8th Annual Symposium on Brain Health

Annual Symposium
Center of Excellence for Translational Neuroscience and Therapeutics (CTNT) and Garrison Institute on Aging (GIA)

Wednesday, April 17th, 2024
Academic Event Center

11:30 am Opening Remarks

Dr. Lance McMahon, Senior Vice President for Research and Innovation
Dr. Volker Neugebauer, Director, CTNT, and Executive Director, GIA

12:00 pm Keynote Lecture *"NIA Alzheimer's Translational Research Program and Funding Opportunities"*

Shreaya Chakroborty, PhD, Program Director, Translational Research, Branch Division of Neuroscience, NIH National Institute on Aging

1:00 pm Q & A Session with Keynote Speaker

1:30 pm CTNT Collaborative Research Presentations

Josh Lawrence, Ph.D., Associate Professor, Pharmacology and Neuroscience
"Vitamin A nutrigenomics and Alzheimer's disease pathogenesis: emerging multi-level preclinical and human studies"

Boris Decourt, Ph.D., Assistant Professor, Pharmacology and Neuroscience
"Translational research on dementia: from drug testing to identifying risk factors"

Jonathan Singer, Ph.D., Assistant Professor, Psychology, TTU
"Investigating the grieving brain utilizing unique methodologies"

3:00 pm Poster Session & Refreshments

5:00 pm Awards Ceremony and Reid L. Norman & Cynthia Jumper Excellence in TNP Scholarship Student Presentation

Distinguished Keynote Speaker

Shreaya Chakroborty, PhD
Program Director
Translational Research Branch
Division of Neuroscience
NIH National Institute on Aging

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Volker Neugebauer, M.D., Ph.D., Director, CTNT, Executive Director, GIA, and Chair, Department of Pharmacology and Neuroscience

12:00 PM   **Keynote Lecture**

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- **Josh Lawrence**, Ph.D., Associate Professor, Pharmacology and Neuroscience
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- **Jonathan Singer**, Ph.D., Assistant Professor, Psychological Sciences, TTU
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3:00 PM   **Poster Session & Refreshments**

5:00 PM   **Awards Ceremony and Reid L. Norman & Cynthia A. Jumper Excellence in Translational Neuroscience and Pharmacology Scholarship Student Presentation**
Brent Kisby, Graduate Student, Translational Neuroscience and Pharmacology Graduate Concentration, TTUHSC
"Role of brain vascular cell types in a neuroimmune mouse model of excessive ethanol consumption"

Table of Content

Welcome and Introduction

The 8th Annual Symposium of the Center of Excellence for Translational Neuroscience and Therapeutics (CTNT), organized jointly with the Garrison Institute on Aging since 2021, is focused on "Brain Health". The symposium provides a unique opportunity for students, trainees, health care and community outreach professionals, and basic science and clinical faculty to inform about this important topic and learn about translational research and other activities at CTNT and GIA. With more than 130 registered attendees, this year's symposium achieved the highest turnout in its history.

Dr. Lance McMahon, Senior Vice President for Research and Innovation, will provide the institutional perspective on research priorities and expertise, research infrastructure and support, and research accomplishments. *Distinguished Key Note Speaker*, Dr. Shreaya Chakroborty, Program Director, Translational Research Branch, Division of Neuroscience, NIH National Institute on Aging, has kindly agreed to share with us information about translational research, resources, and funding opportunities at NIA with a particular focus on Alzheimer's disease. Research presentations by CTNT-GIA teams on brain health-related topics from basic science to translational and clinical studies by Drs. Josh Lawrence, Boris Decourt and Jonathan Singer will update and inform on activities and advances in our understanding of brain health. Posters presentations by

Volker Neugebauer, MD, PhD, Executive Director, Garrison Institute on Aging, Director, Center of Excellence for Translational Neuroscience and Therapeutics, University Distinguished Professor and Chair, Department of Pharmacology Neuroscience. Dr. Neugebauer moved from UTMB Galveston to TTUHSC 10 years ago. A neuroscientist with training in neurology, he has been studying brain functions and dysfunctions in health and neurological and psychiatric diseases for some 30 years. Chronic diseases of interest and expertise include pain, addiction, epilepsy and dementias associated with neurodegenerative diseases. His collaborative research program involves preclinical studies as well as studies in human tissues and in humans, using a multi-disciplinary approach. His work has been published in more than 160 research and review articles (h-index 66, 13389 citations) and presented in nearly 160 invited lectures and workshops. His nationally and internationally recognized research program has been continuously funded by NIH since 1999 and is currently supported by several NIH R01 grants, a USDA grant and Foundations.

trainees in basic science and clinical disciplines will provide additional opportunities to inform about activities at TTU and TTUHSC, share accomplishments, exchange knowledge, identify knowledge gaps, and stimulate innovative collaborative efforts. More than 50 abstracts were submitted this year.

Brain Health

Brain health refers to "the state of brain functioning across cognitive, sensory, social-emotional, behavioural and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders." (World Health Organization, WHO https://www.who.int/health-topics/brain-health). We

Brain Health

Environmental health and Toxicology

Immunology (Immune system and inflammasome)

Neuroscience * Neurology

Translational research
Basic research   Preclinical research   Clinical research   Clinical trials

"Brain health is the state of brain functioning across cognitive, sensory, social-emotional, behavioural and motor domains, allowing a person to realize their full potential over the life course"

Mechanistic insights
Prevention
Diagnosis
Treatment/Management

World Health Organization

Psychology * Psychiatry

Endocrinology (Endocrine and metabolic systems)

Genomics Proteomics Metabolomics

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selected "Brain Health" as the topic for our annual symposium for several reasons. The global burden of conditions affecting brain health is high; these include neurological diseases, which are the leading cause of "disability adjusted

life years" (DALYs) and account for about 9 million deaths per year (WHO). Promoting, preventing, and optimizing brain health requires a concerted effort of specialties such as neuroscience, neurology, psychiatry and psychological sciences for a holistic approach that addresses different determinants that include environmental and social factors as well as biological systems such as genomic, proteomic, metabolomic, endocrine, immune and, of course, neural. CTNT and GIA are well-positioned to coordinate and lead interdisciplinary collaborations from basic to translational to clinical studies to advance knowledge and improve physical and mental health. A focal point of CTNT and GIA is translational research through collaborative and innovative efforts. CTNT continues to bring together basic scientists and clinicians to stimulate scholarly activities, facilitate collaborations, and generate translational research projects related to nervous system functions in health and disease, and some of our members and collaborators bring additional expertise from relevant areas not primarily neuro-related. The GIA offers complementary expertise in aging-related disorders and dementias such as Alzheimer's disease, and these include neurodegenerative diseases that affect brain health. Through collaborations in basic and translational research, education, community outreach and mental health services, the GIA strives to serve as a hub to promote healthy aging and brain health by advancing and disseminating knowledge about aging-related health issues and neurodegenerative diseases, and implementing innovative programs to serve the community.

CTNT

Established in 2015 and based in the Department of Pharmacology and Neuroscience, School of Medicine, TTUHSC, CTNT was designed to bridge the gap between basic science and clinical disciplines related to the neurobiology of clinically relevant disorders (https://www.ttuhsc.edu/centers-institutes/translational-neuroscience-therapeutics). CTNT has grown to 40 members from 16 different departments or institutes at TTUHSC and TTU (27 doing basic preclinical research and 12 working with patients or human subjects). Uniquely focused on translational research, CTNT strives to bridge preclinical "basic science" research and the clinical setting for innovative collaborative efforts to advance knowledge about mechanisms of nervous system functions and dysfunctions, diseases affecting brain health, and other clinically relevant disorders for the development of novel and improved diagnostic and therapeutic tools and strategies. Identifying knowledge gaps and exploring disease mechanisms and potential targets for therapeutic advances are the objectives of translational research. Sharing this information with colleagues and trainees through their participation in this process represents an educational component. To do so, CTNT provides the means and mechanisms to develop innovative research collaborations for publications and competitive grant applications and disseminate knowledge through interactions between basic scientist and clinical partners. CTNT also provides training opportunities in translational research for clinical residents and translational neuroscience graduate students. Mechanisms of support include the Annual Symposium, CTNT Research Meetings and Grant Development Program (Translational Research Club), the Translational Neuroscience and Pharmacology Distinguished Lecture Series, matching seed funds for collaborative translational research by multidisciplinary teams of basic science and clinical faculty, and shared research tools.

Accomplishments (2023) include the following:

- Funding of CTNT members: 48 active grants (29 NIH, 1 NSF, 1 USDA)
    - 46% of the grants involve more than one CTNT member.
- Publications by CTNT members: 137
    - 37% of the articles were co-authored by more than one CTNT member.
- Meeting abstracts by CTNT members: 140
    - 42% of the abstracts were co-authored by more than one CTNT member.
- Recognitions/awards of CTNT members: 59
- Invited talks and oral presentations by CTNT members: 64

GIA

Established in 1999 by the Board of Regents, the Institute for Healthy Aging was renamed the Garrison Institute on Aging (GIA) in 2005 in honor of Mildred and Shirley L. Garrison (https://www.ttuhsc.edu/centers-institutes/garrison-aging/default.aspx). The GIA is well-positioned to play a leadership role in initiatives on aging and aging-related disorders and brain health across TTUHSC and beyond, with a special focus on Alzheimer's' disease (AD). Our mission is to promote healthy aging and address health issues in the aging population through translational research, innovative educational activities, and community outreach programs. The GIA conducts and facilitates clinical and basic research into the possible causes and predictors of neurodegenerative disease and dementias such as AD and related brain disorders. The GIA's educational programs inform the community about aging-related health issues such as dementias and mental health. Our community outreach programs provide services to patients and their care partners to improve quality of life and access to healthcare. The vision of the GIA is to serve as the central hub within the TTU System for innovative initiatives in translational research, interdisciplinary education and community outreach related to healthy aging, aging-related disorders, brain diseases and dementias, and mental health through an inclusive and collaborative environment. The GIA aims to develop and lead programs designed to better understand underlying disease mechanisms and risk factors, and to explore new ways to prevent, diagnose, and manage aging-related diseases - ranging from basic science to clinical trials - to improve brain health and healthy aging overall in the communities of West Texas.

GIA support and resources for collaborations include research laboratories for preclinical behavioral assays, electrophysiology and molecular biology, as well as biobanks for human brain tissues, bodily fluids, and isolated DNA samples to study mechanisms, risk factors, and novel targets for neurodegenerative brain and other aging-related diseases. The GIA Brain Bank provides a unique opportunity for translational research, in addition to serving the families of patients with AD and other forms of dementias through free brain autopsies for a definitive diagnosis. Brain tissues are available for the molecular analysis of mechanisms and targets to validate and guide preclinical lab research. Our research program also includes studies in humans. Project FRONTIER (Facing Rural Obstacles to Healthcare Now Through Intervention, Education & Research) is a laboratory and community based longitudinal study that collects epidemiological, neurological, and biological data on cognitive health and aging in a multiethnic adult group of volunteers from rural communities of West Texas to investigate the prevalence and risk factors of dementia among rural residents. Project FRONTIER data also provide opportunities for trainee and faculty research projects and grant applications. Other programs include providing mental health services for family caregivers of AD and Alzheimer's Disease Related Dementia (ADRD) patients and expanding these services to aging/older adults living in rural counties in West Texas through a new telehealth pilot program, while also investigating biopsychosocial outcomes and the dyadic relationship between family caregivers and persons with AD/ADRD. Our Community Outreach and Education division serves a key goal of the GIA, which aims to support our local communities by informing them about aging-related diseases such as AD, challenges impacting the geriatric population, preventative medicine, and the preparation of pertinent legal documents. Our programs include Healthy Aging Lecture Series, Translational Neuroscience and Pharmacology Lecture Series, a newly implemented Dementia Live Training for caregivers, Care Partner Academy, Caregiver Stress-Busting Dementia Program, Dementia Friendly Lubbock (part of Dementia Friendly America) and Healthy Lubbock Initiative (with Mayor's Fitness Council), Diabetes Self-Management Program (endorsed by the CDC), RSVP (Retired and Senior Volunteer Program, which was established in 1979 under the umbrella of the Corporation for National and Community Service CNCS, now funded as AmeriCorps Seniors Retired and Senior Volunteer Program), and mental health services (TX CARES and Creative Minds).

An impactful new direction is the implementation of clinical studies and clinical trials through a highly collaborative NIH grant application for a new Alzheimer's Disease Research Centers (ADRC) that will add unique values to the existing national ADRC network. The GIA will also participate in the new Guiding an Improved Dementia Experience (GUIDE) program funded by the Centers for Medicare and Medicaid Services (CMS) to improve dementia care management and quality of life by

supporting people living with dementia and their unapid caregivers. Through these programs and activities, the GIA is making a significant difference in the quality of life of the aging population in our rural and urban communities.

Accomplishments (2023) include the following:
- Funded preclinical (16) and clinical (10) GIA projects: 26
  - 63% of the grants are collaborations involving GIA members.
- Publications by GIA members: 35
  - 53% of the articles were co-authored by GIA members and collaborating faculty.
- Meeting abstracts by GIA members: 91
  - 53% of the articles were co-authored by GIA members and collaborating faculty.
- Recognitions/awards of GIA members: 9
- Invited talks by GIA members: 17

Collaborative translational research areas related to "Brain Health"

CTNT and/or GIA members are involved in collaborative projects with >60 faculty across TTUHSC (22 departments/schools/centers/institutes) and TTU (14 departments/institutes). Key areas of expertise and interest are centered on chronic pain and comorbid conditions, substance/alcohol use and addiction, and neuropsychiatric disorders that include neurodegenerative diseases such as AD. To do so, our multidisciplinary teams use state-of-the-art mechanistic, neuromodulatory and interventional tools and strategies and explore common themes and concepts such as neuroplasticity, neuroinflammation, and neurodegenerative processes as well as sex differences and aging.

Brain Health – Areas of Expertise

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Acknowledgements

Keynote Lecturer

Shreaya Chakroborty, Ph.D.

Program Director, Division of Neuroscience
National Institute of Aging | NIH

Shreaya Chakroborty, Ph.D., Program Director in the Translational Research Branch, Division of Neuroscience, at the National Institute on Aging (NIA). She manages a portfolio of drug discovery and drug development for biologics and the Alzheimer's Disease Preclinical Efficacy Database (AlzPED), a publicly available data resource that aims to increase the transparency, reproducibility, and translatability of preclinical efficacy studies of candidate therapeutics for Alzheimer's disease. Dr. Chakroborty earned her Ph.D. in Neuroscience from the Chicago Medical School-Rosalind Franklin University of Medicine and Science in Chicago where she conducted research on the impact of altered calcium signaling on hippocampal synaptic transmission and plasticity in Alzheimer's disease. After her Ph.D., Dr. Chakroborty completed a postdoctoral fellowship at Rosalind Franklin University of Medicine and Science examining the molecular and cellular processes underlying neuronal and network function and dysfunction associated with neurological and movement disorders.

TTUHSC Sr. Vice President for Research and Innovation

Lance McMahon, Ph.D.

Sr. Vice President for Research and Innovation,
TTUHSC

Lance R. McMahon, Ph.D., is the Senior Vice President for Research and Innovation at Texas Tech University Health Sciences Center. He has a tenured appointment as Professor of Pharmaceutical Sciences in the Jerry H.

Hodge School of Pharmacy, and Professor of Medical Education in the School of Medicine. He is chair of the TTUHSC Research Council, member of the Texas Tech Research Park Board, and member of the Steering Committee of the Center for Translational Neuroscience and Therapeutics. Dr. McMahon is committed to TTUHSC's vision to transform healthcare through innovation and collaboration, focusing on advancements in cancer, neuroscience, infectious disease, and cardiometabolic disorders. Dr. McMahon serves on the Department of Defense Chronic Pain Management Programmatic Panel of the Congressionally Directed Medical Research Program, and has over 20 years of service as regular and ad hoc study section member of the National Institutes of Health Center for Scientific Review. He has secured $25M in NIH funding for his research in behavioral pharmacology and central nervous system (CNS) drug discovery and development and has published 135 peer-reviewed publications. He has held leadership positions within the American Society of Pharmacology and Experimental Therapeutics and the American Association of Pharmaceutical Scientists.

Reid L. Norman and Cynthia A. Jumper Graduate Scholar

Brent Kisby, Graduate Student

Translational Neuroscience and Pharmacology
Graduate Concentration, TTUHSC

Brent Kisby Brent is a current 3rd year PhD student in Dr. Ponomarev's lab at TTUHSC in the Department of Pharmacology and Neuroscience. Brent is currently studying how the brain's vasculature network is influenced by neuroimmune perturbations which can result in escalation of ethanol consumption. Brent received his bachelors of science in Behavioral Neuroscience from Northeastern University in Boston, MA and started his PhD in 2021. Brent has received several awards including the John P. McGovern Fellowship from the Texas Research Society on Alcohol, American Heart Association Predoctoral Fellowship, and the Dr. Norman Reid and Dr. Cynthia Jumper Excellence in Pharmacology and Neuroscience Graduate Student Scholarship.

Role of brain vascular cell types in a neuroimmune mouse model of excessive ethanol consumption

Toll-like receptor 3 (Tlr3) – dependent innate immune activation in rodents contributes to escalated ethanol consumption in a sex and genotype-dependent manner. Our preliminary data suggests these effects may be mediated by Tlr3 activation in microvasculature cell types. Micro-vessels consist of cell populations that form the blood brain barrier (BBB), including endothelial cells (ECs), smooth muscle cells, and pericytes. We hypothesize that Tlr3 activation-induced changes in gene expression in these cell types contribute to BBB dysfunction and escalated alcohol intake. The goal of this study was to determine the effects of Tlr3 activation and/or chronic alcohol drinking on gene expression in enriched brain microvasculature in high-drinking FVB/NJ X C57BL/6J F1 hybrid mice. Male mice were randomly assigned to receive repeated injections of Poly(I:C) (PIC), a Tlr3 agonist, or saline (9 injections total). Mice were allowed to choose between alcohol or water every other day (17 dinking sessions) and were assigned to one of four groups: saline/water (SW), saline/ethanol (SE), PIC/water (PW), and PIC/ethanol (PE). Brains were harvested 24 hours after the final alcohol session, micro-vessels from the frontal cortex were purified using mechanical homogenization and density-gradient centrifugation, and RNA sequencing and bioinformatics was performed to compare gene expression between

groups. We identified 1,588 genes differentially expressed (DEGs) between PE and SE groups at nominal p-value of less than 0.05 and 74 DEGs at 5% FDR. The top DEGs were Rsad2, H2-K1, Slc16a1, and Ifi44, which are implicated in the immune response and are cell type-specific to the brain microvasculature. Taken together, these data suggest that vascular cell types are responsive to repeated Tlr3 activation and could contribute to excessive ethanol consumption.

Collaborative Research Presenters

Josh Lawrence, Ph.D.

Associate Professor,

Pharmacology and Neuroscience,

TTUHSC

Dr. Lawrence is a tenured Associate Professor in the Department of Pharmacology and Neuroscience at TTUHSC. He received his B.S. from Allegheny College in 1992 and Ph.D. in 1999 from the Neuroscience Training Program at UW-Madison. As a postdoctoral fellow and staff scientist at the NIH, he focused on interactions between neuromodulatory and inhibitory circuits in the hippocampus. Dr. Lawrence is a cellular and synaptic physiologist by training. His own laboratory has historically focused on excitation/inhibition balance and the contribution of neuromodulation to hippocampal-dependent learning. Since joining TTUHSC, he has become affiliated with the Center of Excellence for Translational Neuroscience and Therapeutics, Garrison Institute on Aging (GIA), and Center of Excellence for Integrated Health, which provided him with an integrative understanding of how Alzheimer's disease (AD) pathogenesis impacts hippocampal learning. Following numerous successful interdisciplinary collaborations over the past 15 years, Dr. Lawrence now leads a multi-disciplinary team that spans molecular to circuit to behavioral level techniques in both preclinical and human studies. He currently has two NIH-funded grants in the areas of nutrition and AD, focusing on protective effects of Vitamin A supplementation in halting the onset and/or progression of AD in mouse models. In collaboration with numerous medical students, Dr. Lawrence also leads several GIA-based Project FRONTIER studies, which seeks to connect nutritional deficiencies with preventable diseases associated with increased AD risk.

Vitamin A nutrigenomics and Alzheimer's Disease pathogenesis: emerging multi-level preclinical and human studies

Converging human and preclinical evidence suggest that Alzheimer's disease (AD) involves a loss of transcriptional control. Numerous transcription factors that maintain neuronal integrity and maturity may be reduced in aging and AD. There is emerging evidence that all-trans-retinoic acid (ATRA), a bioactive metabolite of vitamin A (VA), is altered in the hippocampus in AD. VA and ATRA have antioxidant properties, and oxidative stress (OS), thought to be caused by antioxidant depletion, is a key hallmark of AD. Several studies provide evidence that ATRA itself and agonists of retinoic acid receptors (RAR) promote activation of the non-amyloidogenic pathway by enhancing expression of α-secretase, thereby providing a mechanistic basis for preventing amyloid beta (Aβ)-induced toxicity. In our first study, we use RARE-LacZ mice in which LacZ gene expression is under the control of retinoic acid response elements (RAREs). Using this reporter line uniquely

repurposed for AD studies, we have found that LacZ expression is highest in a subset of mature dentate gyrus granule cells. Studies are ongoing to determine how diet-derived VA alters these cell types in crosses with AD mouse models. Transcriptional control is also disrupted by age- and disease-related epigenetic changes to the genome. In our second study, using an FDA-approved histone deacetylase inhibitor (HDACI), we seek to reverse epigenetic damage to DNA as a means of restoring transcriptional control of gene expression. We find evidence that the HDACI vorinostat possesses antioxidant properties, suggesting its capacity to restore antioxidant-related signaling. Finally, our multi-disciplinary workflow applies machine learning algorithms to multiple human RNA-seq datasets, revealing the contributions of novel AD-related genes. Ultimately, our studies will define the role of Vitamin A nutrigenomics in AD and reveal important molecular mechanisms by which nutritional sufficiency can delay or prevent AD.

Boris Decourt, Ph.D.

Assistant Professor,
Pharmacology and
Neuroscience, TTUHSC

Dr. Boris Decourt is an Assistant Professor in the Department of Pharmacology and Neuroscience at TTUHSC. He is the Director of the Laboratory on Neurodegeneration and Translational Research with a strong emphasis on Alzheimer's disease. He holds a Ph.D. degree in Neuroscience and Pharmacology from the University of Bordeaux. His research interests are focused on biomarker development and in translational drug development approaches using inflammation modulators to study the molecular pathophysiological changes taking place at the early stages of neurological disorders. His ultimate goal is to translate his discoveries from bench to bedside to slow down or cure the diseases via early intervention before severe neurodegeneration and dementia occur.

Translational research on dementia: from drug testing to identifying risk factors
Alzheimer's disease (AD) is an incurable neurodegenerative disorder with several complex brain neuropathologies suspected to develop sequentially but that overlap over time as symptoms progress to dementia. Thus, to be effective, future intervention strategies will likely require combination therapies or pleiotropic agents to tackle several AD molecular pathogenic pathways simultaneously. Most clinical trials for AD have focused on manipulating the synthesis and removal of amyloid beta in the brain, but with limited clinical success. For more than a decade, our group has been exploring the repurposing of immunomodulators for AD and develop new objective peripheral biomarkers. In this presentation, we will quickly introduce clinical trials conducted with two repurposed FDA-approved drugs. First, lenalidomide is an anti-cancer agent used to treat multiple myeloma. In an amyloid mouse model of AD, we observed improved cognitive performance and lower amyloid burden in the brain after drug treatment. This data supported the development of two clinical trials to assess the clinical performance of lenadomide in early AD patients. The second drug is Siponimod, which is used to treat multiple sclerosis (MS). Based on MS clinical trial data, the primary outcome in our clinical trial on mild-to-moderate AD patients is to examine the slowing of neurodegeneration via volumetric MRI. Our clinical trials are complemented by observational studies on rural patients in West Texas to better understand risk factors

possibly leading to dementia, progression of disease, and the investigation of novel peripheral biomarkers for AD. This cohort study is proposed as a new NIH-supported Alzheimer's disease Research Center (ADRC) to improve prevention of AD, as well as healthcare delivery and services to rural dwellers suffering AD and their families. The ultimate goal is to translate our discoveries from bench to bedside to slow down or cure the diseases via early intervention(s) before severe neurodegeneration and dementia occur.

Jonathan Singer, Ph.D.

Assistant Professor,
Psychological Sciences, TTU

Jonathan Singer is an Assistant Professor in the Department of Psychological Sciences at Texas Tech University and clinical faculty in the Department of Pharmacology and Neuroscience. He received his Ph.D. in Clinical Psychology from the University of Nevada, Reno in 2021. Overall, his interdisciplinary research examines the interconnections of multiple biopsychosocial processes within persons with life limiting illnesses (e.g., Dementia; Advanced Cancer) and their care partners. By using various methods (e.g., Ecological Momentary Assessment; Daily Diary), the ultimate goal of his research program is to translate basic and applied research into scalable, evidence-based interventions for persons with life limiting illnesses and their care partners. More specifically, Dr. Singer focuses on reducing pre-death grief in persons with life limiting illnesses and their care providers in order to reduce downstream effects such as prolonged grief disorder. Dr. Singer has 50 peer reviewed publications and 83 conference presentations. He recently was funded by the National Institute on Aging for a 3 year study to reduce indirect suicide ideation in care partners of persons with Dementia.

Investigating the grieving brain utilizing unique methodologies

Dr. Singer will present two unique methodologies, Emotional Counting Stroop task (ecStroop) and the Grief Elicitation, that utilize fMRI to examine pre-death grief and prolonged grief disorder. More specifically, he will present some recent results that utilize these protocols to evaluate pre-death grief in family caregivers of persons with Dementia, advanced Cancer, and prolonged grief disorder in Bereaved individuals. These studies will aid to advance the field, leading to identifying robust neurobiological markers of pre-death grief and prolonged grief disorder, improving our ability to diagnose these psychiatric conditions more accurately.

Round Table – Translational Research

Jeremy D. Bailoo, Ph.D.
Assistant Professor, Cell Biology and Biochemistry, Center of Excellence for Translational Neuroscience and Therapeutics

Environmental determinants of disease, animal behavior and cognition, contributions of genetic and environmental factors to individual differences in health and welfare across lifespan.

Michael Blanton, Ph.D.
University Distinguished Professor, Pharmacology and Neuroscience, Center of Excellence for Translational Neuroscience and Therapeutics

Structural analysis of ligand gated channels. Graduate and postgraduate education.

Boris Decourt, Ph.D.
Assistant Professor, Pharmacology and Neuroscience, Center of Excellence for Translational Neuroscience and Therapeutics

Alzheimer's disease and other neurodegenerative diseases and dementias. Biomarker development, translational drug development approaches, clinical trials, community-based dementia studies.

Petar Grozdanov, Ph.D.
Assistant Professor, Cell Biology and Biochemistry, Center of Excellence for Translational Neuroscience and Therapeutics

Regulation of gene expression by alternative polyadenylation, molecular mechanisms of alternative polyadenylation, Alcohol use disorder, Alzheimer's disease, Intellectual disability syndromes, Epilepsy, Neurodegenerative diseases, Aging.

Josée Guindon, D.V.M., Ph.D.
Associate Professor and Graduate Advisor, Dept. of Pharmacology and Neuroscience, Center of Excellence for Translational Neuroscience and Therapeutics

Behavioral pharmacology, immuno-histochemistry, molecular biology, animal pain models, modulation of pain pathways, kidney physiological pathways.

Andrey Karamyshev, Ph.D.
Associate Professor, Dept. of Cell Biology and Biochemistry, Center of Excellence for Translational Neuroscience and Therapeutics, Center for Membrane Protein Research

Molecular mechanisms of translational regulation, protein interactions in health and disease, protein misfolding in neurodegenerative diseases.

Brent Kisby, Graduate Student
Ph.D. Student, Pharmacology and Neuroscience, Center of Excellence for Translational Neuroscience and Therapeutics.

Neuroimmune signaling, brain's vasculature network, Alcohol Use Disorder.

J. Josh Lawrence, Ph.D.
Associate Professor, Dept. of Pharmacology and Neuroscience, Center of Excellence for Translational Neuroscience and Therapeutics, Garrison Institute on Aging.

Neuromodulation of GABAergic circuits in normal and disease states including Alzheimer's disease

Volker Neugebauer, M.D., Ph.D.
University Distinguished Professor and Chair, Dept. of Pharmacology and Neuroscience, Executive Director and Chief Scientific Officer, Garrison Institute on Aging, Director, Center of Excellence for Translational Neuroscience and Therapeutics.

Neuroplasticity and brain functions in health and disease (chronic pain and comorbid disorders, neurogenerative diseases, and other neurological and psychiatric disorders)

Jonathan Singer, Ph.D.

Assistant Professor, Psychological Sciences, TTU

Center of Excellence for Translational Neuroscience and Therapeutics, Garrison Institute on Aging

Grief and Responses to Illness into Late Life (GRILL), psychological health in aging and illness, interconnection of the biopsychosocial processes within individuals with life limiting illnesses

Hongmin Wang, Ph.D.

Professor, Pharmacology and Neuroscience

Center of Excellence for Translational Neuroscience and Therapeutics

 Interested in the role of proteostasis and some specific transcription factors in the pathogenesis of these diseases.

Poster Judges

Jeremy Bailoo, Ph.D. Assistant Professor, Cell Biology & Biochemistry TTUHSC Lubbock	Michael Blanton, Ph.D. Professor, Pharmacology & Neuroscience TTUHSC Lubbock
Boris Decourt, Ph.D. Assistant Professor, Pharmacology & Neuroscience TTUHSC Lubbock	Petar Grozdanov, Ph.D. Assistant Professor, Cell Biology & Biochemistry TTUHSC Lubbock
Josée Guindon, DVM, Ph.D. Associate Professor, Pharmacology & Neuroscience TTUHSC Lubbock	George Henderson, Ph.D. Professor, Pharmacology & Neuroscience TTUHSC Lubbock
Guangchen Ji, Ph.D. Research Associate Professor, Pharmacology & Neuroscience, TTUHSC Lubbock	J. Josh Lawrence, Ph.D. Associate Professor, Pharmacology & Neuroscience TTUHSC Lubbock
Volker Neugebauer, MD, Ph.D. Professor and Chair, Pharmacology & Neuroscience TTUHSC, Lubbock	Igor Ponomarev, Ph.D. Associate Professor, Pharmacology & Neuroscience TTUHSC, Lubbock
Jonathan Singer, Ph.D. Assistant Professor, Psychological Sciences, TTU Clinical Assistant Professor, Psychiatry, TTUHSC Lubbock	Hongmin Wang, Ph.D. Professor, Pharmacology & Neuroscience TTUHSC Lubbock

Poster Presentation Schedule

Basic Science – Undergraduate students

Posters	Time	Presenter	Judges
1	3:15-3:25	Aarthi Annamalai	Dr. Grozdanov/ Dr. Wang
2	3:00-3:10	Meagan Baggett	Dr. Bailoo/ Dr. Ponomarev
3	3:15-3:25	Isabel Guzman	Dr. Bailoo/ Dr. Ponomarev
4	3:30-3:40	Isabella Makelaar	Dr. Bailoo/ Dr. Ponomarev
5	3:30-3:40	Kara Rodgers	Dr. Grozdanov/ Dr. Wang
6	3:45-3:55	Jordan Sanchez	Dr. Grozdanov/ Dr. Wang
7	4:00-4:10	Andrew Vann	Dr. Grozdanov/ Dr. Wang
8	4:15-4:25	Isabella Zambrano	Dr. Grozdanov/ Dr. Wang
9	4:30-4:40	Charlie Zhang	Dr. Grozdanov/ Dr. Wang

Basic Science – Medical Students

Posters	Time	Presenter	Judges
10	3:45-3:55	Kimberly Brown	Dr. Ji/ Dr. Singer
11	4:00-4:10	Travis Kastner	Dr. Ji/ Dr. Singer
12	4:15-4:25	Maamoon Mian	Dr. Ji/ Dr. Singer
13	4:30-4:40	Farhood Salehi	Dr. Ji/ Dr. Singer
14	4:40-4:50	Alyson Willis	Dr. Ji/ Dr. Singer

Basic Science – Graduate students

Posters	Time	Presenter	Judges
15	3:00-3:10	Philip Adjei	Dr. Grozdanov/ Dr. Wang
16	3:00-3:10	Shahira Arzoo	Dr. Guindon/ Dr. Neugebauer
17	3:15-3:25	Robert Barnes	Dr. Decourt/ Dr. Lawrence
18	3:30-3:40	Hirva Sunilkumar Bhayani	Dr. Decourt/ Dr. Lawrence
19	3:45-3:55	Ema Bidiwala	Dr. Decourt/ Dr. Lawrence
20	3:15-3:25	Fereshteh Dehghani	Dr. Guindon/ Dr. Neugebauer
21	4:00-4:10	Zachary Hurtado	Dr. Decourt/ Dr. Lawrence
22	3:30-3:40	Caezaan Keshvani	Dr. Guindon/ Dr. Neugebauer
23	4:15-4:25	Brent Kisby	Dr. Decourt/ Dr. Lawrence
24	3:45-3:55	Tenley Lehman	Dr. Guindon/ Dr. Neugebauer
25	4:00-4:10	Yash Mahta	Dr. Guindon/ Dr. Neugebauer
26	4:15-4:25	Ehsan Nozohouri	Dr. Guindon/ Dr. Neugebauer
27	4:30-4:40	Kseniia Orbets	Dr. Decourt/ Dr. Lawrence
28	4:40-4:50	Praneetha Pantagani	Dr. Decourt/ Dr. Lawrence
29	4:30-4:40	Fernando Tsurukawa	Dr. Guindon/ Dr. Neugebauer

Basic Science – Postgraduates

Posters	Time	Presenter	Judges
30	3:00-3:10	Quynh Hoa Do	Dr. Ji/ Dr. Singer
31	3:10-3:15	Nermina Sarayli Belirgen	Dr. Ji/ Dr. Singer
32	3:15-3:25	Sam Shanmugam	Dr. Ji/ Dr. Singer
33	3:00-3:10	Linda Yin	Dr. Decourt/ Dr. Lawrence

Clinical/Human studies/tissue – Undergraduate students

Posters	Time	Presenter	Judges
34	3:45-3:55	Jakub Formella	Dr. Bailoo/ Dr. Ponomarev

Clinical/Human studies/tissue – Medical Students

Posters	Time	Presenter	Judges
35	3:30-3:40	Marcos Arciniega	Dr. Blanton/ Dr. Henderson
36	3:45-3:55	Valeria Levin	Dr. Blanton/ Dr. Henderson
37	4:00-4:10	Riley McCready	Dr. Blanton/ Dr. Henderson
38	4:15-4:25	Claudia Morris	Dr. Blanton/ Dr. Henderson
39	3:15-3:25	Foster Ogu	Dr. Blanton/ Dr. Henderson
40	4:40-4:50	Foster Ogu	Dr. Blanton/ Dr. Henderson
41	4:30-4:40	Hannah Seo	Dr. Blanton/ Dr. Henderson

Clinical/Human studies/tissue – Graduate students

Posters	Time	Presenter	Judges
42	3:45-3:55	Lauren Chrzanowski	Dr. Bailoo/ Dr. Ponomarev
43	4:00-4:10	Megha Shah	Dr. Bailoo/ Dr. Ponomarev
44	4:15-4:25	Rubaia Tasmin	Dr. Bailoo/ Dr. Ponomarev
45	3:00-3:10	Antonio Vintimilla	Dr. Blanton/ Dr. Henderson

1. Basic Science – Undergraduate students

Baggett, Meagan

Loss of Dnase1L3 causes neuropsychiatric systemic lupus erythematosus phenotypes in mice

Meagan Baggett
Texas Tech University, College of Arts and Sciences

A primary cause of morbidity and mortality in women is autoimmune disease. Systemic lupus erythematosus (SLE) is one chronic autoimmune disease with multisystemic involvement, frequently affecting the central nervous system (CNS). CNS symptoms such as cognitive dysfunction, headaches, and anxiety disorders subsequently result in neuropsychiatric systemic lupus erythematosus (NPSLE). In more than 60% of patients with NPSLE, the presence of anti-dsDNA antibodies is detected. Anti-dsDNA antibodies build up due to undegraded DNA. DNA is degraded by Dnase1L3, an endonuclease that digests antibody-DNA complexes. The absence of Dnase1L3 contributes to the presence and severity of SLE in humans, however the relationship between Dnase1L3 and NPSLE remains unclear. We hypothesized that the loss of Dnase1L3 in mice causes phenotypes consistent with NPSLE as a result of accumulating anti-dsDNA antibodies. In Dnase1L3 knock-out mice, we measured behavior, immunofluorescence, and brain immunohistochemistry. Behavioral analyses suggest anxiety-like phenotypes in aged Dnase1L3 knock-out mice. We observed an increase in astrocytes and astrocytic hypertrophy, which are primary markers of neuroinflammatory disease. We suggest that the loss of Dnase1L3 contributes to NPSLE-like phenotypes in mice. These findings implicate that the restoration of Dnase1L3 could be a therapeutic target for intervention and management of NPSLE.

Guzman, Isabel

Using Vaginal Cytology to Optimize Reproductive Productivity in an Alzheimer's Disease Mouse Model

Guzman, Isabel[1,2,3], Matthews, Travana[6], Whitaker, Kember[6], Addington Bridgett[6], S. L. Trasti[6], Smith, Shane[1,2], Hindle, Ashly[1,2], Strickland, Jake[1,2], Lawrence, J. Josh,[2,4,5]
[1]Department of Pharmacology and Neuroscience, [2]Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, [3]Department of Animal and Food Sciences, Texas Tech University, Lubbock, TX; [4]Center of Excellence for Translational Neuroscience and Therapeutics, [5]Center for Integrative Health, [6]Laboratory Animal Resource Center, Texas Tech University Health Sciences Center, Lubbock, TX USA

Poor breeding performance can be observed in specific strains of transgenic mice due to strain genetics and/or specific genetic modifications, thereby creating barriers to research progress by increasing the time needed to generate mice for experiments. Analyzing the cells from vaginal smears using microscopic evaluation is an established method of identifying and monitoring the stage of the estrous cycle in female mice. Female mice have short estrous cycles consisting of 4 stages: proestrus, estrus, metestrus, and diestrus, each lasting

approximately one day. By examining vaginal cytology, the estrous cycle transitions from one stage to the next can be tracked. The cells that are shed include leukocytes, nucleated epithelial cells, and cornified epithelial cells. Our goal is to establish a detailed protocol to efficiently identify normal vs. abnormal cycling patterns that may be associated with decreased breeding performance. As a first step in evaluating poor breeding performance, vaginal cytology is used to screen mice to ensure they are cycling normally. In this study, we observed and staged the estrous cycle over a 9 to 10-day period, spanning roughly 2 estrous cycles. These breeder mice consisted of 8 female mice, with 4 being on the CD1 background and homozygous for a LacZ transgene and 4 being on the C57BL/6NJ background and heterozygous for a humanized APP gene. We included both productive and nonproductive breeders, as determined by breeding history. Using breeding history and classification of the stages using cytology, we expect to see abnormal cell densities in less productive females, and normal cytology in highly productive females. By evaluating the estrous cycle over 2 cycles, we hope to quickly eliminate non-viable breeder animals, enabling us to increase our overall litter production over reproductive lifetime. In conclusion, increased knowledge of the estrus cycles in these mouse models will enable us to establish a protocol to increase productivity of breeding pairs, thereby enabling more efficient generation of mice for experiments.

Makelaar, Isabella

Utilizing membrane protein chaperone to prevent and disrupt alpha synuclein protein aggregation in Parkinson Disease

Makelaar, Isabella and Dr. Liang, Fu-Cheng
Midwestern State University, Department of Chemistry

Parkinson's disease (PD) is primarily identified by the accumulation of α-Synuclein (ASyn) protein, which forms aggregates known as Lewy Bodies. These aggregates contribute to the demise of neurons in the substantia nigra, resulting in symptoms like resting tremors, muscle rigidity, and weakness. ASyn protein comprises three distinct segments: the N-Terminus, NAC-central region, and the C-Terminus. Research indicates that interactions between the N- and C-Termini hinder aggregation in the central region of ASyn, and the removal of this central part notably reduces aggregation. However, the precise molecular mechanisms underpinning ASyn aggregation into toxic oligomers and its impact on cellular pathways remain enigmatic. Molecular chaperones play a vital role in maintaining protein homeostasis by facilitating proper protein folding and preventing misfolding and aggregation. A promising avenue for therapeutic exploration involves impeding or reversing the formation of insoluble and hydrophobic ASyn aggregates. Notably, the utilization of membrane protein chaperones to counteract protein aggregation represents an intriguing prospect. Remarkably, certain plant-derived chaperones have exhibited the ability to deter aggregation and promote disaggregation in light-harvesting chlorophyll-binding proteins, without relying on ATP or co-chaperones. This unique functionality sets them apart from other protein chaperones. Our research exploits the potential of membrane protein chaperones as a model system. By harnessing their distinctive anti-folding and disaggregation attributes, we aim to strategically develop and characterize effective therapeutics for disorders characterized by protein aggregation susceptibility. This approach holds promise for advancing our understanding of ASyn-related diseases like PD and could offer novel insights into therapeutic interventions.

Rodgers, Kara

Membrane protein chaperone modulates the kinetics and morphology of tau aggregation: A potential treatment for Alzheimer's disease

Kara Rodgers and Fu Cheng Liang
Department of Chemistry, Midwestern State University, Wichita Falls, TX 76308

Alzheimer's disease (AD), the most prevalent form of dementia, is a progressive neurodegenerative disorder characterized by initial mild memory impairment and eventual loss of communicative and environmental responsiveness. Central to its pathology is the aggregation of Tau, a microtubule-associated protein, which leads to neurotoxicity and, ultimately, neuronal demise. This aberrantly hyper-phosphorylated Tau forms toxic neurofibrillary tangles, driving cell death. The amyloid hypothesis posits that the accumulation of protein aggregates in the brain is the primary driver of AD pathogenesis. Counteracting protein aggregate accumulation emerges as a promising therapeutic strategy. However, a significant knowledge gap pertains to the potential of membrane protein chaperones in preventing and/or disrupting protein aggregation. Notably, the recently discovered protein targeting machinery from chloroplasts, chloroplast signal recognition particle (cp43), serves as an effective membrane protein chaperone. It not only prevents the aggregation of its substrate, the light-harvesting chlorophyll-binding protein (LHCP), but also efficiently reverses aggregation. Through selective binding to hydrophobic amino acids, cp43 stabilizes interactions, impeding aggregation without requiring ATP or co-chaperones. To evaluate its impact on Tau aggregation, we employed Thioflavin T (ThT) dye to assess aggregation kinetics. Our results demonstrated that cp43 inhibits aggregation in a concentration-dependent manner. Further validation through electron microscopy reinforced these findings, highlighting the potential of cp43 in mitigating Tau aggregation. These findings unveil a novel approach to prevent Tau aggregation by harnessing cp43's unique anti-folding and disaggregation capabilities. Moreover, they underscore the pivotal role of membrane protein chaperones in addressing protein aggregation-related diseases.

Sanchez, Jordan

BCS Classification of Butyl Ether Minocycline for Oral Drug Products

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The study explores the pre-clinical development of 10-butyl ether minocycline (BEM) as a treatment for alcohol use disorder (AUD), a prevalent chronic disease associated with comorbidities and a major risk factor for premature death or disability. Our lab demonstrated the pre-clinical efficacy of minocycline and its derivative, BEM, in significantly reducing alcohol consumption in rodent and swine models. Long-term use of minocycline for AUD risks disrupting the gut microbiome and development of antibiotic resistance. Among 17 derivatives, BEM was chosen for its safety, efficacy, and lack of anti-microbial activity. Our goal is to study BEM's physiochemical properties and efficacy to facilitate FDA approval process. The efficacy of BEM was tested in both female and male C57BL/6J mice using a drinking-in-the-dark (DID) paradigm and observed a dose-responsive and significant reduction in alcohol consumption. In preclinical development, assessing physicochemical characteristics and target identification is crucial. BEM's dissociation constant (pKa) was predicted using 'Marvin' software and confirmed by UV spectroscopy. BEM has three pKa values within the range of 5-8, suggesting that most absorption happens in the gastric environment. The Partition coefficient (log

P) of BEM (measured at 0.77 using the shake-flask method) aligns with the concentration of the drug in the brain relative to plasma. In vitro permeability assays by Xenotech further confirmed BEM's high permeability. Moreover, solubility studies indicate BEM is highly water soluble, classifying it as Biopharmaceutical Classification System (BCS) Class-I, ideal for oral drug development. BEM's effect on MMP-9 and microglial activation was evaluated as these mechanisms were identified to be altered in AUD. Colorimetric assays confirmed dose-dependent MMP-9 inhibition, while western blot analysis showed significant reduction in Iba1 expression (marker for microglial activation), surpassing minocycline. These findings collectively suggest that there is a promising avenue for further development of BEM as a therapeutic agent for AUD.

Vann, Andrew

Leveraging Membrane Protein Chaperones to Mitigate Familial Mutant Amyloid Beta Aggregation: A Prospective Therapeutic Approach for Early-Onset Alzheimer's disease

Andrew Vann and Fu Cheng Liang
Department of Chemistry, Midwestern State University, Wichita Falls, TX 76308

Alzheimer's disease (AD) is a progressive and terminal condition marked by the gradual decline of cognitive function. Despite extensive research, AD remains an incurable form of dementia, commonly associated with the accumulation of misfolded proteins in the brain. Notably, Amyloid beta (Aβ) peptides, resulting from the cleavage of larger membrane proteins, aggregate to form extracellular plaques near nerve endings. Among these peptides, the arctic mutant Amyloid beta E22G (Aβ E22G) stands out as highly prone to aggregation. This mutation is linked to aggressive early-onset AD and rapid plaque buildup in the brain, yet the precise pathological mechanisms remain unclear. The amyloid hypothesis posits that the accumulation of misfolded Aβ primarily drives AD pathology, thus targeting and eliminating these aggregates holds promise for disease stabilization and potential cure. Our investigation highlights the effectiveness of an innovative protein targeting mechanism derived from the chloroplast signal recognition particle (cpSRP43). Serving as an ATP-independent chaperone for membrane proteins, this machinery adeptly mitigates the aggregation of Aβ E22G. The core focus of our research is to harness the potential of cpSRP43 as a therapeutic agent to counteract the aggregation processes prevalent in AD patients unable to efficiently clear Aβ aggregates. Our central hypothesis posits that cpSRP43, functioning as a membrane protein chaperone, can impede the misfolding and aggregation of proteins. Notably, our findings illustrate that the introduction of cpSRP43 effectively hinders the aggregation of Aβ E22G peptides, suggesting a promising avenue for the development of innovative AD treatments.

Zambrano, Isabella

Molecular mechanisms of action of flaxseed biochemical components: relevance to the gut-brain-axis and prevention of Alzheimer's disease

Isabella Zambrano[1], Dr. Andrew Shin[1], Dr. J Josh Lawrence[2,3,4,5]
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Introduction: Flaxseeds have numerous dietary benefits. It is rich in both fiber and Ω3 fatty acid content essential to gut bacteria symbiosis. Moreover, flaxseed components are converted to enterolactone (ENL) by gut microbiota (GM). Alzheimer's disease (AD) affects over 6 million Americans today. AD is associated with

both genetic and environmental risk factors. Diet itself plays an oversized role that can increase or reduce onset of AD symptoms. The gut plays a role in digestion and breakdown of nutrients that in turn produce polyphenolic compounds like ENL. Flaxseeds are rich in polyphenols that, once absorbed in the large intestine, are converted to ENL that may have synergistically protective roles in preventing AD. Methods: To investigate the link between flaxseed-derived ENL acting within the gut-brain axis (GBA) and AD, we reviewed multiple articles collected via PubMed.

Results: ENL was found to have numerous mechanisms of action by acting as an anti-bacterial/pro-bacterial compound in the GBA, an antioxidant, an NMDA receptor antagonist, and an acetylcholinesterase inhibitor (AChEI). Moreover, it has anti-estrogenic, anti-nitric-oxide, anti-atherosclerotic, anti-proliferative, and anti-inflammatory properties via multiple metabolic pathways. Finally, modulation by ENL and its other biochemical components can enrich "healthy" gut microbiota, which itself has nutritional benefits. Conclusion: High ENL and fiber content are positively associated with enriched GM and creation of symbiosis within the GBA, thereby suppressing neurodegenerative disease. Additionally, ENL's AChEI activity could have a similar mechanism of action in AD-related pharmaceutical drugs (donepezil and galantamine), thereby promoting acetylcholine release, facilitating cognition and learning. Flax-seed derived lignans strengthen neural protection through myelination and microglia stabilization. These biochemical mechanisms could act synergistically within the GBA against AD. Additional studies would further elucidate the molecular mechanisms of ENL.

Zhang, Charlie

Vitamin K2 in healthy aging and protection against Alzheimer's Disease pathogenesis: potential mechanisms mediated by Osteocalcin

Vitamin K2 (VK2), or menaquinone, is a vitamin abundant in animal and fermented foods but is also produced by a healthy gut microbiome. Initially discovered in 1929, Vitamin K enables the synthesis of proteins critical for blood coagulation and bone metabolism. Importantly, K2 is an essential cofactor in the regulation of osteocalcin (OCN), a hormone regulating glucose homeostasis and bone matrix composition. More recently, with the creation of OCN knockout mice, OCN has been shown to play critical roles in learning and memory. Studies have shown that OCN improved the brain's neural network function in AD mice by amplifying the power of high gamma oscillations, a brain rhythm associated with improved cognition. In addition, in one study in a mouse model of Alzheimer's disease (AD), OCN decreased the accumulation of amyloid β (Aβ) peptides, a molecule widely associated with the onset of AD. OCN-treated AD mice showed increased glycolytic activity, amplifying the pentose-phosphate pathway (PPP) which plays a pivotal role in the reduction of oxidative stress. OCN treatment in AD mice inhibited astrocyte proliferation, reduced Aβ burden, and reduced DNA damage. Notably, a natural source of VK2 is found in many fermented foods such as natto and kimchi. Given the prevalence of VK2 in East Asian diets, the increased VK2-mediated biosynthesis of OCN may contribute to improved protection from osteoporosis, cardiovascular health, and cognitive function frequently observed in aged individuals in East Asian cultures. We hypothesize that increasing VK2 sustains OCN levels and consequently maintains cognitive function in aging populations. In conclusion, VK2 shows promise as a novel and exciting treatment for reducing or preventing neurodegeneration through dietary intervention, potentially improving the quality of life of individuals at risk for or suffering from AD.

2. Basic Science – Medical students

Brown, Kimberly

Impact of Parent Involvement in Therapy on Parent-Child Reporting of Depression and Suicidality

Kimberly Brown BA1, Dr. Regina Baronia M.D.2, Samudani Dhanasekara, M.B.B.S.2, Dr. Sarah Wakefield M.D.2
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Previous studies have shown that child-parent agreement on reporting child mental health varies due to several factors including mental disorder type and child demographics. However, which depressive and suicidal symptoms have a greater impact on child-parent disagreement and whether parent involvement in their child's psychotherapy relates to these discrepancies has been understudied. This study aims to evaluate the relationship between symptom type and parent involvement with parent-child disagreement. Data was collected from the Texas Youth Depression and Suicide Research Network study, Texas Tech University Health Sciences Center node. Data included baseline reports for both parents and children on the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-KID), Concise Health Risk Tracking (CHRT) Behavioral Module, and the Comprehensive Interview Regarding Child Assistive Services (CIRCAS) assessments. Data analysis revealed a moderate agreement was seen when reporting suicide attempts, preparatory acts, and recent suicidal ideation, which remained significant with psychotherapy and parent involvement. There was no agreement when reporting major depressive episodes, even with psychotherapy and parent involvement. Lastly, fair agreement was found when reporting suicidality and severity of suicidality, which became poor with parental involvement. Parent involvement in therapy may have a negative relationship with parent-child agreement when assessing suicidality. Our findings provide further evidence of the importance of using multiple information sources when assessing child depression and suicidality.

Travis, Kastner

Exploring the Impact of Dietary Vitamin E Intake on Neurodegenerative Diseases: A Review of Free Radical Damage Mitigation

Neurodegeneration, a common feature of age-related diseases, is intricately linked to oxidative stress, characterized by heightened levels of reactive oxygen species (ROS) as aging progresses. The brain, with its high lipid content, faces heightened susceptibility to oxidative damage, perpetuating the pathophysiology of conditions such as Alzheimer's, Parkinson's, and stroke. Vitamin E, predominantly -tocopherol, emerges as a pivotal endogenous antioxidant in the brain, safeguarding neuronal membranes against ROS-induced harm. Notably, Vitamin E also exhibits antiplatelet effects, modulating prostaglandin E2 levels. Deficiency presents clinically with neurologic symptoms including ataxia, proprioception loss, and muscle weakness. This review examines the relationship between Vitamin E intake and the development of neurodegenerative diseases. Findings reveal intriguing associations between Vitamin E intake and neurodegenerative disorders. Diminished Vitamin E intake is observed among Parkinson's patients compared to controls. Conversely, Vitamin E exhibits a dichotomous effect on stroke risk, reducing ischemic stroke incidence while elevating hemorrhagic stroke risk, likely due to its antiplatelet properties. Furthermore, an inverse relationship between Vitamin E consumption and dementia risk is delineated. Adequate Vitamin E intake appears

pivotal in mitigating the onset of Alzheimer's and Parkinson's diseases. However, caution is warranted in stroke patients due to the propensity for increased hemorrhagic stroke risk with preexisting hypertension. Further investigation is imperative to delineate optimal therapeutic dosing regimens.

Mian, Maamoon

Overlooked Cases of Mild Cognitive Impairment

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1Department of School of Medicine, Texas Tech University Health Sciences Center, Lubbock, 79430, TX, USA, 2School of Biology, Texas Tech University, Lubbock, 79430, TX, USA.
3Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, 79430, TX, USA.

This meta-analysis investigates the intricate landscape of cognitive disorders, focusing on Mild Cognitive Impairment (MCI) and Alzheimer's Disease and Related Dementias (ADRD).The study aims to understand the signs of MCI, early Alzheimer's disease, and healthy brain aging while assessing factors influencing pathology development and susceptibility. A systematic literature review of over 100 articles was conducted, emphasizing MCI and ADRD within the elderly population. The synthesis of results reveals significant findings regarding ethnicity, gender, lifestyle, comorbidities, and diagnostic tools. Ethnicity was found to influence MCI prevalence, with disparities observed across diverse populations. Gender differences were evident in cognitive performance and decline, highlighting the need for personalized management strategies. Lifestyle factors and comorbidities were identified as crucial influencers of cognitive health. Regarding diagnostic tools, the Montreal Cognitive Assessment (MoCA) emerged as superior to the Mini-Mental State Examination (MMSE) in early MCI detection. Overall, this review provides insights into the multifaceted nature of cognitive disorders, emphasizing the importance of tailored interventions and comprehensive assessment strategies
for effective cognitive health management.

Salehi, Farhood

Examining the relationship between poor air quality and progression of Alzheimer's

Salehi, Farhood; Patel, Rishi; Gundupalli, Prudhvi; Sandhu, Theodore; Mani, Chinnadurai
Texas Tech University Health Sciences Center

Elevated levels of pollutants, including particulate matter, nitrogen dioxide, and ozone, contribute to poor air quality, recognized as a significant environmental factor affecting neurological health. Airborne particles can penetrate the central nervous system, causing inflammation and oxidative stress. This study aims to analyze the relationship between air pollution and neurological health by assessing the internal validity of a published review (1) claiming that particulate matter 2.5 (PM) plays a role in the progression of Alzheimer's. To assess the internal validity of the review, we conducted a comprehensive analysis drawing on a series of scholarly

publications. These included a systematic review(2) examining the impact of air pollutants on human microbiota and the resultant dysbiosis of biological processes, a review publication(3)(6) expanding on the emerging understanding of the involvement of the gut microbiome in neurological disorders such as myocardial infarction (MI), Parkinson's, and Alzheimer's, a translational study(4) utilizing rat models to investigate the effects of air pollution on bile acids and the subsequent neurodegenerative processes, and a second review(5) analyzing the biological hallmark changes induced by particulate matter (PM). The study results validate the review's internal reliability. The systematic review (2) found strong evidence linking environmental contaminants, especially air pollution, to microbiota changes, immunological disruptions, and impaired endocrine function in 24 studies. The primary review (3)(6) highlighted that dysbiosis-induced increased permeability of the gut and blood-brain barrier is a key factor in AD pathogenesis, particularly in aging-related neurodegenerative disorders. Additionally, it shows that imbalances in the gut microbiota contribute to inflammation associated with obesity, type 2 diabetes mellitus, and AD. The translational study (4) revealed that exposure to traffic-related air pollution leads to increased bile acid dysbiosis in rats, with elevated microbial-derived secondary bile acids observed in AD patients. The second review (5) emphasized that PM exposure amplifies AD hallmarks, including amyloid-β deposition, neurofibrillary tangle accumulation, cognitive impairments, microglial activation, inflammation, oxidative stress, immune activation, and behavioral changes. Chronic PM2.5 exposure exceeding guidelines correlates with cognitive impairment, mild cognitive impairment (MCI), and AD scores in young individuals, while older adults in areas with higher PM2.5 concentrations show an increased likelihood of positive amyloid PET scans, indicating neuronal amyloid-β presence. This comprehensive study provides evidence supporting the contention that poor air quality, specifically elevated levels of particulate matter 2.5 is intricately linked to the progression of AD. The amalgamation of findings from various scholarly publications, spanning systematic reviews, translational research with rat models, and analyses of PM-induced biological changes, underscores the profound impact of air pollution on neurological health. Our investigation corroborates the internal validity of a previous review, demonstrating a consistent association between exposure to environmental contaminants and alterations in crucial physiological processes. accumulation, cognitive impairments, and inflammation, provide a comprehensive understanding of the detrimental effects of air pollution on brain health.

Willis, Alyson

Benign Intracranial Hypertension-Associated Chronic Headache in Congenital Cystinosis-A Case Report

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1Texas Tech University Health Center School of Medicine, Lubbock TX , 2Covenant Women and Children's Hospital, Lubbock TX

Congenital nephropathic cystinosis (CNC) is a rare lysosomal storage disorder that is inherited in an autosomal recessive pattern. It manifests during infancy with early onset of end-stage kidney failure, cognitive and focal neurological deficits, neuro-ophthalmic pathologies, and various demineralizing and electrolyte-imbalance conditions. As a result, it is often compounded with secondary ailments and necessitates early kidney transplants. We present the case of a 12-year-old girl with CNC, Fanconi Syndrome, a 3-year prior history of a kidney transplant, and chronic sinusitis who presented with a constantly progressing headache with nausea and vomiting, and hypertension. The patient had a history of chronic sinusitis and secondary ailments, which were all properly managed with medication. After undergoing various differentials following clinical and laboratory workups and ICP monitoring along with a G-tube insertion, the cause of her headache was initially postulated to be intracranial hypotension (ICH) associated with ventriculoperitoneal (VP) shunt over-drainage

and related to the G-tube as well. However, the G-tube was later ruled out as a potential cause. Abdominal ultrasound, radiologic imaging, shunt tap, and clinical and laboratory workups ruled out infections, distal shunt pseudocyst, and shunt malfunctioning. We propose that the over-shunting was due to potential low opening valve pressure or a consequence of benign intracranial hypertension (BIH) or pseudotumor cerebri effect on cystinosis brain tissue quality. Once over-shunting was identified, the shunt was externally increased from 2.0 to 2.5. The patient's clinical symptoms improved, and she was discharged home with a 2-week follow-up. She remained asymptomatic at the 2-week follow-up. Here, we hope to explore the relationship between BIH and congenital cystinosis. That is especially what clinical and neurological effects cystinosis brain quality and rigidity in the presence of BIH had on over-shunting without the development of hydrocephalus while affecting cognition.

3. Basic Science – Graduate students

Adjei, Philip

Effects of TLR3 activation on temporal immune profiles of brain and blood in male and female FVB/B6 mice

Philip Adjei, Sambantham Shanmugam, Igor Ponomarev
Department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center

BACKGROUND: Alcohol use disorder (AUD) is associated with increased inflammation. Alcohol (ethanol) may activate toll-like receptors leading to the release of inflammatory molecules, which may contribute to changes in AUD-related behaviors, such as increased alcohol consumption. Activation of toll-like receptor 3 (TLR3) by Polyinosinic:polycytidylic acid (Poly(I:C), PIC) leads to the release of proinflammatory cytokines associated with changes in alcohol consumption, which is sex- and genotype-specific. For example, male mice of some genotypes drink more ethanol after repeated injections of PIC, while females do not change or decrease ethanol consumption. There is little known about the role of peripheral vs central inflammation in regulation of alcohol consumption. In this study, we investigated the relationship between blood and brain levels of proinflammatory cytokines, chemokines and other immune molecules in male and female mice after TLR3 activation by PIC. Sex differences in the levels of the immune mediators in blood and brain over time may, at least, in part, explain differences in alcohol consumption. We hypothesized that the immune profiles in brain and blood after TLR3 activation will be different between males and females. Male and female mice on mixed genetic background were I.P. injected with PIC. Blood and perfused prefrontal cortex brain tissues were collected at 0, 6, 24 and 48 hours. mRNA and protein levels of several immune genes were measured using qPCR and ELISA respectively. Preliminary experiments in males showed that majority of immune genes induced by PIC, such as, IL-6, IL-1B, TNF-alpha, TLR3 and TLR4, had higher expression in blood than brain, while Chemokine (C-C motif) ligand 5 (CCL5) had higher expression in brain, compared to blood. CCL5 has previously been shown to be expressed in different cell types in brain including astrocytes, microglia and some neurons, suggesting that it may be important for regulation of brain functions and behavior. Taken together, our results showed distinct profiles of TLR3 activation – induced immune genes in blood and brain and suggested disparate roles of these molecules in regulation of alcohol consumption. Direct comparisons of immune profiles between males and females at different time points are underway.

Arzoo, Shahira

Uncovering Altered Nutrient Metabolism in non-obese Nepl15 Mutant Flies Through Metabolomics and Lipidomics Studies

Shahira Helal Arzoo, Chase Drucker, Surya Jyoti Banerjee
Department of Biological Sciences, Texas Tech University

The tissue-specific, catalytically dead, secreted protein Neprilysin like 15 (Nepl15) plays a crucial role in regulating glycogen and glycerolipids storage in Drosophila. A study on isogenized Nepl15 knock-out (Nepl15KO) mutant flies revealed intriguing sex-specific metabolic alterations. While Nepl15KO adult male flies exhibited reduced lipid and glycogen storage compared to controls (w1118), Nepl15KO adult females showed slightly lower lipid levels but higher glycogen storage. Moreover, these mutant flies exhibited anti-obesity

features, including extended lifespan and sustained activity in older age. To delve deeper into these metabolic changes, primary metabolomics and lipidomics analyses were conducted on age-matched mutants and control adult flies of both sexes. The Principal Component Analysis (PCA), facilitated by SIMCA software, uncovered significant differences in metabolite and lipid profiles between mutant and control flies, with notable distinctions between male and female mutants. In male mutants, pathways related to phenylalanine, tyrosine, and tryptophan biosynthesis were impacted, while in female mutants, fructose and mannose metabolism pathways were prominently altered. Interestingly, sex-based profiling using MetaboAnalyst 6.0 revealed that female mutants exhibited more substantial changes in metabolites compared to males, with 10 unique pathways affected in females versus 4 in males. However, both sexes shared alterations in 8 common pathways. This comprehensive analysis highlights the intricate role of Nepl15 in modulating sex-specific metabolic pathways, providing insights into potential therapeutic targets for obesity and metabolic disorders. Further exploration of this data promises a deeper understanding of Nepl15-controlled metabolic pathways, offering avenues for developing novel interventions in metabolic health.

Barnes, Robert

Evaluation of the Role of CB1 and 5-HT1A Receptors in ACEA-Induced Effects on Nociception, Motor Coordination, Locomotion, and Body Temperature

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Chronic pain represents a significant detriment to patient quality of life and its prevalence is increasing. Rheumatic disease, which is among the most common causes of chronic pain, is characterized by inflammatory pain. Due to recent social, political, and cultural changes, the interest in cannabis and cannabinoids for their potential as antinociceptive agents has increased. Though cannabinoids have a number of receptor targets, many of their actions occur through activation of Cannabinoid Receptor 1 (CB1), which is predominantly, but not exclusively, found within the central nervous system. Prior research has attributed some of the antinociceptive effects of cannabinoids to CB1 activation. Additionally, recent research has linked the Serotonin-1A Receptor (5-HT1A), which has been shown to produce antinociceptive effects in its activation, to the Cannabinoid Receptor 2 (CB¬2). However, research into a possible link between CB1 and 5-HT1A, along with investigations into possible sex differences in their activation and side effects, is currently lacking. The dose-dependent antinociceptive effects of arachidonoyl 2'-chloroethylamide (ACEA), a selective CB1 synthetic agonist, was first evaluated in male and female wild-type C57Bl6J mice in the formalin model of inflammatory pain. The most effective dose of ACEA was then identified and further evaluated within the tetrad test, which classically includes models of pain (formalin test), locomotion (open field), motor coordination (rotarod), and temperature (rectal temperature). Finally, the effects of prior blockade of either CB1 (via AM251) or 5-HT1A (via WAY-100635) within this tetrad test was then evaluated. ACEA provided antinociceptive benefit, without any significant sex differences, in both male and female wild-type mice within the formalin inflammatory pain model. ACEA did not produce any significant changes, relative to vehicle, in motor coordination or locomotion. ACEA did produce an increase in temperature, relative to vehicle, in male, but not female, wild-type mice. Evaluation of the effects of prior blockade of either CB¬1 or 5-HT1A is ongoing. As interest in cannabinoid usage continues to grow, it is important to gain a better understanding of both their mechanisms of effects and any sex differences.

Bhayani, Hirva

The Molecularity of Smell, Taste driven by Vision, and Experiential Learning

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Smell and taste are closely linked. We adopted a novel approach to identify the molecularity that drives both these chemical senses. Our novel approach sought to combine visual perception with olfaction and gustation as well as experiential learning by identifying electronic-structural features in molecules that invoke the visual perception of brown following smell and taste tests. We studied electronic structural features for 19 odorant molecules and 18 tastant molecules associated with the chemical sensory perception of "Brown." The structural studies beyond gross molecular features and explores linear, planar, and three-dimensional features defined by atoms within a molecule, while the electronic features are defined by Nuclear Magnetic Resonance chemical shifts. The structural and chemical shift calculations are completed using quantum chemistry methods. We classified these molecules into cooked, vegetable, and sweet tastes and smells. For every molecule, we tabulated a comprehensive list of distances from atom pairs, and angles from atom triads and dihedral angles from atom tetrads. We developed software to find reproducible atom pairs, triads, and tetrads in the entire list of 37 molecules, in order to identify any commonality between these electronic structural features and specific smells and tastes. We discovered significant reproducible electronic structural features across molecules which are responsible for similar smells and tastes, while comparisons with molecules that elicited different smells and tastes were used as controls. Our study shows that we can identify the atoms pair, triads and tetrads that are chemical markers that contribute to specific smells and tastes. Our studies showed that we can identify chemical markers that contribute to smells and tastes and combine these chemical senses with the visual perception as well as experiential, social and geographical background—as the poster will show. Our studies combine the disciplines of quantum and computational chemistry, organic chemistry, chemical senses, neuroscience, and software development.

Dehghani, Fareshteh

BCAAs acutely increase sucrose indulgence in mice: possible role of FGF21?

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Overconsumption of palatable food is a major contributor to the recent spike in obesity prevalence. Circulating levels of branched-chain amino acids (BCAAs) are observed in both human and animal models of obesity and type 2 diabetes. Low protein and/or BCAA-restricted diets have shown to induce the expression of a hepatokine called fibroblast growth factor (FGF21), which negatively regulates simple sugar intake and sweet preference in mice. Whether or not BCAAs can alter reward functions to increase preference for palatable foods and the role of FGF21 in this process have not been explored. Therefore, we tested the effects of a short-term BCAA exposure on the consumption of palatable sucrose solution and plasma FGF21 levels. 8-week-old male C57Bl/6 mice were assigned to two weight-matched groups to receive intraperitoneal injections of either saline or BCAAs (225 nM) twice a day for 7 consecutive days. Before and after intervention, their 10% sucrose intake was measured for two days. Following the completion of the study, mice were sacrificed for plasma and tissue collection. Daily body weight and food intake were measured throughout the study. Blood glucose was checked by a hand-held

glucometer, and plasma BCAAs and FGF21 were measured by enzymatic and ELISA assays, respectively. Plasma BCAA levels tended to be higher in the BCAA group compared to saline group as expected. While sucrose intake was identical between groups at baseline, BCAA treatment increased sucrose intake that was independent of body weight, food intake, or blood glucose. This was associated with lower plasma FGF21 in BCAA group compared to saline group. Our findings suggest that a short-term supplementation of BCAAs may promote indulgence in palatable sucrose solution, and this may be potentially related to the reduction in plasma FGF21 levels. Determining the long-term effects of BCAAs on sucrose preference and FGF21 as a possible mediator is warranted. Our study sheds light on the novel role of BCAAs in food reward.

Hurtado, Zachary

BDNF in the amygdala modulates sensory and affective neuropathic pain behaviors

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Chronic pain is a profound and arduous health care issue to remediate. While many therapies are ineffective with adverse side effects, this requires a better mechanistic understanding to investigate new therapeutic strategies. It is well established now that the amygdala, a limbic brain region, plays a critical role in the modulation of pain, fear, and anxiety behaviors. Mechanisms of pain-related amygdala neuroplasticity are not fully understood. Previous data suggest that Brain Derived Neurotrophic Factor (BDNF) plays a critical role in neuroplasticity and may be dysregulated in chronic pain models and neuropsychiatric diseases such as anxio-depressive disorders. BDNF given exogenously can ameliorate conditions like anxiety, pointing toward the amygdala as a potential target. However, the role of BDNF signaling in the amygdala in pain modulation is not yet known. Typical BDNF signaling involves the tyrosine kinase TrkB receptor. This study examined the effects of BDNF and a TrkB receptor antagonist (ANA-12) in the central amygdala on the modulation of pain- and anxiety-related behaviors, using a chronic neuropathic pain model in rats (spinal nerve ligation, SNL). Adult male rats were implanted with a guide cannula targeting the central amygdala, and after 2 days of recovery, BDNF or ANA-12 were administered by micro-dialysis for 20 minutes. Sensory and emotional-affective behaviors were measured. BDNF, but not ANA-12, had antinociceptive effects in the von Frey test. BDNF, but not ANA-12, had anxiolytic effects on the Elevated Plus Maze. The data suggest that exogenous delivery of BDNF into the amygdala can modulate neuropathic pain behavior while the lack of clear antagonist effects may suggest that this system is not sufficiently activated in the pain condition.

Keshvani, Caezaan

GD3 ganglioside is not a potential cell surface immunotherapeutic target for neuroblastoma

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Neuroblastoma is the most common extracranial solid tumor of childhood. GD2 is a validated immunotherapeutic target for neuroblastoma and use of anti-GD2 antibodies to treat neuroblastoma patients is standard-of-care. GD3 is a precursor ganglioside for GD2, a cell surface antigen commonly overexpressed in neuroblastoma cells. GD3 is synthesized in the endoplasmic reticulum by GD3 synthase (ST8SIA1) and highly overexpressed on cell surface of some cancers (melanomas and T-cell lymphomas). GD3 has been shown to be expressed in neuroblastomas. Anti-GD2/GD3 vaccines are currently being evaluated in clinical trials for high-risk neuroblastoma therapy. As therapy with anti-GD2 antibodies can select for low GD2 expression, it has been postulated that a vaccine stimulating immune cells to target GD3 in addition to GD2 could be effective in preventing recurrence of neuroblastoma in patients. GD3 is hypothesized to be on the cell surface of neuroblastomas with low or high GD2 expression. GD3 expression on the cell surface of 11 patient-derived neuroblastoma cell lines (PDCLs) with both low and high GD2 expression. qPCR was also performed on cell lines to assess expression of GD3 synthase (ST8SIA1). We found that 0 of 11 neuroblastoma cell lines expressed GD3 on the cell surface, but intracellular (cytoplasmic) GD3 was observed in some of the cell lines. ST8SIA1 mRNA expression did not correlate with GD3 expression. GD3 expression on neuroblastoma cell surface based on the cohort of neuroblastomas evaluated indicated that GD3 was not a valid vaccine therapeutic target for neuroblastoma.

Kisby, Brent

Effects of Tlr3-dependent innate immune activation and chronic alcohol consumption on gene expression in brain micro-vessels

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Chronic high alcohol (ethanol) drinking is one of the characteristics of Alcohol Use Disorder (AUD). Toll-like receptor 3 (Tlr3) – dependent innate immune activation in rodents contributes to escalated ethanol consumption in a sex and genotype-dependent manner and our preliminary data suggested that these effects may be mediated by Tlr3 activation in microvasculature cell types. Micro-vessels consist of cell populations that form blood brain barrier (BBB), including endothelial cells (ECs), smooth muscle cells, and pericytes. We hypothesize that Tlr3 activation-induced changes in gene expression in these cell types contribute to BBB dysfunction and escalated alcohol intake. The goal of this study was to determine the effects of Tlr3 activation and/or chronic alcohol drinking on gene expression in enriched brain microvasculature in high-drinking FVB/NJ X C57BL/6J F1 hybrid mice. Male mice were randomly assigned to receive repeated injections of Poly(I:C) (PIC), a Tlr3 agonist, or saline (9 injections total). Mice were allowed to choose between alcohol or water every other day (17 dinking sessions) and were assigned to one of four groups: saline/water (SW), saline/ethanol (SE), PIC/water (PW), and PIC/ethanol (PE). Brains were harvested 24 hours after the final alcohol session, micro-vessels from frontal cortex were purified using mechanical homogenization and density-gradient centrifugation, and RNA sequencing was performed to compare gene expression between groups. Tlr3 activation with PIC resulted in escalated ethanol consumption and we identified 1,588 genes differentially expressed (DEGs) between PE and SE groups at nominal p-value of less than 0.05 and 74 DEGs at 5% FDR. The top DEGs were Rsad2, H2-K1, Slc16a1, and Ifi44, which are implicated in the immune response and are cell type-specific to the brain microvasculature. Subsequent bioinformatics analysis utilized Weighted Gene Co-expression Network Analysis (WGCNA) to identify clusters (modules) of genes correlated with the effects of Tlr3 activation and/or ethanol consumption. We identified a total of 43 modules, many of which were enriched with cell type-specific genes, such as ECs and pericytes, and were associated with Tlr3 activation and escalated ethanol consumption.

Taken together, these data suggest that vascular cell types are responsive to repeated Tlr3 activation and could contribute to excessive ethanol consumption.

Lehman, Tenley

The blood-based telomeric DNA C-circle assay can detect alternative lengthening of telomeres (ALT) in pediatric high-grade gliomas

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High-grade gliomas (HGG) comprise ~10% of pediatric brain tumors; 40% of pediatric HGG use the alternative lengthening of telomeres (ALT) mechanism to maintain replicative immortality. ALT cancers share a unique biology providing potential therapeutic targets. Extrachromosomal telomere DNA repeats, termed C-circles, can be detected by a unique PCR assay, providing a sensitive and specific biomarker for ALT cancers. C-circles have been detected in ALT tumors and serum of ALT patients. We have adapted the C-circle assay (CCA) to provide a sensitive and specific assay with cfDNA in patient plasma. Here we determined if cfDNA in plasma can be used to detect patients with ALT-positive HGG. Frozen plasma samples were collected in Streck tubes at time of surgery prior to resection from patients with HGG. DNA was extracted and quantified. Isothermal rolling C-circle amplification and real-time telomere PCR was performed followed by analysis. The C-circle positive neuroblastoma cell line, CHLA-90, and C-circle negative neuroblastoma cell line, CHLA-20, served as the positive and negative controls respectively. CCA values in plasma of 2 and above indicate positivity for C-circles. Plasma samples were analyzed by CCA from three pediatric patients whose brain tumors were previously biopsied and identified as ATRX mutation positive. ATRX mutation indicates ALT however, not all ALT cancers have ATRX mutations. All plasma samples were above the 2.0 cutoff at 3.37, 3.13, and 4.59 and thus classified as C-circle positive. This preliminary cohort shows that the CCA has potential for identifying ALT pediatric brain tumors using cfDNA from plasma. As novel therapies effective against ALT HGG are developed, the plasma CCA may allow accelerated initiation of neoadjuvant therapy to shrink tumor prior to surgical resection and lessen or prevent the need for tumor biopsy. Expansion of the initial test cohort is underway. Supported by NCI UO1 CA63988.

Mehta, Yash

Beyond Western Blot: Advancing Glucose Transporter -1 (GLUT-1) Quantification with LC-MS/MS in Brain Endothelial Cells

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20% of daily glucose uptake is routed to the brain. Its uptake is limited by the presence of a blood-brain barrier (BBB), and mostly occurring via the recruitment of glucose transporter-1 (GLUT1). Notably, GLUT1 deficiency

syndrome (GLUT1DS) is a rare genetic disease caused by mutations affecting the GLUT1 activity and currently suffers from limited analytical tools to better understand and quantify such transporters in patients. The aim of this study is to develop an LC-MS/MS-based novel, highly specific, selective, and high-throughput confirmative methodology quantify the GLUT1 protein expression in various endothelial cells. The "Bottom-up" approach was applied using trypsin as an enzyme to digest cell membrane proteins. The digested peptides were separated using XBridge Premier Peptide BEH C18 (50*21.mm, 2.5u) column at 55 degrees Celsius and detected using SCIEX QTRAP 7500 mass spectrometer. Water and acetonitrile both having 0.1% formic acid were used as mobile phase in gradient mode for separation of the analytes. Among the trypsin-digested peptides, TFDEIASGFR (459-468 amino acids of GLUT-1 protein) emerged as the signature peptide for GLUT-1, recognized for its specificity and sensitivity. For quantification of GLUT-1 protein, three Multiple Reaction Monitoring (MRM) transitions were chosen based on intensity: 571.8 > 894.3, 571.8 > 537.2, and 571.8 > 650.3. The method specificity and selectivity were confirmed against the GLUT1 knockout cell line samples processed in triplicate. No confirmative peak was observed for signature peptides in the negative controls (Knockout cell lines & experimental blank). To enable accurate quantification of GLUT-1 protein, a calibration curve was prepared. This involved spiking different concentrations of the chemically synthesized TFDEIASGFR peptide into SLC2A1 knockout cell lines, along with similar concentrations of the 15N-labeled TFDEI-A*(15N)-SGFR peptide in all samples. The highest expression of GLUT-1 protein was observed in IMR90-c4 iPSCs followed by iBMECs, hCMEC/D3, and bEnd.3 cells. LC-MS proves to be superior method for absolute quantification of GLUT-1 protein with 3 times faster turnaround, improved specificity, and fewer processing steps than semiquantitative immunoblot analysis.

Nozohouri, Ehsan

The Acute Impact of Propofol on Blood-Brain Barrier Integrity in Mice

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We investigated whether short term infusion of propofol, a highly lipophilic agonist at GABAA receptors, which is in widespread clinical use as anesthetic and sedative, affects passive blood-brain barrier (BBB) permeability in vivo. Mice were anesthetized with an intraperitoneal injection of ketamine/xylazine followed by a continuous IV infusion of propofol in lipid emulsion through a tail vein catheter. Control groups received ketamine/xylazine anesthesia and an infusion of Intralipid, or ketamine/xylazine anesthesia only. [13C12]sucrose as a permeability marker was injected as IV bolus 15 min after start of the infusions. Brain uptake clearance, Kin, of sucrose was calculated from the brain concentrations at 30 min and the area under the plasma-concentration time curve. We also measured the plasma and brain concentration of propofol at the terminal time point. The Kin value for propofol-infused mice was significantly higher, by a factor of 1.55 and 1.87, compared to the Intralipid infusion and the ketamine/xylazine groups, respectively, while the control groups were not significantly different. No difference was seen in the expression levels of tight junction proteins in brain across all groups. The propofol plasma concentration at the end of infusion (10.7 μM) matched the clinically relevant range of blood concentrations reported in humans, while concentration in brain was 2.5-fold higher than plasma. Propofol at clinical plasma concentrations acutely increases BBB permeability, extending our previous results with volatile anesthetics to a lipophilic injectable agent. This

prompts further exploration, potentially refining clinical practices and ensuring safety, especially during extended propofol infusion schemes.

Orobets, Kseniia

Deciphering Molecular Mechanism of Alzheimer's Disease: Early Events During Amyloid Precursor Protein Synthesis

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Alzheimer's disease (AD) is the most common neurodegenerative disorder. One of the molecular hallmarks of the disease is the accumulation of the amyloid β (Aβ) plaques. Amyloid β is the product of the amyloidogenic processing pathway of the amyloid precursor protein (APP). Amyloidogenic processing has been intensively studied, however early steps of APP protein synthesis remain unknown. APP is a membrane protein containing the N-terminal signal peptide. Membrane and secretory proteins follow a specific targeting pathway to reach the endoplasmic reticulum (ER). Signal recognition particle (SRP) dependent and SRP-independent pathways are known. SRP is the most common pathway, and it was assumed it is used for APP. No experimental data demonstrating this assumption were obtained so far. Early steps of APP biogenesis remain uncharacterized, and there is no evidence if APP is targeted to the ER by SRP or by other unestablished factors. Our results demonstrate for the first time that APP is not a regular SRP substrate. While depletion of SRP54, an SRP subunit, leads to mRNA degradation of the typical SRP substrates activating RAPP protein quality control, APP mRNA level evaluated by RT-qPCR remains practically unaltered. APP protein level in cells and in culture medium coincides RT-qPCR data and does not show notable decrease in APP abundance. These data suggest that other unknown factors are involved in APP targeting. To detect and to identify these factors we developed a unique in vitro site-specific photo-crosslinking system. We also tested if APP translocation to the ER lumen is conducted through the ER membrane complex SEC61. The depletion of SEC61 subunit affects APP secretion but not APP synthesis or the abundance inside the cell. Our work provides a first view on early events in APP synthesis and sorting that are crucial for understanding molecular mechanisms of Alzheimer's and other neurogenerative diseases.

Panthagani, Praneetha

A multifaceted approach to evaluate efficacy of BEM as a treatment for Alcohol Use Disorder

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Alcohol use disorder (AUD) is a complex brain disease with limited treatment options and significant societal burden with respect to morbidity, mortality and cost. Here, we test the overarching hypothesis that the lead compound, 10-butylether minocycline (BEM), based on initial efficacy and safety evaluations from a series of modified minocycline analogs, will reduce high alcohol consumption across the spectrum of AUD. The murine models tested were: Drinking in Dark (DID), Immune-Induced Escalation (IIE), and Chronic Intermittent Ethanol (CIE) to represent, initial binge drinking or mild AUD, moderate AUD and dependence or severe AUD respectively. In addition, we completed a pilot test in mini-pigs that had been behaviorally tested to meet a diagnosis of severe AUD having drunk to intoxication for nearly three years. For DID, BEM dose-responsively and significantly reduced alcohol consumption in both female and male mice at 20, 40 and 60 mg/kg i.p. BEM also reduced alcohol consumption in poly(I:C) immune challenged animals (IIE model) at the 6 hr time point but not at 24 hours when administered at 60 mg/kg i.p. These results were consistent with its pharmacokinetic profile, BEM works acutely and may need to be given b.i.d. (twice daily). In our models of severe AUD, BEM significantly reduced ethanol consumption in both mice and minipigs. In the mouse CIE test, female and male mice were given 60 mg/kg i.p. following 4 standard cycles of ethanol vapor exposure and limited access drinking. There were no sex differences and BEM reduced voluntary consumption by nearly 80%. To confirm efficacy in a nonrodent animal model, we treated two female minipigs with a history of nearly 3 years of alcohol consumption. Both met at least six of eleven DSM-V criteria, which indicated a severe AUD diagnosis. At 10 mg/kg p.o. BEM, a reduction in both alcohol consumption and preference were recorded. The results show BEM may be a promising AUD treatment; it is currently undergoing ADMET testing for an FDA Investigational New Drug application.

Tsurukawa, Fernando

Multi-Study Transcriptomic Analysis of Alzheimer's Brain Tissue: Insights and Caveats

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Alzheimer's disease is a progressive neurodegenerative disorder whose molecular landscape is still not very well understood. The majority of existing studies on Alzheimer's transcriptomic data consider differential expression-based analysis, which are univariate by design and often miss the multivariate nature of genetic interactions. Several existing studies report analyses of single datasets but results are often not replicated in other datasets. Our goal is to emphasize the integration of machine learning techniques beyond traditional gene differential expression analyses and report the caveats of using datasets from different studies. We designed a machine learning based pipeline and present the gained insights from the multi-study multivariate analysis of two datasets along with the caveats of such analysis and the recommendations to follow.

4. Basic Science – Postgraduates

Do, Hoa Quynh

A bupropion modulatory site in Gloeobacter violaceus ligand-gated ion channel

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Bupropion is an atypical antidepressant and smoking cessation drug that causes adverse effects such as insomnia, irritability, and anxiety. Bupropion inhibits dopamine and norepinephrine reuptake transporters and eukaryotic cation-conducting pentameric ligand-gated ion channels (pLGICs), such as nicotinic acetylcholine (nACh) and serotonin type 3A (5-HT3A) receptors, at clinically relevant concentrations. Here, we demonstrate that bupropion also inhibits a prokaryotic homolog of pLGICs, the Gloeobacter violaceus ligand-gated ion channel (GLIC). Using GLIC as a model, we used molecular docking to predict binding sites for bupropion. Several clusters of bupropion binding pose within the transmembrane domain were identified, with the predominant cluster being localized to the interface between transmembrane segments M1 and M3 of adjacent subunits. Residues W213, T214 and W217 in the first transmembrane segment, M1, and F267 and I271 in the third transmembrane segment, M3, most frequently reside within 4 Å distance from bupropion. We then used single amino acid substitutions at these positions and two-electrode voltage-clamp recordings to determine their impact on bupropion inhibitory effects. The substitution T214F alters bupropion potency by shifting the IC50 to a 13-fold higher value compared to wildtype GLIC. Residue T214 is found within a previously identified binding pocket for neurosteroids and lipids in GLIC. This intersubunit binding pocket is structurally conserved and almost identical to a binding pocket described for neurosteroids in GABAA receptors. Our data thus suggest that T214 that lines a previously identified lipophilic binding pocket in GLIC and GABAA receptors is also a modulatory site for bupropion interaction with GLIC.

Yin, Linda

Cbln1 alleviates cognitive deficits in J20 mice

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The objective of this study was to investigate the potential impact of neuronal network dysfunction at the early stages of Alzheimer's disease (AD) pathology, with a specific focus on cerebellin1 (Cbln1), a synaptic organizer within the central nervous system. Our recent observations of decreased Cbln1 expression in post-mortem brains of AD patients prompted our hypothesis that restoring Cbln1 levels might ameliorate cognitive decline. To explore this hypothesis, 8-month-old male J20 AD mice were used for this study, because J20 mice show deposition of amyloid-beta and beginning plaque formation and cognitive behavioral deficits by this age. Recombinant human Cbln1 or vehicle (0.9% NaCl) was administered stereotaxically into the lateral ventricles of J20 mice and in age- and sex-matched wild type (WT) mice. Subsequent behavioral assessments, including

the Morris Water Maze and Novel Object Recognition Task, revealed significant learning and memory deficits in vehicle-treated J20 mice, compared with vehicle-treated WT mice and Cbln1-treated J20 mice, suggesting that Cbln1 administration alleviated cognitive deficits of J20 mice. Further electrophysiological recordings of long-term potentiation (LTP) in hippocampal slices from Cbln1-treated J20 mice and vehicle-treated WT and J20 mice showed that Cbln1 could restore LTP in J20 mice. Together, these results suggest that Cbln1 can alleviate cognitive deficits and restore neuroplasticity in 8-month-old J20 AD mice.

Sarayli Belirgen, Nermina

RIC-3 Chaperone Protein Interacts with Serotonin Type 3A Receptor in Neuronal Mammalian Cells

Nermina Sarayli Belirgen1, Hoa Quynh Do1, Austin Dwight Rodgers1, Clinton MacDonald2, Rhea Ramani1, Joshua Theriot1, Petar Grozdanov2, Michaela Jansen1

The serotonin type 3A (5-HT3A) receptor is a distinct member of the serotonin receptor family, present in both the central and peripheral nervous system, specifically in neurons. It operates as a pentameric ligand-gated ion channel (pLGIC), allowing the passage of sodium and potassium upon serotonin binding. The 5-HT3 receptor plays crucial role in neurotransmission and synaptic plasticity, influencing mood, emotions, sleep, appetite, and addiction regulation. Disruptions in serotonin signaling have been linked to central nervous system disorders, including schizophrenia, anxiety and depression. 5-HT3A receptor is integrated into the cell membrane, comprising five subunits surrounding a central pore. Each subunit includes a substantial extracellular portion housing the agonist binding site, four transmembrane segments (M 1-4), a sizable intracellular domain located between M3 and M4, and a short extracellular C-terminal region. The functional surface expression of 5-HT3A channels is regulated by the chaperone protein RIC-3 (Resistant to Inhibitors of Cholinesterase 3) that facilitates plasma-membrane expression, maturation, and trafficking of 5-HT3A receptors and nicotinic acetylcholine receptors within the pLGIC superfamily. As such RIC-3 contributes to fine-tuning neuronal signaling, thus affecting the overall excitability and communication between neurons. Any changes in the levels of RIC-3 or its interactions with the receptor could potentially modify how sensitive or responsive the 5-HT3A receptor is to serotonin. In this study, we utilized synthetic 5-HT3A peptides as research tools to examine and characterize their interaction with RIC-3 derived from heterologous overexpression sources, as well as from cell lines (neuroblastoma, SH-SY5Y cell lines) or tissues (mouse brain) naturally expressing RIC-3.

Shanmugam, Sam

New Interventions to mitigate oxidative damage to the placenta and developing brain (PLACENTA-CORTEX AXIS) by ethanol using polyphenols

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Background: Fetal alcohol spectrum disorders (FASD) refers to impaired fetal brain development due to alcohol (EtOH) exposure leading to lifelong physical, behavioral, and cognitive impairments. "Neuroplacentology" defines the link between placental dysfunction and impaired brain development (Placenta-Cortex Axis). Earlier studies from our lab have confirmed that in utero EtOH exposure induced oxidative stress, which is mechanistically connected to dysregulation of NRF2 and NFAT3 (transcription factors essential for oxidative stress responses and neuronal survival in the developing brain) in both the placenta and fetal brain. Glutathione (GSH), a tripeptide (gamma-Glutamyl-cysteinyl-glycine), is a vital antioxidant present in virtually all systems. GSH synthesis is ultimately controlled by the availability of Cysteine and/or Cystine, which are transported by SLC family genes (SLC1A1/EAAC1 and SLC7A11/xCT) and cysteine synthesis by the transsulfuration pathway. The objective was to elucidate the ability to rescue NRF2 and NFAT3 expression to counteract EtOH-induced oxidative stress and dysregulation of GSH homeostasis in in-utero and in-vitro placental models. Timed-pregnant Sprague-Dawley rats were exposed to intermittent EtOH vapor (IEV) as the in-utero model, daily from GD11-GD20 with a 6h ON/18h OFF in EtOH-vapor chamber. And, in-vitro, HTR8 cells (an early gestation cytotrophoblast model), and Forskolin induced differentiated BeWo cells (a syncytiotrophoblasts model) were used. Activation of NRF2, and NFAT3 were assessed using the polyphenols chlorogenic acid (NFAT3 activation) and resveratrol (NRF2 activation). Samples were then processed for cell growth/proliferation, ROS, MDA, GSH/GSSG assays, transcriptional activation assay, transporter activity, qRT-PCR, and Western blotting for genes governing GSH synthesis. EtOH-induced accumulation of ROS and oxidative damage evidenced by increasing MDA levels, decreased cell viability, decreased basal NRF2 and NFAT3 reporter activity (4xARE-Luc and 3xNFAT-Luc), decreased the Xc- transporter activity, and NRF2 and NFAT3 expression in placental tissue and in the in vitro models. Chip-qPCR revealed binding of NFAT3 on the SLC7A11 promoter and EtOH significantly inhibited this binding. These impacts were prevented by chlorogenic acid and resveratrol treatments. EtOH induced oxidative damage and impaired GSH homeostasis via dysregulation of NRF2/NFAT3-GSH synthesis. Data illustrate that the two transcription factors could be viable targets for optimizing redox homeostasis in the EtOH-exposed placenta and, thereby, normalizing fetal brain development.

Smith, Shane

Vitamin A and Histone Deacetylases in Alzheimer's disease

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In Alzheimer's disease (AD), histone acetylation is disrupted, suggesting impaired transcriptional control. Moreover, evidence suggests an AD-dependent loss of transcription controlled by all-trans-retinoic acid (ATRA), a bioactive metabolite of vitamin A (VA). Antioxidant depletion causes oxidative stress (OS), triggering Nrf2-mediated antioxidant defenses. Here, we investigated roles of VA, histone acetylation, Nrf2, and OS in vitro. Finally, we established a dietary vorinostat dose that promotes histone acetylation in AD mouse brain. For in vitro studies, mouse HT22 cells were treated with vorinostat (up to 40 μM), ATRA, and/or H2O2. MTT and lipid peroxidation assays were performed. Acetyl-histone H3 and Nrf2 levels were examined via western blot (WB) and immunocytochemistry (ICC). For in vivo studies, humanized amyloid beta knock-in (hAbeta-

loxP-KI) AD mice were fed purified diet with 0.18 or 0.36 mg vorinostat/gram of diet for 2 weeks. HDAC enzyme activity in brain tissue was examined via colorimetric ELISA and acetyl-histone H3 level. Vorinostat and ATRA treatment (up to 20 µM) caused no significant cytotoxicity to HT22 cells. H_2O_2 alone (25-50 µM) caused ~30-40% cell death (p<0.0001). ATRA (5 µM), in combination with vorinostat (0.5 µM), protected against H_2O_2 up to 150 µM. Vorinostat increased acetylation of histone H3 with 0.5-3.0 µM treatment for 24h (p<0.001). ROS was significantly reduced. Nuclear translocation of Nrf2 was induced by H2O2 and reduced after ATRA and vorinostat treatment. Both vorinostat diets increased acetyl-histone H3, inhibited HDAC activity, and reduced peroxidation (p< 0.05). Doses of vorinostat used in vitro and in vivo increased histone acetylation without cytotoxicity/toxicity. In vivo, 0.18 mg/g vorinostat diet delivered a tolerable and bioactive dose. VA, alone and in combination with vorinostat, may protect neuronal cells from oxidative stress. Together, our study provides a possible link between oxidative stress, Nrf2 and HDACs as potential contributors to AD progression.

Strickland, Jake

RARE-LacZ Mice as a Model to Study Retinoic Acid Signaling at Cellular Resolution in Alzheimer's Disease

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Disrupted amyloidogenic/non-amyloidogenic balance leads to Alzheimer's disease (AD). Evidence suggests vitamin A (VA) supplementation favors the non-amyloidogenic pathway through upregulation of α-secretase. Originally used to map embryonic retinoic acid (RA) signaling, RARE-LacZ mice possess multiple LacZ genes controlled by retinoic acid response elements (RAREs). We crossed RARE-LacZ mice with AD mouse models to determine their suitability for studies into the effects of VA on dentate gyrus (DG) RA signaling and learning in AD. Relative LacZ gene copy ratio was determined by qPCR. Dietary intervention compared VA-supplemented (20 IU/g) AIN-93M to standard (4 IU/g). Mice were tested at postnatal day (P)125 via water T-maze (WTM, 9 simple discrimination, 9 reversal trials). PFA-fixed sections (40µm) were immunostained for LacZ, doublecortin, and/or calbindin, confocally imaged, and analyzed using ImageJ. RARE-lacZ mice were crossed with C57BL/6J, -NJ, and CD1 mice (wildtype strains of J20, hAβ-KI, and RARE-LacZ mice, respectively). LacZ gene copy ratio was ~2.6:1 between RARE-LacZ mice (N=12) and crosses (N=34). 32/34 offspring fell within ±50% of the mean. Strain affected latency to platform on WTM during simple discrimination and reversal (N=11-12, p<0.05, Friedman), however total distance traveled was unaffected suggesting intact learning in all backgrounds. Hippocampal LacZ immunoreactivity was localized to a subset of mature doublecortin-negative, calbindin-positive DG granule cells, appearing higher on C57BL/6J and -NJ than CD1 backgrounds. Offspring from J20+/- AD and RARE-LacZ mice exhibited impaired learning (N=16, p<0.05, Kolmogorov-Smirnov). No significant differences in behavior between VA-supplemented and standard AIN-93M were observed. RARE-LacZ mice appear to have behavioral and genetic characteristics appropriate for testing VA-mediated interventions in AD models. RA signaling is prominent in mature DG cells associated with successful reversal learning. Although reversal of AD-related learning deficits by VA supplementation was not observed, testing AD mice on a VA deficient (0.4 IU/g) diet is planned.

5. Basic Science - Faculty

Grozdanov, Petar

Changes in alternative polyadenylation in a mouse model of alcohol dependance

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Alternative polyadenylation (APA) is a widespread, but often overlooked mechanism of regulating gene expression. APA within the same 3' terminal exon affects the length of 3' untranslated region (3' UTR). The length of the 3'UTR and sequence elements present into it are important contributors to the regulation of gene expression that impacts essential steps in the mRNA metabolism, i.e., localization within cells, stability, and protein translation. Longer APA transcripts have been shown to be enriched in neuronal processes, while shorter transcripts are often confined to the neuronal bodies. This differential localization of the transcripts may affect neuronal functions including neurogenesis and synaptic plasticity, key processes associated with the development of alcohol use disorder (AUD). The purpose of this study was to investigate the role of APA in AUD using a well-established mouse model of alcohol dependence-induced escalation of ethanol consumption through a chronic intermittent ethanol (CIE) exposure. The model is considered to resemble the experience of alcohol-dependent individuals who participate in episodes of excessive ethanol consumption followed by repeated withdrawals. Our analysis identified hundreds of genes undergoing APA in three different brain regions isolated from alcohol-depended in comparison to non-dependent male mice. In contrast, the number of genes affected by alcohol in female mice was limited. We also identified hundreds of differently expressed (DE) genes in alcohol- vs non-depended brain regions. Strikingly, the APA and DE genes overlapped minimally. Moreover, using previously published cell type-specific single nucleus RNA-Seq datasets, we were able to determine that the APA genes were primarily expressed in neurons in prefrontal cortex, while the DE genes were expressed in mostly in non-neuronal cells, e.g., microglia, endothelial and mural cells. Gene ontology functional group analyses revealed that the pathways associated with APA and DE genes were different: APA genes were involved in cognition, memory, learning, neuronal development, response to alcohol, and behavior with an emphasis on synapse function, organization, and maintenance, whereas the DE genes were involved in processes such as nucleoside biosynthesis, signaling pathways, cell migration and non-neuronal cell functions. In summary, our study suggests that APA is an important molecular mechanism invoked in AUD in both male and female mice that has the potential to regulate localized neuronal protein expression during AUD development. In addition, our study highlights new molecular targets for pharmacological interventions of AUD and other substance use disorders.

Shen, Leslie

Ginger supplementation mitigates spontaneous pain in neuropathic male rats via gut-brain-interaction

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Emerging evidence suggests short-chain fatty acids (SCFA) play a key role in the pathogenesis of neuropathic pain by regulating tight junction integrity and microglial activation: a gut-brain-interaction. We previously reported gingerol-enriched ginger (GEG) improves GI health in diabetic rats (Wang et al. 2022) and reduced mechanosensitivity in rats with spinal nerval ligation (SNL, a model of neuropathic pain) (Shen et al. 2022). In this study, we further evaluated the effects of three dosages of GEG on spontaneous pain sensitivity, fecal SCFA, tight junction integrity, and microglial activation in SNL rats. 36 male rats were divided into: Sham, SNL, SNL+200mg GEG/kg BW, p.o. (GEG200), SNL+400mg GEG/kg BW, p.o. (GEG400), and SNL+600mg GEG/kg BW, p.o. (GEG600) groups for 4 weeks. Spontaneous pain was assessed with the Rat Grimace Scale (RGS). Cecal-feces samples were collected for SCFA analysis using LC-MS. mRNA gene expression levels of tight junction integrity and mitochondrial function in colon and amygdala were determined using qRT-PCR. Data was analyzed statistically. GEG supplementation for 4 weeks significantly mitigated SNL-induced spontaneous pain, evidenced in significantly altered nose bulge, ear position, whisker change, and overall score in the RGS. Compared to the Sham rats, the SNL rats had greater concentrations of fecal SCFA, i.e., acetic acid and propanoic acid. Supplementation of GEG to the SNL rats significantly reduced the SCFA concentrations in feces ($P<0.05$). GEG supplementation improved tight junction integrity of gut and brain, as shown by increased claudin-3 mRNA expression in both the colon and amygdala of SNL rats ($P<0.05$). Furthermore, supplementation of GEG attenuated SNL-induced mRNA expression levels of microglia activation markers, namely CD11b, IBA-1, and GFAP, in the colon and amygdala of rats ($P<0.05$). There were no significant differences in the measured parameters between three GEG dosages. This study suggests that ginger supplementation mitigates spontaneous pain in a rat neuropathic pain model, via decreasing fecal SCFA, improving tight junction integrity, and reducing glia activation.

Sivaprakasam, Sathish

GPR109A induces amyloid-β clearance through macropinocytosis in blood-brain barrier endothelial cells

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Alzheimer's disease is characterized by increased levels of amyloid-β (Aβ) in brain caused by perturbations in the clearance of both soluble and insoluble (Aβ40/42) oligomers, which leads to accumulation and deposition of Aβ plaques as an early event in the pathogenesis of the disease. The Aβ peptides originate from the amyloid precursor protein, and mutations in this protein that enhances generation of the Aβ peptides are known to cause Alzheimer's disease. Similarly, defects in the clearance of Aβ peptides can also contribute to the disease. Chronic inflammation and oxidative stress can influence the rates of Aβ peptide generation and clearance detrimentally so as to initiate and accelerate the disease pathogenesis. Previous studies have demonstrated the uptake of Aβ peptides by different types of cells in the brain via clathrin-mediated endocytosis, caveolar endocytosis and macropinocytosis, with subsequent degradation. Macropinocytosis is initiated by actin polymerization at the plasma membrane and the resultant membrane ruffles trap extracellular fluid with its constituents (~5 μm in size) to form macropinosomes, which then fuse with lysosomes for subsequent

degradation of the macromolecular components in the trapped fluid. Blood-brain barrier (BBB) is a potential site for clearance of Aβ peptides via the endothelial cells that constitute the barrier structure. We examined the possible involvement of macropinocytosis in the clearance of Aβ peptides in BBB endothelial cells using the cell line hCMEC/D3, a widely used model for BBB. In addition, we evaluated the regulation of this process by GPR109A, a G-protein-coupled receptor that is activated by the ketone body β-hydroxybutyrate (βHB), the vitamin niacin, and the bacterial fermentation product butyrate. We undertook this study based on published reports that GPR109A activation by niacin protects against Alzheimer's disease, and we sought to provide a molecular mechanism for this protective effect by testing the hypothesis that the receptor might promote the clearance of Aβ peptides by macropinocytosis across the BBB. For this, we monitored macropinocytosis in hCMEC/D3 cells using the fluorescent probe TMR-dextran as well as FITC-Aβ peptide. The involvement of GPR109A was examined by monitoring the effects of niacin and βHB on the process. We found robust activity of macropinocytosis in these cells. More importantly, activation of GPR109A by its agonists niacin and βHB markedly increased this activity. Previously we have shown that hCMEC/D3 cells possess a carrier-mediated transport mechanism for the uptake of Aβ peptides. The present work uncovers the presence of another novel mechanism for the entry of Aβ peptides into these cells. The activation of this uptake process by GPR109A could be at least partly responsible for the known protective effects of niacin and ketogenic diets against Alzheimer's disease. Once the Aβ peptides enter the BBB endothelial cells, they are eliminated into blood by export via the multidrug export transporter ABCG2. As such, the vectorial clearance of Aβ peptides across the BBB involves multiple mechanisms for the entry (carrier-mediated process, macropinocytosis, and receptor-mediated process with LRP5/6) and ABCG2 for exit. We believe that GPR109A plays a key role in the regulation of all these processes to facilitate the clearance of Aβ peptides. Studies are underway to examine the influence of GPR109A activation in hCMEC/D3 ells on the expression and activity of ABCG2. Our previously published work has unequivocally shown that GPR109A elicits potent anti-inflammatory effects and potentiates differentiation of naïve T cells into immunosuppressive regulatory T cells. The abundant expression of the receptor in colon and its activation by the bacterial metabolite butyrate with resultant changes in immune-cell repertoire to an immnusuppressive phenotype adds another dimension to the participation of this receptor as a protective mechanism against Alzheimer's disease via the gut-brain axis. Taken collectively, our studies underscore the clinical and therapeutic relevance of GPR109A as a promising target for the prevention and treatment of this devastating disease.

6. Clinical/Human studies/tissue - Undergraduate students

Annamalai, Aarthi

Infants' chronic dietary exposure to toxic levels of arsenic: Implications for deleterious health effects

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Multiple epidemiological studies have found associations between early-life arsenic exposure and childhood mental health-related outcomes such as anxiety, depression, and deficits in executive function. Exposure to arsenic from food is expected to be about three times higher for infants and young children than for adults, in part because their intake per unit body mass is higher and their dietary diversity (i.e., the kinds of foods that they eat) is lower than adults. Using inductively coupled plasma mass spectrometry (ICPMS), we evaluated the total arsenic concentration of commonly consumed infant products (formula, teethers and rice cereals) across representative brands (e.g., Similac, Gerber, Enfamil, Kirkland, and Earth's Best) and lots of production. The total arsenic content in infant formula ranged from 2.8-15 ppb, in teethers from 42-314 ppb, and in rice cereals 11-116 ppb. The total arsenic concentrations largely exceeded the 10-ppb regulatory level of arsenic in water set by the United States Environmental Protection Agency (EPA). However, no such regulation currently exists for total arsenic in foods. Arsenic content was generally consistent within brand and across manufacturing lots. As both rice cereals and teethers are primarily rice-based products, we predict, and will confirm using high performance liquid chromatography (HPLC)-ICPMS, that the majority of arsenic in these foods is inorganic arsenic, which is highly toxic and can lead to hypomethylation, DNA damage, neurotoxicity, and chronic inflammation. Our results highlight that infants are likely chronically exposed to arsenic during sensitive periods of organ development which may pre-dispose them to deleterious health outcomes, such as mental illness in adolescence.

Formella, Jakub

Social vulnerability is associated with healthcare disparities in Alzheimer's Disease and Related Dementias

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Neurology is a rapidly evolving field in medicine with new treatment options being developed every year. Yet, access to subspecialty care for Alzheimer's Disease and Related Dementia (ADRD) patients continues to be a challenge for most people struggling with these neurologic conditions. Recent studies have shown vulnerable populations such as patients with low socioeconomic status and minority groups may be at higher risk of delaying treatment for cognitive impairment. Our aim is to conduct a systematic review of the literature and

propose a mechanism through which sociodemographic factors could influence ADRD incidence and mortality. We performed a systematic review of the literature using PubMed research database. The terms used included a combination of "Social vulnerability," "Socioeconomic determinants," "Social frailty," "dementia," "cognitive disorders," using the Boolean operator "AND." We also utilized the medical subject headings (MeSH) terms "Socioeconomic Factors," "Alzheimer's Disease," and "Neurocognitive Disorders."A total of 48 studies were included in the qualitative assessment of the literature review. Most of the articles included in the present review fall into one of six major themes. The direct association between social vulnerability factors and ADRD was supported by 19 of the 48 articles. Studies exploring potential mediators in this association included mental health (n = 2), genetic age and risk (n = 4), healthy lifestyle behaviors and other health factors (n = 9), comorbid chronic conditions (n = 4), education (n = 7), and environmental pollution (n = 3). Results from our study showed both individual and area-level socioeconomic status are linked to higher prevalence and incidence of ADRD, poorer cognitive function at diagnosis, lower adherence to medication and increased mortality rates. Low individual SES potential mediators include lower levels of physical activity, poor diet, smoking, drinking, lower educational attainment, and cognitive reserve. Environmental factors showed an association between pollution and higher ADRD incidence. Racial minorities and women were disproportionately affected by disease severity, access to care, and mortality.

7. Clinical/Human studies/tissue – Graduate students

Bidiwala, Ema

Feature Selectivity in the Far Periphery

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Far peripheral vision (31° to 100° of visual angle; Rutkowski & May, 2017; Loschky *et al.,* 2019) is important in daily tasks including walking, driving, and monitoring our overall environment (Vater *et al*., 2022). For example, before walking across an intersection an individual may widely allocate attention across the far periphery to react to any hazards, such as a car, the color of the signal, and any other people crossing to avoid collision. Despite far peripheral vision's implication in important functional tasks and role in the visual field, a majority of research focuses on the near periphery (5°- 30° eccentricity). A predominant reason for concentrating studies on the near periphery is attributed to the anatomy of the retina and primary visual cortex (V1). Within the retina, the number of cones (related to acuity) decreases as eccentricity increases, leading to diminished acuity in the far periphery (Rosenholtz, 2016). Similarly, V1, a critically important area for visual information processing, is retinotopically organized following the pattern of the retina. Therefore, the amount of information processed by V1 decreases as eccentricity increases. These two physiological patterns lead researchers to hypothesize the far periphery has minimal capabilities. However, a number of studies show the visual area may not be as limited as initially theorized. For example, humans can successfully recognize objects in the far periphery (30-80° of visual angle) despite limited acuity (Boucart et al., 2013; 2016; Baldwin et al., 2016; Rosenholtz, 2016). Notably, orientation selectivity generally serves as a building block for object recognition by critically supporting edge detection. Therefore, we sought to determine if orientation selectivity was possible up to 90° eccentricity. Circular patches of moving or static square wave gratings were presented at 30, 60, and 90° at either cardinal (90° or 180°) or oblique (45° or 135°) orientations. Participants (N=22) reported whether motion was present followed by the orientation of the stimulus. Performance was above chance on all motion and orientation conditions. In the orientation discrimination task, participants performed better on cardinal trials compared to oblique. Our results suggest that despite degraded acuity in the far periphery, representations of visual orientation involved in edge detection are still maintained up to 90° periphery. These representations possibly serve as a building block for object recognition in the far periphery. Our results not only impact vision science but overall research in the far periphery. Far peripheral vision loss is a common symptom in age related vision loss and neurological issues such as brain tumors. Current assessments of peripheral vision are completed via visual field tests (VFT) using contrast sensitivity predominantly in the near periphery. However, contrast sensitivity is one of many perceptual aspects contributing to vision. The present results indicate motion and orientation detection, commonly contributing to important daily tasks such as driving, can operate in the far periphery in individuals with normal vision. Accordingly, orientation and motion tasks similar to ours could be added to VFTs in the future, allowing for more comprehensive measurements of perceptual ability in far peripheral vision. Additionally, our paradigm parallels a VFT procedure while capturing a larger visual area. Due to vision loss operating in an outward to inward fashion (tunnel vision) testing a broader visual field could result in early detection of vision loss. Our method may also be more cost-effective (requiring one to two computers, two monitors, and an eye tracker) and can be adapted to VR headsets saving space and cost. The present research, therefore, produces novel results in vision science with implications for understanding far peripheral vision loss, and possible development of a healthcare tool allowing for timely treatment interventions.

Chrzanowski, Lauren

Investigation of chronic pain biomarkers indicative of cognitive decline in rural Texas: A Project FRONTIER Study

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Chronic pain is becoming increasingly prevalent in older adults. Recent literature has proposed a link between chronic pain and neurocognitive decline in aging; however, the mechanism driving this relationship is unknown. This study hypothesized that chronic pain leads to an increase in inflammation, which leads to neurocognitive decline. However, no existing studies have examined this relationship in rural populations. This study included 1864 participants (561 men, 1295 women; Mage = 59.68 years) 40 and over, living in rural West Texas. Cognitive functioning was measured using the RBANS, TRAILS, and CLOX. We used CRP levels to measure inflammation, which were dichotomized ("standard" below 3mg/L and "high" at or above 3mg/L) to represent inflammation. Chronic pain conditions were reported during a medical examination (1414 no chronic pain; 446 with chronic pain). A MANCOVA was performed to determine the effects of inflammation and chronic pain on cognitive function. CRP values significantly predicted cognitive functioning when controlling for age and gender ($F_{(1,973)}$ = 3.67, p = .006), such that those with high CRP (M=82.03, SD = 14.72) had significantly lower overall cognitive functioning ($F_{(1,1079)}$ = 11.04, p <.001, $\eta p2$ = .13) compared to those with lower CRP (M=85.89, SD =16.10). Also, trails delta (i.e., processing speed; ($F_{(1, 973)}$=4.54, p =.03, $\eta p2$ = .09) has the same results as high CRP (M=78.33, SD =65.31) had significantly slower processing speed than the low CRP group (M=66.84, SD = 54.20). However, the interaction with chronic pain was not significant ($F_{(1,973)}$ = .86, p = .49). These results suggest that there is no interaction between inflammation and chronic pain on cognitive decline in rural populations. However, it appears inflammation markers, specifically, CRP, is a significant predictor of neurocognitive functioning in this rural population. This provides further evidence that rural populations are epidemiologically unique and evidence that inflammation may not be the mechanism by which chronic pain may lead to cognitive decline. Additionally, these results direct future studies to investigate comorbidity and risk factors for cognitive decline other than chronic pain.

Shah, Megha

Life Story Questionnaire Use Improves Depression Symptoms and Physical Therapy Participation in Dementia Facility Residents: A Randomized Control Trial

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Dementia is characterized by a progressive decline in cognitive function. Neuropsychiatric symptoms such as depression, psychosis, agitation, aggression, apathy, sleep disturbances, and disinhibition are common in people with dementia and affects their activity participation and quality of life. Objectives: To evaluate the impact of the Life Story Questionnaire (LSQ), a type of life story book, on (1) physical therapy participation

using Pittsburg Rehabilitation Participation Scale (PRPS); (2) Quality of Life – Alzheimer's Disease Scale (QOL); and (3) depression symptoms using Cornell Scale for Depression in Dementia (CSDD). Design: Randomized Control Trial Methods: A consecutive sample of convenience of 35 patients with mild to moderate dementia (Mini-mental state of examination score 10-24) were recruited from a nursing home facility. Patients were randomly allocated in two groups: (1) Control group (No LSQ), which received standard physical therapy care without LSQ use; and (2) Experimental group (LSQ), where physical therapists used the LSQ during physical therapy care. Participants were treated 3-5x/week for 6 weeks. Each patient's family member received a LSQ to complete prior to the start of intervention. PRPS, QOL and CSDD were measured on day 1, after 3 and 6-week of intervention. QOL and CSDD were also measured 6 weeks following intervention. A licensed occupational therapist blinded to the participants' group measured all three dependent variables. The Mann-Whitney-U test assessed between groups differences in PRPS, QOL and CSDD. Results:Twenty-seven participants (12 women) including 13 in the LSQ group and 14 in the No LSQ group (mean age of 77.6±9.2 years) completed the study. Between groups comparisons showed greater improvement for the LSQ group for PRPS at 6 weeks (p=.045; ES=.44) and less depression at 3 weeks (CSDD; p=.049; ES=.46). There were no between groups differences in QOL at any time point. Discussion-Conclusions: This is the first study to investigate the effect of LSQ usage in physical therapy programs in people with mild to moderate dementia. Using LSQ does not require any additional cost to the patient or facility, improved physical therapy sessions participation and helped improve depression symptoms on the short-term. Further research with larger sample size is needed with longer follow up.

Tasmin, Rubaia

Metabolic Dysregulation Unveiled in a Drosophila melanogaster Model of PLA2G6-Associated Neurodegenerative Disease (PLAN) Through Metabolomics and Lipidomics Analysis

Rubaia Tasmin, Shahira Helal Arzoo, Surya Jyoti Banerjee

The Drosophila melanogaster models of PLA2G6-associated neurodegeneration (PLAN), characterized by loss of function mutations in the calcium-independent phospholipase A2 (iPLA2) VIA gene, exhibit a spectrum of age-dependent phenotypic manifestations, including locomotor deficits, shortened lifespan, and female-specific fertility defects. Notably, our prior investigations have elucidated the localization pattern of wild-type iPLA2-VIA-PB to mitochondria in female germ cells, revealing abnormal mitochondrial aggregation and increased apoptosis in aged iPLA2-VIA null mutant female flies, indicative of disrupted mitochondrial homeostasis. Accordingly, we are investigating the systemic mitochondrial perturbations in iPLA2-VIA null mutants. We hypothesized age-dependent and sex-specific metabolic abnormalities in these mutants. To interrogate this hypothesis, we employed a comprehensive mass-spectrometry-based profiling approach targeting small metabolites and lipids extracted from distinct age groups (< 1 week and 4 week) of iPLA2-VIA null mutant and isogenic control adult male and female flies. Our analyses identified a total of 195 small metabolites and 379 lipids, revealing pronounced alterations in aged control flies relative to their iPLA2-VIA null mutant counterparts. Principal Component Analysis (PCA) of our metabolomic datasets further underscored the distinct metabolic profiles characterizing different age groups and sexes within the iPLA2-VIA mutant and control cohorts. Interestingly, young iPLA2-VIA null mutant female flies exhibited metabolite profiles similar to old control females, suggesting premature aging. This aligns with our observation that iPLA2-VIA knockdown solely in somatic tissues mimicked the ovarian phenotypes of null mutants, reinforcing the concept that age-related changes in female fertility are influenced by somatic metabolic indicators. Increasing amount of isoleucine in the body have been found to increase aging leading to premature aging. Notably, our data unveiled isoleucine degradation was downregulated in old mutant female flies, while isoleucine

biosynthesis and degradation were both upregulated in young mutant females. In the context of iPLA2-VIA deficiency, this subtle variation of isoleucine metabolism across age groups and sexes reveals complex regulatory mechanisms maintaining metabolic homeostasis. In sum, our comprehensive metabolomics and lipidomics analysis shed new light on the intricate metabolic dysregulation underlying PLA2G6-associated neurodegeneration in Drosophila, with a particular emphasis on the regulatory roles of isoleucine metabolism in age-related changes.

Vintimilla, Antonio

The Effect of Exercise-Induced Central Fatigue and Concussion History on Cervical Spine Neuromuscular Function

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TTUHSC School of Health Professions, Department of Rehabilitation Sciences, Doctor of Philosophy in Rehabilitation Sciences

Introduction: Central fatigue is prevalent in sports and poses risks for various injuries, yet its association with concussions is poorly understood. This study explores the interplay between central fatigue and concussion risk, delving into systemic impacts on the cervical spine. The neck's crucial role in force modulation raises concerns, particularly for fatigued athletes facing an elevated concussion risk. This risk may worsen for individuals with a concussion history. The study's primary aim is a comprehensive investigation into exercise-induced central fatigue's effects on head-and-neck neuromuscular function, including vestibular and non-vestibular structures such as the visual system and cervical proprioceptors. Methods: Subjects were divided into two groups based on their concussion history. Both groups underwent assessments on cervical joint position error, strength, and endurance concurrently with myoelectric assessment of cervical musculature. Testing additionally evaluated vestibular domains prior to and following central fatigue. Results: There was a significant main effect for "fatigue state" pre- and post-fatigue across various parameters, including constant ($p > 0.001$, $\eta p2 = 0.48$) and absolute ($p > 0.001$, $\eta p2 = 0.55$) joint position error, neck flexor endurance test time ($p > 0.001$, $\eta p2 = 0.89$), splenius capitis root mean square amplitude during cervical extension muscular strength testing ($p > 0.001$, $\eta p2 = 0.42$), sternocleidomastoid total power spectral density during cervical rotation muscular strength testing ($p > 0.019$, $\eta p2 = 0.17$), and King-Devick test time ($p > 0.009$, $\eta p2 = 0.20$). Discussion & Conclusion: Exercise-induced central fatigue had a negative effect on cervical neuromuscular performance in subjects with and without a history of concussion. Notably, there were no significant differences related to concussion history. Nevertheless, moderate to large effect sizes imply potential differences in neuromuscular responses and movement control strategy for subjects with a history of concussion, despite minimal performance differences versus their non-concussed counterparts. This study underscores the need for further research with more refined concussion history stratification and more sensitive outcome measures.

8. Clinical/Human studies/tissue – Medical students

Arciniega, Marcos

Minimally Invasive, Keyhole Approaches for the Release of Entrapped Peripheral Nerves Using Embalmed Cadavers

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Peripheral nerve surgeries require ample time practicing procedures and understanding variability amongst patients. Minimally invasive procedures have a multitude of benefits, including, but not limited to, reduced blood loss, reduced risk of complications and infections. Medical students, residents, and attendings require an impregnable foundation in anatomy. The use of cadavers in medical education allows for surgical, neuroanatomical procedural practice and assessment. Embalmed cadavers are an achievable, beneficial, and efficient method for medical education and training. Willed cadavers were embalmed through approved methods by the state anatomical board. For each decompression procedure, a 1–2-centimeter keyhole, linear, incision was made. Further methods are described in each nerve entrapment surgery below. Either before or after the minimally invasive procedure, an exploratory session was executed with a wider incision to review anatomy or success of the procedure, respectively. Surgical medical education in neurosurgical techniques and procedures using cadavers allows trainees to learn a medical technique and better enhance their surgical skillset. Cadavers offer the benefit of exploring relative anatomy and correct procedural steps after the minimally invasive surgery has been performed. Embalmed cadavers for medical education and procedural practice for minimally invasive, decompressive nerve release procedures is a purposeful tool for trainees and continuing education. This method of practice allows for a visual, mental, and tactile experience to enhance the trainee prior to operating on a living patient. Limitations: Time for an institution to request and be approved for cadaveric donations from an accredited willed body program by the state anatomical board. The use of surgical tools borrowed from the operating room. Cadaveric tissue does not perfectly resemble live tissue regarding texture, color, and lack of blood flow. Cadavers do not allow electromyography to be performed.

Levin, Valeria

Long Term Brain Ramifications of Arachnoid Cyst and the Benefit of Cystoperitoneal Shunt Placement

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Texas Tech University Health Sciences Center, School of Medicine, 1. Department of Anesthesiology, 2. Department of Neurosurgery

Arachnoid cysts (AC) are the most common type of brain cyst. These are often congenital and present at birth or can form as a result of trauma in the pediatric population. These cysts can vary in size and location leading to a myriad of symptoms. ACs can appear anywhere within the central nervous system; however, they most commonly occur at the middle cranial fossa, the suprasellar fossa and the posterior fossa. The great majority of ACs are asymptomatic and do not require treatment, but those that are symptomatic can be the result of a

direct neurological dysfunction or disturbance of the CSF pathway leading to hydrocephalus. Research has shown that ACs do not generally increase in size over time; however, these can initially present in such a size that it can compromise the arachnoid mater, increase the intracranial pressure and cause a midline shift on the brain, at which point surgical intervention is necessary. The most common and effective surgical intervention to address this is a cystoperitoneal shunt. While this surgical procedure addresses the problem of intracranial pressure caused by the AC, there exists a need for diagnostic methods that can assess and evaluate the brain function and integrity that was compromised prior to the treatment. These tests would allow for early detection of brain damage or dysfunction leading to a possible early intervention. We describe a 4-day-old female neonate born by vaginal delivery at 37 weeks of gestation presenting with a large right hemispheric arachnoid cyst with mass effect. Magnetic resonance imaging (MRI) showed a 6.5 x 3.5 cm. arachnoid cyst over the right cerebral complexity, filling the floor of the right middle cranial fossa and causing mass effect with ipsilateral ventricular compression and effacement. Computed tomography (CT) scans also showed a prominent leftward midline shift. The decision was taken to perform placement of a right parieto-temporal arachnoid cystoperitoneal shunt with a medium pressure Codman Hakim valve without anti-siphon device. During the procedure, xanthochromic arachnoid cyst fluid was found, suggestive of hemorrhage or stagnation. Procedure showed technical success, with minimal blood loss. Post-operative imaging showed an interval decrease in the size of the cyst fluid collection with persistent flattening of the right cerebral convexity. Minimal residual right to left subfalcine shift of midline structures was also present. Patient showed improvement in clinical symptoms and was discharged two days following the procedure. This case presentation and review looks to describe a case in which cystoperitoneal shunting was necessary for alleviating intracranial pressure caused by an AC in a neonate, and explore the current literature on diagnostic methods available for post-operative neurological assessment in the case of ACs treated by cystoperitoneal shunting.

Maheshwari, Akash

Correlation of Eye Examination Frequency and Age

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Regular eye examinations by qualified ophthalmologists and optometrists are crucial to the maintenance of ocular health for individuals of all ages. During adolescence and early adulthood, growth of organ systems, including the eyes, continue as development progresses. As the eye develops, adolescents may experience changes in vision and require prescriptions for corrective lenses. For most individuals, vision tends to stabilize by the early 20s and remains stable for many years. In middle adulthood, individuals may begin to experience further vision changes as normal aging processes often cause noticeable changes. In our study, we conducted an analysis of survey responses completed by undergraduate students, graduate students, faculty members, and staff at the TEXFIT conference at the TTU recreation center in order to capture important demographic data and information regarding eye health. When stratified by age groups, different trends emerged when determining frequency of eye examinations. In the age range of 18-20, 80% of respondents had received an eye examination within the past year, and 20% had received an eye examination longer than 2 years ago. For individuals 21 to 25, 44% had received an eye examination within the past year, 22% within the past 2 years, 22% longer than 2 years ago, and 11% had never received an eye examination. For individuals 26 to 30, 33% had received an eye examination within the last year, 33% within

the last two years, and 33% longer than 2 years ago. For individuals 36 to 60, 40% had an eye examination within the past 6 months while 60% had an eye examination longer than 2 years ago. In this way, we observed a general pattern between age and eye examination; young adults may have more frequent eye examinations initially as their prescriptions change and the eye develops, and older adults may have either frequent eye examinations (every 6 months) or infrequent eye examinations. As humans age and enter middle to late adulthood, the incidence of common ocular conditions increases, perhaps necessitating or encouraging more frequent visitation for optimal ocular health and may explain the relatively high percentage of individuals having frequent eye appointments; however, the individuals who have not experienced noticeable age-related vision changes or ocular problems may be less likely to schedule an eye appointment.

Maheshwari, Akash

Socioeconomic Status and Corrective Lenses

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Health disparities across different socioeconomic classes can impact access to high quality care. For many Americans, corrective lenses are needed in order to achieve high-acuity vision. In our study, we attempted to analyze the correlation between socioeconomic status and utilization of corrective lenses. Survey responses including students, faculty, and staff at the TEXFIT conference at the TTU recreation center were captured and analyzed. Respondents could select the best description of their socioeconomic status from the following four options: disadvantaged, lower middle class, upper middle class, or affluent. Few respondents selected the disadvantaged or affluent categories; for analysis purpose, these individuals' responses were grouped with lower middle class or upper middle class categories, respectively. Respondents were also asked if they wear any corrective lenses, if they wear contact lenses, if they wear eyeglasses, or if they wear blue-light blocking glasses. Of the total respondents, 52% did not utilize any eyewear or corrective lenses, 20% utilized contact lenses, 16% utilized eyeglasses, and 12% utilized blue-light blocking glasses. Of the respondents that belonged to the affluent or upper middle-class categories, 46% did not wear corrective lenses, 23% wore contacts, 15% wore eyeglasses, and 15% wore blue-light blocking glasses. Of the respondents that belonged to the disadvantaged or lower middle-class categories, 58% did not wear corrective lenses, 17% wore contacts, 17% wore eyeglasses, and 8% wore blue-light blocking glasses. From this data, it appeared that there may be a correlation between lower socioeconomic status and decreased utilization of corrective lenses or blue-light blocking lenses. This study has several limitations, and, for future study, we hope to increase our sample size and increase demographic data acquisition to reduce the number of potential confounding variables. In this way, we hope to achieve a higher level of granularity that will aid in the strength of our analysis. Furthermore, we would like to increase awareness and knowledge about programs at clinics such as the Lubbock Impact Free Clinic that can offer services such as eye examinations, updated prescriptions, and free or discounted corrective lenses to uninsured and underserved populations.

Mcready, Riley

Associations between Vitamin D, Diabetes, Cognitive Status, and Hispanic Ethnicity amongst Older Rural West Texans: A Project FRONTIER Study

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Diabetes is associated with cognitive decline, and Vitamin D (VD) deficiency is implicated as a risk factor for diabetes. However, the specifics of the relationships between these variables remain unclear. Additionally, previous studies suggest that Hispanic populations have a higher risk of VD deficiency, diabetes, and cognitive decline. We aimed to assess associations between VD level, diabetes, cognitive status, and Hispanic ethnicity (HE) amongst a sample of aging, rural West Texans from Project FRONTIER (PF; Facing Rural Obstacles to Health Care Now Through Intervention, Education, and Research). Data was obtained from a cohort of 292 PF participants (mean age 62.6±11.8, 70.5% female, 40.1% HE). We examined relationships between VD level, blood-based diabetes-related biomarkers, consensus diabetes diagnosis, Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) total score, and HE status. Logistic and linear regression analyses were performed on binary and continuous variables, respectively. We utilized Spearman correlation for bivariate comparisons and Mann-Whitney U tests for between-group comparisons. Regression analyses indicated significant negative associations between VD and HbA1c (p=0.0004), fasting blood glucose (p=0.0003), consensus diabetes diagnosis (p=0.0060), and HE (p<0.0001). Regression analyses indicated significant negative associations between RBANS and HbA1c (p=0.0282), consensus diabetes diagnosis (p<0.0001), and HE (p<0.0001). A significant positive correlation was indicated between VD level and RBANS score (p=0.0439). HE was associated with significantly lower VD levels (p<0.0001), higher HbA1c (p=0.0003), and higher fasting blood glucose levels (p=0.0011) compared to non-HE participants. HE was associated with lower RBANS scores (p<0.0001), indicating higher levels of cognitive decline. Our results indicate in a West Texas cohort, HE is associated with lower VD levels, higher levels of diabetic indicators, and higher levels of cognitive decline. These disparities are important to consider when investigating areas to improve healthcare in West Texas. Further investigation is necessary to elucidate the connection between VD, diabetes, and cognitive status.

Morris, Claudia

Examining Relationships Between Hispanic/Latino Ethnicity, Healthcare Access, Vitamin D Deficiency, and General Health Rating among Aging Rural West Texans: A Project FRONTIER Study

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Previously, we described health disparities in Vitamin D (VD) status, depression, and Hispanic ethnicity in an aging West Texas population from Project FRONTIER (Facing Rural Obstacles to Health Care Now Through

Intervention, Education, and Research). Using the same sample, we examined relationships between Hispanic/Latino ethnicity(HLE),variables related to health care access, VD status, and a General Health Rating (GHR). Of 299 participants in which serum 25-hydroxyvitamin-D levels were available, we examined relationships between access to care, VD, HLE, and GHR. Logistic and linear regression analyses were performed on binary and categorical variables, respectively. We used Mann Whitney U tests for between group comparisons. A significant negative association was found between the probability of health insurance and VD level ($p=0.0042$). Lower VD levels were observed in uninsured (24.9 ± 1.4 ng/ml) compared to insured (29.4 ± 0.8 ng/ml) participants ($p=0.004$). We found a significant negative association between VD levels and the probability of experiencing a time in the past 12 months when cost prevented seeing a doctor ($n=294$, $p<0.0001$). We found a significant negative association between VD level and the length of time it had been since the participant had seen a doctor ($p<0.0001$). We found a significant negative correlation between VD level and GHR ($p<0.0001$). Lower VD levels were observed in HLE (21.40 ng/ml) compared to non-HLE (34.00 ng/ml) participants ($p<0.0001$). Finally, we found a significant negative correlation between HLE status and GHR ($p<0.0001$). Our results reveal that insurance level, access to care, and length of time since seeing a physician likely impact VD status. Additionally, our results reveal that VD status is correlated with HLE. Finally, our results reveal that HLE status and VD status likely impact GHR. The data highlights areas of healthcare in rural West Texas needing improvement.

Ogu, Foster

Focal Epidural Hematoma Overlaying an Arachnoid Cyst in the Middle Cranial Fossa

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Arachnoid cysts are benign, congenital, cerebrospinal fluid (CSF) filled intracranial mass lesions that develop between the brain's two innermost meninges—the pia mater and the arachnoid mater. Typically asymptomatic, they can become symptomatic following significant growth, especially if greater than 3cm or rupture due to trauma, presenting with an epidural, intracystic, or subdural hemorrhage. Studies indicate large cysts may cause cranial deformation, increased intracranial pressure, and macrocephaly due to hydrocephalus, particularly in the pediatric population due to their developing fontanelles. While no definitive cause for them exists, arachnoid cysts are thought to arise from anomalies during fetal development or post-injury arachnoid membrane shearing in the middle cranial fossa, retro cerebellar region, suprasellar region, or posterior cranial fossa. We present a case of a 3-year-old boy, brought to the emergency department with a fall injury. Initial computed tomography (CT) and magnetic resonance (MR) imaging found an epidural hematoma overlaying an arachnoid cyst. A second imaging study a few hours later indicated more swelling around the cyst. However, a follow-up MRI scan after two weeks showed hematoma resolution without intervention and a stable arachnoid cyst without evidence of mass effect in the left middle cranial fossa. Surgical intervention with or without cystic fenestration is often required to evacuate hematomas to prevent further complications as spontaneous resolution of arachnoid-cysts-associated epidural hematomas is a rare occurrence. Despite this, no medical or surgical interventions were done in this case. The cysts likely cushioned the brain because we cannot see any brain contusion. The soft tissue of the cysts with little resistance could have also caused less resistance with an epidural hematoma, further allowing the expansion of the hematoma. We aim to explore the mechanisms behind this spontaneous self-resolution further.

Ogu, Foster

Surgical Management of Peripheral Nerve Sheath Tumors

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Peripheral nerve sheath tumors (PNSTs) are a diverse group of tumors that arise from the peripheral nerve sheath and may occur sporadically or as part of inherited conditions such as neurofibromatosis type 1 (NF1). The management of tumors associated with NF1, specifically neurofibromas, provides valuable insights that can be applied to the overall management of all PNSTs. Neurofibromas, although benign, present unique challenges due to their involvement in crucial neural structures. In this chart review, we explore the indications for surgery, the principles of resection, as well as the pre-, intra-, and postoperative considerations, focusing on the critical role of neuromonitoring and tumor mapping in preserving functioning nerve roots. Additionally, we underline the importance of regular surveillance imaging in NF1, which can facilitate the early identification of lesions likely to undergo malignant transformation. A retrospective chart review of PNST surgical outcomes at the National Institutes of Health (NIH) was conducted. We identified 29 NF1 patients who collectively underwent surgical resection of 62 lesions between July 2013 to July 2023. Tumors were classified as either PNST or malignant PNST. Clinical symptoms, tumor location, tumor volume, and MRI findings were all collected. Most tumors were resected from the head, neck, and upper torso area (50%). The vast majority represented benign PNST lesions (95%) while a small minority represented malignant PNST (MPNST) lesions (5%). Our complication rate was similar to others, the most common being post-operative hematoma (3/41, 7.3%) and transient weakness or numbness (6/41, 15%). Our analysis underscores the broader implications of these strategies for the management of all PNSTs, pointing towards a future where improved surgical techniques and medical therapy offer enhanced outcomes and quality of life for patients.

Seo, Hannah

Adherence to Recommended Eye Examination Intervals Based on Reported Concerns in Visual Health in Elderly Patients

Current guidelines recommend biannual eye examinations for elderly patients to screen for preventable vision issues; however, adherence to these recommendations remains low. While visual acuity and overall eye health decline naturally with age, the absence of regular screening increases rates of preventable causes of blindness including cataracts and glaucoma. This study evaluates how eye exam frequency correlates with vision-related quality of life in 50 adults aged 55 or above surveyed via phone assisted by Project FRONTIER using the Visual Functioning Questionnaire-25 (VFQ-25). Additional survey questions gather data on demographics, knowledge of guidelines, and ocular conditions. Participants are stratified into four cohorts based on VFQ-25 score and exam frequency. The subgroups with low scores and below-average attendance, along with high scorers with below-average attendance, will inform tailored plans. The evaluation of the relationship between vision-related quality of life and eye exam frequency aids in identifying barriers among rural elderly and informing interventions for increasing eye exam frequency. This research aims to enhance comprehension of cognitive aging in rural communities, offering insights for future interventions to improve health accessibility to rural populations. Future research will analyze rural patients' eye exam outcomes alongside general health exams.