# 2024 UAB AGING RESEARCH SYMPOSIUM

## UAB Alumni House and the Alys Stephens Center

## March 11-12, 2024

UAB
NATHAN SHOCK CENTER
The University of Alabama at Birmingham

UAB
INTEGRATIVE CENTER
FOR AGING RESEARCH
The University of Alabama at Birmingham

UAB
ALZHEIMER'S DISEASE CENTER
The University of Alabama at Birmingham

# AGENDA

## March 11, 2024

**UAB Alumni House**

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| 7:30-8:30 am | **Registration and Continental Breakfast** |
| 8:30-8:35 am | **Welcome**<br>**Thomas Buford, PhD**<br>Professor and Associate Dean<br>Co-Director, UAB Nathan Shock Center of Excellence in the Basic Biology of Aging<br>Director, UAB Center for Exercise Medicine<br>The University of Alabama at Birmingham |
| **SESSION I:** | ***Diversive models of biological aging***<br>**Chair:**<br>**Steven Austad, PhD**<br>Distinguished Professor<br>Protective Life Endowed Chair in Healthy Aging Research<br>Co-Director, UAB Nathan Shock Center of Excellence in the Basic Biology of Aging<br>The University of Alabama at Birmingham |
| 8:35 – 9:35 am | ***KEYNOTE PRESENTATION***<br>**João Passos, Ph.D.**<br>Professor<br>Mayo Clinic<br>**"Mitochondria and Cell Senescence: A Matter of Life and Death"** |
| 9:35-10:00 am | **Abbi Hernandez, Ph.D.**<br>Assistant Professor<br>The University of Alabama at Birmingham<br>**"Metabolism and the Gut-Brain-Axis in Aging and Alzheimer's Disease"** |
| 10:00-10:25 am | **Daniella Chusyd, Ph.D.**<br>Assistant Professor<br>Indiana University Bloomington<br>**"Trunks Up: Elephants for Aging Research"** |
| 10:25-10:45 am | **BREAK** |
| 10:45-11:10 am | **Scott Ballinger, Ph.D.**<br>Professor and Associate Dean<br>Co-Leader UAB Nathan Shock Center Comparative Mitochondrial Health Assessment Core<br>The University of Alabama at Birmingham<br>**"A Quantitative Assay for Determining Mitochondrial DNA Derived Damage Associated Molecular Pattern (DAMP) Levels in Humans and Rodents"** |

11:10-11:35 am **Stanislava Chtarbanova, Ph.D.**
Assistant Professor
The University of Alabama Tuscaloosa
"**As Time Flies By: Studying the Impact of Aging on *Drosophila* Antiviral Defenses**"

11:35-11:50 am **ELEVATOR PITCH**

- **Dean Bunnell,** Graduate Student
  The University of Alabama Tuscaloosa
  **"Evaluating Flock House virus genome changes after replication in young and aged *Drosophila melanogaster*"**
- **Osagie Emokpae,** Graduate Student
  The University of Alabama Tuscaloosa
  **"Sub-neurotoxic exposure to ethyl acetate fraction of soil bacterium metabolite promotes longevity in *C. elegans*"**
- **Tate Lasher,** Graduate Student
  The University of Alabama at Birmingham
  **"Hypoglycemia and impaired glucagon response in a transgenic mouse model of tauopathy"**
- **Angad Yadav, PhD,** Postdoctoral Fellow
  The University of Alabama at Birmingham
  **"Glutamine availability impacts skeletal muscle progenitor cell state transition via Mito-Nuclear communication with advancing age"**

11:50-12:10 pm **Christy Carter, Ph.D.**
Health Scientist Administrator
Division of Aging Biology (DAB)
National Institute on Aging (NIA) | National Institutes of Health (NIH)
***Overview of training at NIA and DAB priority for funding***

12:10 AM – 1:10 pm **LUNCH & NETWORKING**

**SESSION II:** ***Circadian and nutritional-based intervention for maintaining healthy aging***
**Chair:**
**Girish Melkani, PhD**
Associate Professor
Co-Leader UAB Nathan Shock Center Comparative Organismal Energetics Core
The University of Alabama at Birmingham

1:10-2:10 PM **KEYNOTE PRESENTATION**
**Rozalyn Anderson, Ph.D.**
Professor of Medicine
University of Wisconsin-Madison
School of Medicine and Public Health
**"Aging & Delayed Aging by Caloric Restriction"**

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| 2:10-2:35 pm | **Girish Melkani, Ph.D.**<br>"**Chronobiology of Lipid Modulation: Discovering the Role of Time-Restricted Feeding in Aging and Metabolic Disorders"** |
| 2:35-3:00 pm | **Courtney Peterson, Ph.D.**<br>Associate Professor<br>The University of Alabama at Birmingham<br>**"Effects of Time-Restricted Eating on Primary and Secondary Aging in Humans"** |
| 3:00-3:20 pm | **BREAK** |
| 3:20-3:45 pm | **Martin Young, Ph.D.**<br>Professor<br>The University of Alabama at Birmingham<br>**"Circadian Control of Cardiac Physiology and Pathophysiology"** |
| 3:45-4:10 pm | **Karen Gamble, Ph.D.**<br>Professor, F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry<br>The University of Alabama at Birmingham<br>**"Salty Secrets: Impact of High Salt Diet on the Primary Circadian Clock"** |
| 4:10-4:15pm | **Closing Remarks**<br>**Steven Austad, PhD** |

## Alys Stephens Center

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| 4:30-6:30 pm | **POSTER SESSION and RECEPTION** |

# March 12, 2024

**UAB Alumni House**

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| 7:30-8:30 am | **Registration and continental breakfast** |
| 8:30-8:40 am | **Welcome**<br>**Ken Boockvar, MD, MS**<br>Professor, Department of Medicine, Division of Gerontology, Geriatrics, and Palliative Care<br>Gwen McWhorter Endowed Chair in Geriatric Medicine<br>Director, Integrative Center for Aging Research<br>The University of Alabama at Birmingham<br><br>**Seth Landefeld, MD**<br>Professor and Chair of the Department of Medicine<br>The University of Alabama at Birmingham |
| **SESSION I:** | ***Cutting Edge Research***<br>**Chair:**<br>**Ken Boockvar, MD, MS** |
| 8:45 – 9:45 am | ***KEYNOTE PRESENTATION***<br>**Stephanie Studenski, RN, MD, MPH**<br>Professor Emeritus<br>University of Pittsburgh<br>**"There's Something in the Way they Move: Aging and Mobility"** |
| 9:45-10:05 am | **BREAK** |
| 10:10-10:55 am | **FLASH TALK** |

- **Zahra Bassiri,** Graduate Student
  The University of Alabama Tuscaloosa
  **"Subsensory Electrical Noise Stimulation Enhances Postural Control During Visual Perturbations in Older Adults"**
- **George C. Ling, MD,** Resident
  The University of Alabama at Birmingham
  **"Dynamics of Dominant Default Mode Network Linked to Processing Speed in Cognitively Healthy Oldest-Old"**
- **Korijna Valenti, PhD, IPCC, MS,** Instructor
  The University of Alabama at Birmingham
  **"Experiences with culturally based values and preferences for clinician communication and care with lesbian and bisexual older women with serious illness & their care partners"**
- **Belinda Williams, MD,** Postdoctoral Fellow
  The University of Alabama at Birmingham
  **"Lower Urinary Tract Symptoms and Cognitive Impairment among Participants in the REasons for Geographic and Racial Differences in Stroke Cohort Study"**
- **Chunhong Xiao, PhD, RN,** Postdoctoral Fellow
  The University of Alabama at Birmingham
  **"Care-resistant Behavior Trajectories in the Context of Mouth Care of Persons Living with Dementia in Nursing Homes"**

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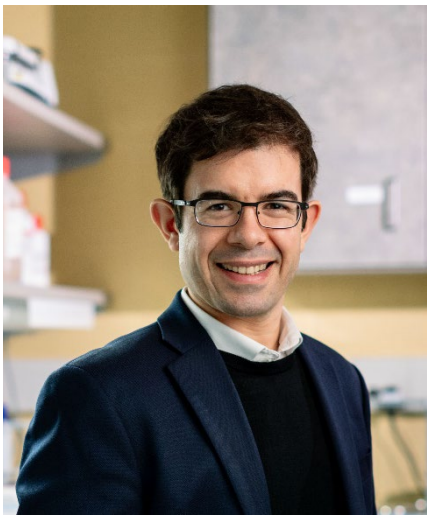
| 10:55-11:20 am | **Alayne Markland, DO, MSc**<br>Professor, Department of Medicine, Division of Gerontology, Geriatrics, and Palliative Care<br>The University of Alabama at Birmingham<br>Birmingham VA Healthcare System Director, Birmingham/Atlanta Geriatric Research, Educational, and Clinical Center (GRECC)<br>**"Improving Access to Urinary Incontinence Treatments through Mobile Health Technology"** |
| 11:25-11:50 am | **Virginia Howard, PhD, FAHA, FSCT**<br>Distinguished Professor of Epidemiology, School of Public Health<br>The University of Alabama at Birmingham<br>**"Recruiting and Retaining Diverse Participants in Longitudinal Studies of Aging and Health - It Takes a Village, $$$ and Advance Planning"** |
| 12:00-1:00 pm | **LUNCH & NETWORKING** |
| 1:00-1:05 pm | **Afternoon Welcome**<br>**Christopher S. Brown, PhD**<br>Vice President for Research<br>The University of Alabama at Birmingham |
| **SESSION II:** | ***Community & Society***<br>**Chair:**<br>**Alayne Markland, DO, MSc** |
| 1:05-2:05 pm | ***KEYNOTE PRESENTATION***<br>**Dr. John Beard**<br>Professor, Columbia University<br>Director, International Longevity Center-USA<br>**"Beyond the absence of disease"** |
| 2:05-2:25 pm | **BREAK** |
| 2:30-2:55 pm | **Pamela Bowen, PhD, CRNP, FNP-BC, BBA**<br>Associate Professor, Acute, Chronic and Continuing Care Department<br>UAB School of Nursing<br>Co-Investigator and Clinical Director, Evelyn F. McKnight Brain Institute at UAB<br>***Brain Health Advocacy Mission (BHAM): Improving Brain Health Through Primary Care*** |
| 3:00-4:00 pm | **PANEL** – Future of Aging Research<br>Moderators: Dr. Ken Boockvar<br>Panelists: Dr. Steve Austad, Dr. John Beard, Dr. Pamela Bowen, Dr. Stephanie Studenski |
| 4:00 pm | **CLOSING REMARKS**<br>**Dr. Ken Boockvar and Dr. Steve Austad** |

# MARCH 11 SESSION I: KEYNOTE SPEAKER



**João Passos, Ph.D.**
*Professor*
*Mayo Clinic*

**Dr. João Passos** is a Professor at Mayo Clinic with nearly 20 years' experience in the field of biology of aging. He directs the Cell and Molecular Aging laboratory at Mayo Clinic and holds the positions of Associate Director of the Robert and Arlene Kogod Center on Aging and director of its Discovery Science Theme. Dr. Passos has led an independent research program focused on cellular senescence and mechanisms of aging since 2010, firstly at the Newcastle University Institute for Ageing in the UK and since 2018 at Mayo Clinic. His laboratory has been continuously funded by several UK, European and US funding bodies since its inception. He has published more than 100 papers about biology of aging.

Dr. Passos' laboratory has made several important contributions to the understanding of the mechanisms driving cellular senescence during aging, with a particular emphasis on telomeres and mitochondria. His investigations have provided critical insights into how chronic DNA damage signaling from irreparable telomeric damage triggers cellular senescence in response to stress. Furthermore, his laboratory has shown that mitochondria are key regulators of the proinflammatory phenotype characteristic of senescent cells.

## Mitochondria and Cell Senescence: A Matter of Life and Death

Senescence is a multi-functional cell fate, characterized by an irreversible cell-cycle arrest and a pro-inflammatory phenotype, commonly known as the senescence-associated secretory phenotype (SASP). Emerging evidence indicates that accumulation of senescent cells in multiple tissues drives tissue dysfunction and several age-related conditions. This has spurred the academic community and industry to identify new therapeutic interventions targeting this process. Senescence is a complex and highly heterogenous phenotype and despite tremendous progress in recent years we are still far from fully understanding it. There is no single, stand-alone marker that allows the identification of senescent cells, posing a challenge to their identification and targeting.

Mitochondrial dysfunction is an often-unappreciated hallmark of cellular senescence which plays important roles not only in the senescence growth arrest but also in the development of the SASP and resistance to cell-death.

In my talk, I will first describe some of our recent efforts to accurately map senescent cells in different tissues, including the application of imaging methods involving artificial intelligence. Additionally, I will describe how mitochondria contribute to the development of senescence and resistance to cell-death.

Finally, I will propose that a detailed road map of mitochondrial biology in senescence will be crucial to guide the future development of therapies targeting cellular aging.

# MARCH 11 SESSION I: PLENARY SPEAKER

**Dr. Hernandez** has been an Assistant Professor in the Department of Medicine in the Division of Gerontology, Geriatrics and Palliative care since August 2023. She received her PhD from the University of Florida in 2018, where she investigated dietary interventions for age-related cognitive decline. Her lab now researches the role of the Gut-Brain-Axis and metabolism in age and AD-related cognitive decline and neuropathology.


**Abbi Hernandez, Ph.D.**
*Assistant Professor*
*Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care*
*University of Alabama at Birmingham*


## Metabolism and the Gut-Brain-Axis in Aging and Alzheimer's Disease

Both aging and Alzheimer's Disease (AD) are often characterized by cognitive decline and altered neurobiology. However, another notable alteration in both aging and AD is altered metabolic function, both systemically and cerebrally. Moreover, gut dysbiosis, or alteration in the gut microbiome composition, is observed in both states. Though there is strong evidence for the existence of a Gut-Brain-Axis, the interplay between gut dysbiosis and cognitive impairment in advanced age is not well understood. Our data demonstrate metabolic impairments driven by gut dysbiosis may mediate this relationship and further compound the negative effects of impaired brain function. In aged transgenic rats expressing genes related to familial AD (TgF344-AD rats), we observe significantly altered microbiome composition and enzyme pathways, as well as significantly altered metabolomes within intestinal and brain samples. Differences in metabolome across genotypes are sex specific, as are systemic impairments in metabolic function. Together, these data indicate the gut microbiome as an important regulator of metabolic, and therefore

# MARCH 11 SESSION I: PLENARY SPEAKER

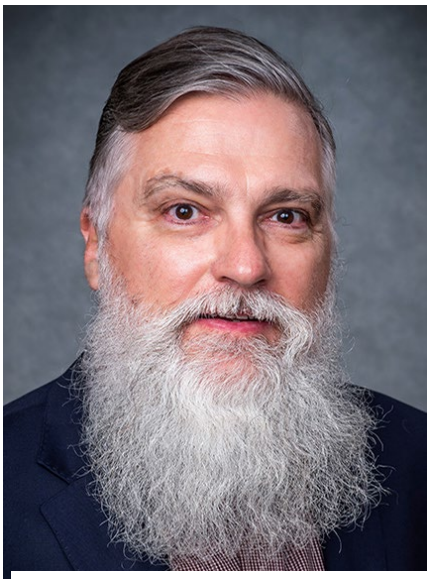
I am a comparative physiologist with experience using both field-based (in range countries and with zoos) and laboratory-based methodologies. Broadly, my research focuses on biotic and abiotic factors that influence elephant physiology and behavior. Specifically, I seek to understand how elephants are capable of living into their 70s and establish elephants as translational model for aging and aging-associated diseases.

**Daniella Chusyd, Ph.D.**
*Assistant Professor*
*Indiana University Bloomington*

## Trunks Up: Elephants for Aging Research

Species that share relevant characteristics with humans can be informative for the comparative investigation of aging and aging-associated diseases. In this regard, elephants are intriguing. Like humans, elephants typically give birth to a single offspring, demonstrate slow maturation, and have a long lifespan, potentially living into their 7$^{th}$ or 8$^{th}$ decade of life. Both species' fitness depends on social bonds, memory, and complex cognition. Elephants' long-term memory for spatial and social information may be related to the specialization of their brain anatomy. A characteristic unique to elephants is their number of copies of the gene *TP53.* Unlike humans with only one copy of *TP53*, elephants have, on average, 20 copies, as variation exists within and between elephant species. Due to these multiple copies, elephants have an enhanced apoptotic response to DNA damage. *TP53* encodes for the protein p53, which either slows cell growth while damage is repaired, or initiates cell death if stress is overwhelming. In addition to the role of p53 in cancer, it is also associated with Alzheimer's disease, cellular senescence, and epigenetic stability. It is possible that *TP53* is one potential mechanism allowing elephants to live to similar ages as certain human populations. Elephants have often been overlooked in aging research but can be potentially transformative and innovative. My current research investigates the association between early-life adversity and later-life health, pace of aging, and behavior by comparing orphaned elephants to similarly age- and sex-matched control elephants. I am also investigating the degree to which elephants develop neuropathology and whether it is associated with total number of TP53 copies. The goal of my research is to establish elephants as a new animal model for comparative and translational aging research and I am always open to new collaborations.

# MARCH 11 SESSION I: PLENARY SPEAKER



**Scott Ballinger, Ph.D.**
*Professor and Associate Dean*
*Co-Leader UAB Nathan Shock Center Comparative Mitochondrial Health Assessment Core*

Dr. Ballinger's received his undergraduate and master's degrees from Texas A&M University in College Station, TX, and PhD from Emory School of Medicine in Atlanta, GA. He performed his postdoctoral studies at the University of Vermont in Burlington, VT as an Alexander Hollaender Fellow (Department of Energy), followed by faculty positions at the University of Texas at Galveston and the University of Alabama at Birmingham. He is also a member of the Academy of Distinguished Former students in the Texas A&M University College of Science. He is currently a Professor in the Department of Pathology, Division of Molecular and Cellular Pathology, and the Associate Dean of Faculty Affairs & Development for the Heersink School of Medicine. His research focuses upon mitochondrial – nuclear genetic interaction processes that influence common disease development. His work explores the influence of "mito-Mendelian" genetics upon bioenergetics, inflammation, metabolism, and nuclear gene expression. He invented and has developed the Mitochondrial – Nuclear eXchange (MNX) model that enables unambiguous testing of mitochondrial and nuclear genetic backgrounds upon cell function and disease development. This research is showing that "mito-Mendelian" genetics influences cell function and response to acute and chronic stimuli. Most recently, he has focused upon studies examining the role of mitochondrial produced factors that initiate sterile inflammation and their impact upon cardiovascular disease development/progression. In this regard, his group has developed quantitative assays for measuring these factors.

## A Quantitative Assay for Determining Mitochondrial DNA Derived Damage Associated Molecular Pattern (DAMP) Levels in Humans and Rodents

Mitochondrial damage associated molecular patterns (mtDAMPs) are molecules released by the mitochondrion in response to stress and play a critical role in the immune response. Notably, mtDAMPs have been implicated in several diseases including cancer, systemic *lupus erytromatosus*, inflammatory bowel disease, cardiovascular disease and most recently, age related neurological function. Fragments of mitochondrial DNA (mtDNA) that are released from the organelle also function as mtDAMPs (mtDNA DAMPs) and recognized by pattern recognition receptors (PRR) which initiate pro-inflammatory cascades of events. We have developed a quantitative assay to detect and measure mtDNA DAMP levels in a variety of tissues, and describe methods for quantification of mtDNA DAMP levels in mice, rats and humans from a variety of tissues using *in vivo*, *ex vivo*, and *in vitro* approaches. In addition to providing methodological approaches, results show that mtDNA DAMP levels are increased in serum and plasma in response to both acute and chronic stressors, and can significantly differ between tissues using an *ex vivo* approach. These results demonstrate the utility of this assay to quantify mtDNA DAMPs in both human and rodent models.

# MARCH 11 SESSION I: PLENARY SPEAKER

Dr. Chtarbanova obtained both her undergraduate (BS in Biochemistry) and graduate (MS in Immunology and PhD in Cell and Molecular biology) degrees at the University of Strasbourg in France. Her graduate work focused on studying the *Drosophila* innate antiviral immunity. As a postdoc she worked in the Department of Genetics at the University of Wisconsin-Madison in the area of *Drosophila* neurogenetics. Dr. Chtarbanova joined the University of Alabama as an assistant professor in 2016. At UA her research focuses on studying the mechanisms of aging innate immunity, and the involvement of the innate immune system in brain health.

**Stanislava Chtarbanova, Ph.D.**
*Assistant Professor*
*The University of Alabama Tuscaloosa*

## As Time Flies by: Studying the Impact of Aging on *Drosophila* Antiviral Defenses

Viral infections represent a significant burden among older individuals and are often associated with higher morbidity and mortality. Importantly, with the increasing number of older populations globally, research in this area could lead to the identification and development of novel interventions that could be used to alleviate the outcomes of infections. In our lab we employ genetic, genomic and molecular approaches to understand how the process of aging shapes host-virus interactions, including immune defenses, and how older organisms survive infection. We have developed a model of aged host-virus interactions using the genetically tractable *Drosophila melanogaster* as the host, and the positive stranded RNA virus Flock House virus (FHV) as the pathogen. Our results implicate modulation of disease tolerance (part of immunity that helps the organism to withstand the pathological consequences of infection but doesn't affect pathogen load) as a major survival strategy in response to FHV of aged flies, which also depends on the regulation of organismal metabolic rate. Furthermore, we discovered that survival of FHV infection has a genetic basis and can be significantly modulated by factors such as colonization by endosymbiotic bacteria or tetracycline antibiotic treatment. We propose that metabolic rates are modulated by these conditions thus playing a major role in the establishment of disease tolerance to FHV. Our work in *Drosophila* is contributing novel insights about the interactions of viruses and their aged hosts and could have long term implications for improving the outcomes of infections among older populations.

# MARCH 11

## OVERVIEW OF TRAINING AT NIA AND DAB PRIORITY FOR FUNDING

**Christy Carter, Ph.D.**
*Health Scientist Administrator*
*Division of Aging Biology*
*National Institute on Aging (NIA) | National Institutes of Health (NIH)*

Dr. Carter is the NIA/DAB Program Officer for Training and Workforce Development. Nationally she serves as the NIA scientific officer on the Research Centers Collaborating Network (RCCN) steering committee. While serving on the faculty at Wake Forest University, University of Florida and the University of Alabama at Birmingham, her research focused on preserving health-span during aging. She helped to define similarities between species in the underlying biological mechanisms of age-related decline in physical performance, cognition, and longevity. She also developed interventions to mitigate loss of health-span using exercise, nutritional, and pharmaceutical approaches. As an educator, Dr. Carter has developed online certificate and masters programs focused on geroscience that are offered nationally.

# MARCH 11 SESSION II: KEYNOTE SPEAKER

**Rozalyn Andeson, Ph.D.**
*Professor of Medicine*
*University of Wisconsin-Madison*

**Dr. Rozalyn Anderson** is a Professor of Medicine and faculty member of the Division of Geriatrics and Gerontology, and the Division of Endocrinology, Diabetes and Metabolism in the Department of Medicine at the University of Wisconsin Madison SMPH. Her research investigates the biology of aging and what creates the age-associated increase in vulnerability to a spectrum of diseases and disorders. A primary focus is on the mechanisms of delayed aging by caloric restriction in mice and in monkeys, with a special emphasis on metabolism as a driver in aging and as a target for interventions to prevent age-related functional loss.

Dr. Anderson is Director of the Metabolism of Aging program, Director of the Biology of Aging and Age-Related Diseases T32 training program, and Associate Director of Research at the William S Middleton Memorial Veterans Hospital GRECC. She is a Fellow and former Chair of the Biological Sciences section of the Gerontological Society of America and a Fellow and former President of the American Aging Association. She is a recipient of the Nathan Shock New Investigator Award (GSA), the Biological Mechanisms in Aging Award (Glenn Foundation), and the Breakthroughs in Gerontology Award (AFAR).

## Aging & Delayed Aging by Caloric Restriction

Aging is associated with increased vulnerability to a host of diseases and conditions, each with independent etiology and investigated as discrete disciplines within biomedical research. A change in metabolism is a unifying theme among age-related disorders including cancer, neurodegenerative diseases, and cardiovascular disease. Caloric Restriction (CR) is a highly effective intervention to delay aging and the onset of age-related disease, and it has a profound impact on metabolism that we hypothesize is causal in its pro-survival and health promoting effects. Our studies focus on the metabolism of aging in mice and monkeys at the tissue and system level and explore mechanisms and insights in cell culture models. Here I will provide the evidence supporting a role for metabolism in the benefits of CR. I will describe data from our nonhuman primate and rodent studies of brain aging, including how metabolism features both in the impact of age and in the impact of neuroprotection by CR. Aspects of metabolic regulation specific to brain will be discussed along with the possibility of using metabolism as a target for age-related neurodegenerative disease. Finally, we explore aspects of peripheral metabolic homeostasis influencing brain aging that might be leveraged for future clinical intervention.

# MARCH 11 SESSION II: PLENARY SPEAKER

**Girish Melkani, Ph.D.**
*Associate Professor*
*Co-Leader UAB Nathan Shock Center Comparative Organismal Energetics Core, UAB*

Dr. Melkani is an associate professor of pathology, and his group has been at the forefront of developing and using clinically relevant Drosophila genetic models of human systemic metabolic abnormalities, cardiometabolic disease, myopathies, neuropathies, and aging. Dr. Melkani group is currently funded with NIH 4 R01 grants (Two PI and Two MPI), and they focused on several aspects of aging and metabolic disorder, and their modulation with time-restricted feeding and circadian rhythms. His research findings have been published in *Science, Nature Communications, Cell Metabolism, Aging Cells, Human Molecular Genetics, Elfie, Physiology,* and *PLoS Genetics.* In addition to his research involvement, Dr. Melkani is deeply committed to fostering the academic growth of students have a strong track record mentoring graduate students and postdocs, and guiding them toward successful careers in academia, biotech, and entrepreneurship. As a faculty member and faculty senator, he also hold leadership roles on university-wide committees, such as the Research Committee and Faculty Advisor Council. Furthermore, his involvement as an Associate Editor and reviewer for scientific journals, as well as his participation in grant review panels for organizations like NIH and AHA, demonstrates his commitment to advancing scientific research and scholarship. He has shared his insights through presentations at universities and conferences, contributing to the dissemination of knowledge in the field of fly research and aging.

## Chronobiology of Lipid Modulation: Discovering the Role of Time-Restricted Feeding in Aging and Metabolic Disorders

Disruptions of circadian rhythms are linked with aging, cardiac, muscle, and other metabolic disorders. We have shown that the time-restricted feeding (TRF) paradigm mitigates age-linked cardiometabolic and muscle disorders. Population-based studies have indicated that midlife-obesity leads to a higher risk of dementia, however, this linkage remains poorly understood, and urgent interventions are required to mitigate these disorders. We demonstrate that middle-aged obese flies have significant cognitive dysfunction. Moreover, obesity causes abnormal lipid accumulation in the brain followed by enhanced inflammation markers and neuroinflammation. As shown for the peripheral tissues, TRF-mediated regulation of circadian rhythm resulted from lessening inflammation markers, neuroinflammation, and abnormal lipid dysregulation in the brain. We have also shown that ApoE, which is a leading genetic risk factor for AD, increases lipid accumulation in neurons. Neuronal accumulation of lipids in ApoE2 and ApoE3, but not ApoE4, depends on Dgat2. TRF decreases ApoE-related lipid accumulation in neurons by reversing aging-related expression of genes related to fatty acids and triglyceride synthesis. We also found that TRF-mediated inhibition of Dgat2 prevents lipid metabolism dysfunction in the periphery and prevents age and obesity-associated dysfunction. These innovative findings are vital to address the pathophysiological lipid dysmetabolism association with aging and metabolic disorders, and its attenuation with TRF.

# MARCH 11 SESSION II: PLENARY SPEAKER

Dr. Courtney Peterson is an Associate Professor in Nutrition Sciences at the University of Alabama at Birmingham and an internationally-recognized researcher in the field of intermittent fasting and meal timing. Dr. Peterson conducted the first controlled feeding trial of intermittent fasting in humans and was the first to test early time-restricted eating (eTRE) in humans. Currently, she is the PI, MPI, or site PI of seven clinical trials on time-restricted eating, including a couple of the largest studies of intermittent fasting in humans. She is also a consultant or collaborator on another five clinical trials on intermittent fasting. Her research has been featured in more than 50 media outlets, including *NBC Nightly News, The New York Times, The Washington Post, Wall Street Journal*, *Good Morning America*, and the *BBC*.

**Courtney Peterson, Ph.D.**
*Associate Professor*
*Department of Nutrition Sciences*
*UAB*

## Effects of Time-Restricted Eating on Primary and Secondary Aging in Humans

Time-restricted eating (TRE) is a form of intermittent fasting that involves eating with a 10-hour or less daily period and fasting for the remainder of the day. Intermittent fasting has greatly increased in popularity, and there are now more than 100 clinical trials on TRE in humans. In this talk, Dr. Peterson will discuss what is known about the effects of TRE on primary and secondary aging in humans. Specifically, Dr. Peterson will discuss the effects of TRE on weight loss, cardiometabolic risk factors, and biomarkers of aging. She will also present data on the feasibility of TRE and how the effects are modulated by the time of day, length of the fasting period, and the degree of calorie restriction.

# MARCH 11 SESSION II: PLENARY SPEAKER

**Martin Young, Ph.D.**
*Professor*
*Medicine - Cardiovascular Disease, UAB*

Martin Young received his Bachelors, Masters, PhD degrees in Biochemistry from the University of Oxford. Following postdoctoral training at Boston University and the University of Texas-Houston, Dr. Young held faculty appointments at the University of Texas-Houston and Baylor College of Medicine, before joining the University of Alabama at Birmingham. Dr. Young is currently a Distinguished Professor of Medicine in the Division of Cardiovascular Disease. He is also the Jeanne V. Marks Endowed Chair of Cardiovascular Disease. Dr. Young has published over 200 peer-reviewed manuscripts in top tier journals. Research in Dr. Young's laboratory is focused on untangling the interplay between time-of-day, nutrient intake, and metabolism, and understanding how these parameters influence the heart. With regards to time-of-day, a series of seminal studies from his laboratory have established that an intrinsic time-keeping mechanism, known as the circadian clock, temporally partitions cardiac metabolism. Fueled with this insight, he has intensified pursuit of the concept that the time-of-day at which nutrients are consumed dictates their metabolic fate and subsequent impact on myocardial form and function.

## Circadian Control of Cardiac Physiology and Pathophysiology

Virtually all aspects of physiology fluctuate with respect to the time-of-day. This is beautifully exemplified by cardiovascular physiology, for which blood pressure and electrophysiology exhibit robust diurnal oscillations. At molecular/biochemical levels (e.g., transcription, translation, signaling, metabolism), cardiovascular-relevant tissues (such as the heart) are profoundly different during the day versus the night. Unfortunately, this in turn contributes towards 24 hour rhythms in both risk of adverse event onset (e.g., arrhythmias, myocardial infarction) and pathogenesis severity (e.g., extent of ischemic damage). Accumulating evidence indicates that cell autonomous timekeeping mechanisms, termed circadian clocks, temporally govern biological processes known to play critical roles in cardiovascular function/dysfunction. During this presentation, a comprehensive review of our current understanding of the cardiomyocyte circadian clock during both health and disease will be detailed. Unprecedented basic, translational, and epidemiologic studies support a need to implement chronobiological considerations in strategies designed for both prevention and treatment of cardiovascular disease.

# MARCH 11 SESSION II: PLENARY SPEAKER

**Karen Gamble, Ph.D.**
*Professor*
*F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry*
*UAB*

Dr. Karen Gamble is the F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry and Vice Chair of Basic Research in the Department of Psychiatry & Behavioral Neurobiology in the Heersink School of Medicine at the University of Alabama at Birmingham in Birmingham, AL. Dr. Gamble's research program is funded largely by NIH and includes both basic and translational research. Basic research interests include how circadian rhythms in physiology, behavior, metabolism, and sleep-wake cycles are regulated in specific brain circuits and affected by nutrition (high salt/fat diets, meal timing), disease (obesity, neurodegeneration, addiction), and the environment. Translational projects address the impact of environmental circadian misalignment (e.g., shift work) or addiction (e.g., smoking and opioid use) on circadian rhythmicity of behavior and physiology. Dr. Gamble is a member of the Sleep Research Society (SRS) and the Society Research in Biological Rhythms (SRBR). She served as the 2014 and 2016 SRBR Professional Development Day director and currently serves as Co-Chair of the SRBR Government Affairs Committee. Dr. Gamble currently chairs the Society for Neuroscience "Sleep and Circadian Biology" annual DataBlitz, which is sponsored by the NHLBI National Center on Sleep Disorders Research.

## Salty Secrets: Impact of High Salt Diet on the Primary Circadian Clock

Diets high in salt, a major component of modern diets, contribute to a very wide range of health complications especially cardiovascular and kidney disease. Salt sensitivity increases with age, and thus, factors important for regulating Na+ homeostasis, such as the internal circadian rhythm network, are important considerations for older populations. Sleep/wake rhythms and other biological rhythms change across the lifespan. Proper alignment of behavioral and environmental rhythms with a regular 24-hour cycle is necessary for maintaining overall health. A critical gap in our knowledge and understanding is fundamentally how high salt intake impacts functional outcomes that depend on a regular circadian cycle. The vasoactive peptide, endothelin (ET)-1 and its isoforms can activate ETB receptors that function in the kidney and vasculature to facilitate renal excretion of Na+ during high salt intake. In the primary circadian pacemaker, the suprachiasmatic nucleus (SCN), the ET-3 isoform is highly expressed in the endothelial cells of in a strong, rhythmic pattern. In addition, we discovered that ETB receptors are highly expressed in SCN astrocytes. Our compelling preliminary data show that high salt diet eliminates the normal day-night difference in firing rate of SCN neurons, and activation of ETB receptors at night increases SCN firing rate. Furthermore, we can restore the normal day-night difference in firing rate when receptors are blocked with a highly selective ETB receptor antagonist. To our knowledge, this is the first evidence of ETB receptor control of SCN output that is regulated by high salt diet. These results point to the need for future studies to improve our understanding of long-term salt homeostasis across the lifespan via an inter-disciplinary and multi-organ approach.

# MARCH 12 SESSION I: KEYNOTE SPEAKER

**Dr. Stephanie Studenski** is a geriatrician and rheumatologist whose practice, teaching and research focus on physical function, mobility, balance disorders and falls in later life. Originally trained as a nurse as well as physician, she also has a Master's Degree in Public Health. Through her research, she strives to understand age-related problems in physical function. Her more recent work focuses on the role of the central nervous system and body composition in mobility and physical function. She recently retired from her position as Chief of the Longitudinal Studies Section of the Intramural Research Program of the National Institute on Aging and Director of the Baltimore Longitudinal Study of Aging and is currently Professor Emeritus at the University of Pittsburgh.

**Stephanie Studenski, RN, MD, MPH**
*Professor Emeritus*
*University of Pittsburgh*

## There's something in the way they move: aging and mobility

Movement changes with aging, but to varying degrees across individuals. This presentation focuses on understanding how and why movement changes, and why these changes provide valuable information to clinicians.

# MARCH 12 SESSION I: PLENARY SPEAKER

**Alayne Markland, DO, MSc**
*Professor*
*Division of Gerontology, Geriatrics, and Palliative Care*
*Department of Medicine*
*The University of Alabama at Birmingham*

**Dr. Markland** is a tenured Professor and holds the Parrish Endowed Professorship in the Division of Gerontology, Geriatrics, and Palliative Care (GGPC) within the Department of Medicine at the University of Alabama at Birmingham (UAB). At the Birmingham VA Health Care System, she serves as the Director of the Birmingham/Atlanta Geriatric Research, Educational, and Clinical Center (GRECC). She is an internationally recognized expert in lower urinary tract disorders and aging.

Dr. Markland's overarching research goal focuses on optimizing community-based life functioning through the prevention and treatment of geriatric syndromes in older individuals with a specific focus on lower urinary tract symptoms and incontinence. She serves as both PI and co-Investigator on a variety of NIH-funded, VA funded, and AHRQ-funded research projects to enhance access to behavioral interventions, while also trying to prevent lower urinary tract symptoms across the lifespan.

In addition, Dr. Markland serves as the GGPC Research Core Division leader. Throughout her career, Dr. Markland has received continual NIH and VA funding, served as an ad-hoc member on the NIH and VA study sections, and published over 150 peer-reviewed publications. She brings clinical geriatric medicine expertise and 18 years of experience treating adults with lower urinary tract symptoms at university and VA-based clinics where she serves as the medical director. As a clinician investigator, her research focuses on analyzing population-based studies, conducting clinical intervention research focused on behavioral and pharmacologic treatments, improving measures related to bladder and bowel symptoms, performing systematic reviews and meta-analyses, and mentoring early-stage investigators.

## Improving Access to Urinary Incontinence Treatments through Mobile Health Technology

Throughout the last 10 years, our team has developed mobile health technology tools to increase access to urinary incontinence (UI) treatments for women and men. We will present our progress from the development, feasibility from pilot-testing, effectiveness results from our pragmatic clinical trial, and current study on implementation of our program with primary care clinics in the VA system. Our current study is part of the AHRQ's EvidenceNow: Managing Urinary Incontinence (MUI) Initiative. Guided by the RE-AIM framework, we will target 50 practices with over 50,000 women Veterans across the three states (Alabama, Georgia, and South Carolina). All primary care practices will receive practice facilitation including (1) a virtual or on-site visit, along with 1-3 practice facilitator visits engaging practices and site champions; (2) MyHealtheBladder education (mobile health application for behavioral treatment of UI); and 3) Online Toolkit, including a clinical dashboard that provides the site champion information about clinic-assigned women Veterans at high risk of UI. Our study team has strong relationships with local and regional leadership in women's health, experts in informatics, industry, and VA information technology infrastructure. To date, we have approached 50 clinics and completed 35 visits across Alabama, Georgia, and South Carolina using our practice facilitation approach. Leveraging leadership support and technology within the VHA healthcare system, we anticipate reaching our goal and improving access to nonsurgical UI treatments. Our online toolkit, remote access to MyHealtheBladder, and consult pathways are scalable throughout the VA healthcare system, if successful at the regional level.

# MARCH 12 SESSION I: PLENARY SPEAKER

**Virginia Howard, PhD, FAHA, FSCT**
*Distinguished Professor*
*Department of Epidemiology*
*School of Public Health*
*The University of Alabama at Birmingham*

**Dr. Howard** is a Distinguished Professor of Epidemiology at the School of Public Health at the University of Alabama at Birmingham (UAB). She received a MSPH degree in Biostatistics from UNC-Chapel Hill and her PhD in Epidemiology from MUSC. She is a stroke epidemiologist with over 30 years' experience in multicenter, multidisciplinary clinical trials and longitudinal cohort studies with a focus on stroke, stroke risk factors, cognitive functioning, and health disparities. Dr. Howard has 450+ publications and an h-index of 98+. She is one of the lead epidemiologists of the long-running NINDS/NIA co-funded REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study started in 2001, and PI or co-I of many REGARDS ancillary studies. She is a co-investigator, member of the Analysis Core and mentor on UAB's Deep South RCMAR (Resource Center for Minority Aging Research) funded by NIA. She has been PI of the statistical and data coordinating center or the leading clinical trial epidemiologist contributor for five major stroke primary or secondary prevention multicenter clinical trials.

Dr. Howard has been a member of the editorial board for the International Journal of Stroke since 2013, the AHA Stroke journal since 2020, and in 2023, she was invited to join the Methodology and Statistics editorial board for the journal Neurology. She has served on numerous NIH and American Heart Association review committees and advisory committees, including most recently the NINDS Steering Committee on Health Disparities, and the subcommittee on Workforce Diversity and Health Disparities, and chairperson of the AHA Heath Equity Research Network on Rural Health. Her research program has included sex differences in the impact of risk factors on stroke risk, and childhood exposures/quality of education on stroke risk and cognitive function, and she was recently awarded an NIH conference grant for Advancing the Study of Stroke in Women to be held in April 2024. Throughout her research career, Dr. Howard has collaborated with multidisciplinary scientists including undergraduates, graduate students, postdocs, early career, and senior investigators, including clinical and basic scientists, and individuals from underrepresented groups, and she is one of the leaders in building REGARDS scientific collaborations and networking, including developing and leading workshops.

## Recruiting and Retaining Diverse Participants in Longitudinal Studies of Aging and Health - It Takes a Village, $$$ and Advance Planning

This presentation will describe our experiences primarily with the national, NIH-funded REGARDS (REasons for Geographic and Racial Differences) cohort study but also a few other national, long-term studies (including clinical trials) related to the planning, conduct, successes, and challenges in enrolling and retaining diverse participants. REGARDS will be described with our approach, lessons learned and budgetary considerations to help with advance planning.

# MARCH 12 SESSION I: KEYNOTE SPEAKER

**John Beard, MBBS, PhD**
*Professor*
*Director, International Longevity Center-USA*

**Dr. John Beard** is Irene Diamond Professor and Director of the International Longevity Center-USA at Columbia University, New York. He was previously Director of Ageing and Life Course with WHO in Geneva. During this time, he led international work to reframe thinking on healthy aging and oversaw the development of multiple global programs including Integrated Care for Older People (ICOPE), and the Global Network of Age-friendly Cities and Communities which now covers over 300 million people. His research considers health from the perspective of functioning rather than the presence or absence of disease and, more recently, seeks to link overt age-related phenotypic and functional change to the complex dynamical changes in biology that drive it.

## Beyond the absence of disease

The field of aging and health is undergoing a major transformation driven by recent advances in geroscience, complex systems thinking, machine learning and our ability to collect and manage big data. This has led to significant advances in understanding how complex age-related dynamic changes in biology drive the aging process and health itself. However, more radical progress is hampered by the dominance of disease-based models for framing health. This presentation will discuss recent thinking on how health can be better considered from the perspective of functioning, how this might best be measured and how it might be linked to the phenotypic and biological change that drives it.

# MARCH 12 SESSION II: PLENARY SPEAKER

**Pamela G. Bowen, PhD, CRNP, FNP-BC, BBA**
*Associate Professor*
*Acute, Chronic, and Continuing Care Dept.*
*School of Nursing*
*Co-Investigator & Clinical Director, BHAM,*
*Evelyn F. McKnight Brain Institute*
*The University of Alabama at Birmingham*

**Dr. Bowen** is a credentialed family nurse practitioner, scientist, associate professor, and researcher at the University of Alabama at Birmingham School of Nursing. At the Evelyn F. McKnight Brain Institute, Dr. Bowen oversees the Brain Health Advocacy Mission (BHAM) as its clinical director.

BHAM strives to engage, educate, and empower individuals in primary care clinics from all aspects of life to improve and maintain their cognitive health. This undertaking is of the utmost importance as it prevents the progression of neurodegenerative disorders such as Alzheimer's by reducing the rate of cognitive decline. Obesity-related chronic diseases are prevalent among individuals of color and those from low-income backgrounds, who represent Dr. Bowen's primary patient population. These health concerns include cognitive decline, hypertension, diabetes, arthritis, and cardiovascular disease.

Promoting emotional and physical health, in her opinion, necessitates the adoption of healthy behaviors, even if they are difficult to make. Dr. Bowen acknowledges the challenges that individuals encounter when attempting to adopt healthier lifestyle habits. Consequently, our team considers establishing BHAM as a resource within primary care clinics to support primary care patients in their journey towards better health as they age to be a promising strategy to preserve overall brain health.

**Brain Health Advocacy Mission (BHAM): Improving Brain Health Through Primary Care**

In the United States, the preservation of brain health among an aging population is a developing concern. Mild cognitive impairment affects an estimated one in five Americans aged 65 or older, while dementia affects one in seven individuals. The projected threefold increase in the prevalence of dementia among the American population by 2050 motivates the Brain Health Advocacy Mission (BHAM) to act. BHAM seeks to encourage individuals to make healthy decisions beginning at age 18 to preserve and improve their brain health as they age. BHAM distinguishes itself by conducting brain health assessments in conjunction with the patient's routine medical appointments with their healthcare provider. BHAM incorporates the American Heart Association Life's Essential 8 and research indicating that the adoption of healthy lifestyles substantially influences the prevention and mitigation of cognitive decline, cardiovascular disease, and dementia, including Alzheimer's disease and Parkinson's disease. Early prevention is therefore of the utmost importance and should begin at young ages.

# MARCH 12

## PANEL: FUTURE OF AGING RESEARCH

**MODERATOR: Kenneth Boockvar**
**PANELISTS: Steven Austad, John Beard, Pamela Bowen, Stephanie Studenski**


**Ken Boockvar, MD, MS**
*Gwen McWhorter Professor in Geriatric Medicine*
*Director, Division of Gerontology, Geriatrics, and Palliative Care*
*Director, Integrative Center for Aging Research*
*The University of Alabama at Birmingham*

**Dr. Boockvar** is the Director of the Division of Gerontology, Geriatrics, and Palliative Care, and Gwen McWhorter Professor in Geriatric Medicine at University of Alabama at Birmingham (UAB) School of Medicine and Physician-Investigator in the Geriatrics Research, Education, and Clinical Center (GRECC), Birmingham Veterans Affairs (VA) Health Care System. Dr. Boockvar's career has been devoted to improving health and quality of care for older adults and those with serious illness. He has pioneered research on the quality of medication prescribing and on the effect of medication reconciliation to improve prescribing. Dr. Boockvar is also an innovator in research and quality in long-term care. He has implemented complex models of care with front-line health care providers, including developing, implementing, and testing interventions in the nursing home setting. He has 25 years of experience treating older adults and adults with serious illness in outpatient, inpatient and long-term care settings and advancing the care of geriatrics syndromes.

**Steven Austad, PhD**
*Distinguished Professor*
*Protective Life Endowed Chair in Healthy Aging Research*
*Co-Director, UAB Nathan Shock Center of Excellence in the Basic Biology of Aging*
*The University of Alabama at Birmingham*

**Dr. Austad** is a Distinguished Professor in the Department of Biology and the inaugural Protective Life Endowed Chair in Healthy Aging Research at the University of Alabama at Birmingham (UAB). He is also Founding Director and current Co-director of UAB's Nathan Shock Center of Excellence in the Basic Biology of Aging. He also co-directs the Nathan Shock Centers' Coordinating Center and is Senior Scientific Director of the New York-based American Federation for Aging Research. Dr. Austad has won multiple national and international awards for his research and published more than 200 scientific papers. He is a fellow of the American Association for the Advancement of Science and the Gerontological Society of America. With an abiding interest in communicating science to the public, he has written more than 150 op-eds and essays for electronic and print media and published four trade books most recently *Methuselah's Zoo: What Nature Can Teach Us about Living Longer, Healthier Lives* (2022). Before his career in science, he put food on the table by driving taxis in New York City and training lions for the Hollywood movie industry.

# POSTER ABSTRACTS

## 1. Subsensory Electrical Noise Stimulation Enhances Postural Control During Visual Perturbations in Older Adults

**Zahra Bassiri[a]***, Qiang (Jason) Zhang[a], Vishesh Vikas[a], Dario Martelli[a]

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**Background:** Sub-sensory electrical stimulation (ES) applied to the lower trunk and lower leg can improve balance control in young adults through stochastic resonance (SR)[1-4]. However, there is a limited understanding of the potential of sub-sensory ES to enhance reactive balance control following unexpected balance disturbances in older adults.

**Research Questions:** How effective does sub-sensory electrical stimulation (ES) improve reactive balance control in older adults experiencing visual perturbations in a virtual reality (VR) environment?

**Methods:** Five healthy older adults maintained balance on a force plate under different visual conditions: eyes closed (EC), eyes open without visual perturbations (EO), eyes open with anteroposterior visual perturbations (AP), and eyes open with mediolateral visual perturbations (ML). They also received either no stimulation (NS), leg stimulation (LS), or trunk stimulation (TS) at 90% of their sensory threshold (ST). The 95% confidence ellipse area (95% EA), the lengths of AP and ML sway path (APPath, MLPath), and the AP and ML 50% and 95% power frequencies (APPF50, MLPF50, APPF95, and MLPF95) were calculated. The analysis involved repeated-measures ANOVA and Tukey post-hoc tests to examine the effects of stimulation and visual conditions.

**Results:** During anteroposterior (AP) perturbations, trunk stimulation (TS) resulted in lower values for APPF50, APPF95, MLPF50, MLPF95, APPath, and EA, while leg stimulation (LS) led to decreases in APPF50, APPF95, MLPF50, and EA. Trunk stimulation (TS) also reduced APPF50, APPath, and EA during mediolateral (ML) perturbations, and both LS and TS caused reductions in MLPF95. Greater instability following AP perturbations correlated with more significant effects of TS and LS.
Significance: Subsensory electrical stimulation (ES) enhanced postural control during anteroposterior (AP) perturbations, with trunk stimulation (TS) proving more effective than leg stimulation in reducing postural sway among older adults. TS emerges as a promising strategy for enhancing balance control during reactive postural tasks, potentially mitigating fall risk in this population.

**Keywords:** Balance; Stochastic resonance; Electrical stimulation; Virtual reality; Visual perturbations.

**Acknowledgments:** We express gratitude to Dr. Sunil Agrawal and Dr. Antonio Prado for their assistance in crafting the virtual reality environment. This research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## 2. Sex-specific changes in mitochondrial bioenergetics in the brain of aging baboons

**Gloria A. Benavides[1,2*]**, Daniel Adekunbi[3], Adam Salmon[3,4], Peter Nathanielsz[4], Laura Cox[4], Jianhua Zhang[1,2], Victor Darley-Usmar[1,2]

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Mitochondria play a crucial role in brain aging due to their central role in energy metabolism and brain steroid synthesis. Mitochondrial dysfunction has been linked to age-related neurodegenerative diseases, including Alzheimer's disease. Changes with age in ATP production, ROS production, and mitochondrial dynamics are associated with altered neuronal signaling, synaptic plasticity, and impaired memory formation. However, there are significant challenges in identifying the proximal causes of these impairments in normally aging brains which hinders our overall understanding of these processes. In this study, we utilized a novel approach, assessment of mitochondrial bioenergetics from frozen banked frontal cortex, from a large cohort (60 individuals) of well-characterized aging baboons (*Papio* sp.) die of natural causes. In samples from animals ranging from 6-23 yr, we find a clear correlation between age at necropsy and reduced activity of Electron Transport Chain (ETC) Complexes I-IV. However, we find no change in activity of citrate synthase, lactate dehydrogenase or CS/LDH ratio suggesting these changes are not due to loss of mitochondrial content with age and represent specific loss of complex function. Interestingly, we find that sex is a significant factor regulating ETC Complex I-IV activity with males showing significantly higher activities of each individual complex. Moreover, when using sex as a covariate, we find that ETC complex activities are preserved with age in females, whereas males show significant and dramatic loss of function with age highlighting a potential molecular mechanism for sexual dimorphisms in brain resilience. Because the aging physiology of these animals was well-studied prior to necropsy, studies are underway addressing the functional impact of these mitochondrial outcomes as well as the extent they are shared among different tissues.

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## 3. HP1a phosphorylation states throughout Drosophila lifespan

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Aging is a biological phenomenon seen in virtually every organism, but the molecular mechanisms behind aging are unknown. Some data suggests that chromatin changes might contribute to aging. Old individuals tend to have less heterochromatin than young individuals. At the same time, increase in heterochromatin, called senescence-associated heterochromatin foci, are more often seen in older individuals. These changes in chromatin can contribute to uncontrolled gene expression that may be the reason age-related diseases arise. Heterochromatin is transcriptionally silenced chromatin characterized by the methylation of lysine 3 on histone 3 (H3K9), which serves as a binding site for heterochromatin proteins (HP1). The HP1 protein family is highly conserved in eukaryotes and functions in transcriptional regulation and chromatin maintenance. Specifically, HP1a is an essential protein in Drosophila that is localized in heterochromic regions and functions in maintaining genome integrity. Drosophila with an overexpression of HP1a have longer lifespan than wildtype animals. HP1a can undergo post-translational modifications (PTMs) but little is known about how these modifications affect HP1a function. HP1a can undergo phosphorylation which is known to modulate protein function. Here, we study the phosphorylation states of HP1a throughout the lifespan using a Phos-tag SDS-PAGE technique. Preliminary data shows that there are two phosphorylation states in 2$^{nd}$ instar, 3$^{rd}$ instar, and adult stages of wildtype Drosophila. Our next step is to assess the level of phosphorylation in aged animals.

## 4. Evaluating Flock House virus genome changes after replication in young and aged *Drosophila melanogaster*

**Dean Bunnell[1]***, Megan Delfeld[1], Janna Fierst[2], and Stanislava Chtarbanova[1]

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Introduction

Aging is associated with progressive changes at the cellular, molecular and physiological levels. How older organisms interact with viruses and the mechanisms they utilize to limit pathogen mutation and spread are currently not well understood. Indeed, a growing aging population could create a reservoir for the emergence of novel viral strains. RNA viruses can rapidly evolve within individual hosts, adapt to new hosts, potentially creating novel diseases. We hypothesize that aging causes deregulation of host physiology, including factors that limit pathogen mutation. We use *Drosophila melanogaster* and Flock House virus (FHV) as a model to investigate the impact of aging on within-host viral evolution.

Methods

Following control/FHV injection of 5d or 30d-old $w^{1118}$ females, hemolymph (HL) transfer into 5d-old flies is performed after 96h. Survival is recorded daily and FHV loads determined by RT-qPCR. Virus mutational analyses using 200Mb next-generation sequencing are carried at 24h and 120h post-FHV injection of 7d- and 30d-old *Oregon R* males. Sequence-specific first-strand cDNA of *FHV RNA2* is synthesized using extracted total RNA, followed by second-strand cDNA synthesis. Virus Recombination Mapper (ViReMa) was used in bioinformatics analysis.

Results

Recipients of FHV-infected HL from an aged host display accelerated mortality and increased FHV titers compared to recipients of FHV-infected HL from a young host. Nucleotide substitutions occur more frequently within aged hosts following infection. The aged cohort shows a higher frequency of deletions and substitutions than the young cohort 120h post-FHV infection.

Conclusions

FHV replication in an aged host could increase viral mutations and pathogenicity.

Future Directions

Click-Seq™, a method of making RNAseq libraries without introducing artifactual chimeric reads, allows more accurate detection of recombination events. Further studies are required to determine the effect of observed mutations on pathogenicity.

Acknowledgments

We thank Dr. Annette Schneemann for sharing FHV stock.

## 5. Alzheimer's Disease: Altered Clock Gene Expression in Parvalbumin Interneurons of the J20 Mouse Model

**Mary B. Cooper[1]***, Eshika Kudaravalli[1], Savannah Crawley[1], Rita Cowell[1], Karen Gamble[2], Erik Roberson[1]

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Alzheimer's disease (AD) features subclinical epileptiform activity predominantly during the inactive circadian phase. Parvalbumin (PV) interneurons are the most abundant interneuron type in the hippocampus and cortex, and therefore, could likely contribute to the imbalance in excitation and inhibition. Because epileptiform activity in AD follows a circadian rhythm of expression, we hypothesized that clock gene dysfunction in PV interneurons of the hippocampus and cortex contributes to AD-related hyperexcitability. To begin testing this hypothesis, we asked if there are alterations in the transcription of core clock genes in PV interneurons in the hippocampus and cortex of the hAPPJ20 mouse model of AD. Mice were entrained using controlled lighting and brains were collected after 2 days of constant darkness across 6 circadian timepoints. RNAscope was then used to measure the gene expression of the chosen clock genes within the PV cells in our respective regions of interest. Our results aim to confirm the existence of clock gene alterations within PV cells to elucidate the connection between circadian dysfunction and epileptiform activity in AD. Future studies include the analysis of additional clock genes and regions of interest.

## 6. The Impact of Serine and Glycine Availability on Skeletal Muscle Cell Composition Following Injury

**Ryan Dannemiller***, Shelby Rorrer, Wenxia Ma, Anna Thalacker-Mercer

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Purpose

Skeletal muscle (SkM) regeneration, an obligatory repair process involving resident SkM stem and progenitor cells (MPCs), is impaired in older adults; therapies are not defined. We confirmed that nutritionally, non-essential amino acids serine and glycine (SG) are reduced in older adult blood and SkM. Additionally, we demonstrated that extracellular SG availability is essential for MPC proliferation and reduced SG availability amplifies intramuscular adipocytes following injury. We hypothesized that adipocyte accumulation in SkM was due to the perturbation of cell composition following injury. Thus, the goal of this research project was to determine the impact of SG availability on immune cells and fibroadipogenic progenitor cells (FAPs) in SkM following injury in aged individuals.

Methods

Young (5-6 mo) and old (20-22 mo) C57BL/6 female mice were randomized to one of three diets: SG-control ($SG_{cont}$), SG-depleted ($SG_{dep,}$ contains 0 SG), or SG-supplemented ($SG_{sup,}$ contains 3x the SG of the $SG_{cont}$). All diets were isonitrogenous and isoenergetic. At the end of 4 weeks of diet, mice received an intramuscular injection, in both tibialis anterior (TA) SkM, with myotoxin. The TA was cryo-sectioned and immunostained for macrophage markers (CD140$\alpha$, CD68, CD11b, and CD206), FAPs (PDGFR$\alpha$), membrane (laminin), and nucleus (dapi).

Results

We observed increased FAPs at early (3-7 days post injury [dpi]) and late-stage regeneration (28 dpi) in mice consuming $SG_{dep}$ diet vs. $SG_{sup}$ diet. Increased early-stage FAPs is obligatory. We also observed disorganization of the laminin within the muscle structure in mice consuming $SG_{dep}$ diet vs. $SG_{sup}$ diet.

Conclusions

The increase in late-stage FAPs suggests SkM degeneration, which corresponds with preliminary transcriptomic data suggesting SkM degeneration occurs with reduced SG availability.

Future Directions

Further studies will vet these results and the relationship with immune cells. Further studies will also be conducted to analyze levels of select proteins and the SkM transcript profile in response to each diet to understand the role of SG in aging SkM.

Acknowledgements

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## 7. The Impact of Ketogenic Diet and Time Restricted Feeding on Multiorgan Gene Expression in Aged Rats

**Sarah Ding[1]***, Anisha Banerjee[1], Abbi Hernandez[1]

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The proportion of adults aged 65 and older is increasing in the United States. Due to this, there is a growing need for therapies to alleviate the deleterious effects of aging, especially decreased cognition. Peripheral interventions that exert system-wide effects are a promising field of therapy for ameliorating cognitive decline. One such intervention, a ketogenic diet (KD) with or without time restricted feeding (TRF), is capable of ameliorating several aspects of age-related declines in function in aged male rats. This includes restoration of cognitive function and altered gut microbiome composition. However, further information about factors contributing to cognitive decline could be obtained by examining changes in gene expression in tissues from these studies, both within and outside of the central nervous system. Therefore, this study expands upon previous work, investigating the impacts of these interventions on gene expression throughout the body. Mechanistic insight as to how these interventions influence cognitive status, or how the resulting changes to the gut microbiome result in improved cognition, is still lacking. Thus, this project evaluated several genes associated with possible contributing factors for decreased cognition with a focus on insulin signaling and glucose uptake. Brain, liver, and muscle tissues from the rats in the study were utilized in quantitative real-time PCR against 14 target genes. Tissue-specific effects were observed for several genes involved in insulin signaling pathways, especially within the CA1 subregion of the hippocampus, where increased AKT and Insr expression were observed following KD and TRF, respectively. These data are aligned with previous work, indicating that these interventions result in brain-region dependent changes in gene and protein expression and further expands this work to include regionally specific effects beyond the brain.

## 8. Sub-neurotoxic exposure to ethyl acetate fraction of soil bacterium metabolite promotes longevity in *C. elegans*

**Osagie A. Emokpae[1]***, Timothy Bushman, Jennifer L. Thies, Lukasz Ciesla, Guy A. Caldwell, Kim A. Caldwell

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**Introduction**. Parkinson Disease (PD) is the second most common neurodegenerative disorder where ~90% of cases are correlated with age. There is a higher incidence of PD in rural areas, where meta-analyses suggest that the increased exposure to terrestrial environmental influences, including well water consumption, agricultural occupations, and, in general, an enhanced interaction with soil microbes might represent a risk factor to vulnerable individuals. We previously discovered that the common non-pathogenic soil bacterium, *Streptomyces venezuelae* (*S. ven.*), produces a metabolite(s) that causes dopaminergic (DA) neurotoxicity in *C. elegans* neurons and human SH-SY5Y cells.

**Methods**. We examined two different concentrations of *S. ven.* metabolite in *C. elegans* for neurodegeneration and lifespan phenotypes. Moreover, chemical fractionation was used identify the biologically active metabolite(s) present within the complex *S. ven* natural matrix.

**Results**. Exposure to a high concentration of *S. ven.* (20X) is associated with increased DA neurodegeneration and decreased lifespan. Interestingly, exposure to a lower metabolite concentration (6X) has no effect on DA neurodegeneration but extends *C. elegans* lifespan. In both cases, the "metabolite" examined was a complex mixture. We have further narrowed down the neurotoxic sub-fraction of *S. ven.* metabolite to consist of 4 molecules using bio-guided fractionation with *C. elegans* neurodegeneration assays.

**Conclusions**. The incidence of PD is strongly correlated with age. The temporal influence of environmental exposures and interaction with intrinsic genetic susceptibility factors likely impact neurodegeneration. Chronic exposures to neurotoxic microbial metabolites released into the environment may represent a potential cause of neurodegeneration, whereas transient or low dose exposures promote longevity.

**Future Directions**. Following chemical isolation of an active molecule, we will perform dose-response lifespan studies to discern the value of the purified form as a chemical tool to evaluate the integration of organismal lifespan and neurodegeneration with genetic variation.

**Acknowledgements**. National Institute on Aging (R36AG073798) to JLT.

## 9. Effects of B-Chromosomal Dosage on Longevity Outcomes in *Drosophila melanogaster*

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Sex-specific longevity is poorly understood across the animal kingdom, with some species having one sex live longer than the other and some species having no sex-based differences in longevity. In humans and many other mammal species, females tend to live longer. This trend is also seen in many strains of *D. melanogaster.* There is, however, no known reason for this variation in sex-based aging differences. One molecular pathway of interest in aging research is heterochromatin maintenance. The heterochromatin loss model of aging was first proposed in 1997 by Villeponteau. This model suggests that chromatin maintenance is lost with age, leading to genomic instability, negatively impacting lifespan. Furthermore, this model suggests that altering the amount of heterochromatin might impact lifespan. One way to test heterochromatin's roles in aging and longevity is by exploiting non-essential B-chromosomes, which are small chromosomes comprised primarily of large amounts of heterochromatin. A small percentage of eukaryotes, such as *D. melanogaster,* can carry B-chromosomes, making them an ideal model organism for testing heterochromatin dosage roles in longevity. We utilized *Drosophila* strains with and without B chromosomes to perform a longevity study. Preliminary data suggest a positive association between B-chromosome dosage and longevity in both sexes. On-going experiments investigate measures of genome stability in these strains to determine if differences in heterochromatin maintenance might explain the lifespan increase seen in the B chromosome strains. Investigating heterochromatin dosage effects in *D. melanogaster* will inform the roles of heterochromatin in aging and lifespan across animal species.

## 10. Sex-specific multisystem alterations in metabolome in aged TgF344-AD rats

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Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by cognitive decline and neuronal dysfunction, as well as increased risk of metabolic impairment and disruption of gut microbiota composition. Moreover, we recently demonstrated systemic metabolic dysfunction may be driven by these alterations in gut microbiome composition. However, how specific metabolite production and utilization is altered with AD, and whether this is regionally specific, remains unknown. Therefore, the primary objective of this study is to assess metabolic impairment within both the central nervous system and intestine through untargeted metabolomic investigation using a transgenic rat model of AD (Tg-F344-AD). These rats exhibit AD-like neuropathology, metabolic impairment and cognitive decline in both adolescence and advanced ages, making it a suitable model for our studies. Tissues of the small intestine, large intestine, hippocampus, and prefrontal cortex of Tg-F344-AD and WT rats were analyzed using liquid chromatography/mass spectrometry (LC/MS). Data normalization and multivariate partial least squares discriminate (PLS-DA) analyses including Variable importance in projection (VIP) and Principal Component (PCA) analyses were performed using MetaboAnalyst 6.0. PCA analysis revealed a statistically significant separation of metabolite profiles between Tg-F344-AD and WT groups in gut and brain tissues, demonstrating regional specificity of metabolic-related alterations in AD. VIP plots illustrated several individual metabolites contributing to the differential metabolite profiles between Tg-F344-AD and WT groups, with VIP scores >1, including inosine and hypoxanthine, found in both brain and gut tissue. Glutamate and nicotinamide in both brain and gut tissue contributed to the metabolite differences between AD and WT group after accounting for sex differences. These data demonstrate AD-related impairments in the metabolome of aged subjects include a broad range of metabolites and are sex- and region-specific. Moreover, this work further highlights targeting the gut for therapeutic interventions aimed at alleviating AD-related dysfunction.

## 11. Unveiling the Neural Mechanisms of Gaze Through EEG and Inverse Reinforcement Learning: Insights for Neurodegenerative Research

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**Introduction**: Understanding the intricate neural mechanisms underlying gaze behavior is crucial for advancing neurodegenerative research and developing diagnostic tools for conditions like Alzheimer's disease. This study leverages inverse reinforcement learning (IRL) applied to electroencephalography (EEG) data to decode the decision-making processes behind human gaze dynamics during cognitive tasks.

**Methods**: Nine participants were monitored using a 64-channel EEG cap and an 8-channel fNIRS device, alongside a gaze tracker, while performing arithmetic tasks (addition and subtraction) at three difficulty levels (easy, medium, hard) according to NIH cognitive toolbox guidelines. The study involved collecting and preprocessing EEG data to analyze gaze behavior. An IRL framework was then meticulously crafted to predict the spatial and temporal dynamics of eye movements in participants across a spectrum of cognitive task complexities.

**Results**: Our IRL-EEG framework demonstrated exceptional accuracy in predicting gaze patterns, underscored by robust performance metrics, including target fixation probability, mismatch probability, and sequence score. The framework's significant enhancement in performance was especially notable in complex cognitive tasks, emphasizing its effectiveness in capturing the nuances of human gaze behavior.

**Conclusions**: This study introduces a novel unified IRL-based information-maximization framework designed to integrate disparate data sources for the analysis of human gaze behavior in specific cognitive tasks, as delineated in the NIH cognitive toolbox. This advanced framework is pivotal in elucidating the complex interconnections among eye movement, visual perception, and brain activities, thereby enhancing our understanding of the cognitive task's influence on human gaze behavior and the associated neural processes.

**Future Directions**: Future efforts will enhance model accuracy and apply them to early neurodegenerative disease diagnosis. By using diverse datasets and increasing interpretability, we seek to merge machine learning with neuroscience, potentially leading to innovative diagnostic and treatment options for neurodegenerative conditions.

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## 12. Exploring the Effects of Arctic Sponge Extracts on *S. cerevisiae* Quiescence

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*S. cerevisiae* (budding yeast) is an excellent model for researching how multiple molecular processes affect aging of eukaryotic cells. In this regard, we are interested about whether cellular quiescence of yeast may be informative regarding the aging of human stem cells. To begin to investigate this possibility, a yeast chronological survival study was conducted to discover potential longevity factors present in extracts of very long-lived antarctic sponges. For this experiment, one prototrophic (FY4) and one auxotrophic (BY4742) strain of *S. cerevisiae* were exposed to a few thousand antarctic sponge extracts. Quantitative high throughput cell array phenotyping (Q-HTCP), a custom technology for growth curve analysis of over 60,000 cultures per experiment was used to assess yeast survival, which was assayed at 5 time points over 56 days of culture. Survival was assayed by plating a sample of the stationary phase yeast culture to fresh media and fitting the resulting growth curve data to a logistic growth function to quantify the time (L) that it takes for the surviving cells to reach half of carrying capacity. By this method, an increase or decrease in L equates to reduced or increased survival efficiency, which is the measure of quiescence. The overall data, which will be presented on my poster, are currently being analyzed, with respect to whether particular extracts were associated with increased or decreased quiescence. The identification of cellular factors from long-lived sponges that increase longevity in yeast may also increase longevity in other eukaryotic species. Quiescence factors identified in these extracts could be purified and studied in greater detail for their effects on quiescence, stem cell survival, and organismal aging in other eukaryotic species, including humans.

We would like to acknowledge Dr. Bill Baker and Benjamin Smith (Univ. S. Florida) for providing the arctic extracts for this study.

## 13. Bmal1 Knockout in Rats Results in Central Fluid and Behavioral Defects Consistent with Premature Aging

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**Introduction:** Disruptions of circadian rhythms in central fluid flow have been implicated in numerous neurodegenerative diseases associated with aging, but links between the two are poorly understood. The essential clock gene, Bmal1, regulates many circadian processes and knockout of the gene in rodents results in accelerated aging phenotypes. We hypothesize that Bmal1 knockout (Bmal1KO) rats have altered circadian control of central fluid homeostasis and increased anxiety.

**Methods:** We used male and female Bmal1KO and wildtype (WT) littermate controls and measured brain water content, blood brain barrier (BBB) permeability with a FITC-dextran perfusion assay, and circadian rhythms of genes involved in central fluid flow. We also performed behavioral tests using open field and elevated plus maze.

**Results:** Bmal1KO had elevated brain water compared to WT (1.54±0.03 vs 1.44±0.03 g, n=8-11; p=0.04). Bmal1KO rats had more FITC-dextran in the brain stem (261.3±18.8 vs 196.4±10.6 ng/mg tissue, n=4-5; p=0.03) and in the spinal cord (331.9±17.1 vs 239.2±31.7 ng/mg, p=0.03) indicating increased BBB permeability. We failed to observe any genotype differences in anxiety using the elevated plus maze. BMAL1KO rats had fewer entries into the center area during the open field test (3.6±0.7 vs 11.0±2.0, n=5-6; p=0.01). Bmal1KO had a blunted aqp4 amplitude (1.2±0.2 vs 0.8±0.2 Ct; p=0.004 comparison of fit). We also found a dramatic blunting of edn1 amplitude in Bmal1KO rats (0.41±0.19 vs 1.31±0.39 Ct; p<0.001 comparison of fit).

**Conclusions:** These results suggest that circadian rhythms are integral in maintaining proper central fluid dynamics and may play a role in neurodegenerative diseases of aging.

**Future Directions:** Genotype difference using RNAseq and sleep differences in patients with normal pressure hydrocephalus will be evaluated.

**Acknowledgments:** This research was supported in part by a pilot award from ICAR to BKB and MTH.

## 14. Impact of *O*-GlcNAcylation elevation on mitophagy in the brain

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**Introduction:** Aging is closely linked with a decline in cellular quality control by mitophagy. This study investigates cell type specific mitophagy and its regulation by protein O-GlcNAcylation, a key nutrient and stress sensing and signal integrating pathway, which modify protein by O-GlcNAc transferase and remove the modification by O-GlcNAcase (OGA).

**Methods:** We use the mito-QC mitophagy reporter mice which express mitochondrial targeted Cherry-GFP. Mitophagy can be scored when Cherry-GFP is targeted to the lysosome in which GFP is quenched leaving red only puncta. We used 3-month-old male and female mito-QC mice, and 24-month-old male C56BL/6 mice, injected intraperitoneally saline or OGA inhibitor thiamet G (TG) at 50mg/kg. After 3 hours, brains were processed for immunostaining. Keyence BZ-X810 microscope and ImageJ software were used for imaging and analysis. Antibodies were used to detect *O*-GlcNAcylation, NeuN (neuron), IBA1 (microglia), TMEM119 (microglia), GFAP (astrocyte), S100b (astrocyte), and LAMP1 (lysosome).

**Results:** TG injections led to increased *O*-GlcNAcylation in both sexes, which reduced mitophagy in the dentate gyrus of the brain and decreased GFAP and S100b levels, indicating remodeling of astrocytes. Importantly, the reduction of GFAP to *O*-GlcNAc was also preserved in 24-month-old mice. We also found a decrease in Iba1 levels, indicating remodeling of microglia.

**Conclusions:** Our findings demonstrate that *O*-GlcNAcylation elevation by TG significantly suppresses mitophagy and alters glial cell homeostasis in the brain, with sensitivity to *O*-GlcNAc and GFAP maintained in aging. These results provide a basis for further understanding how *O*-GlcNAcylation impacts cellular mechanisms supporting neurological health during aging.

**Future Directions:** Future research will delve into the molecular pathways linking *O*-GlcNAcylation with neuroglia and mitophagy in aging, to uncover strategies for promoting healthy brain function in later life.

**Acknowledgements:** We thank our research teams and staff for their invaluable contributions.

## 15. Hypoglycemia and impaired glucagon response in a transgenic mouse model of tauopathy.

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### Introduction

Alzheimer's disease (AD), a prevalent form of dementia, is characterized by a progressive cognitive decline with age. The combination of its prevalence and limited availability of treatment options position AD as a significant public health concern, necessitating an in-depth understanding of this disease. Previous work from our group has shown that defects in peripheral insulin sensitivity exist in transgenic rodent models of AD, with the transgenic rodents displaying insensitivity to insulin compared to age-matched littermate controls. These observations prompted us to further investigate glucose homeostasis in the context of AD.

### Methods

The P301S mouse (Tg), a previously generated transgenic mouse model of tauopathy, was employed. Ambient-fed glycemia monitoring and glucose/insulin/glucagon tolerance testing were employed to assess glucose homeostasis *in vivo*. RT-qPCR analysis of genes known to be involved in hepatic glucose production was carried out to probe mechanisms for observed physiological changes.

### Results

Light cycle hypoglycemia was observed in Tg males and females. No differences in glycemic excursion following a glucose challenge were observed in Tg mice of either sex. Insulin tolerance testing revealed greater reductions in blood glucose of male Tg but not female Tg mice compared to WT littermates. A glucagon challenge revealed that both male and female Tg mice have impaired endogenous glucose production, with a more dramatic effect in males. Consistent with this, gene expression analysis revealed reduced expression of mRNA transcripts involved in hepatic glucose production and fatty acid metabolism in the livers of Tg mice, with a more pronounced difference in males.

### Conclusions & Future Direction

P301S transgenic mice display notable hypoglycemia compared to WT littermates likely caused by dampened hepatic glucose production resulting from reduced expression of genes involved in the program. Future studies restoring this function are warranted to explore the contribution of impaired glucose production to the AD phenotype.

## 16. MicroRNA and Cognitive Impairment

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**Background:**
MicroRNAs are endogenous non-coding RNAs that can regulate gene expression in either normal physiological or pathological processes. In recent years, their potential as promising biomarkers has drawn attention for diagnostic or prognostic purposes for many diseases including cognitive impairments or dementia.

**Methods:**
All participants were recruited from a local homeless shelter. Demographic information (age, gender, ethnicity/race, and education) as well as vital signs were collected from the participants. Two cognitive tests (MMSE and MoCA) were used to measure the cognitive performance from the participants. A nasal swab sample was collected from each participant, which was saved in a -80-degree freezer until the time to do the MicroRNA analysis.

**Results:**
There are four participants who have an age between 54 and 63 years old. Three are Black and one is White. Two participants have cognitive impairments (MMSE is below 25 and MoCA is below 20 for both). In total, 2618 microRNAs were measured with a multiplexing method. 1281 microRNAs are present, and 15 microRNAs are absent from all participants respectively. More importantly, 6 microRNAs are absent in participants with normal cognition but present in participants with cognitive impairments. By contrast, 3 microRNAs are present in participants with cognitive impairments but absent in participants with normal cognition.

**Conclusions:**
Our findings indicate it is feasible for detecting microRNAs from body fluid samples collected with a non-invasive method (nasal swabs). In addition, microRNAs have the potential for being used as biomarkers for purposes of cognitive impairment diagnosis, prognosis, and more.

## 17. Nicotinamide Riboside Does Not Enhance the Effects of Exercise in Hypertensive Middle-Aged and Older Adults (the NEET trial): A Phase II Randomized Clinical Trial

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**Introduction.** Aerobic exercise is an effective treatment for lowering blood pressure (BP), but effects vary among hypertensive middle-aged and older adults. Preclinical evidence suggests that nicotinamide adenine dinucleotide (NAD+) declines with age, and that replenishing it enhances the effects of exercise on endothelial function, which may improve BP control. Thus, this randomized clinical trial (RCT) tested the safety and feasibility of aerobic exercise combined with nicotinamide riboside (NR) (NAD+ booster) to improve BP control in hypertensive middle-aged and older adults.

**Methods.** In this three-group, double-blinded RCT, 54 sedentary adults (≥ 55 years) and mean daytime systolic BP (SBP) ≥130mmHg were randomized to 6 weeks of (1) 1000 mg/day of NR or (2) Placebo combined with 3 days/week of supervised, 30-min walking exercise (NREx), or (3) NR alone (NRa). The primary outcome was daytime SBP (24-hour BP). The secondary outcome was arterial stiffness (pulse wave velocity, PWV). A linear regression model was used to compare between-group differences with a statistical significance set at $p$=0.05.

**Results.** Of 54 participants (mean age 67.3 years, 61% female, 32% Black or American Indian), 49 (NREx: n=15, NRa: n=18, PLEx: n=16) completed all visits. The blood chemistries and reported adverse events were not significantly different between groups. The average adherence to exercise sessions was 93%, and 90% to NR supplementation. NREx did not reduce SBP (mean +4.57 mmHg, $p$=0.113) compared to those receiving NRa and PLEx as well as did not decrease PWV (mean -0.21 meters/second, $p$=0.523).

**Conclusions.** Although we have not observed trends in reductions in SBP and PWV, NREx intervention was safe and feasible in hypertensive middle-aged and older adults. As next, we will perform further analyses of molecular changes in response to NREx taking dietary intake and medications into account to better understand the impact of NREx dosing on BP control.

## 18. Dynamics of Dominant Default Mode Network Linked to Processing Speed in Cognitively Healthy Oldest-Old

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**Background:** Cognition can vary tremendously among the cognitively-intact "oldest-old" in areas such as executive function, memory, and processing speed. Dynamic brain activity can be clustered on the individual time-point level to produce group-averaged "brain states," termed "co-activation patterns" (CAPs), which can provide high resolution temporal information about brain function. Here we present the first study conducted in the oldest-old population that attempts to describe the relationship of brain dynamics to cognition.

**Methods:** 146 cognitively-unimpaired participants aged 85-years or older provided 8-minute, 2.4-second TR, 3T resting-state functional magnetic resonance imaging (rs-fMRI) and completed neurocognitive assessments as part of a 4-site study, the McKnight Brain Aging Registry, a collaboration with UAB, University of Florida, University of Miami, and University of Arizona. CAPs were calculated using a k-means clustering algorithm. Dynamics were defined based on Fraction of occurrence (percentage of time spent in a specific state), persistence (consecutive time spent in a specific state), and transitions (movements from one state to another state).

**Results:** The most stable CAP across models (mean r = 0.92) has highly active DMN (z = 2.2), relatively high activation of the ventral attention network (VAN, z = 1.0) and low activation of every other network (z < -0.6). We compared the dynamics of this dominant CAP to 5 aggregate measures of cognitive performance. Strikingly, these dynamics were strongly correlated only to processing speed, where better processing speed related to greater transition entropy, longer persistence, and greater fraction of occurrence.

**Conclusions:** The default mode network was identified as a stable, common group-wide measure in the oldest-old population, regardless of model. Better processing speed was found to correlate to a dominant and persistent default mode network activity. CAPs add a new, dynamic dimension to fMRI and hold promise as a potential biomarker for cognitive intervention in future studies.

## 19. Constraint-Induced Cognitive Therapy: Pilot Findings Regarding Transfer of Processing Speed Improvements in Daily Living for Stroke Survivors with Cognitive Impairment

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**Introduction:**
Slowed processing speed is a common cognitive impairment that can impede stroke survivors' daily lives. Constraint-Induced Cognitive Therapy (CICT) is a novel technique that combines speed-of-processing training (SOPT) with a transfer package adapted from Constraint-Induced Motor Therapy that focuses to transfer cognitive improvements to activities of daily living (IADL). The goal of CICT is to ensure that improvements made in the clinical setting are applicable to everyday life.
The Useful Field of View Test (UFOV) was used to assess processing speed in this study. The UFOV is a standardized, computer-based test that assesses processing speed, generating scores in milliseconds for Processing Speed, Selective Attention, and Divided Attention.

**Methods:**
Participants were four stroke survivors with chronic mild-to-moderate post-stroke cognitive impairment and difficulties in IADL. Each was given 35 hours of CICT therapy, which consists of SOPT, cognition-based IADL training, and a Transfer Package that includes a behavioral contract, homework assignments, and tracking of IADL functioning.
The UFOV was administered before and after treating three of the participants. A composite score of the Selective Attention and Divided Attention measures was used as the outcome measure due to a floor effect with Processing Speed. One participant was excluded due to a post-stroke visual field cut that interfered with completing the UFOV.

**Results:**
The three participants with valid UFOV data all showed clinical improvement. One went from a composite score of 325.5ms to 23.85ms, one from a composite score of 188.5ms to 121.7ms, and the final from 117.1ms to 85.1ms.

**Conclusions:**
CICT may be a promising technique for improving processing speed for patients with cognitive impairment after stroke.

**Future Directions:**
A randomized controlled trial with a comparison intervention is warranted.

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## 20. *Drosophila* $K^+$-dependent $Na^+/Ca^{2+}$ exchanger, *nckx30c*, is implicated in temperature-sensitive paralysis and age-dependent neurodegeneration

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### Introduction
The correlation between epileptic seizures and neurodegenerative conditions like Alzheimer's Disease (AD) is of growing interest, yet poorly understood. Ion channels regulating intracellular $Ca^{2+}$ levels are crucial for neuronal function and their dysregulation leads to neurological symptoms like, seizures. Additionally, disruptions in $Ca^{2+}$ levels are implicated in AD pathogenesis. Previous research indicates that temperature-sensitive (TS) paralytic *Drosophila* mutants, resembling epileptiform activity, could offer insights into the molecular links between these conditions.

### Methods
Unbiased genetic screen identified mutants exhibiting paralytic behavior at 38°C followed by brain histology. Gene mapping, and DNA sequencing located the mutation in the *nckx30C* gene, encoding the $K^+$-dependent $Na^+/Ca^{2+}$ exchanger. TS paralysis assay, lifespan analysis, climbing assay, brain histology, RT-qPCR and immunohistochemistry for larval neuromuscular junction (NMJ) was used for the analysis of the mutant fly. Knockdown using RNAi established the cell-type specificity of mutant phenotypes.

### Results
Mutant line *426* exhibited TS paralysis and progressive neurodegeneration. Comparing to *wild type*, *426* flies showed reduced lifespan, impaired climbing, lower relative expression of *nckx30c* in the head and changes in NMJ morphology, indicative of synaptic dysfunction. Another *nckx30c* allele exhibited mutant phenotypes. Neuron-specific knockdown of *nckx30c* recapitulated the TS paralytic phenotype with shorter lifespan, while knockdown in both neurons and glia led to early-onset climbing defects.

### Conclusions
*Drosophila nckx30c* gene shares orthology with the mammalian *Solute Carrier Family 24* (*SLC24*), the brain function of which remains poorly understood. This investigation may illuminate the function of *SLC24* while establishing a connection between seizures and neurodegeneration.

### Future Directions
Cellular physiology in the nervous system of *nckx30c* mutant and interactions of *nckx30c* mutations in a fly model of AD will be investigated.

### Acknowledgements
We thank Dr. Robinow for sharing the collection of mutant flies used in the genetic screen. We thank members of the Chtarbanova, Iyengar and Gantezky labs for helpful discussions.

## 21. Early Composite Score to Predict Long-Term Physical Function in Surgical Sepsis Survivors

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**Background:** Sepsis is a dysregulated response to infection, which leads to poor in-hospital and long-term outcomes, including physical disability. There is a lack of early predictors of long-term physical disability in sepsis survivors.

**Methods:** Surgical sepsis survivors underwent physical function assessments at 3 and 12 months by the Short Physical Performance Battery (SPPB) and handgrip strength. Blood biomarkers and severity scores were collected withing 12-48 hours after sepsis onset. Multiple univariate and multivariate regression analyses incorporated seventeen biomarkers to explore their associations with changes in SPPB scores and grip strength between 3 and 12 months. Univariate analysis calculated Area Under Curve (AUC) for SPPB and handgrip strength. A multivariate logistic regression using biomarkers only or established severity scales (SOFA, APACHE, and Charlson Comorbidity scores) developed a predictive score for whether the SPPB change at 3 vs. 12 months would exceed the population median. To construct a composite biomarker score alongside these severity scales, a multivariate logistic regression using both biomarkers and severity scales was adopted.

**Results:** In this secondary analysis of a prospective cohort (356 sepsis survivors; 55% males, 98% White, median age 64), four out of seventeen tested biomarkers (granulocyte colony-stimulating factor receptor (G_CSF) (muscle regeneration), Cystatin C (renal function), albumin (muscle loss), and angiopoietin 2 (angiogenesis) showed comparable association with long-term physical function to biomarkers combined into the model (AUC SPPB 0.587, 95% CI = 0.528-0.647; AUC grip strength 0.515, 95% CI = 0.454-0.575), and biomarkers combined with severity score (AUC SPPB 0.604, 95% CI = 0.545-0.663; AUC grip strength 0.531, 95% CI = 0.470-0.591). In the composite biomarker score, the predictive power attributed to G_CSF was statistically significant (p-value=0.026).

**Conclusions:** Although composite biomarkers comparably predicted physical function decline, G_CSF biomarker had strongest predictive power in a combined model.

## 22. Sniffing out olfactory neuroregeneration: neurogenesis in the context of Alzheimer's disease

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**Introduction:** The loss of smell is an early potential biomarker for Alzheimer's disease (AD), which is perplexing given that the olfactory system is highly regenerative, with a population of basal stem cells responsible for the continuous renewal of olfactory sensory neurons (OSNs). Building on our previous findings of a Notch signaling-Insm1a feedback loop that drives developmental olfactory neurogenesis, we hypothesized that AD-associated Aβ42 peptide disrupts this signaling mechanism.

**Methods:** Aβ42 overexpression was achieved exogenously by treating zebrafish embryos with Aβ42 peptide or endogenously via mosaic expression of the transgenic construct Tg(βactin:mTurquoise2-T2A- Aβ42). The transgenic constructs Tg(Ngn1:nGFP) and Tg(Hsp70I:NICD-myca) were used to mark neurons and overexpress Notch signaling, respectively. Hybridization chain reaction (HCR) detected *her4.1 and insm1a* mRNA expression. HCR and cell number analyses were performed using Imaris (Bitplane, Inc.) software.

**Results:** Exogenous Aβ42 peptide treatment yielded temporally-dynamic changes in the number of basal stem cells and OSNs in developing zebrafish embryos. Endogenous, mosaic overexpression of Aβ42 facilitated *in vivo* comparisons between individual Aβ42-expressing cells, uncovering transcriptional changes and downstream effects that point to a cell autonomous, pro-neurogenic role for Aβ42.

**Conclusions**: Our findings suggest that Aβ42 cell autonomously shifts the olfactory stem cell-neuron balance towards neuronal differentiation.

**Future directions:** Moving forward, we will assay changes in basal stem cells and neuronal progenitors when Aβ42 is overexpressed, including, how particular signaling pathways influence a cell's ability to self-renew or commit to a more differentiated cell fate. Additionally, we will investigate single-cell level transcriptional changes in response to Aβ42 overexpression. Given that previous research on Aβ42 has focused predominantly on neurodegeneration, we hope to uncover new insights into how neurogenic mechanisms might be harnessed to improve outcomes for neurodegenerative diseases.

**Acknowledgements:** This work was supported by the National Institute on Aging, National Institute of Child Health and Human Development, and the Alzheimer's Association.

## 23. High Fat Diet (HFD) contributes to a decline in peripheral metabolism but affects cognition and memory in a sexually dimorphic manner

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### Introduction

Alzheimer's Disease (AD) currently affects 50 million people worldwide, reaching 152 million by 2050. Less than 5% of AD is familial transmission and therefore most AD is not entirely understood. The abnormalities in bioenergetics and endocrine mechanisms caused by insulin resistance tends to eventually lead to the progression of AD. Our previous research has shown sexual dimorphism in peripheral metabolic homeostasis and emergence of AD via cognitive and memory deficits in TgF344 rats. High Fat (Western) Diet (HFD) induces obesity, decreased insulin sensitivity, insulin resistance and type 2 Diabetes. The current study explores the way in which HFD intervention affects the progression of AD in TgF344 rats, delving into the relationships among diet, metabolism and cognition.

### Methods

Male and Female TgF344 rats were fed on a 60% Kcal HFD obtained from Research Diets for 4 months. Insulin and Glucose Tolerance Tests were then performed to assess peripheral metabolism, QMR for body composition and Morris Water Maze, Elevated Plus Maze and Open Field Tests for cognition and memory.

### Results

Females showed more fat mass. Female rats exhibited a decreased insulin sensitivity but improved glucose tolerance while males showed decreased glucose tolerance. Females rats displayed more anxious behavior and males displayed memory deficits.

### Conclusions

High Fat Diet appears to continue to contribute to a decline in peripheral metabolism in female and male TgF344 rats but affects cognition and memory in a sexually dimorphic manner.

### Future Directions

More research should be performed to understand the underpinnings of AD, particularly with relation to the gut-brain axis via microbiome analysis and other molecular mechanisms.

## 24. Deletion of *Socs3* Enhances OSM-induced Astrocyte Reactivity and Severity of Alzheimer's Disease

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Alzheimer's Disease (AD) is the most dementia affecting millions of people in the United States. Pathological hallmarks of AD are extracellular amyloid plaques and intracellular Tau neurofibrillary tangles. Astrocytes are the most abundant cell type in the central nervous system and widely implicated in neurodegenerative diseases, but the role of reactive astrocytes in AD pathogenesis remains largely understudied. The JAK/STAT signaling pathway, negatively regulated by Suppressor Of Cytokine Signaling (SOCS) proteins, is a key player in inducing astrocyte reactivity in response to proinflammatory cytokines, including Oncostatin M (OSM). However, the functions of the JAK/STAT/SOCS pathway in AD-related astrocyte reactivity and AD-related pathology remain unclear. Our studies using astrocytic Socs3 deletion in $App^{NL\text{-}G\text{-}F}$ knock-in ($Socs3^{cKO};App^{KI}$) mice demonstrated an enhanced astrocyte reactivity, increased Aβ deposition and worsened cognitive deficits compared to $App^{KI}$ mice. A specific enhanced OSM-OSMR-induced JAK/STAT activation was identified in $Socs3^{cKO};App^{KI}$ mice, which led to higher expression levels of OSMRβ and several other disease-associated astrocyte (DAA) markers, such as *Gfap*, *Vim* and *Serpina3n*. Our study demonstrates the crucial role of SOCS3 in regulating OSM-induced astrocyte reactivity related to AD and implicate activation of the JAK/STAT pathway in promoting the reactive astrocyte phenotype.

## 25. Challenges in cross-species comparisons of RNA-seq data

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### Introduction

Con-specific lifespan differences between sexes may share common gene signatures across species. Unfortunately, cross-species transcriptome comparisons pose considerable difficulties. Therefore, comparing orthologs, gene ontologies (GO), and conserved pathways have been suggested.

### Methods

To establish an analysis pipeline for cross-species comparisons, RNA-seq data from young and aged flies (*Drosophila melanogaster*) and fish (*Xiphophorus maculatus*) of both sexes were compared. OrthoFinder was used to identify common orthologs, species-specific orthologs were mapped to their genes, and DESeq2 was used to identify significant sex-specific differentially expressed genes (DEGs). Species-specific functional analyses (GO and KEGG pathway) and weighted gene co-expression network analyses (WGCNA) were conducted and compared. WGCNA modules that were significantly correlated to the same trait across species were selected for comparison.

### Results

Male fish had few DEGs in age which hindered downstream comparisons. One cross-species orthogroup in aged females mapped to a DEG. The orthogroup contained the protein sarco/endoplasmic reticulum Ca(2+)-ATPase (SERCA) (FBpp0309946) in fly, and SERCA 1-like and SERCA 2 (ENSXMAP00000033389.1, ENSXMAP00000041537.1) in fish. GO in fish was unsuccessful. KEGG pathway analysis showed no common pathways between species. WGCNA yielded many modules for comparisons, such as one positively correlated module in aged fish compared with two positively correlated modules in aged flies which yielded 48 common KEGG pathways.

### Conclusion

SERCA was significantly downregulated in aged females in both species. This may be a sign of muscle atrophy and muscle weakening occurring in aged females, a consequence of aging that did not occur in males. This idea was strengthened by the KEGG pathway, “amyotrophic lateral sclerosis (ALS),” which was common in aged females only across species according to WGCNA.

### Future Directions

Refine the pipeline, add more species to the pipeline, identify common signatures of age across multiple species, and manipulate those signatures to pinpoint their influence on aging.

## 26. Role of succinylation in MPC cell state

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**Purpose**: Skeletal muscle (SkM) stem and progenitor cells (MPCs), are required for SkM regeneration and the myogenic program. It is recognized that nutrient availability and metabolism impacts MPC function; however, little is known regarding the mechanisms by which nutrients impact MPCs—an important gap in knowledge to address, as MPC number and function as well as nutrient metabolism/availability are impaired in older adults. The post translational modifications (PTMs), succinylation (succinyl- is added to a protein's lysine residue), is a potential link between nutrient metabolism and cell state. Succinylation and the desuccinylase enzyme, sirtuin 5 (SIRT5), are involved in cancer cell state determination. Neither SIRT5 nor the succinylome are characterized during myogenesis. The purpose of this study was to characterize succinylation as a function of cell state in MPCs.

**Methods**: We measured total protein succinylation and SIRT5 levels using Western blot (WB) and the protein succinylome using untargeted proteomics. Follow-up analyses of potential protein targets linking succinylation with cell state were determined with WB and enzymatic activity assays.

**Results**: SIRT5 protein levels increased when cells transitioned from proliferation to differentiation while succinylation decreased. When succinate, a substrate for succinyl-CoA, was provided to cells as they began to differentiate, protein succinylation increased and differentiation was impaired. We demonstrated that under these conditions there were several succinyl- protein targets that may impact the ability of MPCs to differentiate. Under normal culture conditions, succinylated proteins were enriched in metabolic pathways including fatty acid, propionate, and branched-chain amino acid catabolism.

**Conclusions**: In conclusion, succinylation modifications are associated with MPC cell state and are a likely link between nutrient availability/metabolism and MPC state.

**Future Directions:** Confirm protein targets of succinylation during succinate treatment. Determine causality between succinylation modifications and MPC state.

**Acknowledgements:** UAB CDIB, Nathan Shock Center

## 27. Natural Genetic Variation and Sex Influence Diet-Dependent Lifespan Extension Under Methionine-Restricted Conditions in *Drosophila melanogaster*

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**Introduction:** Methionine restriction (MR) has been shown to extend lifespan in a number of experimental models, but the effects of genetic variation and sex has been under researched compared to similar interventions. This study utilizes the Drosophila Genetic Reference Panel (DGRP) to examine the response to MR of diverse genetic backgrounds of both sexes.

**Methods:** Several strains of fruit flies from the DGRP were collected as virgins and sorted onto a low-methionine diet or control diet. The lifespan of these strains was assayed as well as their resistance to the oxidative stressor, paraquat, by recording survival at regular intervals. Their physical performance was also investigated using the natural negative geotaxis response of fruit flies and assaying their climbing ability at different ages under different dietary conditions.

**Results:** Our results show that sex and genotype influence diet-dependent changes in health and longevity under MR conditions. The lab strain, w1118 experienced sex biased improvements in median and maximum longevity and stress resistance on the experimental diet. DGRP strains show a wide range of responses, with some strains seeing a benefit and others seeing no change at all or even impaired survival.

**Conclusions:** The optimized diet for lifespan extension varies in a genotype and sex-dependent manner. The pro-longevity benefits of methionine restriction can be uncoupled from oxidative stress resistance and is more strongly associated with genetic background.

**Future Directions:** Future studies will involve identifying diet-responsive genes that are involved in the regulation of the aging process in other model organisms and inform clinical studies using MR to ameliorate aging-associated illnesses like Alzheimer's and cancer.

**Acknowledgements:** Dr. Steven Austad and members of the Austad lab including Dr. Heather Patterson and Aniyia Good for their help in designing and implementing experiments, as well as the UAB Nathan Shock Center.

## 28. Early Inflammaging and Senescence Transcriptional Response to Ocular Hypertension in Living Human Retina

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**Purpose:**

Aging and elevated intraocular pressure are primary risk factors for glaucomatous optic neuropathy. The acute immune response to elevation in IOP in animal models has been described, however, the exact molecular pathways that trigger these response remains unknown in the human eye. This study evaluates the impact of acute elevation in IOP in the living human eye on transcriptional genes responsible for immune recruitment, inflammaging, and senescence seen with early injury in the retina.

**Methods:**

Research-consented brain-dead organ donors underwent screening for inclusion criteria. Blood pressure was monitored via an arterial line and tonometry was performed using an applanation tonometer. The experimental eye received one hour of manometric pressure elevation at 50 mmHg via pars plana cannulation while the fellow eye served as a control. Electroretinography was performed in regular intervals. Ocular tissues were subsequently procured, dissected, formalin-fixed and paraffin embedded. Peripheral and macular retina was sliced in 5 μm sections, deparaffinized and RNA fluorescent in-situ hybridization was performed according to RNAScope (Advanced Cell Diagnostics) protocol for FFPE tissues.

**Results:**

Acute, 1-hour increase in IOP results in an increase in retinal transcripts involved in innate immune activation, recruitment of peripheral immune effector cells, inflammaging and senescence. To date, we have analyzed 2 donors of 2 different ages and found an increase in chemokine ligand 2 (CCL2), FasR, cluster of differentiation 44 (CD44), and transforming growth factor beta 1 (TGF-β1), which differ between retinal regions. Analysis is ongoing.

**Conclusions:**

Brief, acute increases in IOP results in alteration in the transcription of genes involved in early immune and senescent pathways in the living human retina. Further studies of this acute response within the living human eye could further elucidate early injurious pathways at the onset of ocular hypertension.

## 29. Regulation of Vascular Aging by Runx2 Transcription Factor

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Epidemiology studies have identified aging as is a predominant risk factor that accelerates the pathogenesis of cardiovascular diseases, the leading cause of mortality and mobility in the United States and worldwide. Vascular aging, the age-related molecular, structural and functional changes in the blood vessels, not only impairs normal vascular contraction and compliance but also increases the incidence of cardiovascular disease, including hypertension, coronary artery disease, heart failure, stroke and peripheral artery disease, as well as vascular complications in metabolic diseases, such as diabetes. Therefore, better understanding of the molecular regulation of vascular aging may offer greater opportunities to identify promising targets for potential novel clinical interventions to prevent or retard vascular aging and age-related cardiovascular disease.

Vascular smooth muscle cell (VSMC) proliferation, migration, mineralization, extracellular matrix deposition, and senescence contribute to age-related vascular structural and functional changes. We identified increased expression of the Runx2 (Runt-related transcription factor 2) transcription factor in mouse arteries *in vivo* in an age-dependent manner. In addition, Runx2 upregulation was also determined in the arteries from klotho mutant mice, an accelerated aging mouse model. Furthermore, using a smooth muscle specific (SMC)-Runx2 ablation mouse model, we demonstrated that SMC-specific Runx2 deficiency inhibited vascular complications that are more pronounced in aging, including atherosclerosis, neointimal formation and vascular calcification. To uncover the molecule mechanisms underlying Runx2-regualted VSMC aging phenotype, we utilized a focused microarray analysis, which revealed that increased expression of matrix proteins in the normal aging mice and the klotho mutant aging mice. In contrast, SMC-specific Runx2 deficiency inhibited matrix protein expression in mouse arteries. Furthermore, we found that VSMC from SMC-specific Runx2 mice exhibited reduced senescence and extracellular matrix protein production, two characteristics of vascular aging. Therefore, results from these studies uncovered a new role of Runx2 in regulating VSMC aging phenotype and the pathogenesis of vascular aging, which is beyond its osteogenic function in regulating vascular calcification.

## 30. Compression of morbidity dynamics: Interrogating evidence, measurement challenges, and research horizons

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The compression of morbidity (CoM) hypothesis, proposed by James Fries in the early 1980s, suggests that delaying chronic illness onset in older age results in shorter period of health decline later in life, reducing the overall disease burden. However, empirical evidence on morbidity trends varies, with some studies supporting compression while others suggest an expansion. This inconclusiveness stems from variations in morbidity measurement, data sources, analytical methods, and participant characteristics. Existing studies predominantly measure CoM by focusing on disability. However, there is a growing call for a broader perspective incorporating disease-based definitions, as functional limitations alone may oversimplify the aging process. Most studies on CoM rely on observational data from national surveys or health claims, with a notable gap in primary data specifically collected for evaluating CoM, and lack of experimental studies examining the impact of life-extending interventions on CoM. Statistical analyses of CoM employ both prospective and retrospective approaches. Prospective methods link survival changes to morbidity status over time, estimating lifespan with and without morbidity, while retrospective assessments focus on morbidity occurrence closer to the end of life. Health expectancy, a crucial tool for assessing CoM, evaluates population health trends using prevalence-based life tables (e.g., Sullivan's method) and multistate life tables (e.g., Markov's illness-death model). Despite mixed evidence, there is strong support for prevention efforts aimed at preserving health and reducing disease burden, emphasizing quality of life over longevity. Future research directions include investigating specific health indicators and improving data collection to understand the interplay between morbidity onset and lifespan. Prioritizing systematic reviews, critical evaluations of statistical methods, and conducting experimental studies assessing the impact of life-extending interventions on CoM are recommended. Challenges such as diverse morbidity trajectories, demographic variations, and changing lifestyle necessitate comprehensive research including developing rigorous statistical methods for gaining deeper insights into this complex phenomenon.

## 31. Mitochondria Alternations in Human Explanted Failing Hearts

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Diabetes mellitus (DM) stands out as one of most significant risk factors for heart failure (HF) within the general population. Recent studies indicate that hyperglycemia may account for deleterious changes in mitochondrial functions and dynamics. So far, the alternations in myocardial mitochondrial bioenergetics and proteins in human HF have not been clearly revealed. In this study, myocardial mitochondrial functions were evaluated by an XF96 Extracellular Flux Analyzer. Spectrophotometric enzyme assays were used to determine the activities of citrate synthase (CS), lactate dehydrogenase (LDH), aconitase and total glutathione (GSH+GSSG) amount. Moreover, western blot was performed to measure myocardial mitochondrial protein levels including CS, LDHB, aconitase (ACO2), voltage-dependent anion channel (VDAC), and ETC Complex IV (C-IV). There were no significant statistical changes in LDH and aconitase activities, GSH+GSSG amount, and protein levels of VDAC and ACO2. However, the explanted failing hearts exhibited decreased activities in CS, C-I, C-II and C-IV, and less LDHB, CS, and C-IV proteins. Comparing to the Control group, only LDHB and CS proteins exhibited statistical significance when separated samples based on DM diagnosis. Of note, when normalized by CS activities, there were no differences in ETC complex activities between the Control group and Explanted group. No changes were shown in most enzymatic activities with the normalization by protein levels, except LDH. In conclusion, the decreased activities in ETC complexes and other enzymes in the explanted failing hearts may be due to less cardiomyocyte mass and mitochondrial content. DM related difference was not detected within the Explanted group. Further studies need to confirm cardiomyocyte loss, and whether there is a relationship between mitochondrial content and mitochondrial morphology.

Acknowledgement: We thank the Alabama Organ Center (AOC), the families and donors of the heart tissues used in this study. This study is funded by UAB Nathan Shock Center Exploratory Funds.

## 32. Experiences with culturally based values and preferences for clinician communication and care with lesbian and bisexual older women with serious illness & their care partners

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**Introduction**: Older adults living with serious illness and their chosen caregivers need experienced, receptive, and inclusive support from their health care professionals. Lesbian, gay, bisexual, transgender, queer (LGBTQ+) individuals face lower access to quality care given their risk of discrimination, and LGBTQ+ women are multiply marginalized. The study aimed to understand the perspectives of LB women and their partners in their interactions with health care professionals, focusing on communication, inclusivity, and decision-making.

**Methods**: This community-based participatory research study employed socio-ecological and queer gerontology theoretical frameworks to investigate the experiences of lesbian and bisexual (LB) women from the Deep South aged 50 and above, living with serious illness, and their chosen caregivers. This qualitative study employed focus group interviews to which thematic analysis of data was applied.

**Results**: 18 LGB women participated in four sets of focus group interviews. We identified nine themes and 29 sub-themes: 1) Positive experiences; 2) Navigating sexuality; 3) Continuum of disrespect to discrimination; 4) Advocacy; 5) Decision-making and inclusion; 5) Communication, 6) Health care protocols; 7) Systemic issues; 8) Disparities between rural and urban areas; and 9) Proxy marginalization experienced by older LB women.

**Conclusions**: Findings underscore the necessity for inclusive, patient-centered care, highlighting the importance of training programs for health care professionals to improve cultural competence, communication skills, and shared decision-making. This research emphasizes the urgent need for interventions at multiple levels to address health disparities and promote equitable care for diverse LGBTQ+ populations.

**Future Directions:** Health care professional communication, education, and training is needed at the individual level. In addition, assessing clinician experience and understanding of intersectionality and the needs and preferences of diverse patients including both structural and interpersonal racism is needed to inform change and provide equitable care.

**Acknowledgments**: Authors would like to acknowledge the community advisory board for this research along with the women who shared their stories and perspectives.

## 33. Lower Urinary Tract Symptoms and Cognitive Impairment among Participants in the REasons for Geographic and Racial Differences in Stroke Cohort Study

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**Introduction:** To evaluate the association of cognitive performance with lower urinary tract symptoms (LUTS), we examined cognitive test scores among participants with and without LUTS.

**Methods:** REGARDS is a national, longitudinal cohort study of 30,239 Black and White adults aged 45+ years, who completed telephone/in-home assessments in 2003-2007 and 2013-2016. We analyzed 6062 women and 4438 men who answered validated LUTS questionnaires (ICIQ-Female/Male-LUTS; range 0-28) in 2019-2020. LUTS were dichotomized as absent (0-3) or present (4-28). Six Item Screener (SIS), abbreviated Montreal Cognitive Assessment (MoCA), animal naming, Letter F naming, word list learning (WLL) and delayed recall tests evaluated verbal fluency/executive function and memory. Lower scores represented worse cognitive performance. We performed multivariable linear regression models adjusting for sociodemographics by LUTS status.

**Results:** Among women, 70% reported LUTS (mean age 69.4±7.8 years, 41% Black, 59% White) compared to 62% of men (mean age 62.8±7.3 years, 32% Black, 68% White). Participants who reported LUTS had lower cognitive performance scores on SIS (beta -0.03, CI 0.05, 0.12, p=0.001), animal naming (beta -0.28, CI -0.47,-0.08, p=0.006), Letter F naming (beta -0.34, CI -0.45,-0.11, p=0.002), WLL (beta -0.48, CI -0.50,-0.13, p=0.001), and delayed recall (beta -0.18, CI -0.19,-0.04, p=0.004). MoCA scores were not lower among participants with LUTS (beta 0.03, CI 0, 0.12, p=0.07).

**Conclusions:** The presence of LUTS was consistently associated with lower cognitive test scores for verbal fluency/executive function and memory. Recognizing subtle changes in cognition among older adults with LUTS may impact treatment decisions.

**Future Directions:** We will analyze longitudinal changes in cognition among participants with and without LUTS.

## 34. The effect of B12 availability on skeletal muscle mitochondrial DNA and mitochondrial function in aging

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Loss of mobility and everyday function is the most common reported disability with aging, inevitably leading to the overall decrease of skeletal muscle (SkM) mass. Decreased mobility combined with decreased SkM mass arises then to define sarcopenia: the age-related loss of muscle mass and increased muscle deterioration. Mitochondrial dysfunction is a major hallmark of aging as mitochondrial DNA density, a marker for DNA content, varies in different tissues and is seen to decline with age. The etiology of mitochondrial dysfunction is multifactorial and not well understood. Micronutrient availability, specifically vitamin B12 (B12), could play a vital role in the regulation of mitochondrial function with aging as B12 absorption is naturally decreased with age. Three experimental groups of aged (20-22 months) C57BL/6 male mice were used to examine the effect of B12 availability on mitochondrial function and SkM mass: a control group with a weekly injection of saline, B12 supplemented group receiving a weekly injection of B12, and a depleted group that received a weekly injection of saline and were given a specialized diet containing no B12. All animals were on the specified treatment for 8 weeks and an MRI vor body composition was conducted at weeks 1 and 8. High resolution respirometry (HRR) was conducted on fresh quadricep tissue and histology was conducted on frozen OCT embedded quadricep tissue. From the HRR, no significant difference in complex activity or oxidation levels was observed among the experimental groups. Intriguingly, preliminary data demonstrated an effect of B12 availability on muscle fiber (cell) type, which is currently being further examined. To compliment SkM histological analyses, we are also measuring changes in transcript and protein levels for key SkM and energy pathways.

## 35. Care-resistant Behavior Trajectories in the Context of Mouth Care of Persons Living with Dementia in Nursing Homes

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**Objective:** This study examined day-to-day variation in care-resistive behaviors (CRBs) exhibited by persons living with dementia (PLWDs) during mouth health care and the potential influence of time-of-day on CRB trajectories.

**Methods:** A secondary analysis was conducted on a sample of 75 nursing home-dwelling PLWDs who exhibited CRBs during mouth care activities. Over 21 days, CRBs were measured using the revised Resistiveness to Care Scale (RTC-r) days during morning and afternoon mouth care sessions. Group-based Trajectory Modeling was used to identify trajectory groups of daily CBs over time and assess differences between CRBs observed during morning and afternoon mouth care sessions.

**Results:** A consistently low trajectory (CRBs remained low=50.6% of PLWD), a moderate rise-and-fall trajectory (CRBs increased slightly then decreased to a moderate level=37.5%), and a high-decreasing trajectory (CRBs started at a high level but decreased;=11.9%) were observed during morning mouth care sessions. Similarly, a consistently low trajectory (54.5%) and moderate rise-fall-rise trajectory (CRB increased, decreased, but increased again at the end =38.6%) were observed during afternoon mouth care, but the third trajectory group followed a high-rising trajectory (CRBs started at a high level and continued to increase=6.9%) were observed.

**Conclusions**: CRBs during mouth care are dynamic in nature and vary over time. We identified three distinct trajectory groups for both morning and afternoon mouth care sessions over a 21-day period. Within days CRB patterns were found to vary with differences noted between morning and afternoon mouth care. Thus, it is important to consider the timing of providing mouth care for PLWDs.

**Implications:** Based on characteristics of trajectories, it is suggested that mouth care delivered in the morning may be more efficient because of fewer frequencies of moderate or high levels of CRB. Also, PLWDs who belonged to the high-level trajectory groups were the most sensitive to the time of the day for mouth care.

**Keywords:** Group-based Trajectory Modeling, Care-resistant behavior, mouth care

## 36. Glutamine availability impacts skeletal muscle progenitor cell state transition via Mito-Nuclear communication with advancing age

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**Introduction**: The nutritionally non-essential amino acid glutamine (Gln) is the most abundant amino acid in skeletal muscles; however, it is reduced with advancing age. Intriguingly, extracellular Gln is required by the muscle progenitor cell (MPC) for regeneration. How extracellular Gln availability is communicated within the MPC and impacts on cell state is unclear. Therefore, the objective of this study was to examine how Gln influences the communication between mitochondria and the nucleus through intermediate metabolic factors.

**Methods:** C2C12 cells were cultured in high glucose DMEM with various doses of Gln (0, 2, 6 & 12 mM) We used imaging cytometry and FACS to assess Gln availability on MPC proliferation, which was further validated by using GLS inhibitor. Dose-dependent effect of Gln on GLS was analyzed using immunoblot. Subcellular DLST co-localization was visualized with immunofluorescence, confocal microscopy. Cell senescence (p16, p21), myogenesis (MyoD, PAX7), and proteins involved in de/succinylation (DLST, SUCLA2, KAT2A, SIRT5, SIRT1, SIRT7) were assessed via immunoblot, potentially influencing cell state through epigenetic processes.

**Results:** We observed that MPC proliferation was retarded in the absence of extracellular Gln. There was no difference in cell death count with doses of Gln. Gln deficiency potentially delayed MPC proliferation by inducing senescence and inhibiting myogenesis. Succinyl-proteomics revealed increased DLST succinylation at 0mM vs 6mM Gln. Additionally, DLST in the nuclear fraction increased at 0mM, potentially enhancing succinyl-CoA availability and subsequent nuclear protein succinylation, including histones, which will be verified in subsequent studies.

**Conclusions:** These results suggest that reduced Gln availability with advancing age alters metabolism in the TCA cycle and could trigger nuclear protein modifications that restrict the cell state transition.

**Future directions:** Glutamine could be a potential nutrient therapy to support MPCs and enhance the myogenic program.

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## 37. A Machine Learning-based Control Approach for Hip Exoskeletons to Provide Personalized Assistance and Improve Walking Functions for Elderly People

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**Introduction:** Powered lower-limb exoskeletons are promising devices to improve the walking patterns of aged people with mobility deficits. However, providing optimal personalized external assistance is challenging due to modeling uncertainties and time-varying human-robot interaction. We propose a model-free reinforcement learning (RL)-based hierarchical control framework to provide adaptive and optimal personalized exoskeleton assistance, which can be tailed to flexible control objectives, including a normative range of motion (ROM), maximal spatial/temporal/spatiotemporal gait symmetry, controllable step length/width for elderly individuals with difficulties during walking.

**Methods:** We used a single session for this proof-of-concept investigation. Each participant performed four walking conditions at the preferred walking speed on an instrumented treadmill: (a) free walking without the hip exoskeleton, (b) transparent mode (no assistance) walking with the hip exoskeleton, (c) robotic assistance tuning procedure, and (d) optimal assistance mode walking with a hip exoskeleton. Each participant walked for 3 minutes for conditions (a), (b), and (d), and up to 10 minutes for condition (c).

**Results:** The study was performed in the ENABLE lab in the Department of Mechanical Engineering at the University of Alabama. Four participants with an average age of over 60 years old were included. During the experiments, we collected personalized control parameters, hip joint range of motion, step length, step width, and gait symmetry.

The automatic tuning procedure converged in condition (c) between 4 and 9 minutes for all participants, generating personalized control parameters. Compared to condition (a), the optimal assistance in (d) achieved a normative hip ROM within an error of 5 degrees, resulting in improved stride length by 10% to 17%, hip ROM by 41% to 52%, and gait symmetry by 55% to 89%.

**Conclusion(s):** The proposed tuning method can efficiently configure the optimal control for personalized assistance on the affected side and yield the desired gait pattern and enhanced performance in elderly participants with mobility deficits.

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