LSU

LOUISIANA STATE UNIVERSITY

INAUGURAL

# International Symposium on Epigenetic Inheritance

Mechanisms • Environments • Generations

*Mechanisms and Consequences of Epigenetic Inheritance Across Generations*

JULY 15–17, 2026

BATON ROUGE, LOUISIANA, USA

THE COOK HOTEL & CONFERENCE CENTER AT LSU

3848 WEST LAKESHORE DRIVE

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PROVOST'S FUND FOR INNOVATION IN RESEARCH

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Learn more and register: **lsu.edu/epi2026**

# *EVENT INFORMATION*

## WiFi:

LSUAlumni-Event
User ID: Geaux
Password: Tigers!

## Venue:

The Lod Cook Hotel and Conference Center
3848 West Lakeshore Drive
Baton Rouge, Louisiana 70808

(225) 383-2665
www.thecookhotel.com

## Transportation:

Uber/Lyft

LSU Tiger Trails Bus System

Yellow Cab Taxi Service
(225) 926-6400

## Emergencies:

To contact LSU Campus Police, dial (225) 578-3231

# WELCOME


Dear colleagues, students, and friends,

It is my great pleasure to welcome you to the inaugural International Epigenetics Symposium at Louisiana State University.

This symposium aims to establish a North American sister meeting to the biennial International Symposium on Epigenetic Inheritance founded by Isabelle Mansuy at ETH Zurich in 2017. Held in alternating years, the Baton Rouge meeting is intended to complement the Zurich symposium, strengthen continuity across the international epigenetics community, and provide an additional forum for scientific exchange on this rapidly evolving field.

Our goal is not only to present exciting new discoveries but also to foster thoughtful discussion, refine conceptual frameworks, and promote rigorous, mechanistic understanding of epigenetic inheritance and transgenerational biology. The scientific program spans molecular, cellular, developmental, behavioral, physiological, and evolutionary perspectives on how environmental exposures and life experiences shape phenotypes across generations in both animal models and humans.

The symposium features keynote and invited lectures by internationally recognized leaders in the field, short presentations by early-career investigators, poster sessions showcasing outstanding trainee research, and ample opportunities for scientific discussion and collaboration. To recognize excellence in trainee research, Best Poster Awards will be presented during the meeting.

As organizers, we are particularly committed to supporting the next generation of scientists and fostering interactions that lead to new collaborations across disciplines, institutions, and countries. We hope this inaugural meeting will become a lasting international tradition that advances scientific rigor, conceptual innovation, and global cooperation in epigenetics research.

This symposium has been made possible through the generous support of the LSU Provost's Fund – Big Ideas in Research initiative. We are sincerely grateful for this support, which has enabled us to bring together an outstanding group of international speakers and participants for this inaugural meeting.

I hope you will find the symposium scientifically stimulating, intellectually rewarding, and personally enjoyable. Thank you for joining us and for helping establish what we hope will become a long-standing tradition of international collaboration and excellence in epigenetics research.

On behalf of the organizing committee, I wish you a productive, inspiring, and memorable symposium.

**Alexander Murashov**
Professor and Head,
Department of Comparative Biomedical Sciences
LSU School of Veterinary Medicine
Louisiana State University

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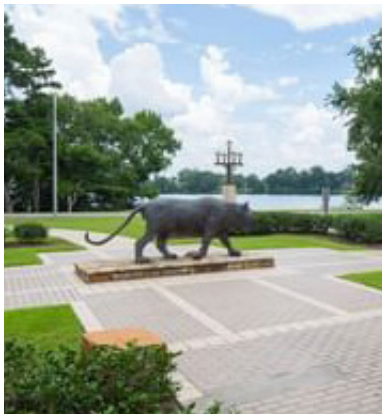
# VENUE

THE COOK HOTEL
and Conference Center at LSU


The Cook Hotel and Conference Center at LSU is a boutique hotel experience on the edge of the LSU campus. Located in the heart of Baton Rouge on the scenic University Lake, the Cook Hotel and Conference Center is Baton Rouge's only independently owned and operated hotel and conference center and the only one wholly owned and operated by an alumni association.

The hotel and conference center opened in 2001 and was funded entirely by private donations. LSU alumnus and benefactor Lod Cook made the lead gift for both the conference center which was opened in 1994 (Lod Cook Alumni Center) and the hotel.

Distinguished guests, including former United States Presidents Gerald Ford, Jimmy Carter, and George H.W. Bush, were in attendance at the dedication of the conference center. In 2001 President George H.W. Bush returned for the dedication of The Cook Hotel.



# PROGRAM

| | | |
|---|---|---|
| **Tuesday, July 14** | **Arrival** | |
| 19:00 - 21:00 | Welcome reception and registration | Conference WIFI: LSUAlumni-Event<br><br>User ID: Tigers<br><br>Password:Tigers |
| **Wednesday, July 15** | | |
| 6:00 | Breakfast buffet at Cook Hotel | |
| 6:30 - 7:30 | Sunrise Yoga | Mats provided out by front fountain (please register on events page) |
| 7:30 - 8:30 | Conference Registration starts | |
| 8:30 - 8:40 | Introduction | |
| 8:40 - 9:20 | Plenary Lecture: Understanding the "sperm RNA code" and epigenetic inheritance with emerging tools | Qi Chen |
| 9:20 - 9:50 | Sperm RNA-mediated intergenerational epigenetic inheritance. | Upasna Sharma |
| 9:50 - 10:20 | Coffee break | |
| 10:20 - 10:50 | Transgenerational Inheritance of Epigenetic Memory in Mammals | Yuta Takahashi |
| 10:50 - 11:20 | Epigenetic Programming in Sperm: Mechanisms of Fertility and Disease Transmission | Sarah Kimmins |
| 11:20 - 11:40 | 2 Early Career Talks (10 min) | Neel Aluru, Humairia Gowher |
| 11:40 - 13:10 | Lunch break | |
| 13:10 - 13:50 | Plenary Lecture: Environmental toxins impact on germline epigenetics (online) | Michael Skinner |
| 13:50 - 14:20 | Sperm RNAs, placentation and fetal growth | Sonia de Assis |
| 14:20 - 14:50 | The Key Role of Placental miRNA in the Crosstalk Driving Fetal Fat Accrual | Perrie O'Tierney-Ginn |
| 14:50 - 15:20 | 3 Flash Talks | Rebecca Robker, Gabriel Peterman (5 Min), Rashmi Joshi (5 Min), Hongbing Liu |
| 15:20 - 16:50 | Coffee and Poster Session | Wed Poster Session participants |
| 18:00 - 21:00 | Dinner | |
| 19:30 | Tour of Tiger Stadium | Please register on the events page |
| **Thursday, July 16** | | |
| 6:00 | Breakfast at Hotel | |

| | | |
|---|---|---|
| 6:30-7:30 | Sunrise Yoga | Mats provided please sign up on website |
| 8:00 - 8:20 | Registration | |
| 8:20 - 8:30 | Provost Welcome | Stephania Cormier |
| 8:30 - 9:20 | Keynote Lecture: How life experiences can influence us and our descendants: An epigenetic perspective | Isabelle Mansuy |
| 9:20 - 9:50 | Investigating the Metabolic Initiation of Transgenerational Epigenetic Inheritance | Patrick Allard |
| 9:50 - 10:20 | Coffee break | |
| 10:20 - 11:00 | Effects of maltreatment during infancy on RNA signatures in rhesus macaques – lessons from EVs | Brian Dias |
| 11:00 - 11:30 | LBRN Lecture: Role of Ribosome Heterogeneity in Epigenetic Inheritance | Eric Greer |
| 11:30 - 12:00 | 3 Early Career Talks (10 minutes) | Megahli Joshi, Alexandre Champroux, Shallinie Thangadurai |
| 12:00 - 13:30 | Lunch break and vendor show | |
| 13:30 - 14:00 | Paternal Epigenetic Inheritance as a Determinant of Metabolic Disease Susceptibility | Valérie Grandjean |
| 14:00 - 14:30 | The Intergenerational Impact of Paternal Pre-Conceptional Health (online) | Rafffaele Teperino |
| 14:30 - 16:00 | Coffee and Poster Session II | Thursday Poster session participants |
| 16:00 - 16:30 | How epigenetic processes enhance natural selection by exposing hidden genetic variation | Benjamin Oldroyd |
| 16:30 - 17:10 | Plenary Lecture: Nongenetic inheritance in evolution and everyday life (online) | Russell Bonduriansky |
| 18:00 - 21:00 | Dinner | |
| 19:15 | Tiger Talk at the Tiger Habitat: LSU is home to the only live tiger mascot in the United States, and he resides on the LSU campus. His care is provided by LSU Vet Med, and Ginger will speak about the history of the live mascot program and how LSU Vet Med provides his care. | Ginger Guttner - sign up on events website |
| **Friday, July 17** | | |
| 6:00 | Breakfast buffet at Cook Hotel | |
| 8:00 - 8:20 | Registration | |
| 8:30 - 9:20 | Keynote Lecture | Eric Miska |
| 9:20 - 9:50 | Diet, Sperm, and Epigenetic Transmission: Mechanisms of Paternal Influence (online) | Anita Ost |
| 9:50 - 10:20 | Intergenerational regulation of brain energy metabolism driven by parental dietary and exercise exposures | Alexander Murashov |
| 10:20 - 10:40 | Coffee break | |

# PROGRAM

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|---|---|---|
| 10:40 - 11:10 | The sins of the fathers: Intergenerational effects of paternal stimulants | Chris Pierce |
| 11:10 - 11:40 | Inter- and Transgenerational Consequences of Adolescent Opioid Exposure on Reward and Addiction Vulnerability | Fair Vassoler |
| 11:40 - 12:10 | Paternal drinking and the epigenetic influences on offspring mitochondrial function, placental health, structural birth defects, and age-related disease | Michael Golding |
| 12:10 - 12:55 | Lunch break | |
| 12:55 - 1305 | Flash Talk | Surjyadipta Bhattacharjee |
| 13:05 - 13:45 | Elovanoid-Mediated Epigenomic Modulation of Mitochondrial Functions and Homeostatic Synaptic Plasticity in Alzheimer's Disease | Nicolas Bazan |
| 13:45 - 14:00 | Awards and Closing | |
| 14:00 - 14:20 | Coffee break | |
| 14:20 - 15:20 | Strategic Forum - Roundtable 1: Toward Mechanistic Resolution of Transgenerational Inheritance | Isabelle Mansuy, Sarah Kimmins, Qi Chen |
| 15:20 - 15:40 | Coffee break | |
| 15:40 - 16:40 | Strategic Forum - Roundtable 2: Building the Next Phase of the Field | Eric Miska, Benjamin Oldroyd, Patrick Allard, Brian Dias |
| 18:30  21:00 | Dinner and Live Music at the Faculty Club | Bus transportation starts Register (additional charge) on website |
| **Saturday, July 18** | **Departure** | |

# MODERATORS

**Wednesday**
Morning: Chris Axelrod, Analisa Taylor, Ph.D.
Afternoon: Alexandra Noel, Ph.D., Anusha Zaman

**Thursday**
Morning: Upasna Sharma, Ph.D., Hafsa Haq
Afternoon: Sonia de Assis, Ph.D., Tolulope Olaolorun

**Friday**
Morning: Shallinie, Ph.D., Shilpa Prakala, Ph.D.
Afternoon: Shallinie, Ph.D., Ugochi Emelogu

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LSU Vet Med is hosting the
2026 Epigenetic Inheritance
Symposium in Baton Rouge,
Louisiana, from July 15-17.
Coffee break
sponsored by Ellis Bio!

# SPONSORS

# POSTER ABSTRACT LIST

| # | Session | Poster# | Name (First) | Name (Last) | Title | Affiliation |
|---|---|---|---|---|---|---|
| 1 | Faculty | 1 | Neel | Alura | Differential DNA Methylation Landscapes in Zebrafish *dnmt3aa* and *dnmt3ab* Mutants | Woods Hole Oceanographic Institute |
| 2 | | 2 | Ethan | Anderson | Inhibiting the histone methyltransferase G9a reduces escalated alcohol drinking in a novel model of alcohol dependence | LSU CBS |
| 3 | | 3 | Surjyadipta | Bhattacharjee | Cell-Specific epigenomic reprogramming of the midbrain periaqueductal gray (PAG) pain neuronal circuit by a novel, non-opioid, non-hepatotoxic analgesic. | LSUHSC NOLA |
| 4 | | 4 | Humaira | Growher | Regulation of DNMT Activity in Development and Disease | Purdue Univ |
| 5 | | 5 | Hongbing | Liu | Hdac1/2 and Ezh2 cooperate to preserve nephrogenesis by restraining β-catenin signaling | Tulane Univ |
| 6 | | 6 | Rebecca | Robker | Perfluoroalkyl and polyfluoroalkyl substances (PFAS) in trace levels via drinking water diminishes mouse embryo mitochondria function across three generations | Adelaide Univ |
| 7 | | 7 | Sarah | Swinford-Jackson | Paternal high fat diet consumption increases susceptibility to drugs of abuse in rat offspring | TAMU |
| 8 | | 8 | Kristie | Willett | Using zebrafish to investigate sex-dependent, epigenetic, and multigenerational adverse outcomes following parental benzo[a]pyrene exposure | Univ of MS |
| 9 | Post Doc | 9 | Ananya | Anmangandla | Dysregulation of the RNA modification m6A promotes cancer progression and provides therapeutic opportunities | Alida Biosciences |
| | | 10 | Amy | Ogle | From Preconception Health to Developmental and Epigenetic Programming Addressing Translational Gaps in Early Reproductive Health Engagement | Preconception Ed Partnership |
| 10 | | P1 | Alexandre | Champroux | Epigenetic Inheritance of Effects of Trauma | Tufts Univ |
| 11 | | P2 | Meghali | Joshi | Chemotherapy-Induced Sperm RNAs Disrupt Embryogenesis and Underlie Reproductive Outcomes in a Pre-Clinical Model of Childhood Cancer Survivors | Georgetown Univ |
| 12 | | P3 | Rashmi | Joshi | Germline influences of paternal high fat high sugar consumption | USC/Children's Hopsital |
| 13 | | P4 | Paulina | Misztak | A Novel Model to Study Epigenetic Transgenerational Inheritance of Alcohol-Related Phenotypes | |
| 14 | | P5 | Russell | Morales | Exosomal miRNAs Released by Alveolar Type II Cells after Exposure to Environmentally Persistent Free Radicals Regulate Nitric Oxide Release from Lung Endothelial Cells | LSU CBS |
| 16 | | P6 | Duane | Pereira | Environmentally-Induced Sperm RNAs Shape Placentation and Fetal Growth | Georgetown Univ |
| 17 | | P7 | Martha | Schwall | Targeting the Epigenetic Regulator G9a Reduces Heroin Seeking | LSU CBS |
| 18 | | P8 | Shallinie | Thangadurai | Sperm-Derived miR-277-3p Is a Candidate Mediator of Paternal Western Diet-Induced Epigenetic Inheritance During the Maternal-to-Zygotic Transition | LSU CBS |
| 19 | | P9 | Shilpa | Thota | Epigenetic Regulation of Treg and Inflammatory Pathways by E-Cigarette Exposure During Pregnancy is Modulated by IL-10 Deficiency in the Lung | LSU CBS |
| 20 | | P10 | Analisa | Taylor | Skeletal Muscle MIRO1 Deletion Protects Against Diet-Induced Hepatic Fibrosis Through Inter-Organ Crosstalk and Epigenetic Remodeling | PBRC |
| | Graduate Student | G1 | Gabriel | Peterman | Neurocognitive Gene Expression in the Brain Tissue of Pediatric Methotrexate Patients and *in vitro* Dopaminergic Neurons | LSUHSC NOLA |
| 22 | | G3 | Angel | Casillo | Exploring the Role of UNC0642 in Mitigating the Developmental Impacts of BPA on Stress Behavioral Responses | LSU CBS |
| 23 | | G4 | Kelly | Estilette | A One Health Systems Framework for Integrating Transgenerational Epigenomic Signals Across Environmental Exposure Pathways | Tulane Univ |
| 24 | | G5 | Joshua | Gill | Uncovering Mechanisms of Increased Healthy Aging in Dietary-Restricted *C. elegans* | LSU Bio Sciences |
| 25 | | G6 | Hafsa | Haq | Paternal Diet-Induced Epigenetic Modulation of Huntingtin-Associated Pathways in *Drosophila melanogaster* | LSU CBS |
| 26 | | G7 | Hannah | Holmberg | Regulation of DNA Damage Response by SPT6 | LSU CBS |
| 27 | | G8 | Md Imran | Hossain | Regulation of Dynein-Dependent HSV-1 Virion Retrograde Transport by Viral and Cellular Kinases | LSU PBS |
| 28 | | G9 | Caiden | Ingram | IL-10 Deficiency Improves Lung Function In Female Offspring Prenatally Exposed to E-cigarette Aerosols | LSU CBS |
| 29 | | G10 | Cheng | Lu | Spn1 represses the Transcription-coupled Nucleotide Excision Repair | LSU CBS |
| 30 | | G11 | Shahrzadossadat | Mirhosseini | In Vitro Testing of Histone Methyltransferase Activity for Future Drug Discovery | LSU CBS |
| 31 | | G12 | Tolulope | Olaolorun | Paternal Western Diet Reprograms Offspring Brain Mitochondrial Bioenergetics in *Drosophila melanogaster* | LSU CBS |
| 32 | | G13 | Lina | Shi | A Conserved Enhancer Cluster Regulates *efnb2* Expression in the Vertebrate Dorsal Retina | LSU Bio Sciences |
| 33 | | G14 | Lindsey | Yoo | KAT8 Associates with WDR5 in Adipocytes and Loss of KAT8 Implicates NSL Complex Activity in Adipose Metabolism | LSU Bio Sciences/PBRC |
| 34 | | G15 | Anusha | Zaman | Prenatal Exposure to E-Cigarette Humectants Alters Placental Methylation Status Correlating with Lung Dysfunction in a Juvenile Mouse Model of House Dust Mite-Induced Asthma | LSU CBS |
| 35 | UG Student | U1 | David | Nguyen | Uncovering the Role of the Aargonaute *rde-1* in the Regulation of Lifespan and Autophagy in *C. elegans* | LSU Bio Sciences |
| 36 | | U2 | Aldrich | Wilberg | Class III PI3K Complex I: a Potential Target for Modulating Autophagy in *C. elegans* | LSU Bio Sciences |
| | | U3 | Laura | Beaubrun | Nicotine Downregulates the Histone Methyltransferase G9a mRNA in the Brain | LSU CBS |

**Dr. Patrick Allard** is a Professor in the Division of Life Sciences at UCLA. Dr. Allard received his BSc from University of Toulouse, France, and his MSc in Biology of Aging from University of Paris. He then completed his PhD degree in Biology from McGill University, Canada, and his postdoctoral fellowship position in the Department of Genetics at Harvard Medical School, before joining UCLA as Faculty in 2012.

Dr Allard's work resides at the intersection of genetics, epigenetics, developmental biology and environmental health. Specifically, his laboratory leverages the tractability of model organisms and stem cell-based approaches to examine the transgenerational reproductive and neurobehavioral impairments following exposure to environmental toxicants. His research has been published in several high-profile journals including Proceedings of the National Academy of Sciences (PNAS), PLOS Genetics, Cell Reports, and Environmental Health Perspectives. Dr Allard has received multiple awards and grants including a Fulbright and a Burroughs Wellcome Innovations in Regulatory Science Award and funding from NIEHS, NIAAA, and the Templeton foundation. The Allard laboratory website can be visited at: https://www.theallardlabatucla.org/

**Dr. Nicolas G. Bazan** has been called "a true Renaissance man." He is an innovative research scientist, inspiring teacher, effective mentor, generous community leader, creative author, screenplay co-writer/executive movie producer, patron of the arts, imaginative entrepreneur, and transformative influencer of knowledge-based economy.

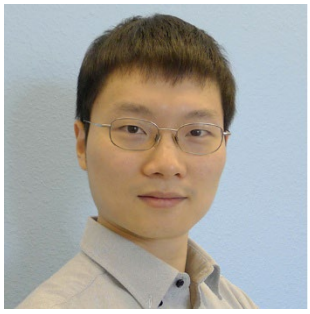
He is the inaugural founder of the Ernest C. and Yvette C. Villere Chair for Research in Retinal Degeneration, the founding Director of the Neuroscience Center of Excellence at the Louisiana State University Health New Orleans' School of Medicine, and has been appointed to the highest academic rank in the LSU System—a Boyd Professor. He also served as a Foreign Adjunct Professor of Neuroscience at the Karolinska Institutet, Stockholm, Sweden (2017-2023).

Dr. Bazan received his MD from the University of Tucuman, Argentina. Then, he trained at Columbia University P&S, New York, and at the Department of Biological Chemistry at Harvard Medical School. At the age of twenty-six, he was appointed Assistant Professor of Biochemistry at the University of Toronto, Canada, and Assistant Director of the Department of Neurochemistry at the Clarke Institute of Psychiatry. He then founded a research institute, a new Biology academic unit, and Master of Science and doctoral graduate programs in Biochemistry in Argentina (1970-1981).

In 1981, he moved to New Orleans. He was the founding Editor-in-Chief of Springer Nature's *Molecular Neurobiology* journal. He was also a founding Senate Member of the Deutsches Zentrum fu¨r

Neurodegenerative Erkrankungen (DZNE) in der Helmholtz-Gemeinschaft for the neurodegenerative diseases research program (2009-2016) in Germany. He was elected President of the American Society for Neurochemistry (1991-2001), and then he was the Elected Chairman on the Board of Governors for the Association for Research in Vision and Ophthalmology (ARVO Foundation) (2011-2014).

**Online) Dr. Russell Bonduriansky** is a professor of evolutionary ecology at the University of New South Wales in Sydney. While carrying out his PhD research at the University of Toronto, he became fascinated with the power of developmental plasticity to shape reproductive and life history traits. This in turn led him to ask whether environmental variation can be transmitted across generations and, if so, what such nongenetic mechanisms of inheritance mean for our understanding of how evolution works. The role of environment in influencing development and fitness, both within and across generations, has been a long-term focus of his lab's research. Alongside his empirical work with insects and other invertebrates, Bonduriansky has been involved in developing new theory on the evolutionary role of nongenetic inheritance in collaboration mathematical biologist Troy Day. Bonduriansky and Day synthesized an emerging model of evolution that incorporates both genetic and nongenetic inheritance in their book monograph Extended Heredity: A New Understanding of Inheritance and Evolution, published in 2018 by Princeton University Press.



**Dr. Qi Chen**, Associate Professor at University of Utah School of Medicine, was trained as a reproductive and developmental biologist, specializes in the study of spermatogenesis, sperm behavior, embryo development, and implantation, primarily using mouse models. His research extends beyond the conventional focus on DNA to explore how small RNAs and RNA modifications in sperm carry hereditary information. Dr. Chen's team has identified a 'sperm RNA code' that transmits paternally acquired traits, like metabolic disorders, to offspring by influencing early embryonic development. His ongoing research aims to understand how specific types of small RNAs in sperm—known as tRNA-derived small RNAs (tsRNAs) and rRNA-derived small RNAs (rsRNAs)—respond to environmental stimuli and regulate early embryonic development. To support this research, his group has developed innovative analytical tools, such as PANDORA-seq, designed to overcome RNA modification-induced biases to comprehensive analysis of these emerging small RNAs. Dr. Chen's team is working on applying this knowledge for disease prevention across generations and in developing new diagnostic biomarkers such as for sperm aging.

**Dr. Sonia de Assis** is a tenured Associate Professor of Oncology at Georgetown University. Her lab pioneered the concept of non-genetic or epigenetic inheritance as it relates to cancer susceptibility. While family history is one of the most important risk factors for cancer, genetic mutations only explain a portion of familial cancers, suggesting that other factors play a role. At conception, each parent contributes their genome to the offspring, but they also transmit a molecular memory of past environmental experiences to their progeny through epigenetic mechanisms. This epigenetic memory can determine the fate of organs in the developing embryo and modulates their risk of developing chronic diseases such as cancer. Dr. de Assis and her team are currently exploring how sperm RNAs affect embryonic and fetal development, ultimately leading to disease after birth. They are also studying whether cancer treatment-induced sperm mitochondrial dysfunction and persistent dysregulation of sperm RNAs explain infertility in male childhood cancer survivors.

**Dr. Brian Dias** is a South Asian-American Associate Professor with Tenure in the Department of Pediatrics at the USC Keck School of Medicine and directs a research laboratory at Children's Hospital Los Angeles (CHLA). Dr. Dias and his team study how legacies of stress echo across generations. From their discoveries, they aim to inform therapeutic and policy interventions to mitigate multi-generational legacies of stress. A recipient of a CIFAR Azrieli Global Scholar Award from the Canadian Institute for Advanced Research (CIFAR), Dr. Dias is a Fellow in CIFAR's Child & Brain Development Program. Sought after as a thought leader and gifted science communicator, among other engagements, Dr. Dias has spoken about legacies of trauma on stage (TEDx), radio (NPR) and TV (Your Fantastic Mind – PBS). Complementing his research, Dr. Dias is deeply invested in knowledge mobilization. He taught Neuroscience to Tibetan Buddhist monastics through the Emory Tibet Science Initiative (2012-2019) and consults for FamilyWise Services – a Minnesota-based organization that aims to strengthen families by promoting wellbeing of children. See www.diaslab.weeblv.com for more information.

**Dr. Michael C. Golding** earned his Ph.D. in Physiology from Texas A&M University in 2003, where he studied how epigenetic errors related to somatic cell nuclear transfer or cloning cause structural and placental defects in bovine fetuses. This research sparked a lasting interest in DNA methylation and the role of abnormal epigenetic programming in birth defects and disease. He completed postdoctoral training at Cold Spring Harbor Laboratory and the University of Western Ontario, focusing on transposable element suppression in the placenta and noncoding RNA regulation of imprinted genes.

Dr. Golding joined Texas A&M's Department of Veterinary Physiology and Pharmacology in 2009 and was promoted to full professor in 2020. He teaches courses in physiology, fetal development, and genetics, and has developed specialized curricula on human pregnancy.

His research sits at the intersection of pregnancy and epigenetics, examining how environmental exposures before or during conception shape offspring health. Using a preclinical mouse model, his lab has demonstrated that chronic paternal alcohol use drives craniofacial birth defects, accelerates aging, and increases cancer susceptibility in offspring. His ongoing work aims to uncover the biochemical mechanisms of sperm-mediated epigenetic inheritance and determine how alcohol and other toxicants alter this process to cause fetal alcohol spectrum disorders (FASDs).

**Dr. Valérie Grandjean** is a researcher at the Institut national de la santé et de la recherche médicale (Inserm), where she investigates the mechanisms of paternal epigenetic inheritance in metabolic diseases. Her research lies at the intersection of epigenetics, reproductive biology, and metabolic pathophysiology, with the overarching goal of understanding how environmental factors shape the health of future generations.

She has contributed to identifying small non-coding RNAs as key sperm-borne vectors in the transmission of metabolic disease risk. Her work has demonstrated that alterations in sperm RNA profiles, induced by paternal nutritional or metabolic disturbances, can reprogram gene expression and metabolic outcomes in the offspring.

By combining experimental models with molecular and functional analyses, her research provides mechanistic insights into intergenerational metabolic inheritance. Her contributions are particularly

relevant to current discussions on developmental origins of health and disease and open new perspectives for prevention strategies and public health interventions.

**Dr. Eric Greer** is an Associate Professor at Washington University in St. Louis. Before joining Wash U, Eric was an Assistant Professor at Harvard and Boston Children's Hospital. Dr. Greer obtained his BA from CWRU and his PhD from Stanford for work done in the lab of Dr. Anne Brunet. During his graduate work he did some of the first work to identify the molecular basis for how dietary restriction, a reduction in nutrients without starvation, can extend lifespan. He also demonstrated that chromatin modifications, particular H3K4 trimethylation, could regulate lifespan. Eric did postdoctoral training in Dr. Yang Shi's lab at Harvard. As a post-doc Eric found that members of the H3K4me3 complex not only regulated longevity in the parental generation, but also in an epigenetic manner for 3 additional generations. Eric began to decipher how non-genetic information is transmitted from ancestors to their descendants. In this search he identified a novel form of DNA modification in metazoan, methylation on adenines, that might be responsible for epigenetic inheritance. The Greer lab focuses on understanding the molecular mechanisms of epigenetics. The lab focuses on 1) identifying what heritable epigenetic cues are inherited across generations, 2) examining the role of chromatin and epitranscriptomic modifications in regulating cellular processes and how dysregulation of epigenetic mechanisms causes developmental defects and diseases to arise, 3) identifying and characterizing new epigenetic modifications and the enzymes that add, remove, and recognize these modifications and what their role is in regulating a variety of biological processes and 4) examining the role of epigenetics in the evolution of multicellularity.

**Professor Sarah Kimmins** is a researcher in the Department of Pathology and Cell Biology at the Université de Montréal and at the Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM). She is Co-Director of the Québec Developmental and Intergenerational Origins of Child Health Research Network (ODISÉ), and Co-Founder and Co-Director of ORIGÈNE.
She completed her PhD at Dalhousie University, where she studied the molecular regulation of the estrous cycle and uterine receptivity to pregnancy, followed by postdoctoral training at the Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC) in Strasbourg, France, investigating epigenetic mechanisms in spermatogenesis and male fertility.

Professor Kimmins' research focuses on how paternal environmental exposures shape sperm epigenetic programming, influence early embryo development, and contribute to intergenerational health and disease risk. Her work sits at the intersection of reproductive biology, developmental biology, and epigenetics, with a particular emphasis on the role of the paternal germline in the developmental and intergenerational origins of health and disease.

**Dr. Isabelle Mansuy** is a professor in Neuroepigenetics at the Medical Faculty of the University of Zurich and the Department of Health Science and Technology of the ETH Zurich. She holds a Ph.D. in developmental neurobiology from the University Louis Pasteur in Strasbourg, France for a doctoral thesis conducted at the Friedrich Miescher Institute in Basel. She trained as postdoc in the lab of Eric Kandel at the Center for Learning and Memory at Columbia University in New York and then established her own lab as assistant professor in neurobiology at ETH Zurich in Switzerland. Dr. Mansuy initially conducted research in molecular cognition and made landmark discoveries on the mechanisms of forgetting by identifying memory suppressors in the mammalian brain. In parallel, in early 2000s, she started to work on epigenetic inheritance and has become one of the pioneers and founders of this new discipline. She is studying the epigenetic basis of heritable traits induced by life experiences. Her work demonstrated that adverse conditions in early life such as traumatic stress can alter behavior, physiology and metabolism across multiple generations in mice, and that inheritance depends on non-DNA factors in germ cells, particularly RNA in sperm. This discovery established the existence of an RNA-based form of heredity in mammals independent from the DNA sequence, similarly to what's known in plants and invertebrates. The fundaments of these findings in mice are being validated by translational studies in trauma patients in humans. This research provides important mechanistic advances about the influence of the environment on brain and body functions and is highly relevant for heritable environmental diseases. It has a major impact on evolution and offers an alternative to classical genetics for rapid organismic plasticity. It also has important societal and ethical implications. Dr. Mansuy co-authored >200 research articles, reviews and book chapters in neurosciences and epigenetics. She published a book on epigenetics for the lay public in French and German "Reprenons le contrôle de nos gènes", Larousse (2019) and "Wir können unsere Gene steuern" Berlin Verlag (2020). She is active in multiple scientific and research funding boards, is member of the Swiss Academy of Medical Sciences, the European Academy of Sciences (EURASC), and the European Molecular Biology Organization. She is Knight in the National Order of Merit and Knight in the Legion of Honor in France.

**Dr. Eric Miska** is the Herchel Smith Professor of Molecular Genetics and Head of the Department of Biochemistry at the University of Cambridge. He studied mathematics, physics and biology at Heidelberg, Berlin, Mainz and Trinity College Dublin, before receiving his PhD in Pathology from the University of Cambridge, working with Sir Tony Kouzarides. He was a postdoctoral fellow in the laboratory of Nobel Laureate Bob Horvitz at the Massachusetts Institute of Technology, and went on to establish his own research group at the Gurdon Institute. His research focusses on RNA, epigenetics and the mechanisms of inheritance. Eric is also a Founder and Director of STORM Therapeutics Ltd., a clinical-stage biotechnology company pioneering cellular reprogramming through RNA modifications to treat disease.

**Dr. Alexander K. Murashov**, M.D., Ph.D., is a Professor and Head of the Department of Comparative Biomedical Sciences at the Louisiana State University School of Veterinary Medicine. He graduated from the 2nd Medical Institute in Moscow, Russia, and earned his Ph.D. in Physiology from the Anokhin Institute of Physiology, Russian Academy of Medical Sciences. He completed postdoctoral training at the Howard Florey Institute (University of Melbourne), Griffith University, and later at Columbia University's Center for Reproductive Sciences, where he served as Associate Research Scientist.

Dr. Murashov spent over two decades at East Carolina University School of Medicine, where he became Full Professor, directed the interdepartmental Neuroscience graduate program, and led the local Society for Neuroscience chapter. In 2023, he joined LSU as department head.

His research focuses on the mechanisms of transgenerational epigenetic inheritance, particularly microRNA-mediated regulation of brain function in response to environmental factors such as diet, stress, and injury. Using Drosophila and integrated behavioral, bioenergetic, and multi-omics approaches, his laboratory investigates how parental exposures shape offspring metabolic and neurological phenotypes. He was among the first to demonstrate functional RNA interference in peripheral nerve axons and to identify a role for exercise in transgenerational epigenetic programming of the "thrifty phenotype."

**Dr. Benjamin P. Oldroyd** is an emeritus professor in the School of Life and Environmental Sciences at the University of Sydney, Australia. His long-term research interest is the evolution and genetics of honeybees. In honeybees, queen-worker dimorphism arises from differential feeding across just two days in the larval stage. Since queen- and worker-destined eggs are genetically identical, larval feeding must initiate an epigenetic process that results in the wildly different phenotypes. Recognizing that epigenetics is central to understanding bee biology, Oldroyd's lab made significant contributions to our understanding of the evolution of worker sterility (ever wondered how an allele that makes you sterile can spread in a population?), the inheritance of epigenetic marks, and the possibility of paternal imprinting as a contributing factor to male-male competition.

In 2020 Oldroyd was a resident fellow at the institute of Advanced Studies in Berlin, where he co-edited a special issue of the Philosophical Transactions of the Royal Society of London entitled 'How does epigenetics influence the course of evolution?' and began writing a popular science book 'Beyond DNA: How epigenetics is changing the way we think about evolution' published by Melbourne University Press in 2023. Ben now lives in far north Queensland, admiring the cassowaries restoring a tropical rainforest to its former glory.

**(Online) Dr. Anita Öst** is a Professor of Cell and Molecular Biology at Linköping University (LiU). Her research focuses on how paternal factors, including diet and lifestyle, influence sperm biology and offspring development. During her postdoctoral training at the Max Planck Institute for Immunology and Epigenetics, she developed a *Drosophila* model to study intergenerational metabolic responses, which continues to inform her work. She also investigates male fertility and strategies to support couples undergoing IVF.

**Dr. Perrie O'Tierney-Ginn**, PhD is the Executive Director of the Woman, Mother + Baby Research Institute (WoMB) at Tufts Medical Center and a Research Associate Professor of Obstetrics & Gynecology and the Friedman School of Nutrition Science and Policy at Tufts University. Her overall interest is to understand the connection between maternal health and the placental regulation of nutrient metabolism and delivery, and to improve cardiometabolic health of offspring.

A self-described "Perinatal Ecologist," Dr. O'Tierney-Ginn is fascinated by the interaction between the mother, baby and placenta and their environment. Her laboratory investigates how miRNAs produced by the placenta influence maternal glucose metabolism and fetal fat accumulation during pregnancy. She has identified specific placental miRNAs linked to maternal insulin resistance and high neonatal fat mass. Recently, her team reported correlations between epigenetic regulators and lipid metabolism drivers (such as SMUG1 and CDS1) in the placentas of mothers affected by obesity.
You can find out more about her work at www.placentascience.com
Bsky: @placentascience.bsky.social
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**Dr. Chris Pierce** is a Professor of Psychiatry at the Rutgers Robert Wood Johnson School of Medicine. He also is a core member of the Rutgers Brain Health Institute, where he is Associate Director for Education and Training, and a member of the Rutgers Addiction Research Center leadership team. Dr. Pierce is the director of a NIDA-funded training program in addiction neuroscience for pre- and postdoctoral trainees. Dr. Pierce's research has been funded by NIDA continually since 1993 (totaling over $35,000,000 of past and allocated funding as principal investigator, mentor or co-investigator). He has published over 100 articles, focusing primarily on cocaine-induced neuronal and behavioral plasticity. Dr. Pierce's publications collectively have been cited over 15,000 times (h-index=64).

Contributions to the field of epigenetic inheritance include the following:

Rich, M.T., S.J. Worobey, S. Mankame, Z.P. Pang, S.E. Swinford-Jackson and R.C. Pierce (2023). Sex-dependent fear memory impairment in cocaine-sired rat offspring. *Science Advances* Epub 18 October 2023.

Vassoler, F.M., S. White, H.D. Schmidt, G. Sadri-Vakili and R.C. Pierce (2013). Epigenetic inheritance of a cocaine resistance phenotype. *Nature Neuroscience* 16:42-47.

**Dr. Upasna Sharma** is an Assistant Professor in the Department of Molecular, Cell, and Developmental Biology at the University of California, Santa Cruz (UCSC). Dr. Sharma's lab investigates how the paternal environment influences offspring health. During her postdoctoral studies, as a Charles H. Hood Postdoctoral Fellow in the laboratory of Dr. Oliver Rando at the University of Massachusetts Medical School, Dr. Sharma utilized genomic approaches to elucidate the mechanism of intergenerational epigenetic inheritance of paternal dietary effects. Her work revealed a role of sperm small RNAs in such inheritance and provided evidence of RNA-mediated soma-germline communication in mammals. Her lab at UCSC is utilizing a unique and powerful combination of genomics, genetics, and assisted reproduction approaches to investigate the mechanistic basis of RNA-mediated soma-germline communication, its influence on sperm epigenome, and the consequences for offspring health. She is a recipient of the NIH Director's Innovator Award, a Searle Scholars award, and a McKnight Foundation's Neurobiology of Brain Disorders award.

**(Online) Dr. Michael K. Skinner** is a professor in the School of Biological Sciences at Washington State University, Pullman Washington, USA. He did his B.S. in chemistry at ReedCollege in Portland Oregon, his Ph.D. in biochemistry / chemistry at Washington State University (WSU) and his Postdoctoral Fellowship at the C.H. Best Institute at the University of Toronto, Canada. He has been on the faculty of Vanderbilt University and the University of California at San Francisco. He is the Founding Director of the Center for Reproductive Biology at WSU and University of Idaho, which is the largest reproduction biology center in the world, with over 100 faculty. Dr. Skinner's current research has demonstrated the ability of environmental exposures (e.g., toxicants) promote the epigenetic transgenerational inheritance (non-genetic form of inheritance) of disease phenotypes due to abnormal germ line epigenetic programming in gonadal development. Dr. Skinner has over 400 peer reviewed publications and has given over 400 invited symposia, plenary lectures and university seminars. Dr. Skinner is the Editor-in-Chief of the Encyclopedia of Reproduction and the Oxford publishing journal Environmental Epigenetics. He has done Ted talks and had documentaries done on his research with BBC Horizon, PBS Nova, Smithsonian, and France ARTE. Dr. Skinner has also founded several biotechnology companies.

Web links:

Website: https://skinner.wsu.edu/

Curriculum Vitae: https://skinner.wsu.edu/principal-investigator-michael-k-skinner/

Publications: https://skinner.wsu.edu/publications/

Press: https://skinner.wsu.edu/public-press-information/

https://skinner.wsu.edu/public-press-information-and-news/

**Dr. Yuta Takahashi** is an Associate Professor at the International Research Center for Medical Sciences (IRCMS), Kumamoto University, where he established his independent laboratory in 2024. His research focuses on the mechanisms of transgenerational epigenetic inheritance in mammals. Dr. Takahashi earned a B.S. in 2006, an M.S. in 2008, and a Ph.D. in 2011 from the University of Tsukuba in Japan. During his postdoctoral training at the Salk Institute, under the mentorship of Professor Juan Carlos Ispisua Belmonte, he demonstrated that epigenetic signatures at gene promoters and their associated phenotypes can be transmitted across multiple generations in mammals using epigenetically modified mouse models (Takahashi et al., Cell, 2023, Science 2017). These findings represent a pioneering contribution to the field of mammalian epigenetic inheritance and may also provide valuable insights into biological evolution and the etiology, diagnosis, and prevention of non-genetically inherited human diseases.

**(Online) Dr. Raffaele Teperino** leads the Environmental Epigenetics group at Helmholtz Munich, where his research focuses on the epigenetic inheritance of complex traits. His work has uncovered the role of seminal plasma in developmental programming (*Science Advances*, 2021) and demonstrated the transfer of epigenetic material from sperm to oocyte during fertilization (*Nature*, 2024). He also showed that at conception represents a distinct risk factor for childhood obesity and diabetes (*Nature*, 2024). Dr. Teperino earned his PhD in Molecular Endocrinology from the University of Napoli Federico II and conducted postdoctoral research at EPFL Lausanne and the Max Planck Institute of Immunobiology and Epigenetics in Freiburg, specializing in developmental biology, epigenetics, and metabolic physiology. He has authored 45 scientific publications, including papers in leading journals such as *Nature*, *Cell*, and *Cell Metabolism*. His work has been recognized with awards and fellowships from the Marie Skłodowska-Curie Actions, the Italian Association for Cancer Research, the Minerva Foundation and

more recently from the German Diabetes Society and the Schmidt-Buddecke Stiftung. Actively engaged in science communication, he contributes to podcasts, exhibitions, and television documentaries. Recognized by the European Commission as an expert in personalized medicine, his research aims to translate discoveries in epigenetic inheritance into strategies for preventing and treating metabolic diseases.

**Dr. Fair M. Vassoler**, Ph.D., is an Associate Professor in the Department of Comparative Pathobiology at the Cummings School of Veterinary Medicine at Tufts University, with a secondary appointment in the Neuroscience Program at the Tufts Graduate School of Biomedical Sciences. Her research lies at the intersection of addiction neuroscience and epigenetics, with a focus on how opioid exposure alters brain function and how these effects can be transmitted across generations. Dr. Vassoler is internationally recognized for her pioneering work demonstrating transgenerational inheritance of addiction-related phenotypes. Her seminal publication in Nature Neuroscience showed that paternal cocaine exposure can alter behavioral and molecular responses to drugs in offspring, helping to establish the field of addiction related epigenetic inheritance. Her current NIH-funded research investigates how sperm microRNAs, including the Let-7 family, regulate offspring opioid vulnerability and relapse risk. Through rodent models of self-administration and relapse, her work integrates molecular, behavioral, and circuit-level approaches to understand and ultimately mitigate the long-term consequences of the opioid epidemic.

## Guest Speaker Abstracts in Program Order – Wednesday

### Understanding the 'Sperm RNA Code' for Epigenetic Inheritance with Emerging Tools

**Dr. Qi Chen**

Recent discoveries have revealed a novel layer of inheritance, showing that mammalian sperm transmit not only DNA but also diverse RNA molecules that mediate the intergenerational effects of paternal condition (e.g., diet, stress, aging, and exercise). Expanding knowledge of sperm RNAs—including miRNAs, tsRNAs, rsRNAs, and lncRNAs—together with their modifications and spatial compartmentalization, supports the emerging concept of a 'sperm RNA code' that programs offspring phenotypes during development. I will discuss the challenges and opportunities in establishing this field, including identifying the key sperm RNAs responsible for paternal phenotype transmission, uncovering their native expression and modification profiles with advanced sequencing tools, and understanding the molecular events they trigger in embryos. Complete deciphering of the sperm RNA code under different paternal conditions could transform our understanding of epigenetic inheritance and open paths toward translational applications and precision medicine, exemplified in the recent decoding a conserved aging signature in mouse and human sperm RNAs.

### Sperm RNA-mediated intergenerational epigenetic inheritance

**Dr. Upasna Sharma**

Environmental exposures experienced by fathers can influence offspring development and health, yet the molecular carriers of this information remain incompletely understood. Small non-coding RNAs carried by sperm are emerging as important mediators of such epigenetic inheritance, linking paternal environmental exposures to offspring development and health. Among these, cleavage products of mature tRNAs, known as tRNA fragments (tRFs), represent a major and environmentally responsive class of sperm RNAs – levels of tRNAs are altered by numerous environmental conditions, such as diet, stress and toxicant exposure. However, the mechanisms governing their biogenesis and function remain poorly understood. In this talk, I will present our work identifying enzymes in the male reproductive tract that regulate the generation of sperm tRFs and demonstrate how disruption of these pathways alters the sperm small RNA landscape and male fertility. I will also discuss how a specific sperm tRF is delivered to sperm during epididymal maturation and how manipulating its levels in the zygote affects early embryonic gene expression and developmental progression. Together, these findings provide new mechanistic insights into how sperm small RNA payload is established and how these small RNAs may influence early development and intergenerational inheritance of paternal environmental effects.

**Transgenerational Inheritance of Epigenetic Memory in Mammals**

**Dr. Yuta Takahashi**

Background: In mammals, it is generally assumed that two distinct phases of epigenetic reporgramming – primodial germ cell (PGC) development and early embryonic development – serve to prevent the inheritance of ancestral epigenetic signatures. Therefore, whether transgenerational epigenetic inheritance occurs in mammals, to what extent epigenetic information can be passed to offspring, and whether it is associated with disease heritability have been longstanding and attractive scientific questions.

Main findings:

We demonstrated that DNA methylation of promoter-associated CpG islands (CGIs) can be transmitted from parents to their offspring in mice (Y.Takahashi, et al., **Cell.** 2023, PMID: 36754048). We generated DNA methylation – edited mouse embryonic stem cells (ESCs) in which CGIs of two metabolism related genes, the Ankyrin repeat domain 26 (Ankrd26) and the low-density lipoprotein receptor (Ldlr), were specifically methylated and silenced using or DNA methylation editing strategy (Y.Takahashi, et al., **Science**. 2017, PMID: 2847583). DNA methylation-edited mice generated by microinjection of methylated ESCs exhibited abnormal metabolic phenotypes. Both the acquired methylation of the targeted CGI and the phenotypic traits were maintained and transmitted across multiple generations. Moreover, the heritable CGI methylation was subjected to reprogramming in parental PGCs and subsequently reestablished in the next generation at post-implantation stages.

Significance:

Using our technology, we generated DNA methylation-edited mice in which the targeted CGI of two different loci are methylated. The edited DNA methylation and ensuing phenotypes observed in the first-generation mice are maintained in subsequent generations, providing experimental evidence that epigenetic information, DNA methylation of CGIs, could be transmitted from parents to their offsprings in mammals. Furthermore, we uncovered that it is not the DNA methylation itself, but rather a transmitted epigenetic memory, that leads to the reestablishment of CGI methylation in the next generation. In this presentation, I will also discuss the potential mechanisms underlying this process.

**Epigenetic Programming in Sperm: Mechanisms of Fertility and Disease Transmission**

**Dr. Sarah Kimmins**

Male reproductive health is declining globally, alongside rising rates of metabolic, developmental, and neurobehavioral disorders in children. Increasing evidence suggests that these trends may be biologically connected through the influence of paternal health and environment on the sperm epigenome. Sperm carries more than DNA alone; it also delivers heritable epigenetic information that may influence fertilization, embryo development, and health trajectories in the next generation.

Our work investigates how environmental and lifestyle factors shape the sperm epigenome and how this may contribute to male fertility, offspring development, and intergenerational disease risk. A central focus is the role of histone H3 lysine 4 trimethylation (H3K4me3) and DNA methylation in sperm in relation to fertility, and health across generations. Although most histones are replaced by protamines during spermatogenesis, a conserved subset of histones is retained at regulatory regions linked to spermatogenesis, embryo development, metabolism, and disease susceptibility. We have shown in both mouse models and human studies that sperm DNA methylation and H3K4me3 marks key developmental and reproductive pathways and is sensitive to environmental and nutritional exposures.

In this talk, I will discuss how perturbations to sperm chromatin and DNA methylation are associated with reduced fertility, altered embryo development, miscarriage risk, and adverse health outcomes in offspring. I will highlight findings from our mouse models, where paternal diet alter sperm epigenetic programming and influence developmental outcomes, as well as our studies in men, which examine the relationship between sperm epigenetic signatures, fertility, overall health, and the transmission of disease risk to the next generation.

A major question in the field is whether environmentally induced epigenetic abnormalities in sperm are permanent or whether they can be repaired. I will also explore emerging evidence for the plasticity of the sperm epigenome and the implications of this work for reproductive medicine, disease prevention, and our understanding of how paternal health before conception can shape the biology of future generations.

**(ONLINE*)***

**Environmental Exposure Induced Epigenetic Transgenerational Inheritance Impacts on Reproduction, Disease Etiology and Evolution**

**Dr. Michael K. Skinner**

Epigenetic transgenerational effects of environmental factors such as toxicants, diet and stress significantly amplify the biological impacts and health hazards of these exposures , as well as influence future generations. One of the most sensitive periods to exposure is during fetal gonadal sex determination when the germ line is undergoing epigenetic programming and DNA methylation alterations. Previous studies have shown that toxicants (e.g., Glyphosate, DDT, Vinclozolin) can transgenerationally increase in adults the onset of disease such as infertility, prostate, ovary and kidney disease, cancers and obesity. Interestingly, these effects are transgenerational (F1, F2, F3 and all further generations) due to a permanent (imprinted-like) altered epimutations in the germline. The transgenerational epigenetic mechanism involves the actions of an environmental compound at the time of sex determination to permanently alter the epigenetic (e.g., DNA methylation) programming of the germline that then alters the embryo stem cells to alter all epigenomes of all developing somatic cells and organs to induce disease susceptibility and development transgenerationally. In addition to DNA methylation, alterations in sperm ncRNAs and histone modifications and retention have also been observed. A variety of different environmental compounds have been shown to induce this epigenetic transgenerational inheritance of disease, including: fungicide vinclozolin, plastics BPA and phthalates, pesticides, DDT, dioxin, hydrocarbons and herbicides like atrazine and glyphosate. Interestingly, exposure specific epigenetic alterations were observed between the specific toxicants. Recently we have identified in human’s epigenetic biomarkers for parental germ cell transmission of offspring disease states such as infertility, autism, and arthritis. These epigenetic biomarkers can be used in preventative medicine. The suggestion that environmental exposures (e.g., toxicants) can reprogram the germline to induce epigenetic transgenerational inheritance of disease is a novel non-genetic paradigm in disease etiology, toxicology, and evolutionary biology that needs to be considered in the future.

**Sperm RNAs, Placentation and Fetal Growth**

**Dr. Sonia de Assis**

Mendelian genetics explain most inherited traits, including disease predisposition, but not all. There is growing evidence for intergenerational epigenetic inheritance occurs and that traits—such as disease susceptibility—are passed between generations through non-genetic mechanisms. Small noncoding RNAs (sncRNAs) in sperm are sensitive to paternal experiences and can mediate inheritance of phenotypes. However, how these environmentally-induced sperm RNAs influence embryonic and fetal development remains poorly understood. In eutherian mammals like rodents and humans, the placenta connects fetus and mother, ensuring exchange of nutrients and gases essential for fetal development. Impaired placental function can result in fetal growth restriction and long-term health effects. While placentation is largely driven by paternal imprinted genes, little is known about how paternal environmental exposures before conception affect placenta formation. Using two paternal exposure models, we demonstrated that environmentally-altered sperm RNAs are functionally linked to placental development. We found that sperm RNA from males exposed to different environmental insults shape placenta efficiency by regulating placenta vascularization and nutrient storage. Our findings provide strong evidence that sperm RNAs shape placental development and fetal growth and offer a potential mechanism for paternally-driven epigenetic inheritance of disease and developmental traits across generations.

**The Key Role of Placental miRNA in the Crosstalk Driving Fetal Fat Accrual**

**Dr. Perrie O'Tierney-Ginn**

Background

How babies grow in the womb (organ development, fat accrual, lean tissue growth) can modify their metabolism, cardiovascular function, neurological development, and their risk of future disease. A difference of 8% body fat at birth is associated with a 20% greater risk for childhood overweight and obesity. Maternal obesity and insulin resistance are well-recognized risk factors for high neonatal adiposity. However, not all obese women have obese babies and the specific maternal and placental factors contributing to fat deposition *in utero* are poorly understood.

Main Findings

Dr. O'Tierney-Ginn's group has identified placental-derived microRNA (miRNA) signatures associated with neonatal adiposity that target stress-response pathways (Alvarado et al. Repro Sci, 2021), impact insulin sensitivity in peripheral tissues (Alvarado et al. Placenta 2025) and correlate with placental lipid metabolism drivers (Spadafora et al, Front Endocrinol, 2026). These findings demonstrate the broad local and peripheral actions through which placental miRNA

impact fetal growth. Through mediation of sensitivity to environmental stressors, alterations in maternal metabolic adaptations to pregnancy, and modification of placental nutrient metabolism, we argue that miRNAs originating in the placenta play a key role in the maternal-placental communication that drives pregnancy outcomes and offspring health.

Significance

Placenta-maternal “crosstalk” throughout gestation is critical for metabolic adaptations to pregnancy and fetal growth. Dr. O’Tierney-Ginn’s talk will focus on her lab’s work to understand this maternal-placental communication and its influence on pregnancy outcomes.

## Guest Speaker Abstracts in Program Order – Thursday

### Keynote Lecture

### How Life Experiences Can Influence Us and Our Descendants: An Epigenetic Perspective

**Dr. Isabelle M. Mansuy**

Behavior and physiology in mammals are strongly influenced by life experiences, particularly experiences in childhood. While positive factors favor proper development and good mental and physical health in adulthood, early life adversity and traumatic events increase the risk for psychiatric, cardiometabolic and autoimmune diseases and cancer. Such disorders can affect directly exposed individuals but also their descendants, in some cases across generations. The biological mechanisms underlying the inheritance of environmentally-induced (acquired) traits involve factors independent from the DNA sequence in the germline. To study these mechanisms, we developed a mouse model of postnatal stress that causes trauma symptoms across generations1–3. The symptoms include increased risk-taking, depressive-like behaviors, cognitive and social deficits, as well as metabolic and cardiovascular dysfunctions in adulthood that persist across life in exposed animals. Some symptoms are also manifested by the offspring of exposed individuals for instance risk-taking behaviors up to the 5th generation in the patriline 4. In humans, comparable symptoms affect people exposed to childhood trauma, suggesting conserved effects across species5. At a molecular level, exposure is associated with epigenetic changes involving RNA and DNA methylation in somatic cells across the body and in germ cells, with sperm RNA being causally linked to symptoms transmission3. MiRNAs are also affected in extracellular vesicles in blood and the reproductive tract6. Circulating factors were identified as mediators of some of the alterations in germ cells. Chronic injection of serum from

trauma-exposed mouse males into control males recapitulates metabolic phenotypes in the offspring, suggesting information transfer from serum to germ cells. Pathways involving peroxisome proliferator-activated receptor (PPAR) are causally involved, with pharmacological PPAR activation *in vivo* affecting sperm transcriptome and metabolic functions in the offspring and grand-offspring5. These results suggest the existence of an ensemble of factors and mechanisms that can carry information about past experiences from the periphery to germ cells for the inheritance of acquired traits7–11.

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**(Online)**

**The Intergenerational Impact of Paternal Preconceptional Health**

**Dr. Raffaele Teperino**

**Background.**

Spermatozoa harbor a complex and environmentally sensitive pool of small non-coding RNAs (sncRNAs) that can influence early embryonic development and long-term offspring phenotypes. However, whether mature spermatozoa residing in the epididymis are directly responsive to environmental exposures remains unclear. In particular, the relative contributions of testicular germ cell development versus post-testicular epididymal maturation to environmentally induced remodeling of the sperm epigenome are poorly understood. Addressing this question is critical for understanding how paternal health at conception contributes to intergenerational risk of metabolic disease.

**Main findings.**

Using two complementary paradigms of acute preconception high-fat diet (HFD) exposure in mice, we dissected the relative contributions of testicular versus epididymal processes to the sperm sncRNA pool and offspring metabolic health. Our results demonstrate that mature epididymal spermatozoa—but not developing germ cells in the testis—are directly sensitive to environmental cues. Small RNA sequencing identified mitochondrial tRNAs and their fragments (mt-tsRNAs) as key sperm-borne factors responsive to dietary stress. In humans, mt-tsRNA abundance in spermatozoa was linearly associated with body mass index, and paternal overweight at conception was sufficient to double the risk of obesity in offspring while compromising metabolic health. Complementary analyses of the epididymal sperm proteome revealed extensive remodeling in response to HFD during post-testicular maturation, affecting 149 proteins in the caput epididymis, 597 during epididymal transit, and 453 in the cauda. These proteomic changes involved pathways critical for sperm function, including zona pellucida binding, sperm motility, and RNA biogenesis. Notably, mitochondrial pathways were strongly affected, with enrichment of metabolic processes and NRF2-mediated oxidative stress responses, indicating mitochondrial dysfunction during sperm maturation under dietary stress. Consistently, sperm sncRNA sequencing in mouse models with genetically perturbed mitochondrial function showed alterations in mt-tsRNAs, suggesting that these RNAs arise downstream of mitochondrial dysfunction. Finally, single-embryo transcriptomics of genetically hybrid two-cell embryos demonstrated the direct transfer of mitochondrial tRNAs from sperm to oocyte at fertilization and implicated them in the regulation of early embryonic transcription.

**Significance.**

Together, these findings demonstrate that epididymal spermatozoa are environmentally responsive and identify mitochondrial tRNAs and their fragments as sperm-borne epigenetic signals linking paternal metabolic health to offspring development. By providing the first evidence of sperm-to-oocyte transfer of mitochondrial RNAs under physiological conditions, this work establishes a mechanistic framework for paternal epigenetic inheritance and underscores the importance of paternal health at conception for offspring metabolic outcomes.

## Effects of maltreatment during infancy on RNA signatures in rhesus macaques – lessons from EVs

**Dr. Brian Dias**

**Authors:** Laura Korobkova, Matthew E. Thornton, Matthew A. Collin, Elyse L. Morin, Hadj Aoued, Soma Sannigrahi, Nabeel Bhinderwala, Kristie M. Garza, Erin R. Siebert, Hasse Walum, Ryan P. Cabeen, Brendan H. Grubbs, Mar M. Sanchez, Brian G. Dias, PhD. (Presenter) [Department of Pediatrics, Division of Endocrinology, Developmental Neuroscience & Neurogenetics Program, Children's Hospital Los Angeles, USC Keck School of Medicine.]

**Background:** Early life adversity (ELA) like maltreatment during infancy significantly increases the likelihood of developing psychosomatic disorders in adolescence and adulthood. Most investigations of these sequelae of ELA profile DNA methylation in whole blood and have disruptions to immune functions as being a conduit via which ELA derails physiology and behavior.

**Methods:** To identify novel molecular signatures that are perturbed by maltreatment in infancy, we leveraged naturally occurring infant maltreatment in rhesus macaques housed in a semi-naturalistic setting at the Emory National Primate Research Center. More specifically, we isolated circulating extracellular vesicles (EVs) from plasma collected from adolescent rhesus macaques that had been recipients of either nurturing maternal care (CONT, n=7, 4M 3F) or maltreatment in infancy (MALT, n=6, 3M 3F). We then profiled the RNA found in these EVs.

**Results:** RNA linked to genes governing mitochondrial activity and immune regulation showed reduced expression in circulating EVs from adolescent macaques exposed to maltreatment in infancy, whereas RNA related to ion transport, metabolic processes, and cellular differentiation were elevated. Moreover, a substantial fraction of EV RNA mapped to microbial origins, and

maltreatment during infancy influenced the diversity of microbiome-associated RNA profiles within these EVs.

**Conclusions:** Our research indicates that changes in RNA linked to immune function, cellular energy, and the microbiome in circulating EVs could act as lasting indicators of previous ELA. Consequently, disruptions in these RNA patters might provide new molecular understanding of how biological systems can stay altered long after exposure to ELA has passed.

### Role of Ribosome Heterogeneity in Epigenetic Inheritance

**Dr. Eric Greer**

Heritable non-genetic information can regulate a variety of complex phenotypes. However, what specific non-genetic cues are transmitted from parents to their descendants are poorly understood. Here, we perform metabolic methyl-labeling experiments to track the heritable transmission of methylation from ancestors to their descendants in the nematode *Caenorhabditis elegans*. We find heritable methylation in DNA, RNA, proteins, and lipids. We find that parental starvation elicits reduced fertility, increased heat stress resistance, and extended longevity in fed, naïve progeny. This intergenerational hormesis is accompanied by a heritable increase in N6′-dimethyl adenosine (m6,2A) on the 18S ribosomal RNA at adenosines 1735 and 1736. We identified DIMT-1/DIMT1 as the m6,2A and BUD-23/BUD23 as the m7G methyltransferases in *C. elegans* that are both required for intergenerational hormesis, while other rRNA methyltransferases are dispensable. We further find that DIMT-1 is necessary for transgenerational hormesis. This study labels and tracks heritable non-genetic material across generations and demonstrates the importance of rRNA methylation for regulating epigenetic inheritance.

### Paternal Epigenetic Inheritance as a Determinant of Metabolic Disease Susceptibility

**Dr. Valérie Grandjean**

**Background:**

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) is rapidly becoming a global health crisis, with prevalence projected to affect up to 50% of the population within the next decade. While obesity and insulin resistance are well-established risk factors, they do not fully explain the variability and progression of the disease. Emerging evidence suggests that paternal epigenetic inheritance may contribute to this susceptibility.

**Main findings:**

Here, we investigated whether paternal multi-generational exposure to a Western-Cholesterol Diet (WCD) induces transgenerational hepatic epigenetic reprogramming that increases vulnerability to MASLD. Histological and molecular analysis demonstrate that successive progenies progressively develop aggravated hepatic inflammation and fibrosis, despite comparable environmental exposure. Genome-wide epigenomic profiling revealed extensive remodeling of hepatic H3K27 acetylation (H3K27ac). These chromatin alterations were associated with coordinated transcriptional activation of pro-inflammatory and pro-fibrotic pathways, suggesting that sustained WCD exposure across generations reshaped the hepatic H3K27ac landscape in offspring, rendering them more susceptible to severe liver injury upon metabolic stress.

**Significance**

This work provides evidence that dietary exposure can durably reprogram the hepatic chromatin landscape across generations, thereby amplifying disease risk independently of genetic variation.

## Deciphering the Metabolo-Epigenetic Rules Underlying Environmental Epigenetic Alterations and Inheritance

**Dr. Patrick Allard**

**Background.**

Environmental exposures can disrupt epigenetic regulation in ways that persist long after the initial exposure and, in some cases, across generations. A central challenge in environmental epigenetics is understanding how these alterations arise and why some epigenetic changes resist the extensive epigenetic reprogramming that normally occurs during germline development. Increasing evidence suggests that environmental toxicants perturb metabolic pathways that provide essential substrates and cofactors for chromatin regulation, linking cellular metabolism with the control of epigenetic states.

**Main findings.**

In this presentation, we address two connected questions: how environmental agents alter the epigenome and how exposure induced changes can be maintained across generations. We focus on two toxicants of interest, inorganic arsenic (iAs) and ethanol, and integrate mammalian stem cell models with the genetically tractable organism *Caenorhabditis elegans*.

Using inorganic arsenic as a model epigenetic toxicant, we examine how environmental exposures reshape the metabolic environment that supports chromatin regulation. Arsenic exposure has long been associated with disruption of one carbon metabolism and reduced levels

of the universal methyl donor S-adenosylmethionine (SAM), which has been proposed to explain global DNA hypomethylation. Our findings support a more nuanced model in which arsenic exposure prominently impacts chromatin regulation through changes in histone post translational modifications, and in which effects on DNA methylation can arise secondarily through exposure driven changes in cell state and differentiation trajectories.

In parallel, we use *C. elegans* to dissect the metabolic requirements for environmentally induced transgenerational phenotypes. Specifically, we show that ethanol metabolism, and the associated production of key chromatin relevant metabolites, is required for the inter and transgenerational inheritance of ethanol induced neurobehavioral outcomes. These results support a direct mechanistic link between exposure metabolism and the persistence of exposure memory across generations.

**Significance.**
Our work supports a unified model in which environmental exposures disrupt metabolic pathways that regulate chromatin-modifying enzymes, leading to altered histone and DNA methylation landscapes which can produce persistent developmental and reproductive dysfunctions and heritable phenotypes. By linking metabolic disruption and chromatin regulation, this work provides a mechanistic framework for understanding how environmental exposures can shape epigenetic inheritance.

## How Epigenetic Processes Enhance Natural Selection by Exposing Hidden Genetic Variation

**Benjamin P. Oldroyd**

*Background.* The Modern Synthesis (MS) of evolution was first laid out by Ronald Fisher in 1930. It holds that the mechanism underlying natural selection is that phenotypes are influenced by many genes, each of small effect, and each with multiple alleles. As the environment changes, alleles that enhance fitness in current environmental conditions increase in frequency at the expense of those that decrease fitness. Beneficial alleles may occasionally arise by fortunate mutation and then spread in a population. However, it's been argued that evolutionary change is too speedy to be 'nothing more than sorting out of random mutations by the natural selective filter' (Waddington 1942).

*A conceptual framework.* I don't want to replace the MS. Rather, I would like to elevate 'plasticity first' evolution promoted by West-Eberhard (2003). It holds that individuals under stress may phenotypically change to meet that stress, a process called 'phenotypic accommodation'.

Phenotypic accommodation isn't the result of changed gene sequence at the individual level, nor of allele frequency change at the population level, but of gene regulation at the individual level. If a population is exposed to a novel environmental change, individuals may regulate gene expression in different ways to achieve the same or similar phenotypic outcome; there is no 'best way' to regulate a gene network to achieve a phenotype. By chance, individuals will accentuate different genes for changed expression. Now imagine a gene that was formerly down-expressed and played a minor role in producing phenotype. Existing allelic variation in this gene was invisible to natural selection because it was expressed at low levels and in concert with a constellation of other genes that could compensate for its low expression. With environmental change, this gene is now up-expressed and is therefore more strongly exposed to selection because its relative importance to phenotype has been elevated. In other individuals, another gene may assume importance, and this gene will now be exposed to selection. I contend that this can lead to rapid changes in allele frequency, gene regulation and potentially population subdivision.

*Significance.* Plasticity-led evolution is underappreciated and under-supported by data. Note that you don't need epigenetic inheritance for it to work, but where regulatory mechanisms are heritable, it can speed adaptation.

**(Online)**

**Nongenetic Inheritance in Evolution and Everyday Life**

**Dr. Russell Bonduriansky**

19th century biologists believed that the environment generates heritable variation, but the 20th century's Modern Synthesis of evolutionary biology restricted the environment's role to direct effects on development (i.e., classic plasticity) and natural selection of random genetic variants. Yet, this Modern Synthesis view is now contradicted by a great deal of empirical evidence, showing that many types of phenotypic variation can be transmitted to descendants through nongenetic inheritance. Nongenetic inheritance encompasses a diversity of mechanisms, including epigenetic inheritance in the narrow sense as well as somatic, cytoplasmic, environmental, symbiont, structural, behavioral and cultural inheritance. Such phenomena were long ignored by both biology and medicine (sometimes with disastrous consequences), but the reality of nongenetic inheritance is now widely accepted. However, the role of nongenetic inheritance in evolution remains controversial and poorly understood. Theory suggests that nongenetic inheritance could influence evolution in a variety of ways, highlighting a need to incorporate both genetic and nongenetic mechanisms of inheritance in evolutionary theory. I will

discuss recent steps towards this new model of evolution, and outline some novel questions raised by this model.

## Guest Speaker Abstracts in Program Order – Friday

### The Role of RNA and Chromatin in Transgenerational Epigenetic Inheritance

**Keynote Lecture – Eric Miska**

Caenorhabditis elegans is an established model to investigate transgenerational inheritance beyond DNA sequence: C. elegans has a small genome, short generation time and homozygous imbred laboratory strains are available. My group and others have done extensive work over the last twenty years demonstrating that RNA-based information can be inherited transgenerationally in C. elegans. Here, I will focus on how chromatin state contributes to RNA-based transgenerational memories. I will also highlight how transgenerationally inheritance might be relevant to adaptation and evolution, how there are striking differences in different species and how our work might relate to vertebrates and mammals.

### (Online)

### Sperm Mitochondrial RNAs Link Paternal Diet to Intergenerational Metabolic Programming

**Dr. Anist Ost**

Paternal metabolic state at conception can influence offspring health, but the mechanisms transmitting environmental information through sperm are poorly understood. Sperm carry diverse small non-coding RNAs, and among these, mitochondrial-derived small RNAs are highly sensitive to dietary changes, despite their low abundance. Paternal high-sugar feeding triggers rapid remodelling of mitochondrial-derived RNAs, alters chromatin regulation and metabolic gene expression in early embryos, and leads to persistent metabolic effects in offspring, including changes in lipid storage. Using *Drosophila melanogaster*, we characterized mitochondrial-derived small RNAs in sperm and find many to have piRNA characteristics. Furthermore, genetic perturbations show that the germline regulators Piwi and Aubergine contribute to their biogenesis.

In humans, a one-week high-sugar diet similarly remodels sperm small RNAs, with mitochondrial tRNA fragments among the most responsive. These changes coincide with shifts in proteins regulating metabolism and redox balance, as well as altered mitochondrial reactive oxygen species production.

Our results support a model in which sperm mitochondria act as sensitive environmental sensors, reshaping RNA cargo in response to diet. Mitochondrial-derived RNAs may thus provide a conserved mechanism linking paternal nutrition to intergenerational metabolic programming.

**Intergenerational regulation of brain energy metabolism driven by parental dietary and exercise exposures**

**Dr. Alexander Murashov**

Parental nutritional state can influence offspring physiology across generations, yet the cellular mechanisms underlying this inheritance remain poorly defined. Using *Drosophila melanogaster* as a model system, we investigated how paternal exposure to a Western diet (WD) alters brain mitochondrial function, molecular profiles, and behavior in first-generation offspring. We found that paternal WD exposure produces persistent alterations in offspring brain metabolism accompanied by sex- and lineage-dependent molecular remodeling. Measurements of mitochondrial function using high-resolution Oroboros O2k respirometry demonstrated significant deficits in multiple respiratory states, with the largest reductions observed in Complex I-linked respiration. Offspring also exhibited reduced ATP/$O_2$ efficiency, consistent with impaired oxidative phosphorylation. These bioenergetic changes were accompanied by reduced mitochondrial DNA copy number, altered expression of mitochondrial respiratory genes, and reduced NAD/NADH ratio, indicating disruption of mitochondrial metabolism. Integrated transcriptomic and proteomic analyses revealed coordinated changes in mitochondrial ribosomal proteins and metabolic regulators, pointing to disruption of core bioenergetic pathways and neuronal homeostasis. These molecular signatures were associated with behavioral alterations in offspring, including increased feeding behavior and changes in locomotor activity. To investigate mechanisms underlying this intergenerational inheritance, we identified spermderived microRNAs that are altered by paternal Western diet. Small RNA sequencing and RTqPCR identified miR-277-3p as a diet-responsive miRNA that is increased in sperm from WD-fed fathers and transmitted to early embryos. Single-cell RNA sequencing and in situ hybridization demonstrated altered gene expression during the maternal-to-zygotic transition, with *mei-P26*identified among the predicted targets of miR-277-3p. Together, these findings identify inherited mitochondrial dysfunction and sperm-derived microRNAs as components of the molecular response to paternal Western diet and provide a framework for investigating the mechanisms by which parental environmental exposures regulate offspring brain energy metabolism across generations.

**The Sins of the Fathers : Intergenerational Effects of Paternal Stimulants**

**Dr. Chris Pierce**

We previously demonstrated that male progeny of cocaine-experienced sires resisted cocaine, expressed as delayed acquisition of cocaine self-administration. Here, we sought to determine whether this phenotype extended to another psychostimulant, methamphetamine (meth). Surprisingly, male, but not female, meth-sired offspring demonstrated increased susceptibility to meth taking. Single nuclei RNA- and ATAC-sequencing of the nucleus accumbens was used to identify molecular drivers of phenotypes in cocaine- and meth-sired offspring. Sequencing results revealed unique profiles of gene expression and open chromatin in offspring nucleus accumbens. Differential gene expression in cocaine-resistant, cocaine-sired offspring and meth-susceptible, meth-sired offspring illuminates potential novel treatment targets for psychostimulant use disorders.

**Inter-and Transgenerational Consequences of Adolescent Opioid Exposure on Reward and Addiction Vulnerability**

**Dr. Fair Vassoler**

**Background:**

The opioid epidemic has had profound societal consequences, yet its potential impact across generations remains underexplored. Emerging evidence indicates that preconception opioid exposure can alter behavioral and molecular phenotypes in subsequent generations via epigenetic mechanisms. MicroRNAs (miRNAs) in sperm are particularly compelling candidates for mediating such transmission. Members of the Let-7 family regulate the mu opioid receptor (OPRM1), a central mediator of opioid reward and relapse vulnerability. This work investigates whether adolescent opioid exposure alters sperm miRNAs and whether these changes contribute to intergenerational differences in opioid-related behaviors.

**Main Findings and Conceptual Framework:**

Using a rat model, adolescent morphine exposure in males produced persistent increases in Let-7g expression in testes and sperm during adulthood. Offspring (F1) of morphine-exposed sires exhibited increased Oprm1 expression in mesolimbic reward regions early in development and elevated oxycodone self-administration in adulthood in both sexes. In contrast, F2 grandoffspring demonstrated reduced oxycodone intake, accompanied by decreased Let-7 family expression in F1 sperm, suggesting dynamic and generation-specific regulation of miRNA-mediated inheritance. Complementary pilot analyses of human sperm samples revealed increased levels of OPRM1-targeting miRNAs, including Let-7 family members, in men with a history of illicit drug use

compared to drug-naïve controls. Together, these findings support a model in which sperm miRNAs encode prior drug exposure and influence offspring opioid system development and behavioral vulnerability.

**Significance:**
These data identify sperm miRNAs as mechanistic mediators linking paternal opioid exposure to altered reward circuitry and drug-taking behavior in descendants. By integrating rodent mechanistic studies with preliminary human observations, this work advances a translational framework for understanding intergenerational addiction risk. Elucidating the molecular substrates of epigenetic inheritance may reveal biomarkers of vulnerability and inform strategies to mitigate the long-term consequences of the opioid crisis across generations.

## Paternal Drinking and the Epigenetic Influences on Offspring Mitochondrial Function, Placental Health, Structural Birth Defects, and Age-Related Disease.

**Dr. Mike Golding**

**Background**: Fetal alcohol spectrum disorders (FASDs) are among the most preventable causes of developmental disability, yet the contribution of paternal alcohol use to adverse offspring outcomes remains poorly understood. While maternal drinking has long been the focus of FASD research, emerging evidence suggests that epigenetic mechanisms of paternal inheritance are a significant and underappreciated driver of birth defects and long-term disease.

**Conceptual Framework & Main Findings**: To address this gap, our laboratory developed a preclinical multiplex mouse model enabling direct comparison of offspring outcomes following maternal, paternal, or dual parental alcohol exposure. Both maternal and paternal alcohol consumption independently impaired placental development and disrupted craniofacial patterning in a dose-dependent manner. Notably, male offspring of dual-exposed parents showed defects exceeding those caused by either parent's alcohol use alone, revealing an additive interaction between maternal and paternal exposures. At the cellular level, parental alcohol exposure heritably disrupted mitochondrial complex I activity in both the placenta and fetal brain. Critically, these bioenergetic deficits do not resolve after birth—they persist into adulthood, manifesting as elevated oxidative stress, chronic inflammation, and accelerated cellular aging in the brain and liver. Our recent work demonstrates that paternal Nrf2 loss-of-function phenocopies alcohol-induced effects in offspring, with both conditions altering similar cohorts of sperm noncoding RNAs targeting redox homeostasis and mitochondrial function. Moreover, we identified a novel liver-germline signaling

axis, as liver-specific Nrf2 deletion modified sperm RNA profiles in patterns overlapping with those seen in alcohol-exposed males.

**Significance**: These findings fundamentally reframe our understanding of alcohol-related birth defects and long-term disease risk. We demonstrate that disruptions in paternal mitochondrial redox signaling—whether environmentally induced by alcohol or genetically triggered through Nrf2 deficiency—converge on shared germline pathways that program lasting bioenergetic dysfunction in offspring. This mitochondrial reprogramming extends well beyond the developmental window, elevating susceptibility to chronic disease across the lifespan. Importantly, our data establish that FASD-related harm can be transmitted through either parent, underscoring the critical importance of both maternal and paternal health in preconception planning and calling for a broader public health approach to alcohol use before conception.

## Elovanoid-Mediated Epigenomic Modulation of Mitochondrial Functions and Homeostatic Synaptic Plasticity in Alzheimer's Disease.

**Dr. Nicolas Bazan**

Neurodegenerations arise when endogenous mechanisms that preserve neuronal integrity fail. We have asked whether the nervous system deploys a molecular logic of resilience at the onset of damage to restore homeostasis. We have identified elovanoids (ELVs), key components of this protective response. ELVs are bioactive lipid mediators derived from very-long-chain polyunsaturated fatty acids (C32–C34) synthesized by the neuronal-specific enzyme ELOVL4, whose mutations lead to mental retardation, other severe neurological diseases, and blindness. ELVs act as damage-responsive signals that coordinate cell-survival pathways, redox homeostasis, and epigenomic remodeling. ELVs enhance pro-survival mediators, including Sirtuin 1, Iduna, and Prohibitin 2, and selectively modulate TXNRD1, a central redox effector at the top of oxidative stress defenses. ELV biosynthesis is downregulated in Alzheimer's disease models and in retinal cells from age-related macular degeneration, underscoring their relevance to neurodegeneration.

Using experimental traumatic brain injury, a leading cause of disability and the largest non-genetic, non-aging-related cause of cognitive impairments and Alzheimer's -like dementia, we combined histopathology, synaptosomal mitochondrial functions, and single-cell multiome to define ELV bioactivity. Intranasal ELV-N34 administration reduced immune-cell infiltration and lipid peroxidation, improved neuronal survival, protected synaptosomal mitochondrial functions, and preserved synaptic proteins, including PSD95 and synaptophysin. At single-cell resolution, ELVs restored and induced gene programs linked to synapse organization, neuronal connectivity, and glial support in glutamatergic neurons, GABAergic neurons, astrocytes, oligodendrocytes, and

OPCs. At the same time, chromatin accessibility revealed increased activity and NRF2- and AP-1-associated regulatory networks, particularly in glutamatergic neurons, identifying an epigenomic framework through which ELVs strengthen antioxidant defenses, promote mitochondrial competence, and sustain homeostatic synaptic plasticity.

Thus, ELVs are epigenomic resilience mediators that couple oxidative-stress responses to mitochondrial performance, synaptic maintenance, and neural cell survival. Our work also indicates that ELVs modulate transcriptome architecture, dendritic integrity, senescence-associated gene programming, autophagy, extracellular matrix remodeling, inflammaging, and pathological Aβ- and tau-related signaling, while contributing to telomere integrity and chromatin-linked regulation. Because mitochondrial dysfunctions, maladaptive glial responses, oxidative stress, and synapse loss are central drivers of Alzheimer's disease, ELV signaling may define a broader protective axis relevant to disease onset and progression. This work highlights how damage-activated lipid mediators shape chromatin-linked transcription that preserves neural function and suggests a framework for understanding homeostatic synaptic plasticity in neurodegeneration.

# POSTER ABSTRACT LIST

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| 2 | | 2 | Ethan | Anderson | Inhibiting the histone methyltransferase G9a reduces escalated alcohol drinking in a novel model of alcohol dependence | LSU CBS |
| 3 | | 3 | Surjyadipta | Bhattacharjee | Cell-Specific epigenomic reprogramming of the midbrain periaqueductal gray (PAG) pain neuronal circuit by a novel, non-opioid, non-hepatotoxic analgesic. | LSUHSC NOLA |
| 4 | | 4 | Humaira | Growher | Regulation of DNMT Activity in Development and Disease | Purdue Univ |
| 5 | | 5 | Hongbing | Liu | Hdac1/2 and Ezh2 cooperate to preserve nephrogenesis by restraining β-catenin signaling | Tulane Univ |
| 6 | | 6 | Rebecca | Robker | Perfluoroalkyl and polyfluoroalkyl substances (PFAS) in trace levels via drinking water diminishes mouse embryo mitochondria function across three generations | Adelaide Univ |
| 7 | | 7 | Sarah | Swinford-Jackson | Paternal high fat diet consumption increases susceptibility to drugs of abuse in rat offspring | TAMU |
| 8 | | 8 | Kristie | Willett | Using zebrafish to investigate sex-dependent, epigenetic, and multigenerational adverse outcomes following parental benzo[a]pyrene exposure | Univ of MS |
| 9 | Post Doc | 9 | Ananya | Anmangandla | Dysregulation of the RNA modification m6A promotes cancer progression and provides therapeutic opportunities | Alida Biosciences |
| | | 10 | Amy | Ogle | From Preconception Health to Developmental and Epigenetic Programming Addressing Translational Gaps in Early Reproductive Health Engagement | Preconception Ed Partnership |
| 10 | | P1 | Alexandre | Champroux | Epigenetic Inheritance of Effects of Trauma | Tufts Univ |
| 11 | | P2 | Meghali | Joshi | Chemotherapy-Induced Sperm RNAs Disrupt Embryogenesis and Underlie Reproductive Outcomes in a Pre-Clinical Model of Childhood Cancer Survivors | Georgetown Univ |
| 12 | | P3 | Rashmi | Joshi | Germline influences of paternal high fat high sugar consumption | USC/Children's Hopsital |
| 13 | | P4 | Paulina | Misztak | A Novel Model to Study Epigenetic Transgenerational Inheritance of Alcohol-Related Phenotypes | |
| 14 | | P5 | Russell | Morales | Exosomal miRNAs Released by Alveolar Type II Cells after Exposure to Environmentally Persistent Free Radicals Regulate Nitric Oxide Release from Lung Endothelial Cells | LSU CBS |
| 16 | | P6 | Duane | Pereira | Environmentally-Induced Sperm RNAs Shape Placentation and Fetal Growth | Georgetown Univ |
| 17 | | P7 | Martha | Schwall | Targeting the Epigenetic Regulator G9a Reduces Heroin Seeking | LSU CBS |
| 18 | | P8 | Shallinie | Thangadurai | Sperm-Derived miR-277-3p Is a Candidate Mediator of Paternal Western Diet-Induced Epigenetic Inheritance During the Maternal-to-Zygotic Transition | LSU CBS |
| 19 | | P9 | Shilpa | Thota | Epigenetic Regulation of Treg and Inflammatory Pathways by E-Cigarette Exposure During Pregnancy is Modulated by IL-10 Deficiency in the Lung | LSU CBS |
| 20 | | P10 | Analisa | Taylor | Skeletal Muscle MIRO1 Deletion Protects Against Diet-Induced Hepatic Fibrosis Through Inter-Organ Crosstalk and Epigenetic Remodeling | PBRC |
| | Graduate Student | G1 | Gabriel | Peterman | Neurocognitive Gene Expression in the Brain Tissue of Pediatric Methotrexate Patients and *in vitro* Dopaminergic Neurons | LSUHSC NOLA |
| 22 | | G3 | Angel | Casillo | Exploring the Role of UNC0642 in Mitigating the Developmental Impacts of BPA on Stress Behavioral Responses | LSU CBS |
| 23 | | G4 | Kelly | Estilette | A One Health Systems Framework for Integrating Transgenerational Epigenomic Signals Across Environmental Exposure Pathways | Tulane Univ |
| 24 | | G5 | Joshua | Gill | Uncovering Mechanisms of Increased Healthy Aging in Dietary-Restricted *C. elegans* | LSU Bio Sciences |
| 25 | | G6 | Hafsa | Haq | Paternal Diet-Induced Epigenetic Modulation of Huntingtin-Associated Pathways in *Drosophila melanogaster* | LSU CBS |
| 26 | | G7 | Hannah | Holmberg | Regulation of DNA Damage Response by SPT6 | LSU CBS |
| 27 | | G8 | Md Imran | Hossain | Regulation of Dynein-Dependent HSV-1 Virion Retrograde Transport by Viral and Cellular Kinases | LSU PBS |
| 28 | | G9 | Caiden | Ingram | IL-10 Deficiency Improves Lung Function In Female Offspring Prenatally Exposed to E-cigarette Aerosols | LSU CBS |
| 29 | | G10 | Cheng | Lu | Spn1 represses the Transcription-coupled Nucleotide Excision Repair | LSU CBS |
| 30 | | G11 | Shahrzadossadat | Mirhosseini | In Vitro Testing of Histone Methyltransferase Activity for Future Drug Discovery | LSU CBS |
| 31 | | G12 | Tolulope | Olaolorun | Paternal Western Diet Reprograms Offspring Brain Mitochondrial Bioenergetics in *Drosophila melanogaster* | LSU CBS |
| 32 | | G13 | Lina | Shi | A Conserved Enhancer Cluster Regulates *efnb2* Expression in the Vertebrate Dorsal Retina | LSU Bio Sciences |
| 33 | | G14 | Lindsey | Yoo | KAT8 Associates with WDR5 in Adipocytes and Loss of KAT8 Implicates NSL Complex Activity in Adipose Metabolism | LSU Bio Sciences/PBRC |
| 34 | | G15 | Anusha | Zaman | Prenatal Exposure to E-Cigarette Humectants Alters Placental Methylation Status Correlating with Lung Dysfunction in a Juvenile Mouse Model of House Dust Mite-Induced Asthma | LSU CBS |
| 35 | UG Student | U1 | David | Nguyen | Uncovering the Role of the Aargonaute *rde-1* in the Regulation of Lifespan and Autophagy in *C. elegans* | LSU Bio Sciences |
| 36 | | U2 | Aldrich | Wilberg | Class III PI3K Complex I: a Potential Target for Modulating Autophagy in *C. elegans* | LSU Bio Sciences |
| | | U3 | Laura | Beaubrun | Nicotine Downregulates the Histone Methyltransferase G9a mRNA in the Brain | LSU CBS |

## 10 Minute Short Talks Listing

| Presenter | Career Level | Affiliation |
|---|---|---|
| **Rebecca Robker** | Faculty Member | University of Adelaide |
| **Alexandre Champroux** | Postdoctoral Fellow | Tufts University |
| **Megahli Joshi** | Postdoctoral Fellow | Georgetown University |
| **Neel Aluru** | Faculty Member | Woods Hole Oceanographic Institution |
| **Humaira Gowher** | Faculty Member | Purdue University |
| **Shallinie Thangadurai** | Postdoctoral Fellow | LSU Comparative Biomedical Sciences |
| **Surjyadipta Bhattacharjee** | Faculty Member | LSU Health Sciences Center – New Orleans |
| **Hongbing Liu** | Faculty Member | Tulane University |

## 5 Minute Short Talks Listing

| Presenter | Career Level | Affiliation |
|---|---|---|
| **Gabriel Peterman** | 3rd-Year Medical Student | LSU Health Sciences Center |
| **Rashmi Joshi** | Trainee / Postdoctoral Research Fellow | Children's Hospital Los Angeles |

# Faculty Submitted Abstracts

## #1 Neel Alura (Short Talk)

### Differential DNA Methylation Landscapes in Zebrafish *dnmt3aa* and *dnmt3ab* Mutants

Neel Aluru, Biology department, Woods Hole Oceanographic Institution, Woods Hole, Massachusetts 02543 USA

DNA methylation is a critical epigenetic mechanism involved in vertebrate development, cellular differentiation, and genome regulation. *De novo* DNA methyltransferases DNMT3A and DNMT3B are known to establish tissue-specific methylation patterns during development; however, their distinct and overlapping functions in non-mammalian vertebrates remain incompletely understood. To investigate the role of *de novo* methyltransferases in zebrafish, we performed comparative DNA methylation profiling in *dnmt3aa*, *dnmt3ab*, and double-mutant animals. Genome-wide analyses identified distinct differentially methylated regions (DMRs) across all mutant lines, with both unique and overlapping methylation signatures observed between genotypes. Single mutants exhibited a predominance of hypermethylated regions, whereas double mutants displayed a greater proportion of hypomethylated regions, suggesting partially redundant and compensatory functions between paralogs. Several DMRs showed large methylation differences, with some regions exceeding 60–70% methylation change relative to controls. Functional enrichment analyses associated DMRs with pathways related to signaling, ion transport, lipid metabolism, and developmental regulation. In particular, double mutants demonstrated broader enrichment across biological processes, consistent with increased disruption of epigenetic regulation when both paralogs are absent. These findings provide insight into the role of zebrafish dnmt3 paralogs in shaping tissue-specific methylation landscapes and establish a framework for future studies examining how altered epigenetic programming influences development, physiology, and environmental responses.

## #2 Ethan Anderson

**Inhibiting the histone methyltransferase G9a reduces escalated alcohol drinking in a novel model of alcohol dependence**

Paulina Misztak, Laura Beaubrun, and Ethan M. Anderson

Not available for public view at this time

## #3 Surjyadipta Bhattacharjee (Short Talk)

**Cell-Specific epigenomic reprogramming of the midbrain periaqueductal gray (PAG) pain neuronal circuit by a novel, non-opioid, non-hepatotoxic analgesic**

Surjyadipta Bhattacharjee1, Hernan A. Bazan2, Brian L. Giles1, Nicolas G. Bazan1
1Neuroscience Center of Excellence, LSU Health, New Orleans, LA – 70112.
2Department of Vascular and Endovascular Surgery, Heart and Vascular Service Line, Sutter Health, San Francisco, CA – 94109

We discovered a non-opioid analgesic (now entering FDA-approved phase II clinical trials: SRP-001). Now we investigated cell-specific epigenomic remodeling of the PAG pain circuit. Pain is an environmentally induced reshaping of neural circuits through epigenomics. Inflammatory injury, stress, metabolic state, and repeated nociceptive input alter chromatin accessibility, transcription factor activity, and cell–cell communication within pain-modulatory regions such as the PAG, change how neurons and glia encode, amplify, or suppress nociceptive signals. Using a complete Freund's adjuvant-induced inflammatory pain, single-cell RNA and ATAC sequencing of the midbrain PAG, we define coordinated transcriptomic and chromatin-accessibility signatures associated with analgesia. Three major transcription factor families emerged as central epigenomic nodes. In oligodendrocyte-lineage cells, inflammatory pain altered SOX-family transcription factors, while SRP-001 restored patterns associated with myelination, and circuit support. In neurons, SRP-001 and acetaminophen restored SP/KLF-family, including SP1-associated regulatory activity, suggesting pro-survival and neuronal maintenance detectable by chromatin accessibility. Conversely, they reduced activity of AP-1-family factors and TFEB/3-associated programs, consistent with suppression of pain- and inflammation-linked regulatory states without requiring parallel changes in gene expression, uncovering

an epigenomic mode of regulation. These findings identify the PAG as a site of analgesic-induced epigenomic plasticity and demonstrate that SRP 001 produces acetaminophen-like genomic and epigenomic analgesic signatures while avoiding NAPQI formation and preserving hepatic tight junction integrity. These data suggest that non-opioid analgesia can be achieved through targeted, cell-specific modulation of chromatin accessibility, transcription factor activity, and neuronal communication in central pain circuits. Thus, inflammatory pain circuitry may retain a therapeutically targetable form of epigenomic plasticity, in which analgesic intervention block pain transmission, and actively preprograms chromatin regulatory states toward neuronal resilience, synaptic stability, and reduced inflammatory drive. Funded by NIH Small Business Technology Transfer R42NS119103 (HAB and NGB) and the EENT Foundation, New Orleans (NGB).

## #4 Humaira Growher (Short Talk)

**Regulation of DNMT Activity in Development and Disease**

**Purdue University**

The timing and location of DNA methylation are critical parameters controlling cell differentiation. Dysregulation of these processes has widespread consequences ranging from developmental disorders to cancer. DNMT3A and 3B methyltransferases catalyze DNA methylation and have essential roles in embryonic development and differentiation. Our lab focuses on understanding how DNMT3A and 3B use their reader and writer domains to coordinate their activity with TFs and chromatin modifiers at specific locations in response to environmental signals, including those of cellular differentiation. Our data showed that during embryonic stem cell differentiation, DNMT3A-mediated DNA methylation is regulated by the upstream activity of the Lsd1-Mi2/NuRD complex at the enhancers of pluripotency genes, and that this mechanism is disrupted in cancer cells. Similarly, in normal cells, the cooperative catalytic mechanism that supports the high catalytic turnover and DNA sequence preference of DNMT3A is disrupted by the DNMT3A R882H mutation in AML cells, and the variant enzyme gains DNMT3B-like properties. Our recently published work described how the lncRNA *Dnmt3bas* controls the inducible expression and alternative splicing of Dnmt3b during epiblast differentiation. We have ongoing projects to understand the mechanism by which chromatin conformation

regulates DNA methylation during early differentiation. We are also systematically determining the mechanistic variations that regulate the specificities of DNMT3A and 3B enzymes, and studying the role of *Dnmt3bas* in gating early differentiation.

## #5 Hongbing Liu (Short Talk)

**Hdac1/2 and Ezh2 cooperate to preserve nephrogenesis by restraining β-catenin signaling**

Associate Professor of Pediatrics, Section of Pediatric Nephrology
Louisiana Cancer Research Center - Gene X Environment Research Program; The Tulane Center of Excellence in Sex-Based Medicine Investigator Tulane Cancer Center

**Background:**
Nephron progenitor maintenance and differentiation require precise coordination between developmental signaling pathways and epigenetic regulators. Histone deacetylases 1 and 2 (Hdac1/2) and the Polycomb repressive complex 2 (PRC2) methyltransferase Ezh2 are critical chromatin regulators of nephron progenitor cell (NPC) identity and fate. However, their cooperative roles in nephrogenesis remain poorly understood. We hypothesized that Hdac1/2 and Ezh2 coordinately control NPC fate by restraining Wnt/β-catenin signaling.

**Methods:**
The compound knockout of Hdac1/2 and Ezh2 in NPCs were generated via sequential removal of Hdac1 and/or Hdac2 allele(s) from Ezh2 conditional knockout mice using Six2-Cre–mediated recombination. These mutant mice are designated 5-alleles mutants. Renal morphology and nephrogenesis were evaluated by histology, immunofluorescence and RNAscope. Protein level was quantitated by Western Blot.

**Results:**
NPC-specific compound loss of three Hdac1/2 alleles together with biallelic Ezh2 deletion (5 allele mutants) resulted in severe nephrogenic defects characterized by reduced nephron endowment, tubular cyst formation, and disrupted nephron patterning. 5-allele mutant kidneys exhibited increased protein levels of active β-catenin and elevated expression of the Wnt targets such as Lef1 and Wnt4, indicating sustained activation of Wnt/β-catenin signaling. Mechanistically, mutant NPCs and

nascent nephrons exhibited loss of the repressive histone markers H3K27me2/3, with a reciprocal and significant increase in H3K27ac, consistent with reduced Hdac1/2 and Ezh2 activity. Furthermore, we observed increased acetylation of β-catenin at Lys49, a modification known to promote its activation. In addition, 5-allele mutant NPCs demonstrated ectopic induction of Six1, an early nephrogenic transcription factor normally extinguished during nephron progenitor differentiation.

**Conclusions:**

Hdac1/2 and Ezh2 cooperate to preserve nephrogenesis by restraining β-catenin signaling through both epigenetic and non-epigenetic mechanisms and maintaining transcriptional programs necessary for nephron progenitor differentiation and maturation. Sustained Six1 expression suggests developmental arrest and prolonged maintenance of immature progenitor state, potentially reflecting broader dysregulation of transcriptional and epigenetic states essential for nephrogenesis. Disruption of the regulatory network results in sustained developmental signaling, impaired lineage progression, and defective nephron formation. These findings provide new mechanistic insight into kidney development and establish Hdac1/2–Ezh2 cooperation as a critical safeguard of nephrogenesis.

## #6 Rebecca Robker (Short Talk)

**Perfluoroalkyl and polyfluoroalkyl substances (PFAS) in trace levels via drinking water diminishes mouse embryo mitochondria function across three generations.**

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Perfluoroalkyl and polyfluoroalkyl substances (PFAS), synthetic and resistant to degradation, are present at trace levels in municipal drinking water. PFAS exposure is associated with female infertility and developmental anomalies, yet how these compounds influence ovarian function and embryogenesis is not understood. Thus, the impact of exposure to PFAS via drinking water on oocyte viability and embryo development was examined. The local tap water was found to contain ~3ng/L PFAS, primarily PFOS, PFOA, and PFHxS. Female mice were then given purified water

containing 5ng/L or 50ng/L of these same three PFAS compounds or drinking fountain (tap) water for 4 weeks or 6 months. Ovulation, oocyte quality, embryo development and fetal weight were analyzed across three generations. Embryos from PFAS-exposed females (5ng/L or 50ng/L PFAS or tap water) exhibited impaired mitochondrial function, DNA damage and fewer cells, and reduced fetal weight. Embryo phenotypes were similar whether females were PFAS-exposed for 4 weeks, 6 months or just the first 4 weeks of the 6 months. Offspring drank purified water, yet fertility analysis showed similar embryonic and neonatal phenotypes in the F1 'daughters' of the PFAS-exposed females, and in the embryos of F2 females ('granddaughters' of PFAS-exposed females). To determine causality and whether defects are reversible, embryos were treated mitochondria-modulating compounds, with responses indicating that PFAS exposure irreversibly impairs key aspects of mitochondrial function. These findings identify cellular targets and mechanisms by which PFAS disrupt female fertility; reveal that PFAS cause intergenerational changes in mammalian embryos; and have important implications for water quality policies. Environmental Research (2026) Apr 1;296:124043.

## #7 Sarah Swinford-Jackson

**Paternal high fat diet consumption increases susceptibility to drugs of abuse in rat offspring**

Sarah Swinford-Jackson[1,2], Tyler J. Sacko[1], Samantha de Guzman[1], Rafael Solis Laybon[1], R. Christopher Pierce[1]

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Maternal consumption of a high fat diet (HFD) has been shown to produce hyperphagia and susceptibility to diet-induced obesity in mouse offspring. Maternal overnutrition during gestation also appears to influence offspring susceptibility to other rewarding substances, including alcohol, amphetamine, and cocaine. We and others have previously demonstrated that paternal drug exposure alters drug self-administration in offspring, but the effect of preconception paternal HFD intake on reward-related behaviors in offspring is unknown. We hypothesized that paternal

consumption of a high fat diet would alter drug self-administration in offspring. Sires had access to a HFD or a low fat diet (LFD) in addition to lab chow for 60 days, after which special diet was removed and sires were mated with naïve females to generate offspring. As expected, body weight of HFD sires was significantly higher than LFD sires, but there was no difference in offspring weight. Paternal HFD increased self-administration of cocaine (1.0 mg/kg/inf) in male, but not female, offspring relative to LFD-sired offspring. Morphine self-administration and motivation for morphine were also higher in HFD-sired vs. LFD-sired male offspring at a high unit dose (0.75 mg/kg/inf). Importantly, sucrose self-administration was not altered by paternal HFD consumption. Ongoing experiments use single nuclei RNA-sequencing of the nucleus accumbens from naïve male HFD- and LFD-sired offspring to identify differences in gene expression that may drive increased drug self-administration. Taken together, these results suggest that paternal consumption of a high fat diet before conception reprograms neurobiological mechanisms of reward to increase drug self-administration in male offspring. Funding: NIH grants R01 DA033641 (RCP) and K01 DA058168 (SESJ).

## #8 Kristie Willett

**Using zebrafish to investigate sex-dependent, epigenetic, and multigenerational adverse outcomes following parental benzo[a]pyrene exposure**

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Benzo[a]pyrene (BaP), a known carcinogenic polycyclic aromatic hydrocarbon (PAH), represents a class of ubiquitous environmental contaminants derived from the incomplete combustion. We have used zebrafish, assessed at different life-stages and variable routes of parental exposure (water vs diet), to study BaP's sex-dependent and multigenerational developmental toxicities. Following a continuous waterborne parental and larval exposure, BaP significantly reduced F1 global DNA methylation and altered gene specific methylation status. Dietary parental BaP exposure resulted in dose-dependent multigenerational adverse phenotypic impacts in F1 and F2 offspring with body deformities being the most severe. A crossover breeding design following a parental dietary BaP exposure yielded F1 cohorts of control and three crosses from BaP-exposed parents. Significant hyperactivity (light-dark assay) was

detected in F1 96 hpf fish resulting from both crosses with paternal BaP exposure. Gene expression and DNA methylation (RRBS) was measured in F0 gonads and 10 hpf F1 embryos resulting from each cross. F1 embryos from the BaP male x control female cross had the most differentially methylated regions and differentially expressed genes. Bioinformatic analysis highlighted impacts on genes associated with epigenetic processes and those critical during early development and provide new molecular pathways to mechanistically validate. Overall, we found that BaP exposure resulted in adverse outcomes that are multigenerational, and paternal exposure contributed most significantly to these adverse outcomes. *Supported by NIEHS 1R21ES030154.*

# Post Doc Submitted Abstracts

## #9 Ananya Anmangandla (Not Judged)

**Dysregulation of the RNA modification m6A promotes cancer progression and provides therapeutic opportunities**

Ananya Anmangandla[1], Ayush Raman[1], Roshan Vaid[3], Eric Davis[1], Zachary Miles[1], Sean Uryu[2], Marguerite A. Hutchinson[2], Eric S. Martin[2], Tanmoy Mondal[3,4], Matthias Fischer[5,6,7], Byron Purse[1], Gudrun Stengel[1]

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The objective of this study is to determine how sensitive detection and quantitation of the RNA modification *N*6-methyladenosine (m6A) can enable cancer detection, mechanistic insights into tumor biology, and improved monitoring of treatment

responses. RNA modifications, which are co- and post-transcriptional alterations to nucleobases or ribose, are key regulators of nearly all aspects of RNA metabolism, including transcription, splicing, localization, translation, stability, and interactions with RNA-binding proteins. Among these, m6A is the most abundant modification in human mRNA and long noncoding RNA and is frequently dysregulated in cancer. To enable comprehensive analysis of RNA modifications, we applied a multiplexed proximity-barcoding assay that enriches for modified RNA fragments, encodes modification sites during cDNA synthesis, and quantifies their abundance at each locus using synthetic spike-in controls for calibration. This approach allows concurrent detection of m6A, inosine, and pseudouridine, providing a multidimensional, high-sensitivity view of the cancer epitranscriptome. Application of this assay to neuroblastoma samples and cell line-derived xenograft tumor models revealed consistent increases in m6A abundance across all tumor types examined. Notably, m6A peak patterns also distinguished MYCN-amplified ($MNA^+$) from ALT-activated ($ALT^+$) and low-risk neuroblastomas, demonstrating that the method can resolve biologically and clinically distinct subgroups. Treatment of neuroblastoma cell lines and xenograft-derived samples with STC-15, a small-molecule inhibitor targeting the primary m6A writer enzyme METTL3, led to a dose-dependent reduction in m6A levels measurable by this assay. METTL3 inhibition was associated with decreased tumor cell viability and increased sensitivity to chemotherapeutics such as doxorubicin. Sensitive, quantitative measurement of m6A and related RNA modifications provides a powerful strategy to detect cancer-associated epitranscriptomic dysregulation, to dissect molecular heterogeneity in neuroblastoma, and to monitor therapeutic responses to METTL3-targeted interventions.

## #10 Amy Ogle (Not Judged)

**From Preconception Health to Developmental and Epigenetic Programming**

***Addressing Translational Gaps in Early Reproductive Health Engagement***

Amy Ogle, MS, RDN, Dietitian & Exercise Physiologist

Preconception Education Partnership (PEP) / PartnerPepTalk.org

Research in developmental origins of health and disease (DOHaD), reproductive biology, and epigenetic inheritance increasingly implicates preconception influences in shaping placental, fetal, and potentially multi-generational developmental

trajectories. Emerging evidence involving parental metabolic health, nutrition, psychosocial stress, sleep, environmental exposures, and gamete-related factors has expanded scientific interest in how developmental and epigenetic programming may begin prior to conception. At the same time, paternal preconception influences remain comparatively underrepresented in many reproductive health discussions despite growing investigation into sperm-mediated and seminal fluid-related pathways.

While mechanistic understanding continues to evolve, translational pathways for earlier interdisciplinary engagement remain limited. Many conversations surrounding reproductive and developmental health continue to occur only after pregnancy recognition, potentially narrowing opportunities for earlier health-supportive engagement and informed decision-making. Scientific concepts related to developmental programming also remain difficult to communicate outside specialist settings without oversimplification, stigma, or deterministic interpretation.

This conceptual and translational poster explores the gap between emerging mechanistic science and real-world engagement surrounding preconception health. The presentation outlines a prevention-oriented, stigma-aware communication framework designed to support earlier interdisciplinary discussion of upstream reproductive health influences while acknowledging scientific complexity and uncertainty. Particular attention is given to shared parental contributions, translational challenges involving paternal preconception health, and opportunities for collaboration across research, clinical, educational, and community-facing settings. The poster also considers opportunities for interdisciplinary collaboration involving translational research, clinician engagement, implementation approaches, and trainee participation.

# P1 Alexandre Champroux (Short Talk)

## Epigenetic Inheritance of Effects of Trauma

Champroux Alexandre[1], Mitra Sadat-Sadat Shirazi[1], Aidan Chen[2], Denny Sakkas[2], Tammy M. Scott[3], Emily Mellen[4], Abigail Kaija[5], Larisa Ryzhova[5], Lucy Liaw[5], Arturo Hernandez[5] , Larry Feig[1]

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Susceptibility to psychiatric disorders has traditionally been attributed to inherited genetic variation and individual life experiences. However, classical genetics alone cannot fully explain their heritability. While transgenerational inheritance of environmentally induced traits is well established in lower organisms, its mechanisms in mammals, particularly humans, remain incompletely understood**.**

Over the past decade, rodent studies have provided compelling evidence supporting a role for sperm non-coding RNAs, especially microRNAs (miRNAs), in this process. Male mice exhibit stress-specific alterations in sperm miRNA profiles that induce stress-specific behavioral and neurobiological changes in their offspring, even in the absence of paternal contact. In our laboratory, we use a paternal **Chronic Social Instability** (CSI) stress model, which reduces levels of miR-34/449 in sperm and preimplantation embryos derived from them that lead to anxiety-like behavior and social deficits specifically in female offspring across generations through the male germ line. Supporting the translational significance of these findings, we found that men with high **Adverse Childhood Experiences** (ACEs), whose offspring display elevated risk for mental health disorders, also display reduced sperm levels of the miR-34/449 family.

To test whether stress-specific changes in sperm miRNA content that leads to stress-specific behaviors in offspring occurs in humans as well as in mice, we performed small RNA sequencing on sperm from 51 men exposed to **adult trauma**, assessed with the **Trauma History Questionnaire** (THQ). High THQ scores, which predispose one to PTSD, were positively correlated with four sperm miRNAs: miR-532-3p, miR-491-5p, miR-375-3p, and miR-361-3p. And sperm from men reporting the highest THQ scores overexpressed all four miRNAs (4- to 130-fold)**.** Microinjection of these miRNAs

into mouse zygotes at levels comparable to those delivered to zygotes by human sperm induced anxiety- and depression-like behaviors in offspring, along with reduced body size and weight specifically in males.

We will report on using these mouse models to reveal how changes in these sperm miRNAs alter offspring development to produce sex-specific phenotypes. Finally, ~20% of men report either ACE or THQ scores in ranges we showed lead to changes in sperm miRNAs that in mice cause harmful effects in offspring, suggesting a large at-risk human offspring population.

## #P2 Megahli Joshi (Short Talk)

### Chemotherapy-Induced Sperm RNAs Disrupt Embryogenesis and Underlie Reproductive Outcomes in a Pre-Clinical Model of Childhood Cancer Survivors

Meghali Joshi[1], Duane Gischewski Pereira[1], Lu Jin[1], Susana Galli[1], Bridget Ferguson[1], Isabella Tuzzio[1], Alka Gupta[3], Andrew D. Holmes[3], Nagi G. Ayad[1], G. William Rebeck[2], Anton Wellstein[1], Upasna Sharma[3], Burton Appel[4], Nina Kadan-Lottick[1] and Sonia de Assis[1*]

The adverse effects of alkylating chemotherapy on reproductive function of male pediatric cancer patients who have limited fertility preservation options, are well documented and impact their quality of life. Yet, comprehensive studies examining the molecular mechanisms by which these chemotherapies disrupt germ cell development and sperm maturation remain scarce. Here, we used cyclophosphamide (CY), an alkylating drug widely employed to treat pediatric cancers, to develop a preclinical mouse model of childhood cancer survivors (CCS) and examine how CY impairs male fertility. We demonstrate that peri-pubertal CY causes testicular damage, sperm mitochondrial dysfunction and persistent dysregulation of sperm mitochondrial-derived tRNA and rRNA fragments. Mechanistic experiments show that CY-induced sperm RNAs disrupt preimplantation embryo development and viability. We also report that surviving offspring of CY-treated males develop metabolic dysfunction, highlighting the potential intergenerational epigenetic consequences of chemotherapy. These data suggest that sperm RNAs underlie reproductive outcomes in male CCS.

**Keywords:** Childhood chemotherapy, alkylating agents, sperm, small non-coding RNAs, male infertility, preimplantation embryo, intergenerational inheritance, epigenetics.

# #P3 Rashmi Joshi (5 Min Short Talk)

**Germline influences of paternal high fat high sugar consumption.**

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**Background.** Pre-conceptional paternal High Fat High Sugar (HFHS) consumption increases the likelihood of offspring developing type 2 diabetes mellitus (T2D)-associated phenotypes. Mechanisms for this relationship remain unclear. We and colleagues have demonstrated roles for sperm RNA as conduits for propagating paternal legacies of stress in mice. To probe sperm RNA-based legacies of paternal HFHS consumption we asked how different durations of HFHS diet affect metabolic health and sperm RNA profiles in male mice.

**Methods.** Adult male mice were fed either Control (CD) or HFHS diet for either 10 days or 16 weeks. We assessed weight gain, glucose metabolism and insulin sensitivity in these mice. Sperm were harvested from an independent cohort of mice on CD or HFHS diet for 10 days or 16 weeks. RNA from sperm of the CD-10d and HFHS-10d mice was isolated and subjected to small RNA sequencing. RNA from sperm of CD-16w and HFHS-16w has been isolated and sent for small RNA sequencing.

**Results.** Compared to CD-10d mice, HFHS-10d mice did not show excessive weight gain but showed impaired glucose metabolism without evidence of insulin resistance. HFHS-16w mice weighed significantly more than CD-16w and showed insulin resistance. Ten days of exposure to HFHS altered sperm small noncoding RNA.

**Conclusion.** Short-term exposure to HFHS impaired glucose tolerance without affecting insulin sensitivity, suggesting disruption of insulin secretion. Long-term exposure to HFHS decreased insulin sensitivity with persistent glucose intolerance, suggestive of insulin resistance in peripheral tissues. While short-term exposure to HFHS was sufficient to cause perturbations in the sperm RNA profile, comparing and contrasting these changes with sperm RNA profiles after longer-term exposure will shed light on sperm RNA-initiated alterations of specific metabolic endpoints. Understanding these relationships will provide an opportunity to attenuate and prevent the inheritance of detrimental metabolic disruptions in progeny.

## #P4 Paulina Misztak

### A Novel Model to Study Epigenetic Transgenerational Inheritance of Alcohol-Related Phenotypes

**LSU Comparative Biomedical Sciences Department**

**Background:** Alcohol-use disorder(AUD) is a global medical, social, and economic problem afflicting people of all ages. AUD is heritable, with a 50% prediction of risk in offspring. However, less is known about epigenetic influences on AUD inheritance. We aimed to develop a new model to study the effects of alcohol dependence on epigenetic transgenerational inheritance.

**Methods:** Female and male adult C57Bl/6J mice were subjected to a novel model of dependence-induced escalation of alcohol drinking. We have combined: 1) two-bottle choice (2BC) and 2) the Lieber-DeCarli diet(LDC), a forced alcohol consumption diet. For 4 weeks/5days/2h, mice had 2BC drinking(15% ethanol in water vs water) to establish baseline. Mice were divided into two equivalent groups based on ethanol intake and sex: control(CNT, 0% ethanol liquid diet) vs LDC(liquid diet with 5% ethanol). Mice received a 1-week CNT vs LDC liquid diet, then returned to regular food and 2BC for the next week. We completed 4 cycles of LDC/2BC for a total of 8 weeks to mimic the commonly used chronic intermittent ethanol(CIE) model of alcohol dependence. At the end of 8 weeks, 2 female and 3 male mice from both conditions were chosen and bred with non-alcohol exposed C57Bl/6J mice. We measured the number of pups delivered, the time to delivery, and the body weights.

**Results:** The Lieber-DeCarli diet significantly increased ethanol intake in LDC mice in the 2BC protocol($p>0.001$). We did not observe any significant changes in delivery time or litter body weight (both $p>0.05$). However, the LDC diet may reduce the number of pups as there was a trend for significance($p=0.0985$).

**Conclusion:** Our combined 2BC-LDC model is a novel way to produce dependence-escalated alcohol drinking. This alcohol dependence-induced effect may lead to a reduction in the number of pups in the F1 generation and could lead to other epigenetic translational inheritance changes in future cohorts. Next steps are to introduce some of these F1 mice to 2BC to analyze ethanol intake, but we will also retain other F1 mice as alcohol-naïve to produce an F2 generation to assess epigenetic inheritance of alcohol dependence in our new model.

## #P5 Russell A. Morales

### Exosomal miRNAs Released by Alveolar Type II Cells after Exposure to Environmentally Persistent Free Radicals Regulate Nitric Oxide Release from Lung Endothelial Cells

Russell A. Morales[1], Alexandra Noel[1], Tammy R. Dugas[1] [1]Department of Comparative Biomedical Sciences, Louisiana State University School of Veterinary Medicine, Baton Rouge, Louisiana 70803, USA

Background and Purpose: Particulate matter containing environmentally persistent free radicals (EPFR) is produced when organic matter or pollutants are incompletely combusted and adsorb onto the surface of particles containing redox-active metals. Previous studies in mice have shown that EPFR-induced aryl hydrocarbon receptor (AhR) activation in alveolar type II (ATII) cells can lead to vascular endothelial dysfunction beyond the lungs. We hypothesize that EPFR alters the profiles of exosomal miRNAs released into plasma, thereby modulating gene expression essential for nitric oxide regulation in lung vessels. Methods: To test our hypothesis, we isolated and cultured mouse ATII cells at the air liquid interface (ALI) and exposed them to aerosolized EPFR (~30 $\mu g/cm^2$) using a Vitrocell exposure system. At 24 h after ALI exposure, exosomal miRNAs from the basal medium were isolated and characterized, then exposed to commercially sourced murine lung microvascular endothelial cells (mLMVE). The expression and activation of vascular eNOS, as well as

NO production, were then measured. Results: Exosomes released by ATII cells following EPFR exposure exhibit a distinct miRNA profile. We identified miR-1906, miR-1900, and miR-32-5p as having potential mRNA targets involved in regulating nitric oxide signaling. Furthermore, miRNAs within these exosomes can be taken up by mLMVE cells, leading to reduced nitric oxide production, decreased expression of Nos3 and Pik3r2 mRNA, and lower eNOS phosphorylation levels. Conclusions: Our findings highlight the role of exosomal miRNAs in regulating lung vascular function after EPFR exposure, particularly by targeting genes that control nitric oxide release. These studies aid in evaluating human risk and could offer an intervention to help communities address the health impacts of EPFR exposure.

## #P6 Duane Gischewski Pereira

**Environmentally-Induced Sperm RNAs Shape** P**lacentation and Fetal Growth**

Duane Gischewski Pereira[1], Raquel Santana da Cruz[1], Meghali Joshi[1], Lu Jin[1], Elaine Chen[1], Rong Hu, Susana Galli and Sonia de Assis[1*]

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Sperm RNAs are environment-sensitive and mediate paternally-induced epigenetic inheritance of traits. The sperm RNA cargo is delivered to the oocyte during fertilization but precise mechanisms by which the 'epigenetic memory' it carries alters embryonic development to shape the progeny phenotypes remains poorly understood. In eutherian mammals like rodents and humans, the placenta is a crucial organ that connects fetus and mother, ensuring exchange of nutrients and gases essential for development. Impaired placental function can result in fetal growth restriction and long-term health effects. While placentation is largely driven by paternal imprinted genes, little is known about how paternal environmental exposures before conception affect placenta formation. Here, we used two mouse paradigms of male pre-conception experiences to study whether environmentally-induced sperm RNAs regulate placenta development. Using zygotic injections, we show that the sperm RNA load from DDT-treated and obese males impacts placenta function and fetal growth in opposite ways. Mechanistically, these environmentally-driven sperm RNAs disrupt early embryonic development and cell lineage specification. They also dictate the mature placenta cellular composition, nutrient stores, vascularization and imprinted genes landscape.

Furthermore, paternal sperm RNAs not only affect embryonic and placental development, but also modulate maternal physiological adaptations during pregnancy. In this context, our findings provide direct evidence that sperm RNAs shape placentation, offering a mechanism by which fathers influence their progeny beyond their shared genome. These data also highlight the role of paternal non-genetic factors in pregnancy outcomes.

## #G1 Gabriel Peterman (5 Min Short Talk)

### Neurocognitive Gene Expression in the Brain Tissue of Pediatric Methotrexate Patients and *in vitro* Dopaminergic Neurons

Gabriel Peterman[1], Gabrielle Sheets[1], Joe Vaccaro[1], Jovanny Zabaleta[2], Matthew Stark[3], Chindo Hicks[1], and Fern Tsien[1].

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**Background:** The chemotherapy drug methotrexate (MTX) is associated with long-lasting cognitive symptoms in some pediatric cancer survivors. These adverse effects include audiological impairment, decreased attention span, and lower measured intelligence. The present study hypothesizes that MTX deregulates the expression of several neurocognitive genes and may show an epigenetic relationship with the neurological late-effect outcomes experienced by pediatric cancer survivors.

**Methods:** White matter paraffin blocks from MTX-treated patients and age-matched controls were received from the Pathology Department at Manning Family Children's Hospital in New Orleans. DNA and RNA were purified utilizing the Covaris truXTRAC® FFPE total NA Kit. DNA methylation CpG sites and mRNA expression were analyzed with the Infinium Human MethylationEPICversion 2.0 microarray and the mRNA-targeted Nanostring Neuroinflammation Panel, respectively. ACS-5006 neural progenitor cells from ATCC were cultured and differentiated into dopaminergic neurons for *in vitro* MTX dose-curve studies of gene dysregulation.

**Results:** The mRNA expression for multiple neurocognitive genes was dysregulated in MTX patients when compared to controls. Furthermore, DNA CpG sites were generally more methylated in MTX patients, but methylation did not always correlate

with mRNA suppression. Four neurocognitive genes of interest were discovered to share both abnormally methylated and decreased mRNA suppression: MSR1, BDNF, TCIRG1, and PSEN2. For example, BDNF, which has been found to be decreased in Alzheimer's disease, was 6.9% hypermethylated on a CpG site and exhibited a 6% decrease in mRNA expression. Immunocytochemistry using the TH and Tuj1 antibodies confirmed the successful differentiation into dopaminergic neurons for future use.

**Conclusion:** This work desires to guide clinical follow up with pediatric cancer survivors into adulthood to screen for potential neurological risks. The present results indicate that early interventions are necessary for reducing neurological adverse effects, including auditory, medical, and neurocognitive assessments. Future work will focus on isolating DNA and RNA from the differentiated dopaminergic neurons to analyze epigenetic dysregulation after the administration of varying MTX doses.

## #P7 Martha Schwall

### Targeting the Epigenetic Regulator G9a Reduces Heroin Seeking

Martha A. Schwall, Ethan M. Anderson

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Substance use disorders (SUD) are a major public health crisis, and current treatments have staggeringly high rates of relapse. The persistence of SUDs in patients is likely due in part to lasting epigenetic changes in neurons caused by repeated substance use. One important epigenetic alteration involves reductions in levels of the histone dimethyltransferase, G9a, in nucleus accumbens (NAc) after chronic morphine administration using a forced administration procedure. We first tested the effects of heroin vs saline self-administration on NAc G9a levels using western blotting. Next, we tested the effects of downregulating NAc G9a by using an adeno-associated virus expressing a short-hairpin RNA to G9a (AAV-shG9a) or a control RNA (AAV-shLUC). We tested the effects of a G9a knockdown on both heroin taking/seeking and sucrose taking/seeking. Finally, we tested the effects of a daily systemically-administered G9a inhibitor, UNC0642 (4mg/kg, i.p.) on heroin seeking behavior. We found that NAc G9a was downregulated by heroin self-administration. Mimicking this downregulation with

a NAc G9a knockdown had no effect on heroin-taking behavior, but significantly reduced heroin-seeking behavior. Control experiments showed that NAc G9a knockdown had no effect on sucrose taking or sucrose-seeking behavior. Finally, daily systemic administration of UNC0642 also reduced heroin seeking behavior, suggesting that G9a can be therapeutically targeted to reduce heroin craving. These data support previous findings that NAc G9a downregulation is a common feature of all major classes of addictive drugs including psychostimulants, alcohol, and opioids. These data also demonstrate that mimicking the heroin-induced reduction of NAc G9a with AAV shG9a reduces heroin seeking, but not sucrose seeking, suggesting that these effects are drug specific and do not alter normal reward-seeking behavior. Finally, the effects of a daily G9a inhibitor suggest the potential to reduce drug craving in individuals with SUD, which should be pursued clinically.

## #P10 Analisa Taylor

### Skeletal Muscle MIRO1 Deletion Protects Against Diet-Induced Hepatic Fibrosis Through Inter-Organ Crosstalk and Epigenetic Remodeling

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**Background:** Liver disease is a prevalent complication of obesity and type 2 diabetes, affecting over 50% of patients and progressing from steatosis to steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. This continuum is driven, in part, by disrupted systemic metabolic homeostasis. Inter-organ communication between skeletal muscle and liver is a key regulator of this process, yet mechanisms linking muscle metabolic function to hepatic disease progression remain poorly defined. Mitochondrial Rho GTPase 1 (MIRO1), a ubiquitously expressed mitochondrial trafficking protein involved in maintaining cellular energy homeostasis, has emerged as a novel mediator of metabolic dysfunction. We have previously demonstrated that accumulation of skeletal muscle MIRO1 exacerbates whole-body insulin resistance and impairs glucose uptake in cells, mice, and humans with obesity and type 2 diabetes. However, the role of skeletal muscle MIRO1 in mediating liver disease progression remains completely unknown. The purpose of this study was to investigate whether skeletal muscle MIRO1 regulates liver disease progression through systemic metabolic remodeling.

**Methods:** Male Miro1$^{flfl}$ and Miro1$^{SkM-/-}$ C57BL/6J mice were randomized to 20 weeks of a 40% fat, 20% fructose, and 2% cholesterol (HFHC) diet as a model of metabolic dysfunction-associated steatohepatitis (MASH), or a sucrose-matched low-fat diet (LFD) at 8 weeks of age and housed at thermoneutrality. Body weight and food intake measurements were taken weekly, while body composition was measured every 6 weeks. A glucose tolerance test (GTT) was performed at 16 weeks and animals were housed in a metabolic chamber for 8 days at 18 weeks of diet. At study endpoint, liver mass was measured and histologically assessed for steatosis and fibrosis. Hepatic triglyceride content and expression of lipid metabolism genes were quantified. Untargeted metabolomics was performed to evaluate global hepatic metabolic remodeling. To assess histone status, H3K27ac and H3K27me3 were measured by Western blot and normalized to total H3 protein.

**Results:** HFHC Miro1$^{SkM-/-}$ mice exhibited increased body weight ($p<0.0001$) driven by elevated fat mass ($p<0.0001$) and absolute lean mass ($p=0.0093$), compared to Miro1$^{fl/fl}$ controls. LFD Miro1$^{SkM-/-}$ animals displayed higher blood glucose over time ($p=0.0210$) compared to Miro1$^{fl/fl}$ controls, but there was no difference in the HFHC Miro1$^{SkM-/-}$ animals compared to HFHC controls ($p=0.5156$). Independent body weight or food intake, HFHC Miro1$^{SkM-/-}$ displayed increased energy expenditure ($p=0.0100$), respiratory exchange ratio (RER) ($p=0.0275$), and oxygen consumption ($p=0.0078$). Liver mass was increased in HFHC Miro1$^{SkM-/-}$ mice compared to Miro1$^{fl/fl}$ controls ($p<0.0001$); however, histological analysis revealed increased vacuolization ($p=0.0235$) alongside reduced hepatic triglyceride content and decreased fibrosis ($p=0.0130$). Expression of lipid metabolism genes was elevated, consistent with enhanced lipid turnover (FASN; $p=0.0078$, PNPLA2; $p=0.0061$). Untargeted metabolomics revealed reductions in glycolytic intermediates, purine and pyrimidine metabolites, and fatty acid transport-associated metabolites. Consistent with hepatic metabolic remodeling, HFHC Miro1$^{SkM-/-}$ mice also exhibited reduced hepatic H3K27 acetylation and trending decreased H3K27 methylation, suggesting altered epigenetic regulation associated with protection from advanced liver disease.

**Conclusion:** Skeletal muscle deletion of Miro1 protects against diet-induced progression of advanced hepatic fibrosis by remodeling substrate preference, hepatic lipid handling, and hepatic epigenetic landscape despite increased adiposity. These

findings identify skeletal muscle MIRO1 as a novel regulator of liver disease progression via inter-organ metabolic crosstalk.

## #P8 Shallinie Thangadurai (Short Talk)

**Sperm-Derived miR-277-3p Is a Candidate Mediator of Paternal Western Diet-Induced Epigenetic Inheritance During the Maternal-to-Zygotic Transition**

**Paternal Western Diet-Induced Epigenetic Inheritance During the Maternal-to-Zygotic Transition**

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Growing evidence across species indicates that transgenerational inheritance of metabolic traits is a conserved phenomenon, with small RNAs emerging as the strongest-supported carriers of heritable information via paternal germ line. Here, we investigated whether paternal miRNAs influence offspring development during the maternal-to-zygotic transition (MZT), a critical developmental window characterized by degradation of maternal RNAs and activation of the zygotic genome. Using a *Drosophila* model of paternal Western diet (WD) exposure, small RNA sequencing identified miR-277-3p as a candidate diet-responsive miRNA. Subsequent RT-qPCR validation demonstrated a consistent ~1.5-fold increase in miR-277-3p expression in sperm from WD-fed fathers. Furthermore, in situ hybridization revealed that miR-277-3p puncta were predominantly localized within spermatocytes and were significantly more abundant in testis of Western diet fathers than in controls. To identify embryonic pathways potentially regulated by miR-277-3p, we performed single-cell RNA sequencing of early embryos. Differential gene expression analysis revealed substantial transcriptional changes during the maternal-to-zygotic transition (MZT), including genes involved in dorsal-ventral axis formation. FlyEnrichr identified miR-277-3p as a putative upstream regulator of several differentially expressed genes, including *vimar*, *mei-P26*, and *brat*. Using a uracil phosphoribosyltransferase (UPRT)-based metabolic labeling system to trace paternal RNAs, we found that miR-277-3p was

significantly enriched among paternally miRNAs in 0–2 h embryos from WD fathers, providing direct evidence for its paternal transmission and supporting its potential role during MZT. Consistent with these findings, in situ hybridization revealed elevated miR-277-3p expression in early embryos, particularly in the ventral neurogenic region that gives rise to the neuroblasts of the ventral nerve cord. Furthermore, spermatocyte-specific overexpression of miR-277 in fathers using Topi-GAL4 resulted in downregulation of *mei-P26* expression (~-1.3 fold) in early embryos. In contrast, spermatocyte-specific knockdown of miR-277 did not alter *mei-P26* expression in early embryos. Together, these findings identify miR-277-3p as a paternally transmitted, diet-induced miRNA and support its potential role as a mediator of paternal WD-induced epigenetic inheritance during MZT, supporting a mechanism by which paternal diet influences early embryonic gene regulation through sperm-derived miRNAs.

**Keywords:** miRNAs, Wester-diet, sperm, embryogenesis, epigenetic inheritance, MZT

## #P9 Shilpa Thota

### Epigenetic Regulation of Treg and Inflammatory Pathways by E-Cigarette Exposure During Pregnancy is Modulated by IL-10 Deficiency in the Lung

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**Rationale:** E-cigarette (e-cig) use during pregnancy is increasingly prevalent, yet its impact on pulmonary immune regulation in expecting mothers remains poorly understood. Following exposure to inhaled toxicants, the lung's ability to maintain precise immune tolerance governed by epigenetic mechanisms including DNA methylation may be disrupted. Chromatin-modifying enzymes regulate gene accessibility for immune homeostasis. Interleukin-10 (IL-10), among others, coordinates T-regulatory (Treg) cell activity through the TGF-β–STAT5a–FOXP3 axis and is essential for epigenetic immune homeostasis. Disruption of these pathways by e-cig exposure during pregnancy may impair DNA methylation-dependent and chromatin-level immune regulation, potentially impacting the pulmonary health of mothers and fetuses.

**Methods:** Pregnant wild-type (WT) and IL-10 knockout (IL-10KO) dams were exposed to e-cig aerosols (third generation: free-base nicotine or fourth generation: nicotine salt) or filtered air 14 days before plus throughout pregnancy. Lungs were collected to assess global DNA methylation (%5-mC) and gene-specific promoter methylation by bisulfite conversion followed by methylation-specific PCR (MSP). Chromatin-modifying enzyme expression was evaluated using $RT^2$ PCR Arrays.

**Results:** Global methylation (%5-mC) was significantly elevated in WT dams exposed to free-base nicotine and nicotine salt ($p<0.01$), whereas IL-10KO dams showed a significant reduction in global methylation across both exposure groups ($p<0.01$), indicating that IL-10 deficiency reverses the maternal methylation response to e-cig aerosols. Within the Treg axis, *Foxp3* promoter methylation was markedly hypomethylated in IL-10KO dams in both free-base nicotine and nicotine salt groups ($p<0.001$), and *Stat5a* was significantly hypermethylated in IL-10KO-nicotine salt dams ($p<0.01$), consistent with impaired Treg transcriptional programming. *Il-1β* and *Arg1* promoter methylation were significantly elevated in IL-10KO-nicotine salt dams ($p<0.0001$; $p<0.05$), reflecting dysregulated inflammatory gene silencing. $RT^2$ PCR Array analysis revealed broad chromatin enzyme dysregulation in IL-10KO-free-base nicotine lungs, including upregulation of *Aurkc* (5.28-fold), *Smyd1* (4.38-fold), alongside downregulation of *Kmt5b* (−5.74-fold) and *Carm1* (−2.35-fold), suggesting a shift in the histone methylation landscape.

**Conclusion:** Overall, e-cig exposure modulates epigenetic regulation of the Treg and inflammatory axes in maternal lungs, amplified by IL-10 deficiency. Nicotine salt-based aerosols induced greater epigenetic dysregulation than free-base nicotine, suggesting nicotine formulation differentially impacts maternal pulmonary immune homeostasis. These findings underscore IL-10's role in preserving DNA methylation-dependent immune tolerance in pregnancy.

# Graduate Student Submitted Abstracts

## #G3 Angel Casillo

### Exploring the Role of UNC0642 in Mitigating the Developmental Impacts of BPA on Stress Behavioral Responses

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Bisphenol A (BPA), a pervasive environmental contaminant detected in >90% of human samples, has been widely implicated in multiple adverse health outcomes, including neurodevelopmental disorders. Previously, we have shown developmental exposure to .04 µM & 1 µM BPA in larval zebrafish (Danio rerio) alters stress reactivity to acoustic, visual, and peripheral stimuli. RNAseq analysis showed multiple disrupted pathways, including mechanisms associated with epigenetic reprogramming; such as chromatin activation, histone acetylation (driven by an upregulation of kat8), and reduced histone methylation driven by downregulation whsc1 and other related genes. UNC0642 is a small-molecule inhibitor of G9a/GLP histone lysine methyltransferases, which play a critical role in chromatin regulation–thereby influencing gene expression by methylating histones. This compound has been linked to stress-induced behavioral alterations, including previous studies where we found that exposure to 1.56 µM UNC0642 yielded the opposite behavioral profile that BPA exposure elicited in acoustic and visual motor response assays. As such, it can be hypothesized that UNC0642 exposure in tandem with BPA exposure may elicit functionally antagonistic physiological responses.

In the current study, we exposed developing zebrafish larvae to .04 µM and 1 µM BPA, as well as 1.56 µM UNC0642, and assessed both developmental and acute UNC0642 effects (114 & 24 hr exposures). At 120-hour postfertilization, morphological defects, acoustic and visual motor response, and locomotor capacity endpoints were collected. To our knowledge, no studies have investigated the interaction between UNC0642 and BPA. Given the overlapping molecular pathways influenced by these

compounds, this work has the potential to elucidate the role of epigenetic regulation in BPA-induced stress behavioral alterations and provide insight into potential therapeutic and mitigation strategies.

## #G4 Kelly Estilette, DrPH(c), MPH, MCHES

**A One Health Systems Framework for Integrating Transgenerational Epigenomic Signals Across Environmental Exposure Pathways**

Tulane University Weatherhead School of Public Health & Tropical Medicine
Genetic Alliance

Epigenetic inheritance describes how environmental factors influence gene regulation across generations. Strong evidence is available from studies in non-human animals and plants, whereas findings in humans remain limited and context-dependent. Although mechanisms such as DNA methylation, chromatin remodeling, and RNA pathways have been identified, these processes are often examined in isolated biological contexts, limiting their integration into broader ecological and population-level models. Building on these translational and conceptual limitations, this study introduces a structured conceptual framework that situates transgenerational epigenomic processes within a One Health systems context. This approach explicitly links environmental exposures, developmental timing, and cross-species biological responses. Instead of conceptualizing epigenetic inheritance as a discrete molecular phenomenon, the framework organizes it as a component of a multi-layered system comprising (1) upstream exposure environments, (2) biological and developmental processes, and (3) downstream phenotypic and population-level implications. Evidence from controlled experimental models demonstrates that specific exposures, such as endocrine-disrupting chemicals, nutritional variation, and stress-related inputs, can induce heritable epigenetic modifications across multiple generations in non-human animal systems. In parallel, human studies, particularly epigenome-wide association studies, consistently identify associations between environmental exposures and epigenetic variation, although causal and multigenerational pathways remain less clearly established. The primary contribution of this study is the articulation of a systems-level bridge model that connects mechanistic epigenetic processes to exposure pathways across species and environments. This model provides a structured approach to interpreting and

integrating epigenomic signals as both molecular outcomes and indicators of cumulative and distributed environmental inputs across biological scales within interconnected human, animal, and environmental systems. Consequently, by aligning mechanistic epigenetics with ecological, developmental, and population-level perspectives, this framework enables more precise integration of epigenomic data and underscores the necessity for interdisciplinary approaches to understanding non-genetic inheritance. Additionally, it offers a conceptual foundation for investigating how environmentally induced biological variation may contribute to phenotypic diversity under conditions of rapid environmental and societal change.

## #G5 Joshua Gill

**Uncovering Mechanisms of Increased Healthy Aging in Dietary-Restricted *C. elegans***

**LSU Department of Biological Sciences**

Joshua P. Gill, Olga Dubuisson, Kathryn DeLeo, P. Kerr Wall, K. Adam Bohnert, and Alyssa Johnson

The average human lifespan has notably risen within the last century largely because of modern medical advancements and declining birth rates. As a consequence of having an aging population, the prevalence of age-related diseases has also seen a significant uptick, meaning humans spend a larger proportion of their life in an unhealthy state; this has created a lifespan-healthspan gap that needs to be addressed. To target and improve healthy aging, researchers have used model organisms to uncover molecular pathways that promote longevity. One of the most well-studied longevity paradigms is dietary restriction (DR), which refers to eating less than normal without causing malnutrition. Remarkably, DR causes significant epigenetic changes that alter gene expression in the aging adult. Also, dietary-restricted adults pass on epigenetic changes to their progeny that promote healthy aging, indicating a significant transgenerational epigenetic effect. Using the *eat-2* mutant, a genetic model of DR in *C. elegans*, I show that loss of the *adenine nucleotide translocator 4* (*ant-1.4*) further extends DR-dependent lifespan and healthspan, though similar changes are not seen when *ant-1.4* is lost in other longevity mutants. Although loss of *ant-1.4* improves healthy aging in a DR background, it also causes early developmental stress resulting in significant embryonic lethality. This

increase in embryonic lethality can be suppressed by feeding the worms HT115 bacteria, which contain significantly more vitamin B12 compared to the standard OP50 diet, suggesting alterations to vitamin B12-dependent metabolic pathways occur when *ant-1.4* is lost in a DR background. By studying healthy aging resulting from loss of *ant-1.4* in a DR background, mechanisms that enhance healthy aging during DR, including potential epigenetic changes, will be uncovered.

## #G6 Hafsa Haq

**Paternal Diet-Induced Epigenetic Modulation of Huntingtin-Associated Pathways in *Drosophila melanogaster***

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Environmental factors can induce epigenetic modifications that alter gene expression and contribute to long-term changes in physiology and behavior across generations. Our previous proteomic analysis revealed reduced levels of endogenous Huntingtin (HTT) and Huntingtin Interacting Protein K (HYPK) in female offspring from Western diet-fed fathers (WFO) with a parallel increase in feeding behavior, suggesting that paternal dietary exposure might disrupt huntingtin-associated pathways in a sex-specific manner. HTT is a conserved protein crucial for neuronal stability, trafficking, and synaptic function, and is subject to post-transcriptional regulation by microRNAs (miRNAs). Bioinformatic analysis identified miR-10 as a putative regulator of *htt* mRNA. We therefore investigated whether altered HTT expression contributes to inherited feeding phenotypes and whether miR-10 functions as an upstream regulator of this pathway.

*Drosophila* huntingtin (dhtt) was manipulated using the pan-neuronal nSyb-GAL4 driver and monitored locomotor activity under a 12 h light/12 h dark cycle. Pan-neuronal overexpression of dhtt increased locomotor activity in both sexes, increasing total activity by approximately ~30**%** relative to controls. The effect was most pronounced at night, where nocturnal locomotor activity increased by approximately ~50%. Conversely, pan-neuronal knockdown of *dhtt* reduced total locomotor activity by ~10–15%, with nighttime activity decreasing by ~25%.  Thus, suggesting a role for

huntingtin in regulation of circadian activity. To determine whether these changes were accompanied by altered food intake, consumption was quantified using the Consumption–Excretion (ConEx) assay. Pan-neuronal overexpression of *dhtt* significantly increased standard diet (CD) consumption in females by ~60% compared with controls, whereas no significant differences in Western diet (WD) consumption were observed, indicating a sex-specific effect of huntingtin on nutrient intake. Given that miR-10 is predicted to target htt mRNA, we examined whether its manipulation recapitulates htt deficiency. Pan-neuronal overexpression of miR-10 significantly suppressed feeding behavior in both sexes, reducing total feeding events by ~60% relative to controls ($p < 0.05$), disrupting circadian locomotor rhythms, and elevating rest time. Daytime and nighttime feeding events were similarly reduced by 58–65%. In contrast, miR-10 knockdown showed an increase in feeding, approximately 20–30%. Importantly, qPCR analysis demonstrated that pan-neuronal miR-10 overexpression significantly reduced endogenous htt mRNA expression ($p <0.05$), providing direct experimental evidence that miR-10 negatively regulates huntingtin expression. These findings demonstrate that neuronal miR-10 regulates feeding and locomotor behaviors and produces phenotypes that overlap with those observed following dhtt manipulation. Collectively, these data suggest that miR-10-mediated regulation of huntingtin and associated pathways may underlie the metabolic and behavioral phenotypes induced by paternal diet.

## #G7 Hannah Holmberg

**Regulation of DNA Damage Response by SPT6**

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Many different DNA damaging agents constantly attack cellular DNA. Ultraviolet light represents one of the most common DNA damaging agents that produce UV induced damage. UV irradiation causes large helix distorting damage lesions of two main types: 6,4 Photoproducts and cyclobutane pyrimidine dimers (CPDs). Nucleotide Excision Repair (NER) repairs most of these lesions but requires genetic and epigenetic factors to allow recruitment of repair proteins and allow access to the DNA for repair to occur. Spt6 acts as a highly conserved histone chaperone present in

organisms from simple eukaryotes to complex mammals. Spt6 plays rolls in transcription, nucleosome remodeling and mRNA processing. Additionally, Spt6 is known to be essential for H3k36 trimethylation. Previous data has shown that mutations in Spt6 cause alterations in transcription and abnormal histone remodeling. This study aimed to elucidate if Spt6 plays a role in NER by using the Spt6 mutant spt6-HhH to observe effects on NER and histone modifications. CRISPR/Cas9 deleted AA931-994 of the Spt6 gene (Spt6-HhH). Preliminary studies tested the UV sensitivity of the Spt6 mutants. These studies showed that Spt6-HhH mutation caused increased UV resistance in rad16Δ rad26Δ cells and rad16Δ but showed increased UV sensitivity in otherwise wild type cells. Following these studies, researchers mapped the repair speed of spt6-HhH cells across the entire genome. Results show faster TCR in spt6-HhH cells than in WT cells. Additionally, mapping the nucleosome regions showed irregularly positioned nucleosomes in the spt6 mutant cells, suggesting a possible defect in nucleosome reassembly after repair. mRNA seq on spt6 revealed that proper ribosome biogenesis requires spt6. Further studies should map the nucleosome accessibility across the genome to observe the nucleosome positioning in the WT and spt6-HhH mutant.

## #G8 Md Imran Hossain

**Regulation of Dynein-Dependent HSV-1 Virion Retrograde Transport by Viral and Cellular Kinases**

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Herpes simplex virus 1 (HSV-1) establishes lifelong infection by invading peripheral neurons and relying on dynein-driven retrograde axonal transport to reach neuronal cell bodies. While dynein is essential for this process, how incoming virions are dynamically regulated to engage the motor complex and sustain efficient retrograde transport remains a major unresolved question. Here, we investigated phosphorylation-dependent control of retrograde transport by the viral serine/threonine kinase US3 and

the host kinase glycogen synthase kinase-3β (GSK-3β), a key regulator of cytoskeletal dynamics and motor function. Using biochemical interaction assays and infection-based analyses, we demonstrate that US3 physically associates with both GSK-3β and dynein components during HSV-1 infection. Disruption of US3 function alters kinase–dynein interactions and impairs efficient retrograde trafficking of incoming virions, indicating that US3 is a critical modulator of transport regulation. Our findings further suggest that US3 influences dynein activity through coordinated interactions with GSK-3β, supporting a model in which viral and cellular kinases act together to fine-tune motor engagement during neuronal infection. Ongoing studies in neuronal culture systems and in vivo mouse infection models aim to define how US3-dependent phosphorylation events regulate dynein motor activity and viral neuroinvasion. Collectively, this work identifies viral kinase–host motor signaling as a critical regulatory axis in HSV-1 transport and highlights US3-mediated modulation of dynein function as a potential target for antiviral intervention.

## #G9 Caiden Ingram

### IL-10 Deficiency Improves Lung Function In Female Offspring Prenatally Exposed to E-cigarette Aerosols

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**Background**: Prenatal exposures to e-cigarette (e-cig) aerosols introduce nicotine, carbonyls, and metals that can cross the placenta. These exposures can cause epigenetic modifications and impair lung and immune cell development, ultimately heightening the risk and severity of allergic asthma in offspring. This study aims to investigate the role of IL-10 during prenatal e-cig exposure on mouse lung development and asthma susceptibility.

**Methods**: C57BL/6 wild type (WT) and IL-10 knockout (KO) dams were exposed to either air, tobacco-flavored 3$^{rd}$-generation (gen) e-cig aerosol containing free base nicotine (24 mg/mL) or tobacco-flavored 4$^{th}$-gen e-cig aerosol containing nicotine salt(24 mg/mL). Exposures were conducted 14 days prior to conception plus during gestation.

Female offspring were sacrificed at birth, 14-16 days, and 7-8 weeks following saline or house-dust mite (HDM) treatment to induce asthma.

**Results**: At birth, WT offspring exhibited significantly increased lung tissue complexity following 3$^{rd}$- and 4$^{th}$-gen e-cig exposures, whereas only the 4$^{th}$-gen exposures caused this effect in IL-10 KO offspring. These results indicate smaller airways and delayed lung development. Lung RNA sequencing data revealed mild gene dysregulation in female WT and IL-10 KO offspring exposed to 3$^{rd}$-gen e-cigs (20 and 23 genes, respectively), while 4$^{th}$-gen e-cig induced robust molecular changes in IL-10 KO compared to WT offspring (99 and 11 genes, respectively). At 14-16 days in WT offspring, 3$^{rd}$-gen e-cig significantly increased respiratory resistance, while 4$^{th}$-gen e-cig induced this effect in IL-10 KO. In 7-8-week-old WT offspring 3$^{rd}$-gen e-cig exposures plus HDM significantly increased respiratory resistance. Globally, IL-10 deficiency maintained lung function within control levels. Lung molecular changes were exacerbated by HDM in WT offspring with 231 and 237 dysregulated genes for 3$^{rd}$-gen and 4$^{th}$-gen e-cig exposures, respectively, compared to 162 genes in the air + HDM group. Gene dysregulation was more pronounced in IL-10 KO offspring but showed a reduction in the number of dysregulated genes following the e-cig + HDM exposures with 421 and 138 dysregulated genes for 3$^{rd}$-gen and 4$^{th}$-gen e-cig exposures, respectively, compared to 441 genes in the air + HDM group.

**Conclusion**: Prenatal exposures to e-cigs impair lung development, with 4$^{th}$-gen causing more severe effects than 3$^{rd}$-gen at birth. IL-10 deficient offspring displayed improved lung function even after allergen exposure. Overall, prenatal e-cig exposures, mainly 3$^{rd}$-gen, exacerbated asthmatic responses later in life, likely due to epigenetic changes during fetal lung development.

# #G10 Cheng Lu

**Spn1 Represses the Transcription-Coupled Nucleotide Excision Repair**

Cheng Lu, Shisheng Li

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The major pathway for the repair of DNA damage caused by UV is nucleotide excision repair(NER). NER has two sub-pathways, transcription-coupled repair (TCR) and global genomic repair (GGR). Spn1 is a transcription elongation factor and histone chaperone that plays essential roles in RNA polymerase II-mediated transcription, chromatin remodeling, and mRNA processing. As a transcription elongation factor, it helps Spt6 bind to RNA Pol II, thus it may play a role in TCR. Spn1 is also a histone chaperone, which helps Spt6 to assemble the histones after the RNA Pol II passes the transcribed DNA region, and this may also affect both TCR and GGR. In this study, we found that Spn1 can inhibit the TCR in yeast. We truncated the C terminal of Spn1 which led to a higher survival of the mutants. We also found that the C terminal truncation of Spn1 facilitate the repair of UV induced-damage in RPB2 and YEF3 genes which transcribe at moderate and high rates respectively, via Lesion-Adjoining Fragment Sequencing(LAF-Seq). We further found that the repression of TCR by Spn1 is not limited to specific genes, but occurs in all actively transcribed genes in the genome. Our research reveals a new function of Spn1 in TCR and suggests that this a transcription elongation factor and histone chaperone may play a broader part in DNA damage response in addition to its known function in transcription.

# #G11 Shahrzadossadat Moeinzdeh Mirhosseini

**In Vitro Testing of Histone Methyltransferase Activity for Future Drug Discovery**

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G9a (Euchromatic Histone Lysine Methyltransferase 2, EHMT2) is a histone methyltransferase that interacts with G9a-like-protein (GLP/EHMT1) to regulate gene expression by adding repressive histone H3 lysine dimethylation marks, including H3K9me2. Through controlling these epigenetic marks, G9a and GLP influence chromatin accessibility and stabilize transcriptional programs that contribute to cellular identity and plasticity. Dysregulation of G9a-mediated repression has been implicated across multiple disease, including neuropsychiatric disorders, cancer progression, alcohol use disorder, and and other substance use disorders. In addiction-related models, G9a-dependent methylation has been associated with persistent transcriptional remodeling that can support maladaptive behavioral phenotypes, motivating interest in G9a as a druggable epigenetic target for neuroscience-focused therapeutic discovery. UNC0642 and UNC1479 are selective small molecule inhibitors of both G9a and GLP, i.e. they pharmacologically suppress H3K9 dimethylation. To assess their use in vitro for drug discovery of other agents that reduce H3K9me2, HEK293 cells were treated with several doses of either UNC0642 of UNC1479 and the levels of H3 total protein plus H3K9me2 levels were analyzed by Western blot. We found that UNC0642, but not UNC1479, produced a dose-dependent reduction in H3K9me2. Collectively, these data support UNC0642 as a useful compound for studying G9a-regulated epigenetic repression and provide a foundation for future investigations of G9a-targeted strategies in addiction- and disease-relevant systems. Future studies will use this assay to test novel G9a inhibitors that could potentially be used to treat diseases like cancer or substance use disorders.

# #G12 Tolulope Olaolorun

## Paternal Western Diet Reprograms Offspring Brain Mitochondrial Bioenergetics in *Drosophila melanogaster*

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Previously, we have shown that paternal exposure to Western diet (WD) alters feeding behavior, brain proteomic profiles, and microRNA expression in the offspring; indicating that paternal dietary experience can be transmitted through epigenetic mechanisms. However, the underlying mechanisms through which these inherited signals impair offspring brain metabolism remain unclear. Here, we show that paternal WD epigenetically reprograms offspring brain mitochondrial bioenergetics by remodeling electron transport system function, with Complex I emerging as a primary target of this metabolic reprogramming. Adult male *Drosophila melanogaster* were fed either control diet or WD for five days before mating with control-fed females. Fathers and adult offspring were assessed using behavioral assays, high-resolution respirometry (Oxygraph 2K), mitochondrial DNA copy number analysis, qRT-PCR, proteomics, and immunoblotting. WD increased food consumption and locomotor activity, while brain respiration was unchanged in fathers. In contrast, offspring of WD-fed fathers showed reduced brain mitochondrial respiration across multiple respiratory states. High-resolution respirometry revealed reductions in leak respiration, oxidative phosphorylation (OXPHOS) capacity, and electron transfer (ET) capacity. The strongest deficits were observed in pyruvate/malate-supported respiration, with male offspring showing approximately 60-70% lower Complex I-linked respiratory flux compared with controls. Although respiratory deficits were observed across multiple substrate-supported respiratory states, the largest reductions occurred during NADH-linked respiration, identifying the electron transport system entry point as the primary focus of this study. To identify molecular changes associated with the respiratory phenotype, we examined mitochondrial abundance and respiratory machinery. Mitochondrial DNA copy number was reduced in WD

fathers and male offspring. qRT-PCR revealed differential expression of genes encoding Complex III and IV subunits, together with increased expression of the glycolytic enzyme HEX-A in both fathers and male offspring, suggesting compensatory metabolic remodeling. Whole-fly NAD/NADH ratio was reduced by approximately 30% in WD fathers, consistent with redox imbalance. These findings demonstrate that paternal WD exposure is sufficient to reprogram offspring brain metabolism. By combining high-resolution respirometry with molecular and biochemical analyses, we identify defects in mitochondrial respiration accompanied by changes in mitochondrial DNA abundance, respiratory gene expression, and Complex I respiratory state. These findings extend our previous observations of paternal diet-induced inheritance by identifying brain mitochondrial bioenergetics as a downstream target of paternal epigenetic programming.

## #G13 Lina Shi

### A Conserved Enhancer Cluster Regulates *efnb2* Expression in the Vertebrate Dorsal Retina

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The vertebrate retina is patterned along its dorsal-ventral (DV) axis by signaling centers that provide each domain with distinct molecular and functional properties, including differential photoreceptor composition and opsin expression. Although the key DV patterning genes are well studied, the *cis*-regulatory mechanisms that establish and maintain these territories in the adult retina remain poorly understood. To explore this regulatory landscape, we leveraged the four-eyed fish *Anableps anableps*, whose large, protruding eyes and expanded ventral retina facilitate dissection of dorsal and ventral halves for spatially resolved genomics. Bulk RNA-seq of the *Anableps* dorsal and ventral retina regions showed expression of canonical DV markers, while bulk ATAC-seq revealed hundreds of differentially accessible

chromatin regions, including dorsally enriched ATAC-seq peaks residing within a gene desert region between *efnb2a* and *gtpbp8*. These putative *cis*-regulatory elements located to a 29 kb interval forming a contiguous enhancer cluster. Via Hi-C analysis, we identified a topologically associating domain (TAD) encompassing *efnb2a*, *gtpbp8*, and *slc10a2*, with a dorsal-enriched chromatin contact linking the enhancer cluster to the *efnb2a* promoter. Comparative genomics showed that the *efnb2*-s*lc10a2* synteny and TAD boundaries are maintained from human to zebrafish. Notably, the orthologous human interval contains a genome-wide significant association with retinal thickness (rs2575134, $P = 2 \times 10^{-14}$), providing independent genetic evidence that this conserved regulatory domain contributes to human retinal architecture. To enable functional testing of this long regulatory interval, we strategically turned to the spotted green pufferfish (*Tetraodon nigroviridis*), a species with one of the most compact vertebrate genomes, allowing nearly the entire orthologous enhancer cluster (~13 kb) to be cloned intact. Transgenic assays in both zebrafish and mouse demonstrated that this *Tetraodon* enhancer cluster drives dorsal retina-specific eGFP expression, underscoring the deep conservation of its regulatory function across vast phylogenetic distances. Together, these results highlight how a multi-species approach leveraging complementary strengths of model and non-model organisms can illuminate ancient regulatory mechanisms underlying vertebrate eye patterning.

## #G14 Lindsey Yoo

### KAT8 Associates with WDR5 in Adipocytes and Loss of KAT8 Implicates NSL Complex Activity in Adipose Metabolism

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Lysine Acetyltransferase 8 (KAT8) acetylates histone H4 at lysine 16 (H4K16ac) and functions as the catalytic subunit of the Non-Specific Lethal (NSL) and Male-Specific Lethal (MSL) transcriptional complexes. Despite extensive study in other systems, the roles of these complexes in adipocytes remain poorly defined. Adipocyte-specific

deletion of KAT8 in mice decreases fat mass and induces insulin resistance, and KAT8 protein expression in adipose tissue responds dynamically to nutritional state, implicating it in energy metabolism. To identify candidate KAT8-associated proteins, immunoprecipitation (IP) was performed in mature 3T3-L1 adipocytes under endogenous conditions, and publicly available transcriptomic datasets were analyzed to assess NSL/MSL complex expression in adipose tissue. IP identified WD Repeat Domain 5 (WDR5), a known NSL scaffold protein, as a candidate KAT8-interacting protein; WDR5 co-precipitated with KAT8 predominantly in nuclear fractions. NSL and MSL complex members were detected across white adipose tissue cell types by single-nucleus RNA sequencing and throughout 3T3-L1 differentiation by western blot. RNA-seq following KAT8 depletion showed that *Kat8* transcript is reduced without broadly affecting other complex members, suggesting effects are not due to transcriptional loss of NSL/MSL components. Additionally, differentially expressed genes from KAT8 depletion in white adipose tissue show significant directional concordance with a *Kansl3* liver-specific knockout signature, supporting a link between KAT8 and NSL-related transcriptional programs. Upcoming quantitative proteomics will map the adipocyte KAT8 interactome, and direct adipose-specific NSL perturbation will test whether this complex underlies KAT8-dependent transcriptional and metabolic phenotypes relevant to insulin resistance and type 2 diabetes.

## #G15 Anusha Zaman

### Prenatal Exposure to E-Cigarette Humectants Alters Placental Methylation Status Correlating with Lung Dysfunction in a Juvenile Mouse Model of House Dust Mite-Induced Asthma

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Epigenetic reprogramming is increasingly recognized as a central mechanism linking prenatal exposures to later-life respiratory conditions. Building on our prior finding that prenatal exposure to e-cigarette hypomethylated Il10ra, increased Il10 expression, and exacerbated asthmatic responses in offspring, we investigated whether

propylene glycol (PG)/glycerin (VG) alone reprograms the developing immune-respiratory axis. C57BL/6 dams were exposed to HEPA-filtered air or 30/70 PG/VG aerosols (0.20 mg/puff) 1.5 h/day for 14 days preconception plus gestational days 1-20. Offspring received weekly intranasal PBS or 50 µg house dust mite (HDM) instillation during postnatal weeks 3/4-5/6. Placental global DNA methylation, lung/placental gene expression, bronchoalveolar lavage fluid (BALF) cytology, and lung function were assessed. Across the maternal-placental-fetal interface, PG/VG dysregulated chromatin writers and developmental markers in tissue-specific patterns. Maternal lungs downregulated chromatin writers (Dnmt1, Dnmt3a, Hdac1/2) and retinoic acid (RA) regulators (Cyp26b1, Pparg) with Il10/13 induction. Placentas showed global DNA hypomethylation paired with upregulation of 7 chromatin writers and altered RA/steroid signaling (Cyp26a1, Hsd17b1 upregulated; Il2 downregulated). PG/VG-exposed offspring lungs at birth had significantly increased mean linear intercept, showing disrupted lung maturation. RA signaling critical to this process was dysregulated: females exhibited Cyp26b1 upregulation, suggesting sustained RA catabolism when RA is necessary for alveolar septation; males exhibited downregulated Rxrb, Pparg, suggesting impaired signaling necessary for AT2 cell and surfactant maturation. Overall, 15 genes mediating RA metabolism, T helper cell differentiation, inflammatory response, and oxidative stress were dysregulated.

Though alveolar morphometry normalized by 5-6 weeks, HDM challenge demonstrated that prenatal PG/VG exposure programs allergic susceptibility independent of structural changes, potentially through inflammatory mechanisms. PG/VG+HDM exposure dysregulated 27 genes enriched in pathways observed at birth, in addition to sex-specific Th1/Th2/Th17 activation. Females exhibited airway obstruction: upregulated Il10 (31.7-fold), Hdac1, Cyp26a1 and downregulated RA signaling genes; BALF eosinophilia; elevated pressure-volume (PV) loop and tidal volume, indicating Th2-dominant activation. By contrast, males demonstrated lung restriction: upregulated Il10 (23.7-fold), Dnmt1, Dnmt3a, Hdac1; mixed neutrophilic-eosinophilic BALF inflammation; multipolar Th1/Th2/Th17 activation; reduced PV-loop; increased elastance and tissue damping.

In conclusion, prenatal exposure to nicotine-free e-cigarette aerosols may transmit susceptibility to exacerbated allergic asthma through epigenetic mechanisms involving chromatin changes at immune and developmental loci.
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# Undergraduate Student Submitted Abstracts

## #U1 David Nguyen

**LSU Department of Biological Sciences**

**Uncovering the Role of the Aargonaute *rde-1* in the Regulation of Lifespan and Autophagy in *C. elegans***

David Nguyen, Joshua P. Gill and Alyssa Johnson

An aging population poses an issue for society and economic stability. Thus, it is more important than ever to address lifespan extension methods to combat the overall trend of age-related diseases becoming prominent. A major driver of aging is a loss of protein homeostasis (proteostasis), which leads to increased cellular damage. Using the short-lived *C. elegans* as a model system, I am investigating the role of the argonaute *rde-1* in protein homeostasis. In preliminary work, I show that *rde-1* is essential for basal autophagic cargo turnover and loss of *rde-1* shortens *C. elegans* lifespan. Typically, *rde-1* is thought to only function in the RNAi pathway; however, my research has implicated *rde-1* in autophagy regulation. In future work, I will determine how *rde-1* regulates autophagy and whether these functions are dependent on its canonical roles in small RNA processing.

## #U2 Aldrich Wilberg

**Class III PI3K Complex I: a Potential Target for Modulating Autophagy in *C. elegans***

Cristian Ricaurte – Perez, Joshua Gill, P. Kerr Wall, Olga Dubuisson, K. Adam Bohnert, and Alyssa Johnson

LSU Department of Biological Sciences – Johnson Lab

Over the past century, human lifespan has increased dramatically. However, this increase is not observed in human healthspan, the time that an individual lives free from disease. Caloric restriction, without causing malnutrition, has been shown in multiple model organisms to decrease the lifespan-healthspan gap. The beneficial effects due to caloric restriction are shown to be fully reliant on functional autophagy; if autophagy is upregulated, like during caloric restriction, then there will be a further reduction in the lifespan-healthspan gap. Furthermore, during caloric restriction, the canonical vesicular morphology of lysosomes shifts into a network of tubules. These tubular lysosomes (TLs) allow for increased autophagic turnover and aid in the beneficial effects of caloric restriction. Remarkedly, in C. elegans, when the parental generation of worms is subject to caloric restriction, TLs are passed on transgenerationally in well-fed offspring. Using a genetic model of caloric restriction in C. elegans, the eat-2 mutant, in combination with a strain over expressing a Drosophila transgene, SVIP, that has constitutive TL formation, I show that the formation of TLs is reliant on the activities of the class III PI3K complex I. Further research of how this complex behaves to promote TL formation could provide insight into any epigenetic changes that occur to allow for transgenerational TL induction.

## #U3 Laura Beaubrun

**Nicotine Downregulates the Histone Methyltransferase G9a mRNA in the Brain**

Laura Beaubrun, Alexandra Noel, and Ethan M. Anderson

LSU Comparative Biomedical Sciences Department

The rising prevalence of e-cigarette (e-cig) use or vaping among American adults (~7%) underscores the urgent need for further neuro-epigenetic research. This popular lifestyle choice, mainly driven by the exposure to nicotine, can permanently rewire adult reward pathways, fuel lifelong addiction, and accelerate cognitive decline. G9a (EHMT2) is a histone methyltransferase responsible for the di-

methylation of histone H3 at lysine 9 (H3K9me2), a repressive epigenetic mark involved in gene silencing and chromatin remodeling. While G9a has been implicated in addiction-related plasticity and emotional memory in reward circuitry, its transcriptional regulation in the amygdala following nicotine exposure is unknown. Adult male BALB/c mice were exposed by inhalation for 4 months to either 1) air, 2) fourth-generation e-cig aerosols alone or 3) cigarette smoke (CS) plus third-generation e-cig aerosols (dual usage). Each exposure condition was optimized to yield similar cotinine levels in all mice and very low levels of carbonyls were detected in the e-cig aerosols. All vaping products had a tobacco flavor and contained 30 mg/mL of either nicotine salt (fourth-generation) or free base nicotine (third-generation). Tissue was collected from the amygdala, nucleus accumbens, dorsal striatum, and prefrontal cortex. We then used quantitative PCR (qPCR) to examined G9a mRNA levels, normalized to a housekeeping gene (GAPDH). We found that G9a mRNA expression in the amygdala was significantly downregulated in both nicotine-exposed groups. These findings demonstrate that exposure to repeated nicotine by either e-cigs or dual-use (cigarette smoke + e-cigs) suppresses G9a transcription in the amygdala, suggesting a shift toward a more transcriptionally permissive chromatin state in this region. Given the amygdala's central role in fear memory, emotional regulation, and addiction behavior, downregulation of G9a may contribute to the neurobiological changes underlying nicotine dependence and tobacco-related affective dysregulation. Future studies should test whether pharmacological or genetic restoration of G9a activity in the amygdala attenuates affective or dependence-related behaviors associated with nicotine exposure, which would establish a causal link between this epigenetic change and behavior.