix adhesion. It provides the physical linkage between the extracellular matrix (ECM) and cytoplasm. The stiffness of ECM is sensed by cells pulling on the ECM via focal adhesions. Cells typically exert higher tension force on a more rigid ECM. The PRL region of vinculin, thus, plays an essential role in delivering mechanical information to the cell inside. This study aims to characterize the in vivo role of the PRL region. In *C. elegans*, the *deb-1* gene encodes for an ortholog of human vinculin, expressed in muscles and gonads. Twenty-five amino acids from 782 to 806 of the putative deb-1 PRL region were deleted in *deb-1* ΔPRL mutant, *deb-1(kq782)*, using the CRISPR-Cas9 system. Behavioral analysis revealed that *deb-1* ΔPRL mutant displayed defects in touch sensitivity and motility when the body wall compared to the N2 wild type.
Furthermore, upon treating exogenous serotonin and tricyclic antidepressant imipramine, *deb-1(kq782)* failed to show increased egg-laying. A high percentage of matricidal hatching events was observed in the mutant animals. Our study suggested that the DEB-1 PRL region is crucial for responding to external mechanical stimulus and egg-laying machinery. The study of the vinculin PRL region indicates a new possibility in understanding human disease and embryonic development linked to mechanotransduction.

Lianzijun Wang

melinawangbaylor@gmail.com

Undergraduate Student

P4. Small effective population size drives chromosome number evolution in carnivores

Michelle M. Jonika 1,2*, Kayla T. Wilhoit 1, Abhimanyu Arekere 1,3, and Heath Blackmon 1,2,4

1 Department of Biology, Texas A&M University, College Station, Texas, USA, 2 Interdisciplinary Program in Genetics and Genomics, Texas A&M University, College Station, Texas, USA, 3 Department of Biomedical Engineering, University of Texas, Austin, Texas, USA, 4 Ecology and Evolutionary Biology Interdepartmental Program, Texas A&M University, College Station, Texas, USA

Chromosome number is a fundamental genomic trait that is often the first recorded characteristic of a genome. Across large clades, a common pattern emerges: many or even most lineages exhibit relative stasis, while a handful of lineages or species exhibit striking variation. Despite recent developments in comparative methods, most of this heterogeneity is still poorly understood. It is essential to understand why some lineages have rapid rates of chromosome number evolution, as it can impact a variety of other traits. Previous research suggests that biased female meiotic drive may shape rates of karyotype evolution in some mammals. However, Carnivores exhibit variation that cannot be explained by this female meiotic drive model. We hypothesize that variation in effective population size may underlie rate variation in Carnivores. To test this hypothesis, we estimated rates of fusions and fissions while accounting for range size, which we use as a proxy for effective population size. We reason that fusions and fissions are deleterious or underdominant and that only in lineages with small range sizes will these changes be able to fix due to genetic drift. In this study, we find that the rates of fusions and fissions are elevated in taxa with small range sizes relative to those with large range sizes. Based on these findings, we conclude that 1) naturally occurring structural mutations that change chromosome number are underdominant or mildly deleterious, and 2) that when population sizes are small structural rearrangements may play an important role in speciation and reduction in gene flow among populations.

Michelle Jonika

Michelle19@tamu.edu

Graduate Student

P5. Investigating the role of Hsp90 in mutation accumulation in yeast

Morike Ayodeji (1,3), Beryl John (1), and Georgios Karras PhD (1,2,4)

(1) Department of Genetics, The University of Texas MD Anderson Cancer Center, Houston, TX
(2) Genetics and Epigenetics Graduate Program, The University of Texas MD Anderson Cancer Center, UTHealth Houston Graduate School of Biomedical Sciences, Houston, TX
(3) Rice University, Houston, TX
(4) correspondence: gkarras@mdanderson.org

Hsp90 is a highly conserved chaperone that assists in the folding and maturation of ~10% of proteins within yeast and human cells, referred to as “clients”. Hsp90’s versatility while helping its clients allows it to also influence the phenotypic expression of genetic variations in both clients and non-client proteins alike, thus shaping the course of evolution and disease. We previously reported that Hsp90 can buffer, thus mitigate, disease-associated mutations in human patients. Here we hypothesize that in buffering cancer mutations, Hsp90 enables their accumulation within tumors, thereby fostering tumor evolution. Indirect evidence suggests that Hsp90 promotes mutation accumulation in model organisms. However, there is uncertainty regarding the ecological conditions and evolutionary timescales in which Hsp90 enables the accumulation of “useful” mutations. It is also unclear if the buffering capacity of Hsp90 evolves over extended periods of proteotoxic stress, such as those found in the tumor microenvironment. To understand the role of Hsp90 in mutation accumulation, we evaluated spontaneous changes in the efficiency of maltose utilization in *S. cerevisiae* cell populations cultured under both relaxed and Hsp90 stress conditions over 50-100 generations. We chose to pass these populations through widely permissive bottlenecks to minimize the effect of genetic drift. Maltose utilization efficiency was assessed in clonal isolates from each of two populations growing in parallel to compare mutation accumulation in a wild-type industrial strain and a mutant derivative lacking four seemingly redundant genes encoding the transcription factors required for maltose metabolism. This was followed with a western blot to determine the expression of Hsp90 in the final samples, after several generations. Our results suggest that chronic Hsp90 stress slightly increased the rate at which deleterious mutations emerge within the population. We also observed a slight increase in yeast growth in later generations, suggesting modest adaptation of cells to chronic stress. However, this occurred well before any significant number of deleterious mutations were observed. No significant difference in the expression of Hsp90 following its generational exposure to basal, stressful, and inhibitory conditions was observed. A future component of this study will examine the changes in Hsp90’s buffering capacity upon stress. We will employ an assay of Hsp90 activity based on the heterologous expression of the glucocorticoid receptor (GR) in yeast. This study establishes a controlled system to evaluate Hsp90’s role in mutation accumulation and the eco-evolutionary factors shaping the manifestations of this function.

Morike Ayodeji

MEAyodeji@mdanderson.org

Undergraduate Student

P6. Development of an inducible nano-luciferase spore tagging system for tracing the biodistribution of *Clostridioides difficile* spores in the GI tract during infection

Osiris K. López-García and Daniel Paredes-Sabja

Interdisciplinary Graduate Program in Genetics and Genomics, Texas A&M University, Department of Biology, Texas A&M University

During *Clostridioides difficile* proliferation in the GI tract, high cellular stress levels will induce toxin production and/or sporulation. After colonization, sporulating cells lead to the production of dormant spores responsible for high rates of recurrent C. difficile infections (R-CDI). Mechanisms for spore adherence and internalization into intestinal epithelium, which have been shown to be key aspects of the recurrence of CDI, remain understudied. Luciferase-labeled bacteria can be used to monitor the viability and distribution of target bacteria in real-time and in situ. Nano-luciferase (NLuc) was proven to have ultra-brightness, stability, and better penetrating ability in comparison to commonly used luciferases for labeling bacteria. To date, no studies are taking advantage of a nano-luciferase-involved reporter system in Clostridia species in vivo. The capabilities of NLuc paired with a Tet-element control system will allow visualization of the biodistribution of C. difficile spores during CDI to understand target sites for the persistence of spores. For this, we have constructed a spore tagging system using the N-terminal of BclA1, one of three collagen-like proteins in the exosporium of the spore, as an anchor for the NLuc reporter protein. The system is controlled by sporulation-dependent bclA1 or cdeC promoters and results in the expression of NLuc protein during sporulation. To control and induce the expression of the spore tag, we will take advantage of the constitutively expressed repressor protein, TetR, and the addition of tetO sequences in the promoters controlling the expression of the NTDbclA1-NLuc fusion protein. Expression of fusion protein occurs in the mother cell during the early stages of sporulation, allowing its anchoring to the outermost layer of the spore exosporium layer. Tagged spores are expected to be surrounded by reporter proteins along with hair-like projections. The addition of the repressor protein and operator sequences allows the reporter's expression to be dependent on the presence of the inducer anhydrotetracycline. This inducible spore tagging system will allow the visualization of dormant spores produced during infection and identify reservoirs that could lead to recurrent infections. Understanding the biodistribution of C. difficile spores during pathogenesis in the GI tract will shed light on the persistence of spores and their role in disease recurrence.

Osiris K. Lopez-Garcia

osiris.lopez@tamu.edu

Graduate Student

P7. Quantitative assessment of HSP90-stress-induced genome instability

Zoe Wang (1,3), Tin Pham, PhD (1,3), and Georgios Karras, PhD (1,2,4)

(1) Department of Genetics, The University of Texas MD Anderson Cancer Center, Houston, TX
(2) Genetics and Epigenetics Program, The UTMDACC UTHealth Graduate School of Biomedical Sciences, TX
(3) equal contribution
(4) correspondence: gkarras@mdanderson.org

The Heat Shock Protein 90 (HSP90) has been proposed to alter the course of evolution by influencing the phenotypic expression of genetic variation. In shaping evolutionary processes, HSP90 acts as a potentiator, a buffer and a capacitor of genetic variation, roles that have been demonstrated in multiple model organisms, including yeast, plants, fish, and humans. However, the impact of HSP90 as a potentiator, a buffer and a capacitor in shaping the clinical course of genetic diseases in humans remains poorly understood. Genome instability is a major hallmark of cancers that enables tumor evolution. Yet, accumulation of deleterious mutations can also drive genomically unstable tumor sub-lineages towards extinction. Hence, genome instability provides a quantitative system to evaluate the evolutionary role of HSP90. We previously described a role for HSP90 in buffering mutations associated with Fanconi Anemia, a cancer-predisposition disease. We showed that HSP90 buffers (that is-mitigates) certain mutations in FANCA, which encodes a scaffold protein required for DNA repair. Since the FANCA is critical for fixing DNA interstrand cross-linking (ICL) damage, cells lacking a functional FANCA copy are hypersensitive to and accumulate genome instabilities upon exposure to ICL-induced reagents such as mitomycin C and carboplatin. Here, we expressed HSP90-buffered FANCA mutants as sole source of FANCA protein in head and neck squamous cell carcinoma cells and evaluated the accumulation of chromosomal aberrations in vitro under conditions of mitomycin C exposure and HSP90 stress as compared to controls. Cytogenetic analysis was performed to determine the number of chromosomal aberrations per metaphase under each condition. We show that by buffering FANCA mutations, HSP90 renders genome instability conditional upon cell exposure to proteotoxic environmental stressors. These results demonstrated a clinically relevant mechanism for stress-induced genome instability in which proteotoxic environmental stressors hinder HSP90’s ability to buffer mutations in DNA repair genes.

Zoe Wang

ZYWang@mdanderson.org

Undergraduate Student

P8. Communication is key: Singleminded2s maintains the integrity of mitochondria associated membranes for proper differentiation

Lilia Sanchez, Jessica Epps, Scott Pearson, Cole McQueen, Steven Wall, Elizabeth Wellberg, H. Ross Payne, Rola Barhoumi, Monique Rijnkels, and Weston Porter

Texas A&M University, College Station, TX 77843-4458, USA

Investigating the regulatory mechanisms involved in cell differentiation and the role played by inter-organelle communication is essential for understanding both normal development and breast cancer etiology. Singleminded-2s (SIM2s), a member of the bHLH family of transcription factors, is a key regulator of differentiation and is lost in breast cancer. To investigate Sim2s role in lactation, we developed tissue-specific transgenic mouse models and found that loss of Sim2s was detrimental for lactation performance, even though we observed no significant change in epithelial content, proliferation, or cell death. Therefore, it seems SIM2s is necessary for proper lactation function through another mechanism. Electron microscopy analysis of glands during lactation revealed differences in mitochondrial number, ER organization, and ER mitochondria contact sites (MERCs), suggesting loss of SIM2s disrupts inter-organelle communication. We anticipate SIM2s' involvement is through directly interacting with mitophagy components at MERCs, and insights from our studies will contribute to our understanding of mitochondrial homeostasis and its role in determining cell fate during normal development and cancer progression, which can be exploited for therapeutic purposes.

Lilia Sanchez

Lilia.sanchez01@tamu.edu

Graduate Student

P9. Examining trehalose accumulation in the *Saccharomyces cerevisiae pgm2Δ* mutant

Lara I. Shehadeh, Micaiah M. Wetzold, Niki M. Hamraei, Shruti Raghavan, 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

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 (*pgm2*Δ), 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 *pgm2*Δ mutant defects. While we observed a rescue, we don't see a significant decrease in glycogen, however, we did see an increase in trehalose levels. 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 *pgm2*Δ growth sensitivities, while tps1Δ mutation exacerbates *pgm2*Δ mutant phenotypes, supporting our hypothesis that increased trehalose can suppress *pgm2*Δ growth defects. Looking in the other direction, at trehalose breakdown, there are two enzymes that hydrolyze trehalose to free glucose: an acid vacuolar trehalase encoded by ATH1 and a neutral cytosolic trehalase encoded by NTH1. The goal of this project is to further examine the hypothesis that increasing trehalose levels rescues the *pgm2*Δ mutant. To do that we overexpressed and made knockouts of ATH1 and NTH1. Loss of ATH1, preventing the breakdown of trehalose, partially rescues the growth defects of the *pgm2*Δ mutant. Overexpression of both ATH1 and NTH1 exacerbates growth defects but ATH1 overexpression resulted in worse defects. Observations with the knockouts and overexpression of each of these continues to support the hypothesis that it's related to trehalose accumulation. Further work will examine calcium and glycogen/trehalose levels to see what the effects are of increasing or decreasing trehalose on calcium homeostasis problems present in the *pgm2*Δ mutant.

Lara Shehadeh & Micaiah Wetzold

lshehadeh19@austincollege.edu

Undergraduate Student

P10. Wright was right: over one thousand datasets support the critical role of epistasis in genetics and evolution

Jorja Elliott 1, Maximos Chin 1, Brian E. Fontenot 3, Sabyasachi Mandal 1, Thomas D. McKnight 1, Jeffery P. Demuth 3, and Heath Blackmon 1 2

1) Department of Biology, Texas A&M University, College Station, TX USA
2) Interdisciplinary Program in Ecology and Evolutionary Biology, Texas A&M University, College Station, TX USA
3) Department of Biology, University of Texas at Arlington, Arlington, TX USA

Much of evolutionary theory is predicated on assumptions about the relative importance of simple or additive genetic architectures versus complex or epistatic genetic architectures. Previous theoretical and empirical work suggests a pattern where life history traits (because they are tightly linked with fitness) lack any standing additive genetic variation. Instead, these traits are expected to exhibit primarily epistatic variation. In contrast, morphological traits (less tightly linked with fitness) are expected to exhibit more additive genetic variation. We use a quantitative genetics method Line Cross Analysis to infer genetic architectures that contribute to trait divergence. By parsing over 1000 datasets by trait type (life history or morphological), clade (plant or animal), and cross divergence (within species or between species), we were able to estimate the role of epistasis across the tree of life. We confirmed that life history traits were explained more by epistasis than morphological traits. A comparison between plants and animals showed nearly identical genetic architecture between the two clades. Lastly, crosses made between species showed more epistatic variation than crosses made within species. While many scientists (e.g. Fisher, Coyne, Turelli) have argued that epistasis is of little importance, our results show that epistatic interactions are a dominant mode of trait divergence and must be accounted for in our theory and in practical applications like domestication and conservation breeding design.

Jorja Elliott

jorjaelliott@tamu.edu

Graduate Student

P11. Exploring sexual antagonism as a driver of sex chromosome – autosome fusions in mammals using stochastic mapping techniques

Max Chin, Mathew Marrano, and Heath Blackmon

Texas A&M University Department of Biology, Texas A&M Ecology and Evolutionary Biology Graduate Program, Texas A&M Department of Biology

Sex chromosome – autosome fusion as a means of resolving intra-locus sexual antagonism has been hypothesized for decades, but today remains a highly debated within the field of evolutionary biology. Mathematical models have recently been developed which allow for the approximation of null proportions associated with fusions between sex chromosomes and autosomes given no selection on such fusions. Comparing these null proportions with observed proportions within taxonomic clades allows for the evaluation of whether observed proportions are elevated, which is a possible signature of historic or ongoing selection on fusions of this type. Most studies following this methodology have been limited in nature to smaller taxonomic clades, which inhibits evaluation of the hypothesis on a broader scale. Here, we expand on existing techniques for phylogenetically informed analysis of trait evolution to facilitate the exploration of the likelihood of fusions between sex chromosomes and autosomes across a large mammalian phylogeny.

Our analysis builds off of previous studies in our lab which have developed a Markov model describing transitions between different karyotypic states, which we define as a combination of haploid autosome number and fused/unfused nature of the sex chromosome system. This Markov model incorporates four rate parameters, each associated with a different type of transition between states. We compile karyotype data for 950 mammal species, with representation from most major mammalian clades, and assign karyotypic states to each species. A recently published species-level mammalian timetree was pruned to our karyotypic dataset. Using our Markov model, phylogeny, and dataset of karyotypic tip states, we estimate values for our four rate parameters using an MCMC approach. We then use our parameterized model, phylogeny, and karyotypic tip states to reconstruct possible ancestral evolutionary trajectories of karyotype using stochastic mapping techniques. We develop methods which allow for the identification and resolution of tree edges which are unresolvable using existing software to build stochastic maps, broadening the applicability of this analytical technique. Proportions of fusions which fuse sex chromosomes and autosomes are extracted from our stochastic maps and compared against null proportions given no selection for fusions of any type. We find that our observed proportions of sex chromosome – autosome fusions are significantly lower than proportions calculated from our null model. We hypothesize that this is driven by extremely high rates of autosome – autosome fusions estimated and incorporated into our model, which is in turn a result instability in rates of karyotypic evolution across our large tree.

Max Chin

maxchin@tamu.edu

Undergraduate Student

P12. The membrane distal NPxY in β integrin cytoplasmic domain plays an essential role in reproductive behavior

Josh Bumm, Myeongwoo Lee, Arlyn P. Alcid, Catherine Ravikumar, Daniel Lee, and Brynne McWhirter

Baylor University
Department of Biology

Proper regulation of cell-matrix interaction is mediated by integrin, a αβ heterodimeric cell surface receptor that binds to the matrix ligands. Upon binding, the integrin attracts linker proteins such as talin and kindlin to the NPxY (Asn-Pro-x-Tyr) motifs in the cytoplasmic domain. The NPxY is a tyrosine phosphorylation site where mutations from tyrosine (Y) to alanine (A) is known to cause severe phenotypes such as embryonic lethality in mice. However, mutations from tyrosine (Y) to phenylalanine (F) show no discernable defects. To analyze the phosphorylation of the NPxY motif in vivo, the membrane distal NPxY was edited by the CRISPR-Cas9 system. The two mutants of the β integrin/*pat-3(kq8041, Y804A)* and β integrin/*pat-3(kq8042, Y804E)* showed defective egg-laying behaviors. The kindlin/*unc-112(kq715, L715E)* mutation also displayed egg-laying defects comparable to *pat-3(kq8041)* or *pat-3(kq8042)*. In contrast, the *pat-3(kq24, YY792/804FF)* non-phosphorylatable mutant showed wild-type egg laying but completed egg-laying in two days and retained a higher number of unlaid eggs. Further analysis of *kq24* showed deteriorated motility on day three after the initial egg-laying, suggesting that the mutant caused progressive muscle defects. Our analysis suggests that NPxY phosphorylation is necessary for a proper function of integrin.

Josh Bumm

Josh_Bumm@baylor.edu

Graduate Student

P13. A characterization of mutating the NID-1 protein on the behavior of *C. elegans*

Nicholas Griffin and Garrick Owen

Baylor University Department of Biology, Myeongwoo Lee lab

In the organism *C. elegans*, the *nid-1* gene encodes for NID-1, a protein which plays an essential role in laminin's ability to bind to collagen IV in the basement membrane. NID-1 binds to integrin, a cell surface receptor protein on the basement membrane through its RGD tripeptide domain. It is also speculated that the NID-1 protein has a role in cell interactions in the extracellular matrix. Mutations within human homologues of the nid-1 gene have shown a link to diseases in humans, such as gastrointestinal cancer. In order to assess the functional consequences of mutations in *C. elegans nid-1*, two mutations were created via microinjection of the CRISPR-Cas9 system into the gonads of wild type (N2) *C. elegans*. The first mutation, *cg118*, created via the excision of amino acids 59 through 692, resulted in a truncated NID-1 protein length which reduced the proteins ability to bind. The second mutation, ΔRGD, created via the excision of amino acids 714 through 716, resulted in the removal of the RGD domain preventing the ability of *C. elegans* to bind integrin. The consequences of these mutations were observed in the behavior of *C. elegans* through egg laying assays in Serotonin and Fluoxetine solutions, egg retention assays in an M9 buffer, and nose contraction analyzes in a Fluoxetine solution. Results from the truncated NID-1 protein from the *cg118* mutation caused only slight behavioral variations compared to N2 *C. elegans*, with its most significant differences being observed in its egg laying capabilities within Fluoxetine solution and in its egg retention. However, the removal of the RGD binding domain resulting from the ΔRGD mutation caused more significant differences in behavior, with its most significant difference being a reduction in egg laying abilities in both Serotonin and Fluoxetine solution. These findings highlight the importance of the *nid-1* gene and its corresponding NID-1 protein in mediating the interaction between integrin and the basement membrane, in addition to its potential relevance to human health. This study provides a basis for further research in investigating consequences of mutations in the *nid-1* gene in *C. elegans* and other organisms.

Garrick Owen

garrick_owen1@baylor.edu

Undergraduate Student

P14. Impact of mitochondrial homeostasis on the immune response during mammary epithelial cell differentiation

Ramiah Vickers, Jessica Epps, Lilia Sanchez, Elizabeth Wellberg, Monique Rijnkels, and Weston Porter

Texas A&M University

There is increasing evidence that mitochondria have an underrecognized function as activators of innate immune pathways. Activation of the innate immune system necessitates an increase in cellular energy output as well as significant metabolic reprogramming, and thus, requires communication between mitochondria and innate immune pathways. However, the key mechanisms involved in the dialogue between mitochondria and the innate immune response during normal mammary gland development have yet to be elucidated. Therefore, the goal of this research is to advance understanding of the mechanism by which the immune response functionally contributes to lactation. Single-minded 2s (SIM2s), a transcription factor of the bHLH-PAS family, has been shown to possess significant roles in the development of the mammary gland and is also proposed to be a fundamental component in mediating stress responses during mammary epithelial cell (MEC) differentiation. Evidence employing a pMitotimer construct illustrated that Sim2s overexpressing cells exhibited a higher basal turnover rate, likely triggered by oxidative damage, that was maintained throughout MEC differentiation. Recent studies have since highlighted a vital role of mitophagy in regulation of the immune system. Under conditions of severe stress, mitochondria release damage associated molecular patterns such as mtDNA, which has been shown to activate cytosolic DNA sensors of the innate immune system. Activation of specific innate immune pathways, such as the cGAS-STING pathway, is known to result in downstream production of type I interferons and proinflammatory cytokines, which have shown to be required for functional lactation. Based on this knowledge we examined expression of the stimulator of interferon genes (STING) across normal mammary gland development and we observed that STING expression was low during virgin development and pregnancy and increased at lactation day 1. Moreover, during peak lactation (day 10), STING expression was decreased in mammary gland specific SIM2sfl/fl mice. In vitro, we have evidence of increased expression of several interferon-stimulated genes throughout MEC differentiation. Due to high energetic demand, we hypothesize that lactation serves as a prime environment for a mitochondrial-dependent immune response. We have evidence demonstrating that STING expression during differentiation is in part due to mitochondrial-specific reactive oxygen species (mtROS), as we observed a decrease in STING expression following treatment with a mitochondrial-specific ROS scavenger, Mitoquinol. We have SIM2 overexpressing SUM159 cells that exhibit basally high levels of STING expression that is dramatically decreased with Mitoquinol treatment. These data are indicative of an interesting dynamic between STING, mtROS and SIM2. Together, our preliminary data suggests that SIM2s influences innate immunity in the mammary gland via its role in mitophagy, potentially as a result of prolonged metabolic stress during lactation. We anticipate that continued efforts to elucidate the mechanism of the dialogue between mitophagy and the innate immune response will facilitate the exploitation of mitochondrial quality control mechanisms to mediate innate immunity and inflammation during lactation. Overall, this research is significant because it will enhance knowledge of how the immune response functionally contributes to normal mammary gland development, and thus, will provide insight into the development of post-natal pathologies associated with the breast.

Ramiah Vickers

ramiahvickers@tamu.edu

Graduate Student

P15. Characterizing the substrate target of BRCA1/BARD1 in *C. elegans*

Caitlin Lightle, Russell Vahrenkamp, Owen Falkenberg, and Mikaela D. Stewart

Texas Christian University

BRCA1 and BARD1 are proteins involved in the repression of genes associated with increased risk for breast and ovarian cancers. This is accomplished through ubiquitination of H2A and subsequent changes in chromatin compaction. BRCA1 and BARD1 form an E3 ligase (BCBD complex), and mutations affecting the enzymatic functions of this complex can predispose women to these cancers. The model organism *C. elegans* contains orthologs of these proteins, BRC-1 and BRD-1, which makes it a useful organism for studies of protein function; however, little is known about the mechanism of ubiquitination in *C. elegans* as compared to humans. This project used nucleosome assays to provide more insight on the ubiquitination of H2A by the BCBD complex in *C. elegans*. The objectives of this project included characterizing the interaction of the BCBD complex with H2A and identifying a specific lysine target in *C. elegans*. The conserved lysine targets were mutated out of H2A and nucleosome assays were performed to identify potential reductions in ubiquitination activity. In addition, we hypothesized that enzyme-substrate interactions, specifically between H2A and BRD-1 in *C. elegans*, are important in directing ubiquitin to the target site. Amino acid residues in BRD-1 thought to be important for these interactions were mutated out, and assays were performed to assess changes in ubiquitination activity. The H2A nucleosome assays showed that the mutations of conserved lysines in the H2A N-terminus and C-terminus in *C. elegan*s did not significantly reduce ubiquitination activity, and a definitive target could not be identified. However, the BRD-1 assays identified amino acid residues in *C. elegans* that participate in directing the ubiquitination process. Further studies are needed to determine if *C. elegans* has any preferential lysine targets at a non-conserved residue or if it is truly nonspecific in its activity. Currently, mass spectrometry analysis is being performed as a complementary method to attempt to pinpoint the location of lysine ubiquitination.

Caitlin Lightle

Caitlin.Lightle@tcu.edu

Undergraduate Student

P16. Activation of CREB signaling controls a feedback loop required for the homeostasis of connective tissues of the spine

Valeria Aceves, Zhaoyang Liu, and Ryan S. Gray

1Department of Nutritional Sciences, Dell Pediatric Research Institute, University of Texas at Austin Dell Medical School, Austin, TX. 2Center for Craniofacial Molecular Biology, Ostrow School of Dentistry, University of Southern California, Los Angeles, CA

Adolescent idiopathic scoliosis (AIS) is the most common spine disorder affecting children worldwide. We report new molecular insights for AIS based on our analysis of two independent genetic mouse models: (i) generated by Col2-Cre conditional ablation of the Adhesion G-coupled protein receptor Adgrg6; and (ii) a novel microdeletion of allele *Sox9*. To better understand the functional role of ADGRG6 in the spine, we performed spatial transcriptomics with the 10x Genomics Visium platform on sectioned spines from *Cre(-)* control mouse and *Col2-Cre;Adgrgf/f* mutant mice with scoliosis. We found 266 genes were altered >2-fold comparing wild-type and scoliosis samples, including the downregulation of *Sox9* and dysregulation of several known SOX9 target genes in the intervertebral discs. *Sox9* is a known CREB target gene and we show that CREB activation is diminished in *Col2-Cre;Adgrgf/f* mutant mice. SOX9 is an essential transcriptional regulator of cartilage development and homeostasis, and dysregulation of SOX9 is associated with a broad spectrum of skeletal dysplasia. In the mouse, we isolated an in-frame (p.Asp272*) microdeletion of the SOX9 TAM domain (*Sox9Asp272del*), which displayed recessive adult-viable skeletal dysplasia, including scoliosis. *Sox9Asp272del* mutant mice showed alterations in several factors essential for cartilage and extracellular matrix development and exhibited reduced ADGRG6 expression in the intervertebral discs. Altogether our studies demonstrate that the ADGRG6-dependent CREB signaling pathway involving regulation SOX9 is vital for maintaining spine alignment in the mouse. Future directions will focus on asking whether the increased expression of *Sox9* can ameliorate the onset and severity of scoliosis in *Col2Cre; Adgrg6f/f* mutant mice and define the mechanistic role of the TAM domain of SOX9 for transcriptional regulation of gene important for intervertebral disc homeostasis.

Valeria Aceves

valeria.aceves@austin.utexas.edu

Graduate Student

P17. Characterization of DUF4585 genes in zebrafish

Phoebe Nguyen, Jessilyn Tran, Yasmine Bukhari, and Kelli Carroll

Austin College

There are a multitude of muscle diseases, many of which have an unknown cause. Here, we characterize the DUF4585 genes, which are a family of genes expressed in muscle that are still almost entirely uncharacterized. Previous research has found that mice have three DUF4585 genes: C10Orf71 (*orf71*), 1110002E22Rik (*e22*), and Prob1 (*prob1*). These genes were found to be expressed primarily in skeletal muscle, where they localized to the z-disk in sarcomeres. They have also been found to be expressed in cardiac muscle, with overexpression leading to cardiomyocyte hypertrophy, indicating that Orf71 plays a role in cardiac function (Dierck et al., 2017). Due to a partial genome duplication, the DUF4585 family of genes in zebrafish consists of four genes: C10Orf71 (*orf71*), C10Orf71 (*orf71b*), 1110002E22Rik (*e22*), and Prob1 (*prob1*). qPCR (quantitative polymerase chain reaction) on the DUF4585 genes indicated that they are expressed in the first three days of development. This study seeks to determine the localization and function of the DUF4585 genes in zebrafish (*Danio rerio*) using whole-mount in situ hybridization (WISH). Initial results showed that Orf71 and Orf71b were expressed in somites of developing embryos, which suggests the genes play a role in skeletal muscle formation. By characterizing these novel genes, it would further elucidate mechanisms of muscle development and potential disease in myoblasts.

Phoebe Nguyen and Jessilyn Tran

jtran21@austincollege.edu

Undergraduate Student

P18. Fitness relationship between genome fragmentation and environmental stability

Andres Barboza-Pereira, Juliette Strope, and Heath Blackmon

Department of Biology, Texas A&M University

There is a chromosome number variation across the tree of life, but it is unclear what evolutionary benefits this variation provides. There is insufficient information about the relationship between the degree of environmental stability, the type and strength of gene interactions, and the number of chromosomes in a genome. This study seeks to understand the fitness relationship between genome fragmentation and environmental stability and genome fragmentation and interactions between genes, informing into the evolutionary benefits chromosome number variation provides across the tree of life. The investigation consists of simulations of a diploid 100-locus population genetic model with four different models of gene interactions under a wide range of environmental stability probabilities. The population is selected towards a varying optimal phenotype, generating a mean fitness, mean squared error of the optimal phenotype, and mean phenotype datapoint at each generation. The data provides insight into the overall mean fitness of a population across multiple chromosome numbers for each model and environmental stability probability.

Andres Barboza Pereira

andresdbp@tamu.edu

Graduate Student

P19. Glyphosate's effects on the development of zebrafish (*Danio rerio*)

Mia Hibner, Cody Dean, Kelli Carroll

Austin College

Glyphosate is a nonselective herbicide that has been popular in the United States since the early 2000s. Glyphosate, the active ingredient in the popular herbicide Roundup, kills plants by targeting the plant specific EPSP enzyme belonging to the Shikimate pathway. Although animals do not have a Shikimate pathway, Roundup exposure has deleterious effects on humans and other vertebrates, and exposure to Roundup has been associated with the development of non-Hodgkin's lymphoma. However, its mechanism of toxicity in humans and other vertebrates is unknown. Previous research reveals that exposure of developing zebrafish (*Danio rerio*) embryos to Roundup resulted in decreased body length while glyphosate exposure resulted in an abnormal spinal curvature. To assess specific central nervous system abnormalities following glyphosate exposure, zebrafish were immunostained at 48 hours post-fertilization (hpf) to visualize motor neurons with a znp 1 antibody. Exposure to glyphosate resulted in less intense staining along the spine and somites of the exposed embryos, suggesting that glyphosate hinders normal development of the central nervous system. In the future, we hope to better understand the different effects of pure glyphosate exposure compared to roundup exposure on zebrafish embryogenesis. Together, this work will provide an in-depth analysis of the effects of glyphosate on zebrafish development to aid in identifying the detrimental effects that may result from glyphosate exposure.

Cody Dean

cmccasland20@austincollege.edu

Undergraduate Student

P20. The tissue-specific role of SMN-1 in *C. elegans*

Anusha Iyengar, Lindsey Philips, Jane Liu, and Adam Norris

Southern Methodist University

Spinal muscular atrophy (SMA) is an autosomal recessive disease that results from mutations in the Survival of Motor Neuron (smn-1) gene. SMN is a ubiquitously expressed protein, but SMA is characterized by the selective degeneration of motor neurons of the lower spinal cord. Despite a clear understanding of the genetic causes underlying SMA, the mechanisms associated with low SMN levels to disease pathogenesis remains unclear. We focused on examining the effect of deleting SMN in neuronal (*unc-17*, *unc-47*, *rgef-1*), muscular (*myo-2*, *myo-3*), hypodermal (*dpy-7*) and intestinal (*elt-2*) tissues. We characterized each tissue-specific deletion using both behavioral assays (to measure locomotion and eating), as well as transcriptomic analysis (RNA sequencing) to further elucidate the role of the SMN protein at the molecular level. Surprisingly, we found that loss of smn-1 in neurons did not result in any strong phenotypes, but loss of *smn-1* in the intestine caused strong defects, similar to that of null *smn-1* mutants. This prompted us to survey which transcripts are dysregulated and/or aberrantly spliced as a result. RNA-sequencing data revealed a set of proteins—produced in the intestine—involved in the intracellular pathogen response (IPR) that provide resistance against proteotoxic stress and are highly upregulated in *smn-1* mutants. These mutants also exhibit thermotolerant properties, as might be predicted by such a gene expression profile. Through further experimentation we hope to uncover how organisms cope with stress, as part of the IPR, as it relates to SMN deficiency in the intestine.

Anusha Iyengar

aiyengar@smu.edu

Graduate Student

P21.Identifying the role of SOX9 in neural crest EMT

Hannah Herron, Heddy Menendez, and Crystal Rogers

Austin College, University of California Davis

Neural crest (NC) cells are a population of stem-like, transient, multipotent cells originating from the dorsal side of the neural tube in developing vertebrate embryos. After undergoing an epithelial to mesenchymal transition (EMT), where the cells transition from tightly bound to migratory invasive cells, they travel long distances and differentiate into craniofacial bone and cartilage and the peripheral and enteric nervous systems, among other derivatives. However, errors in NC development result in structural defects such as craniofacial cleft or the development of lethal congenital disorders such as Campomelic Dysplasia. Our project focuses on understanding the role of SOX9, a transcription factor linked to NC EMT. Previous work identified that SOX9 overexpression drives migration of NC cells, but the mechanism is unknown. We hypothesized that SOX9 drives migration by regulating the expression of cell-cell adhesion molecules. To test the necessity and sufficiency of SOX9 in NC EMT we performed SOX9 overexpression and knockdown in chick and quail embryos. We used immunohistochemistry (IHC) and histological analyses to identify the effects of SOX9 perturbation on cellular adhesion markers (cadherin proteins). At early stages, reduction of SOX9 results in reduced expression of both N-cadherin (CDH2) and E-cadherin (CDH1) in a non cell-autonomous manner. At later developmental stages, SOX9 knockdowns result in shorter NC migration distances. We predict that SOX9 may be affecting transcription of a morphogen, which causes non-cell autonomous decreases in epithelial markers, and future work will test this prediction. This work illuminates the molecular mechanisms that drive NC cell formation and will increase our understanding of how cells transition from tightly epithelial to migratory, invasive cells during development.

Hannah Herron

hherron20@austincollege.edu

Undergraduate Student

P22. Elucidating the evolution of the recombinational landscape of placental mammals using comparative genomics

Isabella R. Childers (1, 2), Kevin R. Bredemeyer (1, 2), and 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

A long-standing issue in comparative genomics is how best to accurately infer the relationships between species from whole genome data. Emerging literature has discovered a pattern where the local recombination rate is negatively correlated with the frequency of the actual species history, often referred to as the “species tree”. However, we have a poor understanding of how recombination rates evolve over more extended evolutionary time frames, especially in the context of variable rates of karyotypic evolution across lineages. We aim to identify regions of genomes where recombination rates are historically stable over tens of millions of years that might be selected to infer species relationships more reliably. To better elucidate the evolution of historical recombination rates in relation to chromosome evolution, we reconstructed the ancestral placental mammal genome from existing and novel high-quality genome assemblies. We selected species previously identified as having slowly evolving karyotypes based on molecular cytogenetic data: the domestic cat (*Felis catus*), human (*Homo sapiens*), aardvark (*Orycteropus afer*), Hoffmann’s two-toed sloth (*Choloepus hoffmanni*) and blue whale (*Balaenoptera musculus*). These five species sample the four principal placental mammal clades. Highly contiguous genome assemblies exist for three of these species: human, cat, and whale. However, aardvark and sloth lack chromosome-level genome assemblies, so we applied PacBio long-read sequencing and Hi-C scaffolding to obtain chromosome-length assemblies. The aardvark assembly had a length of 4.23 Gbp and a scaffold N50 value of 386 Mbp. The two-toed sloth assembly had a length of 3.11 Gbp and a scaffold N50 value of 154 Mbp. We reconstructed an ancestral placental mammal karyotype showing syntenic alignments between all five species sharing chromosome-length tracks of collinearity where chromosome reshuffling was rare for over 100 million years of evolution. Our ancestral reconstructions will provide the basis for the future study of recombination rate evolution during placental mammal history.

Isabella R. Childers

ichilde@tamu.edu

Graduate Student

P23. The effects of mutation in *mec-9* Kunitz domains on mechanosensation in *C. elegans*

Hunter Hennig

Baylor University, Myeongwoo Lee lab

Kunitz domains are formed when sulfur atoms on two adjacent cysteine amino acids bond to form disulfide bridges. This structure is capable of protecting proteins against protease activity, preventing their degradation. In this study, four different *C. elegans mec-9* mutant types (*kq45*, *kq109*, *kq337*, and the double mutation *kq109/45*) were analyzed, all of which involve a mutation in Kunitz-domain-coding regions related to touch receptor neuron development. These mutations were obtained by utilizing microinjections to alter a key cysteine residue to instead code for serine, thereby preventing disulfide bridge bonding that is crucial in Kunitz domain formation. Thus each of these mutations prevents the development of one or more Kunitz domains in touch receptor proteins, allowing for protease activity to commence and subsequent degradation of the protein to occur. Soft-touch and thrashing assays were then conducted on each of the mutations to determine the severity of touch inhibition and the effect of the mutation on motor-function. It was observed that the studied *mec-9* mutations resulted in a drastically decreased touch response due to the inhibition of proper touch-receptor neuron development, as well as slightly altered thrashing patterns associated with improperly regulated motor function.

Hunter Hennig

hunter_hennig1@baylor.edu

Undergraduate Student

P24. Odd Pair (Opa) and Ocelliless (Oc) dynamics in Drosophila brain development

Shiva Abbasi, Kelli D. Fenelon, Fan Gao, and Theodora Koromila

Department of Biology, University of Texas at Arlington, Arlington, TX, and Caltech Bioinformatics Resource Center (CBRC), Caltech, Pasadena, CA

Neural progenitor specification and differentiation occur early in development with detectable neuroblasts arising a mere one hour post gastrulation in the Drosophila embryo. The roles of transcriptional activators, such as Bicoid (Bcd)/PITX2, Odd paired (Opa)/ZIC3 and Ocelliless (Oc)/OTX2, are largely conserved across animals. A previous study showed that a group of Anterior-Posterior axis (AP) enhancers are initially activated by Bcd, and later activation is transferred to Oc via a feed-forward relay. In addition, gene replacement experiments show that the Drosophila oc gene and orthologous mammalian Otx2 gene are functionally equivalent in the developing procephalic head region. Opa is a late-acting pioneer factor that drives the transcriptional landscape to undergo a dramatic shift to prepare the syncytial nuclei for cellularization and transitioning the embryo into gastrulation. Opa and Oc are transiently coexpressed in the neuronal precursors during cellularization but their role is largely unexplored. Our hypothesis is that Opa and Oc are both regulating gene expression and promote brain cell specification before gastrulation occures in the early embryo. Super-resolution, high-speed 4D imaging of both fixed and living embryos helped us quantify the overlapping expression regions before and after gastrulation in the Drosophila embryo. Single-embryo RNA-seq data reveals a subgroup of Opa-bound genes to be brain specific. Interrogation of these genes against pioneer factor ChIP-seq datasets and expression databases suggests that Opa acts together with Oc for the regulation of a subgroup of genes, in both AP and DV axes, at cellularization. Additionally, this study showed that Oc supports gene regulation by binding to brain-specific Bcd/Opa-independent enhancers during gastrulation at a third wave of zygotic activation. The proposed research has clear potential to elucidate the mystery of brain specification during embryogenesis.

Shiva Abbasi

sxa1511@mavs.uta.edu

Graduate Student

P25. Investigating the effects of the HOG and CWI MAPK cascades on growth defects observed in the Saccharomyces cerevisiae *pgm2Δ* mutant

Wenqi Ding, Madelyn G. Oliver, Mandy R. Eckhardt, and David P. Aiello

Austin College Biology Department

In *Saccharomyces cerevisiae*, the interconversion of glucose-1-phosphate (Glc-1-P) and glucose-6-phosphate (Glc-6-P) is catalyzed by the enzyme phosphoglucomutase (PGM). Previous research has shown that cells lacking PGM2, the major isoform of PGM, display a slow growth phenotype and changes in the ratio of glucose metabolites when grown on galactose. Defects in calcium homeostasis are also present in the *pgm2*Δ mutant, including altered calcium uptake, calcium accumulation, and sensitivity to the calcineurin inhibitor cyclosporin A (CsA). Previous studies revealed that the loss of HOG1, the main effector of the HOG MAPK cascade, resulted in a partial rescue of the *pgm2*Δ mutant on galactose media, suggesting that overactive signaling through the HOG MAPK cascade is harmful to the *pgm2*Δ mutant. Contrastingly, the loss of SLT2, the main effector of the CWI MAPK cascade, was found to be lethal for the *pgm2*Δ mutant, suggesting that signaling through the CWI MAPK cascade is essential to the *pgm2*Δ mutant. The loss of PTP2, which encodes the major phosphatase responsible for the inactivation of both HOG and CWI MAPK cascades, exacerbates the growth defects of the *pgm2*Δ mutant. The unregulated activity of these stress response cascades might be deleterious to the *pgm2*Δ mutant. These findings indicate that the hyperactivation of stress response cascades may be harmful to the *pgm2*Δ mutant. This study further characterizes the roles of HOG and CWI MAPK stress response cascades in the *pgm2*Δ mutant by comparing the phenotypes of knockouts and overexpressions of HOG1, SLT2, and PTP2 in the context of the *pgm2*Δ mutant.

Wenqi Ding

wding21@austincollege.edu

Undergraduate Student

P26. The evolution of chromosome number and sex chromosome system in Odonata

Matthew Marano and Heath Blackmon

Interdisciplinary Program in Ecology and Evolutionary Biology at Texas A&M University, Department of Biology at Texas A&M University

The eukaryotic genome typically exists as multiple discrete chromosomes. Unfortunately, we need to understand more about the processes that drive the evolution of chromosome number if we hope to know why some clades are highly variable and others are almost static. To fill this gap in our understanding, we inferred rates of chromosomal fusion and fission across the insect order Odonata (dragonflies and damselflies). Odonata's most recent common ancestor is hypothesized to have had an XO/XX sex-chromosome system. However, many taxa within Odonata have transitioned to XY/XX, likely by the fusion of an autosome with the X chromosome. Based on a theory proposed by Charlesworth and Charlesworth in 1980, autosome-to-sex-chromosome fusions (and therefore, sex-chromosome system transitions) will be overrepresented in the presence of sexually antagonistic loci on autosomes. We improve stochastic mapping methods to account for limitations related to extreme rate heterogeneity among branches of many empirical phylogenies. We then leverage this improved approach to assess support for the hypothesis that sexually antagonistic variation is present and driving fusions of sex chromosomes and autosomes.

Matthew Marano

matthew.marano@tamu.edu

Graduate Student

P27. Modelling the *Caenorhabditis elegans* gonad over developmental time using the Distal Tip Cell marker *lag-2p::gfp*

Elaine Tennyson, Robert Page, Tanya Carvajal, Payton Davis, Jannatul Ferdush and Matt Crook

Texas A&M University-San Antonio

The effect of mutations can be expressed at different time points during development but are often not measured or observed until development is complete. Knowing when these defects occur could help answer why they occur and how different genes interact during development. *Caenorhabditis elegans* is a hermaphroditic, free-living nematode used as a model organism in science because of their transparent bodies, short reproductive cycles, and invariant cell lineage. We use *C. elegans* to study the molecular control of hermaphrodite gonad development. Our study aims to map gonad development in *C. elegans* over time to assist in characterizing the roles of different genes in gonad development.

During their development *C. elegans* progress through four larval stages, L1- L4, before molting into the adult hermaphrodite. Gonad development begins in late L1, with the growth of the two gonad arms being led by the Distal Tip Cells (DTCs). The gonad arms grow anteriorly and posteriorly until L4 stage where they turn dorsally and then again back to the mid-point, ending development dorsal to the vulva.

We used the Distal Tip Cell marker, *lag-2p::gfp*, to develop a model of gonad development over time in relation to larval size. We did this by selecting the GFP tagged nematodes at different larval stages and capturing brightfield and GFP images of each animal. Merging the brightfield and GFP images of an individual nematode allowed us to measure the length of the gonads and pharynx-vulva length in ImageJ. The pharynx-vulva length was used as a quantitative measure of larval growth. When we studied the various ages of larvae tagged with the GFP protein, we found that gonad length revealed two distinct growth phases in relation to larval length. The breakpoint between the two growth phases is in the mid-L3 stage. After this point the rate of gonad growth increases until the gonads are fully developed in late-L4 stage. In other studies of *C. elegans*, using molecular control of gonad development, only the endpoint of gonad development in late L4 and adult nematodes is studied, and it is unclear at what larval stage the desired phenotype was expressed. Our study aids in more precisely mapping *C. elegans* gonad development over developmental time. Our hope is that this model will help future research to determine which stage in gonad development genes of interest act.

Elaine Tennyson

etenn01@jaguar.tamu.edu

Undergraduate Student

P28. Comparative genomics of *C. rectus*, an “emerging Campylobacter species”

Casey Hughes Lago, Deborah S. Threadgill

Texas A&M University Interdisciplinary Program of Genetics and Genomics, College Station, TX

Texas A&M University Department of Cell Biology and Genetics, College Station, TX, USA;

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

P29. Possible roles of the proprotein convertase KPC-1/Furin and transcription factor EOR-1/PLZF in Compartmentalized Cell Elimination

Nathan Rather, Piya Ghose

The University of Texas at Arlington

Programmed cell death is a critically important event for normal development and homeostasis of organisms. We discovered a ‘tripartite’ killing program that eliminates the morphologically complex tail-spike cell (TSC) and the sex-specific CEM neurons during *C. elegans* embryonic development. This program, Compartmentalized Cell Elimination (CCE), is characterized by three distinct morphological regions each dying in stereotypic ways. The single process/dendrite of these cells displays two very different elimination morphologies in its two segments. The proximal segment fragments in a manner that is strikingly reminiscent of developmental pruning or injury-induced Wallerian degeneration of axons; whereas the distal segment retracts, much like axons do following nutrient deprivation.

One of the characteristic phenotypic cell death regions of CCE is that of the cell body. It was revealed through a forward genetic screen that a specific mutant’s (*ns957*) phenotype exhibits a rounded and enlarged cell body where the other distal and proximal sections are removed. Whole genome sequencing provided a list of genes mutated in the above mutant. Testing possible candidates has revealed that loss of function mutants for the genes *kpc-1* and *eor-1* both modestly phenocopy *ns957*. The *kpc-1* gene encodes a conserved proprotein convertase KPC-1/FURIN whereas *eor-1* encodes for the zinc finger transcription factor EOR-1/PLZF. Both LOF mutants exhibit TSC persistence with cell body rounding in L1 *C. elegans* larvae that are consistent with the *ns957* phenotype. Additionally, all three of these mutants appear to exhibit temperature dependency, with higher TSC persistence occurring at higher growth temperatures as well as certain heat stressors. My immediate next steps include rescue and expression experiments.

Nathan Rather

nbr5014@mavs.uta.edu

Undergraduate Student

P30. Utilizing a F2 population to investigate the genetic regulation of diet-induced thermogenesis in mice exposed to a ketogenic diet

Alexandra Naron1,2*, Anna C. Salvador1,3, Emanuele Baldassarri5, Thomas V. Wong1, Ryan McGovern1, Aaron Van Wettering1, Ahmed Elsaadi1, and David W. Threadgill1,2,3,4

1Department of Cell Biology and Genetics, Texas A&M University, College Station, TX, USA, 2 Interdisciplinary Department of Genetics, Texas A&M University, College Station, TX, USA, 3 Department of Nutrition, Texas A&M University, College Station, TX, USA, 4 Department of Biochemistry and Biophysics, Texas A&M University, College Station, TX, USA, 5 School of Biosciences and Medicine, University of Surrey, Gulliford, Surrey, England

Precision nutrition is the customization of nutrition guidance through individualized plans based on unique metabolic characteristics to improve general health. The dietary guidelines for Americans have been formulated around population-level evidence of nutrients and health to prevent illness and disease. However there, is still a significant lapse in knowledge of how genetics impacts diet. This prevents further refining of nutrient guidelines from the level of populations to unique characteristics of individuals. Genetically heterogenous mouse models have demonstrated significant variation in metabolism, activity, and body fat composition across different strains and diets. Genetic regulation of thermogenesis may contribute to the variation seen in response to diet. Investigating the role that genetics plays in individual consumption of energy, production of heat, and body composition will provide knowledge to better individualize nutritional approaches.

Previously C57BL/6J (B6), A/J, FVB/NJ (FVB), and NOD/ShiLtJ (NOD) mice were exposed to human comparable diets varied in macronutrient content including an American (high fat, high carbohydrate) and ketogenic (high fat, no carbohydrate) diet to investigate the impact diet plays on thermogenesis rates. Phenotyping included measurements of body composition measurements via EchoMRI to determine fat and lean mass present during the feeding trial and metabolic chamber measurements were performed at the conclusion of their diet exposure to determine rates of heat expenditure and activity via the TSE Phenomaster.

We observed that the ketogenic diet increased rates of heat expenditure in A/J mice without a corresponding increase in activity relative to their A/J counterparts exposed to the American diet. B6 mice showed a more modest response to the ketogenic diet relative to the American diet with regards to thermogenesis rates. Percentage of body fat was also observed to have decreased in both A/J and B6 mice fed the ketogenic diet relative to their counterparts exposed to the American diet.

To further investigate genetic regulation of diet-induced thermogenesis, an F2 population of C57BL6/J x A/J was generated. F2s were genotyped at 7854 markers on Mouse Universal Genotyping Array (MUGA). Linkage analysis was conducted with R/qtl2 and revealed several overlapping quantitative trait loci (QTL). QTL overlapping on Chr 7 were identified for heat expenditure and body fat gain. QTL overlapping on Chr 1 were identified for activity and heat expenditure.

To narrow the overlapping QTL of interest we are generating a subconsomic line from chromosome substitution strains (CSS) for A/J Chr1 and Chr7. This will allow us to validate previously identified QTL of interest and assist in identification of genes regulating diet-induced thermogenesis.

These mice will be exposed to the ketogenic diet for 6 weeks. Body composition measured prior to their diet exposure and again after 5 weeks on the ketogenic diet. Metabolic chamber measurements will be performed at the conclusion of the exposure. The phenotyping of our population will allow us to validate previously identified QTL of interest and assist in identification of genes regulating diet-induced thermogenesis.

Alexandra Naron

anaron@tamu.edu

Graduate Student

P31. Project Gen: looking at cognitive function and memory

Shubhi Nanda

University of Texas- Austin

Memory is a critical part of our cognitive function, and many neurobiological mechanisms play a role in how human minds retain and encode memory. However, there need to be more studies done into the recall rates of different populations and how the brain changes with age regarding cognitive function.

This project aims to observe and conduct experiments examining the cognitive and neural basis of learning and memory. Through various learning tasks, the project looks at overall declarative memory and recall time for college youth and the aging population. Using various randomization methods and incentivizing the study, more than 30 and counting participants have been studied for both populations. The college population has been found through UT

Sona (a participant database), particularly the psychology classes. The aging population has been found through outreach amongst senior homes and the city. In addition, incentives through course credit and monetary compensation have been given. The study is given through three days, with the first day having tasks that help to develop a neurocognitive profile. On the second and third days, cognitive tasks related to declarative memory, recall time, and accuracy are administered. After the initial data is collected, the administered tasks are scored and rated amongst the standard score for the tasks to set a threshold score that is high enough to have the data valid for the study. If the score is not above that threshold, it is not used in comparing the two studies. While the study is still being administered, through the preliminary scoring and comparing of some of the data of the three-day study, there is a correlation where the college population has an overall higher cognitive function than the aging population. Once this study is entirely administered and analyzed, it can provide some more insight into how the brain changes over time and if there are ways we can better memory and cognitive function even as the brain ages.

Shubhi Nanda

shubhi.nanda.901@gmail.com

Undergraduate Student

P32. Using CRISPR Cas9 to investigate the role of an evolutionary conserved SNORD115 cluster in the regulation and expression of the paternally imprinted gene UBE3A

Alasdair J Taylor, Sarah G Christian, Scott V Dindot

Department of Veterinary Pathobiology, School of Veterinary Medicine, Texas A&M University.

Loss of function or expression of the maternal UBE3A allele is the primary cause of Angelman Syndrome (AS), a neurodevelopmental disorder characterized by severe developmental, intellectual, and cognitive impairments. UBE3A is paternally imprinted in neurons of the CNS through a mechanism dependent on the transcription of the UBE3A antisense transcript (UBE3A-ATS), found on the distal end of the polycistronic long noncoding RNA host gene, SNHG14.

Recent efforts to develop a therapeutic for this condition have focused on reactivating the paternal allele by targeting and disrupting UBE3A-ATS transcription. Therapies such as the Gapmer ASO GTX-102 target the believed start point of the UBE3A-ATS, the evolutionary conserved 2nd cluster of exons of an orphan C/D box small nucleolar RNA (SNORD) within SNHG14, SNORD115.

The aim of this study is to investigate the role of SNORD115 cluster 2 in the regulation and expression of the UBE3A-ATS and the paternal UBE3A.

CRISPR Cas9 gene editing was used to selectively delete exons in SNORD115 cluster 2 in a HEPG2 cell line before the effect on the relative expression of UBE3A and the UBE3A-ATS were measured using RT-qPCR.

With this study ongoing, the next steps will include quantifying the effect of additional exon specific deletions, creating deletion stable cell lines and also replicating these experiments in both control and AS patient derived iPSC neurons.

Alasdair J Taylor

ajtaylor1@tamu.edu

Graduate Student

P33. Exploring the diversity of soil microbiota in cadaver decay islands (CDI) located in central Texas

Katherine E. McBroom, and David P. Aiello

Austin College

Decomposition is a highly variable process based on the local temperature, weather patterns, manner of death, presence of clothing, and burial conditions. As a cadaver progresses through decomposition the body begins to putrefy. Pressure from the buildup of gases forces cadaveric fluid from natural orifices, ruptures in the skin, and wounds. The cadaveric fluid creates a nutrient rich area underneath and around the cadaver called the cadaver decay island (CDI). Effects of the cadaver decay fluid on the soils underneath and around the body have gained interest as a method for determining the post-mortem interval (PMI) of the cadaver. The postmortem interval is defined as the amount of time that has passed since death at the time of discovery. This study examines the effects of cadaveric fluid on bacterial diversity based on PMI, distance from the cadaver, and location of soil sample around the cadaver. Soil samples were analyzed for changes in bacterial diversity via 16s rRNA sequencing. Results contribute to the ongoing conversation regarding using the changes in the microbiome of the CDI to measure PMIs.

Katherine E. McBroom

kmcbroom19@austincollege.edu

Undergraduate Student

P34. Studying dysregulated gene expression in the frontal cortex of a pig model of Angelman syndrome using single-cell RNA sequencing

Ashley Coffell, Sarah Christian, and Scott Dindot

Interdisciplinary Graduate Program in Genetics and Genomics, Texas A&M University, College Station, TX, USA
Department of Veterinary Pathobiology, Texas A&M University, College Station, TX, USA

Angelman syndrome is a rare neurodevelopmental disorder caused by the loss of the maternal allele of the Ubiquitin-protein ligase E3A (UBE3A) gene. The UBE3A gene is imprinted in a cell type-specific manner: only the maternally inherited allele expressed in central nervous system (CNS) neurons but it is biallelically expressed in all other cells. Genetic or epigenetic loss of the maternally inherited allele leaves neurons without a source of UBE3A and causes the phenotypic characteristics of Angelman syndrome such as developmental delay, speech impairment, and movement disorder. The genes and molecular pathways affected by the loss of UBE3A expression in CNS neurons remain unclear. Since Angelman syndrome neurons are the only cell type with a total lack of UBE3A and the extent to which other cell types are affected is unclear, the greatest knowledge can be gleaned with the application of technology with single-cell resolution. Here, we describe the use of single-cell RNA sequencing to analyze cell type-specific gene expression in the frontal cortex of a pig model of Angelman syndrome. Results from this study aim to improve our understanding of how the loss of UBE3A affects brain function and to inform biomarker development for Angelman syndrome therapies.

Ashley Coffell

acoffell@tamu.edu

Graduate Student

P35. Yeast p24 family proteins and CSG2 in relation to *pgm2*Δ phenotypic defects in the secretory pathway

Shruti Veera Raghavan and Dr. David P Aiello

Austin College

In *Saccharomyces cerevisiae*, phosphoglucomutase (PGM) is the key metabolic enzyme that allows the cell to interconvert glucose-1-phosphate (G1P) and glucose-6-phosphate (G6P). Loss of its major isoform encoded by PGM2 presents carbohydrate metabolism defects including a slow growth phenotype and increased G1P:G6P ratio when cells use galactose as the sole carbon source. Additionally, *pgm2*Δ exhibits calcium homeostasis defects including sensitivity to cyclosporine A and increased Ca2+ uptake and accumulation. The mutant has also been shown to have elevated unfolded protein response (UPR) in the endoplasmic reticulum (ER) and is sensitive to UPR inducer dithiothreitol. The p24 family proteins regulate protein trafficking across the early secretory pathway organelles, the ER and Golgi apparatus. Primary literature suggests that the receptor p24A facilitates calcium sensing receptor (CaSR) maturation and stabilisation in the early secretory pathway and p24Δ activates UPR. These findings suggest a link between p24 proteins to UPR and calcium homeostasis and warrant an investigation into the role of p24 family members involved in transport through the secretory pathway. In order to examine whether the Ca2+ and UPR issues of the *pgm2*Δ mutant stem from issues of transport through the secretory pathway, knockouts of p24 family proteins were constructed. Contrary to preliminary data indications, it was found that the loss of select p24 family proteins did not play a significant role in conjunction with *pgm2*Δ. Stress response was considered as an alternative possibility in addressing the Ca2+ and UPR issues in the secretory pathway of the *pgm2*Δ mutant. The *pgm2*Δ strain has been shown through RNA sequencing analysis to activate a multitude of genes involved in a variety of stress responses. CSG2, a gene involved in calcium homeostasis and localised to the secretory pathway, was found to be necessary for yeast growth at high calcium concentrations. The effect of the loss and overexpression of CSG2 on *pgm2*Δ was examined under a variety of different extracellular stress inducers. Preliminary results suggest that the loss of CSG2 makes the slow growth phenotype of *pgm2*Δ on galactose sicker, and overexpression of CSG2 rescues the slow growth phenotype. This study investigates the loss of select p24 family proteins and the loss and overexpression of CSG2 in relation to *pgm2*Δ defects in a variety of stress conditions to understand what is involved in addressing the *pgm2*Δ calcium homeostasis and UPR issues in the secretory pathway.

Shruti Veera Raghavan

sraghavan19@austincollege.edu

Undergraduate Student

P36. Antisense oligonucleotide quantification via splint-ligation and PCR

Thomas Jepp, Sarah Christian, and Scott Dindot

Department of Veterinary Pathology, School of Veterinary Medicine & Biomedical Sciences, Texas A&M University

Angelman syndrome is a neurodevelopmental disorder characterized by developmental delay, movement disorder, speech impairment, and an atypical happy disposition. Antisense oligonucleotides (ASOs) are a promising therapeutic approach being explored to treat this disorder, via termination of the transcription of UBE3A-AS. ASOs are single-stranded oligonucleotide molecules, typically 18-22 nucleotides in length and containing several highly modified bases and bonds. ASOs are designed to be complementary to a target RNA, bind to create an RNA:DNA hybrid, and induce RNA degradation via the RNase H enzyme. To treat Angelman syndrome, they are administered intrathecally into the cerebrospinal fluid, whereupon they diffuse throughout the entire central nervous system (CNS). Because PCR cannot be performed on ASOs, due to their length and modifications, the quantification of ASOs in tissues and biofluids is usually determined by an ELISA assay, which is expensive, labor-intensive, and has a limited dynamic range. Therefore, improved methods to quantify ASO concentrations are needed. Here, we describe a splint-ligation PCR assay to quantify ASO concentration in the CNS of non-human primates. To achieve this, two long oligonucleotide probes are designed so that the ASO will hybridize to the ends of the probes in a manner that holds them together, facilitating their ligation by SplintR ligase. The two probes are then combined with SplintR ligase and tissue lysate of animals dosed with gapmer ASOs, then hybridization and ligation reactions are performed. The ligated probes are then quantified using a TaqMan qPCR assay. Results from this study show that this assay is accurate and sensitive, as well as having a greater dynamic range, cheaper reagents, and using less tissue per sample relative to an ELISA. This will lead to an increase in the volume and quality of pharmacokinetic data that is able to be generated in ASO pre-clinical studies.

Thomas Jepp

tomjepp@tamu.edu

Graduate Student

P37. The role of RNA Polymerase I in lifespan extension of *Caenorhabditis elegans*

Amanda Leonita, Qiuxia Zhao, Elif Sarinay Cenik

Department of Molecular Biosciences, University of Texas at Austin, Austin,

RNA Polymerase I (Pol I) is responsible for the synthesis of pre-ribosomal RNA (rRNA), the first step in ribosome biogenesis. Reducing Pol I activity has been linked to longevity but the downstream mechanisms through which lifespan extension is achieved has yet to be determined. Utilising an auxin-inducible degron tagged *Caenorhabditis elegans*, we were able to specifically reduce Pol I availability globally and tissue specifically. We found that treatment with a mild concentration of auxin to partially reduce Pol I levels globally resulted in a slight development delay and lifespan extension. Interestingly, specific reduction of Pol I in multiple tissues was sufficient to extend lifespan. We are currently testing the hypothesis whether the cell non-autonomous life span extension may be caused by organism-wide inactivation of TORC1 or activation of proteotoxic stress responses.

Amanda Leonita

amandaleonita@utexas.edu

Undergraduate Student

P38. The membrane distal NPxY motif in β integrin cytoplasmic domain plays important role in reproductive behavior

Josh Bumm, Jeancarlo Gutierrez, Arlyn P. Alcid, Soohyun Lee, Julia Mendes, Catherine Ravikumar, Lianzijun Wang, Zhongqiang Qiu, and Myeongwoo Lee

Department of Biology, Baylor University, Waco, Texas 76798, U.S.A.

Cell-matrix interaction is mediated by integrin, a receptor molecule binding to the matrix ligands. Upon binding, the integrin attracts linker proteins such as talin and kindlin to the NPxY motifs in the cytoplasmic domain. The NPxY is a tyrosine phosphorylation site where mutation to alanine (A) generally causes severe phenotypes such as embryonic lethality. In contrast, mutations to phenylalanine (F) show no discernable defects. To analyze the NPxY motif function, the membrane distal NPxY was edited by the CRISPR-Cas9 system. Our analysis revealed that the β integrin/*pat-3*(YY792/804FF) non-phosphorylatable mutant showed wild-type egg laying but retained a high number of unlaid eggs in the uterus. The β integrin/*pat-3*(Y804A) or β integrin/*pat-3*(Y804E) inhibition mutant showed defective egg-laying. In addition, the kindlin/*unc-112*(L715E) mutation displayed the same egg-laying defects as *pat-3*(Y804A) or *pat-3*(Y804E). Our data suggest that the intact NPxY is required for the regulation of vulva contraction via kindlin/UNC-112 while the mutations in the tyrosine appear to inhibit or facilitate the process. Our findings present the egg-laying behavior as an experimental model to study cell adhesion and cell-matrix interaction.

Arlyn Alcid

arle_alcid1@baylor.edu

Undergraduate Student

P39. In vivo genetic analysis of schizophrenia through a novel developmental cell death paradigm

Hannah Selvarathinam, Karen Juanez, Piya Ghose

The University of Texas at Arlington

Schizophrenia is a mental disorder that affects a person's thoughts and actions. Compartmentalized Cell Elimination (CCE) is a novel cell death program, where three compartments of the cells die differently. CCE can be used as a tool to address questions about psychiatric illness. Through a forward genetic screen looking for CCE defects, the endoplasmic reticulum (ER) network stability gene atln-1/atlastin and microtubule (MT) severing ATPase spas-1/spastin, were found to be linked to Hereditary Spastic Paraplegia (HSP). To explore the question of links between developmental cell death and psychiatric illness a schizophrenic behavioral assay was performed on CCE mutants including *ptl-1*, *sel-12*, and *hop-1*. The gene *ced-3*, which is essential for CCE, did not show schizophrenia-like behavior. The *atln-1*/atlastin and *ptl-1*/tau mutants did show schizophrenic tendencies. This suggests novel links between schizophrenia, the ER, tau.

Hannah Selvarathinam

hannah.selvarathinam@uta.edu

Technician

P40. Transgenerational effects of a small RNA mediated feedback loop on the homeostasis of 22G-RNAs levels in *C. elegans*

Ha Meem and Alicia K. Rogers

Department of Biology, University of Texas at Arlington, Arlington, TX 76019, USA.

Endogenous and exogenous RNAi pathways are important regulators of cellular and genetic processes. Homeostatic balancing of these RNAi pathways is important in maintaining the stability of regulation since they share resources for 22G-siRNA biogenesis. RNA helicase ERI-6/7 is required for the synthesis of one class of endogenous 26G-siRNAs, the ERGO-1-class. Disruption in ERI-6/7 function, or the ERGO-1 pathway, causes animals to display enhanced RNAi (Eri) phenotype. The genomic locus encoding eri-6, contains two distinct regions (sensor of siRNA-1 (*sosi-1*) and *eri-6[e-f]*), targeted by 22G-siRNAs, that allow for fine-tuning of 22G-siRNA production from distinct branches of RNAi pathways within the mutator focus by modulating the expression of *eri-6*. Production of ERGO-1-class 26G-siRNAs is disrupted upon loss of 22G-siRNAs targeting *sosi-1* and *eri-6[e-f]*, and in turn the yield of 22G-siRNAs from other classes of small RNA pathways is amplified. The sosi-1 and eri-6*[e-f]* regions are sensitive to changes in 22G-siRNA populations and small RNA-mediated chromatin changes. Indeed, it was previously observed that mutants for the nuclear Argonaute responsible for directing the establishment of repressive chromatin at siRNA-targeted genomic loci, HRDE-1, displayed a 50% decrease in ERI-6/7 activity. This defect could be associated with the function of the sosi-1 and eri-6[e-f] feedback mechanism. RNAi pathways play a major role in maintaining appropriate gene expression in the germline, thus, we are examining the transgenerational effects of disrupting the small RNA-mediated sosi-1 and *eri-6[e-f]* feedback loop to further understand the importance of maintaining proper levels of different classes of siRNAs in physiological processes, such as development and fertility.

Ha Meem

hxm5000@mavs.uta.edu

Graduate Student

P41. ER network stability promotes organized microtubule disassembly during Compartmentalized Cell Elimination

Karen Juanez, Madison Jones, Hannah Selvarathinam, Nathan Rather and Piya Ghose

The University of Texas at Arlington

Programmed cell death is vital for development and homeostasis. Morphologically complex cells are characterized by elaborate processes, such as axons and dendrites in neurons. While complex cells are common, their programmed as well as pathological or injury induced elimination is poorly understood. Microtubule (MT) disassembly is linked to region-specific neurite pruning, but the exact nature of this relationship is unknown. We discovered a 'tripartite' killing program with stereotyped cellular dynamics that eliminates the morphologically complex tail-spike cell (TSC) and the sex-specific CEM neurons in the *C. elegans* embryo. This program, called Compartmentalized Cell Elimination (CCE), is characterized by three cell regions dying in three disparate ways. Notably, the single process/dendrite of these cells displays two very different elimination morphologies in its two segments. The proximal segment fragments in a manner strikingly reminiscent of developmental pruning or injury-induced Wallerian degeneration of axons; whereas the distal segment retracts, much like nutrient-deprived axons. Here we report that MTs have stereotyped dynamics throughout the development and death of the TSC. Through forward genetic screens, we found that genes promoting endoplasmic reticulum (ER) network stability, *atnl-1*/Atlastin and *lnp-1*/Lunapark, which encode the homologs of human Atlastin GTPase and Lunapark, promote process dismantling during CCE. We find that *atnl-1*/Atlastin and *lnp-1*/Lunapark promote the function of the conserved MT-severing ATPase SPAS-1/Spastin in facilitating CCE. Human Atlastin, Lunapark and Spastin are all associated with neurodegenerative conditions. Fluorescent reporters for the ER, SPAS-1/Spastin and MTs dynamically change in distribution as the TSC develops and dies and MTs shows abnormally gross enrichment in the TSC process in ER network stability and SPAS-1/Spastin mutants, suggesting hyperstability of MTs. We propose that the stable ER network and ER network stability proteins anchor SPAS-1/Spastin to allow for precisely targeted and organized MT disassembly, culminating in the highly defined dynamic demise of the TSC process during CCE. Our findings shed new light on the localized elimination of complex cells and illuminate the link between MTs, pruning and neurodegeneration through an unexpected connection with the ER.

Karen Juanez

karen.juanez@uta.edu

Technician

P42. Elucidating the mechanism of MUT-16-dependent regulation that fine tunes the ALG-3/4 pathway to maintain proper spermatogenesis in *C. elegans*

Trilotma Sen and Alicia K. Rogers

Department of Biology, University of Texas at Arlington

In hermaphroditic *C. elegans*, spermatogenesis occurs during the L4 developmental stage, followed by oogenesis during the adult life stage. Gametogenesis is a thermosensitive developmental process, and small RNA pathways have been shown to play a key role in maintaining thermotolerant fertility. Small RNA pathways use Argonaute proteins complexed with primary and secondary small RNAs, termed 26G-RNAs and 22G-RNAs, respectively, to regulate target genes. The ALG-3/4 small RNA pathway is critical for proper spermatogenesis and relies on the Argonautes ALG-3 and ALG-4. We have found the genes encoding ALG-3 and ALG-4 have 91% sequence identity and are both targeted by 22G-RNAs and 26G-RNAs. The populations of small RNAs targeting *alg-3* and *alg-4* are sensitive to heat stress or disruption of mutator complex-dependent 22G-RNA amplification. The combination of heat stress and mutation of *mut-16* results in immediate male sterility and developmental misregulation of spermatogenesis-enriched gene expression. We propose that small RNA-mediated regulation of *alg-3* and *alg-4* acts to control ALG-3/4 pathway function and restrict spermatogenesis gene expression to the L4 developmental stage. We are investigating whether ALG-3 and ALG-4 are autoregulated through 26G-RNAs and aim to understand how this mechanism is thermosensitive. Understanding the molecular mechanisms by which developmental processes are controlled and coordinated is an active area of investigation. This work will shed light on how small RNA regulation maintains sperm development and fertility and be foundational to our understanding of how small RNA pathways maintain robust, homeostatic gene regulation throughout development during stress.

Triltoma Sen

trilotma.sen@uta.edu

Graduate Student

P43. The co-evolution of phylogenomic signal, gene linkage, and recombination rate in placental mammals

Nicole M. Foley, William J. Murphy

Veterinary Integrative Biosciences, Texas A&M University, College Station, TX, USA., Interdisciplinary Graduate Program in Genetics, Texas A&M University, College Station, TX, USA.

An emerging theme in the field of phylogenomics is that individual genomes are a mosaic of evolutionary histories. Whole-genome analyses assume the dominant phylogenomic signal is the species tree. However, numerous studies have shown that in the presence of gene flow and incomplete lineage sorting, the true species tree may be masked from standard phylogenomic analyses. Emerging research in butterflies, cats, wolves, bats, and monkeyflowers have demonstrated that recombination rate is among the most reliable predictors of which genomic sequences best represent the relationships among living species. Until now, recombination-aware phylogenomic analyses have been unfeasible for many lineages due to the lack of phylogenetically spaced, high-quality genome alignments that also have corresponding recombination maps. To address this, we identified 10 non-model mammalian clades, representing all mammalian superorders, which had a chromosome-level genome assembly, whole-genome data for multiple species, and contained a species for which population-level genomic data was available. First, using a sliding-windows phylogenomic approach we interrogated genome-wide variation in phylogenomic signal across all 10 clades. Then, we used machine learning to generate a recombination map for a representative species from all 10 clades. We used a comparative genomics approach to 1) determine if there is a relationship between genomic architecture and recombination in mammals, 2) discern if the X chromosome, which has remained mostly collinear during placental evolution, has a conserved recombination landscape and 3) if recombination-aware phylogenomics can provide unexpected insights into the evolution of diverse mammalian clades. Our analysis across clades revealed that the most frequent topology, assumed to be the species tree by recently published whole-genome analyses, was often not the species tree. Our analysis also provides support for a conserved low recombining desert on the X chromosome in mammals. Notably this region, which is known to harbor loci associated with reproductive isolation, consistent with the large X-effect, was consistently enriched for signal consistent with the species tree. Further analyses are required to characterize this unusual region and determine why it has been conserved over deep evolutionary time.

Nicole Foley

nfoley@cvm.tamu.edu

Postdoc

P44. Mitochondrial transport, endoplasmic reticulum shape, and mitochondria-endoplasmic reticulum contacts regulate Compartmentalized Cell Elimination

Aladin Elkhalil, Rashna Sharmin, Karen Juanez, and Piya Ghose

University of Texas at Arlington

Developmental pruning is a critical facet of brain sculpting. The role of subcellular structures in such localized cell elimination is an open question. We present a novel program of cell death, Compartmentalized Cell Elimination (CCE), we discovered in the nematode *C. elegans* as an in vivo genetic setting to study region-specific cell elimination. CCE is a highly ordered and stereotyped developmental program, observed in two cell types, an epithelial cell and a set of sex-specific sensory neurons. In this program, the cell soma rounds as a simple apoptotic cell; but the single process/dendrite exhibits two pruning-like degeneration morphologies, with the proximal segment beading and fragmenting and the distal segment retracting.

Our forward genetic screens have revealed that two opposing conserved kinesins and the main nematode caspase protease, CED-3, prepare the cell for CCE by transporting and restricting presumably protective mitochondria to the cell soma: mitochondria are found in the process/dendrite early in development but not prior to death. Failure of the function of the retrograde transport motor causes persistence of mitochondria-containing process/dendrite fragments.

In addition, our data support the hypothesis that the endoplasmic reticulum and endoplasmic reticulum shaping proteins position a microtubule-severing ATPase, the homolog of mammalian Spastin, SPAS-1, to allow for the dismantling of microtubules to execute cell death. ER shaping gene and spas-1 mutants have visibly stabilized microtubules and CCE defects such as a persisting process/dendrite.

To test for a possible link between between the endoplasmic reticulum and mitochondria, specifically mitochondrial-endoplasmic reticulum contact sites, and CCE we examined mitochondria in endoplasmic reticulum-shaping gene mutants. Intriguingly, mitochondria appear highly exaggerated, and persisting in the intact cell process/dendrite.

Our next steps include determining if the observed mitochondrial expansion is associated with enhanced biogenesis or fusion dynamics as well as assessing the quality and functionality of these mitochondria and their transport efficiency.

Our study underscores the importance of organellar dynamics in CCE, and by extension pruning, and implicates mitochondria and their association with the endoplasmic reticulum in the prevention of such localized cell elimination.

Aladin Elkhalil

aladin.elkhalil@mavs.uta.edu

Graduate Student

P45. 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 and Tina L. Gumienny

Texas Woman's University, Division of Biology, 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.

Tina L. Gumienny

tgumienny@twu.edu

Faculty

P46. Developing genetic biocontrol tools for suppression of invasive rodents

Ana M. Velasquez and David W. Threadgill

Texas A&M University Department of Cell Biology and Genetics

Islands are home to a disproportionate amount of the world's biodiversity despite covering a small portion of the earth's landmass. Thanks to their commensal relationships with humans, mice have managed to establish populations on even the most remote islands in part due to human exploration. Their predatory tendencies are detrimental to the stability of endemic island populations of both animal and plant species. They are also an important food source to other larger, oftentimes more injurious, invasive species, providing consistent nourishment to these concerning species.

Current population control methods rely on the spread of bait carrying anticoagulant toxicants and trapping. Although these methods have shown success on some islands, they have potential to harm off-target, potentially endangered, species, and have a negative public view as a response to a slow death. Contamination of large areas of land can cause lasting damage preventing safe usage for agricultural purposes. The risk of harm to endemic island populations, as well as geographic and demographic complexity, increases the need for species-specific population control of invasive rodents on islands.

Novel genome editing technologies have led to a boom in research on the potential of genetic biocontrol of undesired traits or species. Current research investigates the use of gene drives, or selfish genetic elements, as a tool for endogenously driven population control. This project aims to generate a species-specific mouse population control tool. We use the mouse t-haplotype, a naturally occurring selfish element in mice, to engineer a mouse that produces disproportionately more male progeny than female progeny (that is, a daughterless mouse).

The t-haplotype comprises the proximal third of Chromosome 17. It achieves biased transmission on heterozygous males by disrupting motility of sperm that do not carry it (it is commonly described as a toxin/antidote system). Although in heterozygous mice, sperm with the t-haplotype show better motility than sperm with the wild type haplotype (+/+), the effects of the toxins cause abnormalities in the morphology and motility of all gametes relative to +/+ mice, potentially reducing fitness of heterozygous mice.

We will introduce biased inheritance of Sry, the male determination gene, by inserting its sequence into the chromosome 17 of a heterozygous t-mouse. Due to the complexity of the Y-chromosome, the specific promoter and enhancer regions of Sry have not been properly identified, for that reason, we look to express Sry using a Sf1 promoter, which has similar expression patterns in the mouse urogenital ridge.

Using a naturally occurring gene drive overcomes the challenge of depending on specific DNA repair pathways for CRISPR-based homing drives, to carry desired genetic modifications into target populations. Rather, it takes advantage of natural genetic processes already existing in mice. If effective, a t-haplotype/Sry heterozygous male mouse will produce over 95% male offspring upon reproduction and serve as a genetic biocontrol tool. Targeted release of these mice in areas where invasive mice reside would be an equally effective and more humane alternative for species-specific eradication with fewer off-target implications than anticoagulant toxicants.

Ana Velasquez

avelasquez1086@tamu.edu

Graduate Student

P47. A novel PPARγ-β-catenin signaling in placenta development, regarding preeclampsia

Yushu Qin1, Naomi McCauley1,†, Zehuan Ding1,†, Lauren Lawless1,3, Zhimin Liu1,2, Ke Zhang1,3, and Linglin Xie1

1. Department of Nutrition and Food Science, Texas A&M University, College Station, TX, 77840, USA
2. Department of Colorectal Surgery, The Sixth Affiliated Hospital of Sun Yat-sen University (Gastrointestinal and Anal Hospital of Sun Yat-sen Unversity), Guangzhou 510655, China
3. Center for Epigenetics & Disease Prevention, Institute of Biosciences & Technology, Texas A&M University, Houston, TX

Abnormal placenta development has been recognized in pre-eclampsia (PE) and gestational diabetes (GDM), which are both leading causes of maternal death during pregnancy. GDM is recognized as a risk factor for PE. Peroxisome proliferator-activated receptor γ (PPARγ) is a ligand-dependent transcription factor, strongly expressed in both human and mouse placentas. In placentas from our GDM mouse model, we observed an impaired migration ability of spiral artery-associated trophoblast giant cells (SpA-TGCs) with a decreased expression of PPARγ. To further explore the function of PPARγ in placenta development, we utilized a PPARγ+/- mice model, which replicates human PPARγ insufficiency. In the PPARγ+/- pregnant mice, defective SpA remodeling is observed, accompanied by elevated blood pressure during mid-gestation, which resolved after delivery. Importantly, PE-like symptoms (elevated BP and proteinuria) were noted in the PPARγ+/- pregnant mice under hyperglycemia. Interestingly, SpA-TGCs progenitor-specific knockdown of PPARγ did not develop elevated BP. To understand the molecular mechanism that leads to defective SpA remodeling, we performed Mass-Spec Pull-down Analysis using anti-PPARγ and identified potential interaction with β-catenin. β-catenin maintains intercellular tight junctions in forming the membranous E-cadherin/β-catenin complex and facilitates the transcription of migratory genes of Wnt signaling when translocated to the nucleus. Insufficient PPARγ in the placenta repressed β-catenin translocation and degradation resulting in the retention of β-catenin in the cytoplasm. Increased membrane-bound β-catenin indicated a stronger formation of the E-cadherin/β-catenin complex which enhanced cell-cell adhesion, while less nuclear translocation of β-catenin supports the reduced expression of migratory genes. In summary, the study disclosed the role of PPAγ in the SpA remodeling, contributing to the etiology of elevated blood pressure in pregnancy.

Yushu Qin

yushu@tamu.edu

Graduate Student

P48. Winning against unbalanced datasets in a machine learning de novo genes prediction algorithm in angiosperms

Adekola Owoyemi, Alan Pepper, Thomas Ioerger, and Claudio Casola

Department of Ecology and Conservation Biology, Department of Biology, Interdisciplinary Doctoral Degree Program in Ecology and Evolutionary Biology, Department of Computer Science and Engineering, Interdisciplinary Graduate Program in Genetics and Genomics, Texas A&M University, College Station

De-novo genes (DNGs) are a subset of novel protein-coding or RNA genes that have been defined as evolved from DNA sequences which were previously non-coding. Recent studies have shown that DNGs form a substantial fraction of novel genes in eukaryotes, particularly in flowering plants. The identification of de-novo genes is typically based on comparative genomic homology and syntenic searches. As these approaches tend to be computational and time intensive, large-scale surveys of DNGs have not been performed. Thus, our understanding of de novo gene birth processes and their phenotypic impacts remains largely centered around a few model organisms. Machine learning algorithms (MLAs) have proven useful in accelerating discovery in several areas of genomics, but its potential in identifying DNGs has not been explored. In a previous analysis, we have shown that both decision tree (DT) and neural network (NN) models perform well in identifying species-specific DNGs in gene set analyses of the angiosperms *Arabidopsis thaliana*, *Brassica rapa* and *Oryza sativa*. However, these models generated a high number of false positives. Here, we sought to both explore novel MLA methods and develop strategies to reduce the number of false positives in plant DNGs identification surveys. To this aim, we trained and tested the additional MLAs, including random forest (RF), light gradient boost machine (LGBM), and naive bayes (NB). To facilitate the discovery of DNGs in species with limited functional genomic data, our dataset included only DNA and protein sequence features that can be easily obtained from genome and gene annotation data. Because DNGs represent a minority of all genes in a genome, gene datasets are inherently unbalanced. To tackle this issue, we created a new dataset with equal minority and majority classes using different synthetic minority over-sampling (SMOTE) algorithms including SMOTE, SMOTE-Tomek, SMOTE-ENN, BorderlineSMOTE (1 and 2), and SMOTE-NC. Although techniques for additional data synthesis vary among SMOTE algorithms, they typically involve synthetizing k-random neighbors for randomly selected datapoints. All MLA shared accuracy and recall scores above 90% without SMOTE resampling. LGBM classifier had the best performance (accuracy, recall and F1 scores all above 95%). However, precision rates remained consistently below 90% across MLAs. We found that some combinations of SMOTE resampling methods and MLAs significantly lower the number of false positives and improved precision scores with recall remaining above 80%. Importantly, RF had precision scores above 97% when used with SMOTE-Tomek or SMOTE-NC and recall scores of 81.8% and 86.4%, respectively. Precision and recall scores were also high in LGBM-SMOTE-ENN ensemble (96.1% and 89.1% respectively), NN-SMOTE-ENN ensemble (94.5% and 94.5% respectively) and NN-SMOTE-NC ensemble (95.1% and 88.2% respectively). Thus, RF-SMOTE-Tomek, RF-SMOTE-NC, LGBM-SMOTE-ENN, NN-SMOTE-ENN or NN-SMOTE-NC combination represents a substantial improvement in the application of MLAs to the discovery of DNGs and could be candidate ensemble approaches for DNG annotation surveys in angiosperms based on readily available genome and protein features.

Adekola O. Owoyemi

ludtson@tamu.edu

Graduate Student

P49. Identifying candidate genetic mechanisms and modifier genes underlying genetic context-dependent colorectal cancer progression in the absence of ERBB3

Kaitlyn Carter, Michael P. McGill, and David W. Threadgill

Interdisciplinary Graduate Program in Genetics and Genomics, Department of Cell Biology and Genetics

Erbb3 was investigated as a potential therapeutic target for colorectal cancer after epithelial-specific ablation in the ApcMin/+ mouse model showed reduced to absent tumor growth in comparison to control mice. Due to these findings, pharmaceutical companies developed an EGFR/ERBB3 dual inhibitor and a pan-ERBB inhibitor as therapy for patients diagnosed with colorectal cancer. Patients treated with the inhibitors experienced phenotypes that ranged from reduced to accelerated tumorigenesis and a wide variation in tumor size. It was shown in one clinical trial that those treated with the pan-ERBB inhibitor experienced a decrease in survival time compared to the placebo group. Often, pre-clinical studies are performed and do not consider the heterogeneity in genetic background of their study participants. Upon the findings of this clinical trial, additional work was completed in two different mouse genetic backgrounds to determine if there was a genetic background-dependent effect upon ablation of ERBB3. In the C57BL/6J background, loss of ERBB3 led to increased tumor count and size while the 129S1 background experienced reduced tumor counts and size. The F1 generation of this cross led to an intermediate tumor count and growth phenotype. It was confirmed through further work that loss of ERBB3 saw a positive correlation between polyp number and epidermal growth factor receptor (EGFR) expression. Deletion of EGFR confirmed that the increase in polyp number that we see upon loss of ERBB3 in the C57BL/6J background is mediated by EGFR. These findings show that tumor growth is genetic background dependent in terms of ERBB3 ablation.

This project will use an innovative breeding scheme to determine the background-dependent effect of ERBB3 ablation on colorectal cancer. Using this breeding scheme, I will identify the candidate genetic mechanisms and underlying modifier genes/polymorphisms that lead to background-dependent tumorigenesis during loss of ERBB3 in colorectal cancer.

The first component of this project will be to generate a breeding scheme using the C57BL/6J background, which resulted in increased tumorigenesis upon loss of ERBB3, and the 129S1/SvImJ background, which leads to a significant reduction in tumorigenesis. The result of this cross with be B6129F1 mice that represent the intermediate tumor growth and count phenotype. Mice from the F2 population with the genotype Erbb3flox/flox, Apc Min/+ ,Tg(Vil1-Cre+/-) will be necropsied at 100 days, where we will record tumor count in the colon, small intestine, and measure tumor size. We anticipate based on previous findings that mice with the highest tumor count will have the B6 alleles that are driving increased tumorigenesis and mice with the lowest tumor count will have the 129 alleles that are driving reduced tumorigenesis.

To that end, we will leverage these results and an innovative breeding strategy to identify modifier genes/polymorphisms that predict disease severity in the context of Erbb3 ablation. In this way, modifier alleles/polymorphisms could serve as a proof of concept of the power of genetics to predict response to therapy and allow us to further our knowledge of precision medicine when it comes to colorectal cancer treatment and prevention.

Kaitlyn Carter

kcarter2017@tamu.edu

Graduate Student

Visiting Austin!

Scan the QR code for Austin attractions

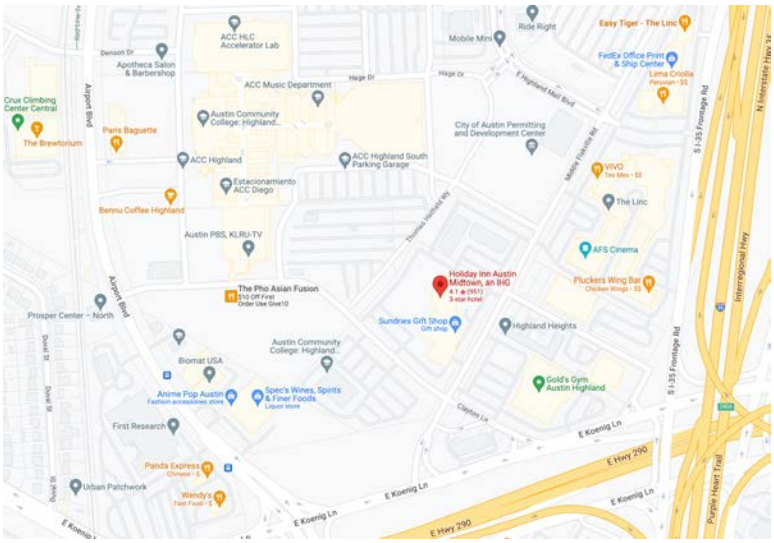
Restaurants within safe walking distance:

Feng Cha Highland
609 Highland Ln.
11 AM–9 PM
Boba tea and foam cakes

Bennu Coffee Highland
109 Jacob Fontaine Ln suite 600
open 24 hours
Relaxed 24-hour coffee house serving sustainable, fair trade coffee, and locally sourced food

Paris Baguette
110 Jacob Fontaine Ln
7 AM–9 PM
South Korean bakery chain known for its Korean and French baked goods — fruit and cream-filled brioches, mochi doughnuts, red bean buns, croissants, tarts,and so much more. Cakes are available by the slice or whole, as well as different types of bread, sandwiches, wraps, and salads. Drinks include hot and iced coffee and espresso beverages, matchas, teas, and hot chocolates.

The Pho Asian Fusion
609 Clayton Lane Suite 100
10 AM–9 PM
Vietnamese/Chinese fusion



Restaurants within a 10-minute drive:

Easy Tiger Bake Shop & Beer Garden (Linc) (~ 2-minute drive)
7 AM–10:30 PM (9:30 PM Thursday)
6406 N IH 35, Ste. 1100
Artisan bread bakery, locally-roasted coffee, housemade meats, full bar, craft beers; centrally located; huge patio.

The Brewtorium (~ 3-minute drive)
6015 Dillard Circle, Ste. A
12 PM–11 PM (4 PM–10 PM Thursday)

The Brewtorium is a locally-owned brewpub featuring award-winning house-brewed beer, modern pub cuisine, wine, cider, mead and great times for all.
LGBTQ+ friendly, identifies as women-owned.

Habesha Ethiopian restaurant and bar (~ 3-minute drive)
6019 N Interstate Hwy 35
11 AM–9 PM

Ethiopian fare served family-style, with injera instead of utensils, against a modern backdrop.

East Side Pies (~ 3-minute drive)
5312 Airport Blvd
10 AM–10 PM (10 AM–9 PM Thursday)

Hopping pizza outpost offering offbeat toppings, plus Chicago-style & gluten-free pies. LGBTQ+ friendly.

Jewboy Burgers (~ 3-minute drive)
5111 Airport Blvd
11 AM–10 PM (11 AM–9 PM Thursday)

Combine a traditional (reform) Jewish upbringing with the El Paso border and you have JewBoy Burgers. Burgers, burritos, cerveza and chutzpah. With a large patio, covered outdoor seating, additional outdoor tables.

Stiles Switch BBQ & Brew (~ 5-minute drive)
6610 N. Lamar
11 AM–8 PM

Austin's original, Stiles Switch BBQ & Brew.
Specializing in slow smoked meats and cold craft beer.

Black Star Co-op Pub & Brewery (~ 6-minute drive)
7020 Easy Wind Dr., Suite 100
11 AM–11 PM (12–10 PM Thursday)

The world’s first cooperatively owned and worker self-managed brewpub with pet-friendly patio. Serving Texas pub fare and unique house-brewed beers as well as guest drafts and bottles. Become a member-owner today and waltz in like you own the place.

Uchiko (~ 8-minute drive)
4200 N. Lamar Blvd.
4–11 PM (4–10 PM Thursday)

Chef and owner Tyson Cole presents offerings fresh from farm and sea inspired by Japanese farmhouse cuisine.

Fonda San Miguel (~ 8-minute drive)
2330 W. North Loop Blvd.
5–10:30 PM (5–9:30 PM Thursday)

Founded in 1975, Fonda San Miguel was the first restaurant in Texas to focus exclusively on true regional Mexican cuisine from Mexico's interior culinary epicenters: Oaxaca, Puebla, Veracruz and Yucatan. The restaurant also features Gilliland's carefully curated collection of museum-quality artwork, exotic plants and international décor, garnering national and international acclaim. Two cookbooks and more than forty years later, Fonda San Miguel continues to explore the authentic tastes and developing trends of Mexico.