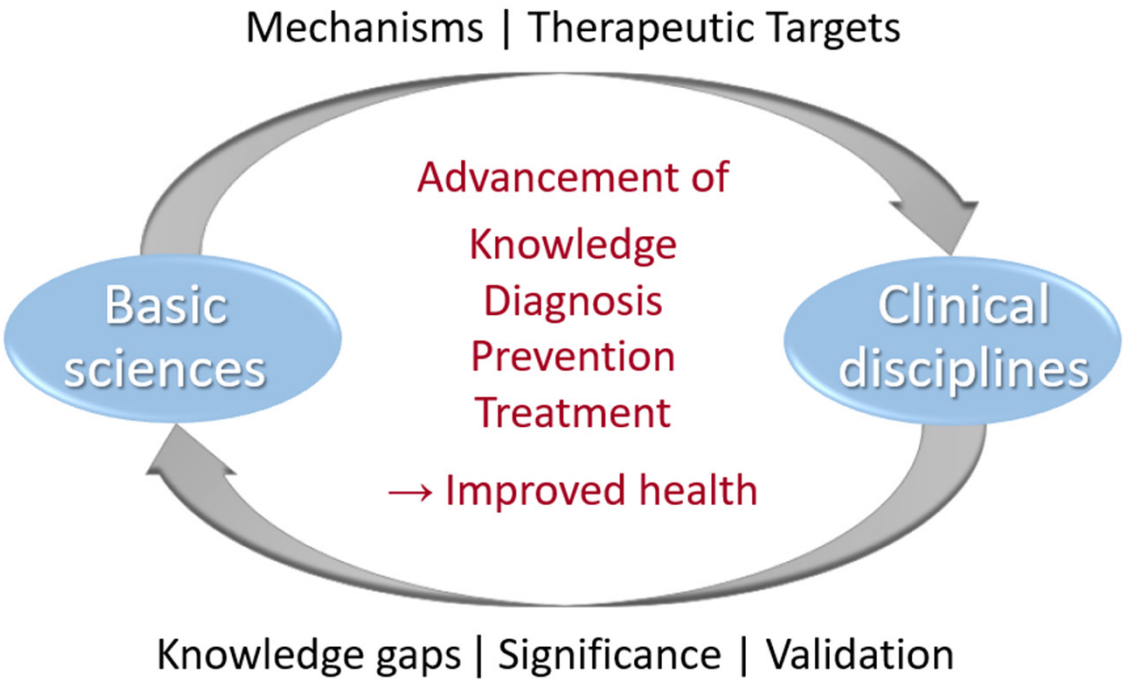
TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER

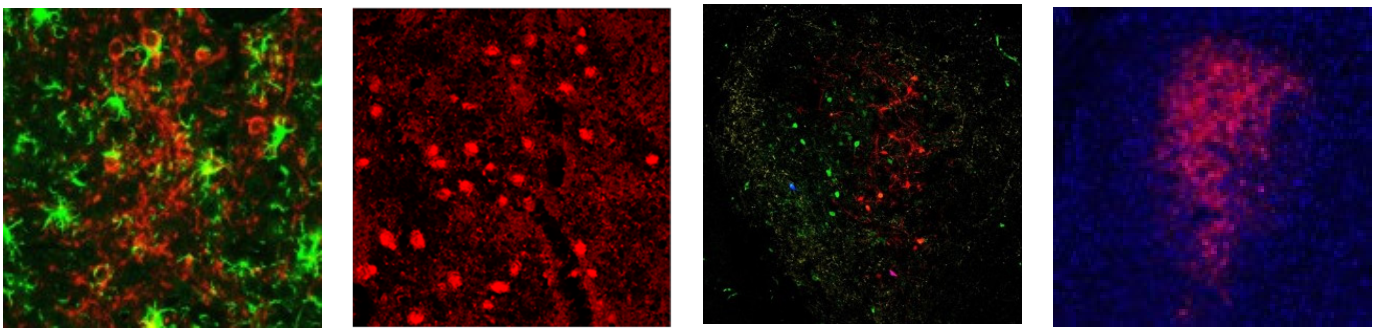
Center of Excellence for Translational Neuroscience and Therapeutics (CTNT)
and Garrison Institute on Aging (GIA)

5th Annual Research Symposium

Wednesday, May 5, 2021

Aging-Related Health Issues and Alzheimer's Disease





Department of Pharmacology and Neuroscience 3601 4th Street | Stop 6592 | Lubbock, Texas 79430

TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER™

Aging-Related Health Issues and Alzheimer's Disease

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

Virtual Event - May 5th, 2021

Zoom Link: https://ttuhscgsbs.zoom.us/j/94479461014

Opening Remarks • 11:30 AM

Min Kang, PharmD – Interim Senior Vice President for Research, Professor, Pediatrics, TTUHSC

Volker Neugebauer, MD, PhD - Director, CTNT, Professor and Chair, Pharmacology and Neuroscience, Executive Director and Chief Scientific Officer, GIA, TTUHSC

Thomas Tenner, PhD - Professor, Department of Medical Education, TTUHSC

Distinguished Keynote Speaker and ADK Lecturer • 12:00 PM

"Progress and opportunities towards advancing the National Plan to Address AD/ADRD by 2025"

Eliezer Masliah, MD

Director, Division of Neuroscience (DN)
National Institute on Aging, National Institutes of Health

Questions and Answers Session with Keynote Speaker and ADK Lecturer • 1:00 PM

CTNT Collaborative Research Presentations • 1:30 PM – 3:00 PM

Maria Manczak, PhD – Research Assistant Professor, Neurology, Garrison Institute on Aging, TTUHSC
"Mitochondrial dysfunction and Mitophagy in Tau -pathology of Alzheimer's Disease"

Gabriela Ashworth, PhD – Research Assistant Professor, Pharmacology and Neuroscience, TTUHSC
"Biopsychosocial Predictors of Mild Cognitive Impairment, the Precursor to Alzheimer's Disease and Other Dementias: A Project FRONTIER Study"

Andrey L. Karamyshev, PhD – Assistant Professor, Cell Biology and Biochemistry, TTUHSC
"Deciphering molecular mechanisms of neurodegenerative disease"

Poster Session • 3:15 PM – 4:45 PM

Morning Session • 10:00 AM

Keynote Speaker and ADK Lecturer with CTNT Steering Committee, GIA Members and Collaborators

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TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER

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

April 26, 2021

Welcome to the *Fifth Annual Symposium of the Center of Excellence for Translational Neuroscience and Therapeutics (CTNT).* The Center continues to bring together basic scientists and clinicians to stimulate scholarly activities, facilitate collaborations, and generate translational research projects. As a result of our collaborative efforts, CTNT has teamed up with the *Garrison Institute on Aging* to host this year's annual symposium focused on aging-related health issues and neurodegenerative disorders such as Alzheimer's disease.

Our collaborative and innovative efforts to bridge basic science and clinical entities in areas such as chronic pain, substance/alcohol use disorders, neurodegenerative diseases, and other neurological and psychiatric comorbidities could not have been accomplished without the dedication and support from Dr. Steven Berk, Dean of the School of Medicine and Executive Vice President for Clinical Affairs, and Dr. Leslie Shen, Associate Dean for Research, School of Medicine. We also value the support of research activities at TTUHSC by the Office of Research headed by Dr. Min Kang, Interim Senior Vice President for Research. We would like to thank Dr. Lori Rice-Spearman as former Provost and current President of TTUHSC and Dr. Michael Evans in his role as Interim Provost for their care and support of the Garrison Institute on Aging (GIA). The GIA seeks to serve as the central hub to promote healthy aging and advance knowledge about aging-related health issues and neurodegenerative diseases through collaborative initiatives in research, education and community outreach.

Necessitated by the COVID-19 pandemic, this year's annual symposium is a virtual event without the typical interactions of faculty, staff and trainees at this meeting. Nevertheless, we hope that the key note lecture, translational research presentations by CTNT-GIA teams, and posters by trainees in basic science and clinical disciplines will help to inform about CTNT and GIA and stimulate innovative collaborative efforts.

It is a great pleasure to welcome this year's *Key Note Speaker*, Dr. Eliezer Masliah, Director of the Division of Neuroscience at the National Institute on Aging. Dr. Masliah has kindly agreed to share with us advances, goals and strategies in Alzheimer's disease and related dementias in his lecture and in meetings with basic science and clinical CTNT and GIA team members.

A special thank-you goes to our CTNT Coordinator, Tiffany Denton, who worked closely with Dr. Josee Guindon, CTNT Steering Committee Member and GIA Research Collaborator, for creating the program and organizing the event. We thank our CTNT-GIA speakers, Drs. Maria Manczak, Gabriela Ashworth and Andrey Karamyshev, for sharing information about their research. And we are very grateful to our colleagues who generously agreed to serve as judges for the poster session.

Thank you for your interest and participation in our activities!

Volker Neugebauer, M.D., Ph.D.

Chair, Department of Pharmacology and Neuroscience
Director, Center of Excellence for Translational Neuroscience and Therapeutics
Executive Director and Chief Scientific Officer of the Garrison Institute on Aging

Acknowledgements

Steering Committee

- Susan Bergeson, Ph.D., Professor, Dept. of Cell Biology and Biochemistry, Director of Biotechnology, Lubbock campus, Associate Dean, GSBS, Editor In Chief, Alcoholism Treatment Quarterly, TTUHSC
- Vadivel Ganapathy, Ph.D., Professor and Chair, Dept. of Cell Biology and Biochemistry, TTUHSC
- Josee Guindon, DVM, Ph.D., Associate Professor, Dept. of Pharmacology & Neuroscience, TTUHSC
- George Henderson, Ph.D., Professor, Dept. of Pharmacology & Neuroscience, TTUHSC
- Michael O'Boyle, Ph.D., Professor, Dept. of Human Development & Family Studies, Associate Dean for Research, College of Human Sciences, TTU
- Leslie Shen, PhD, Professor, Dept. of Pathology, TTUHSC

Organizing Committee

- Tiffany Denton, CTNT Coordinator
- Josee Guindon, Associate Professor

Institutional Support

- Steven L. Berk, M.D., Dean, School of Medicine
- Leslie Shen, PhD, Associate Dean for Research, School of Medicine
- Min H. Kang, Pharm.D., Interim Senior Vice President for Research and Innovation
- TTUHSC President's Office (Lori Rice-Spearman, Ph.D.)
- TTUHSC Provost's Office (Michael Evans, Ph.D., R.N., FAAN, and Darrin D'Agostino, D.O., MPH, MBA)
- Garrison Family Foundation

CTNT Factsheet

The Center of Excellence for Translational Neuroscience and Therapeutics (CTNT) serves 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 and neuropsychiatric disorders for the development of novel and improved diagnostic and therapeutic tools and strategies (https://www.ttuhsc.edu/centers-institutes/translational-neuroscience-therapeutics).

Founded in 2015 and based in the Department of Pharmacology and Neuroscience, School of Medicine, TTUHSC, our Center has grown to 41 members from 17 different departments or institutes at TTUHSC and TTU, including 22 faculty doing basic preclinical research in 9 departments and 13 faculty working with patients or human subjects in 9 departments (https://www.ttuhsc.edu/centers-institutes/translational-neuroscience-therapeutics/leadership-members.aspx).

CTNT provides the expertise and infrastructure for multidisciplinary translational research for translational research from molecular to systems levels and to clinical disciplines. Mechanisms of support include the Annual Symposium, CTNT Research Meetings and Grant Development Program (Translational Research Club), the Translational Neuroscience and Pharmacology Lecture Series, Seed Funds for collaborative translational research and scholarly activity by teams of basic science and clinical faculty, and shared facilities (https://www.ttuhsc.edu/centers-institutes/translational-neuroscience-therapeutics/research-support.aspx).

CTNT support and core facilities are available for innovative collaborative research projects by teams of basic scientists and clinicians to generate translational scholarly activities and external funding to support the mission of the Center and TTUHSC.

Accomplishments (2020)

Publications by CTNT members considered by the author(s) as related to CTNT activities:
108 (nearly 30% co-authored by several CTNT members)

Presentations by CTNT members:
53 invited talks

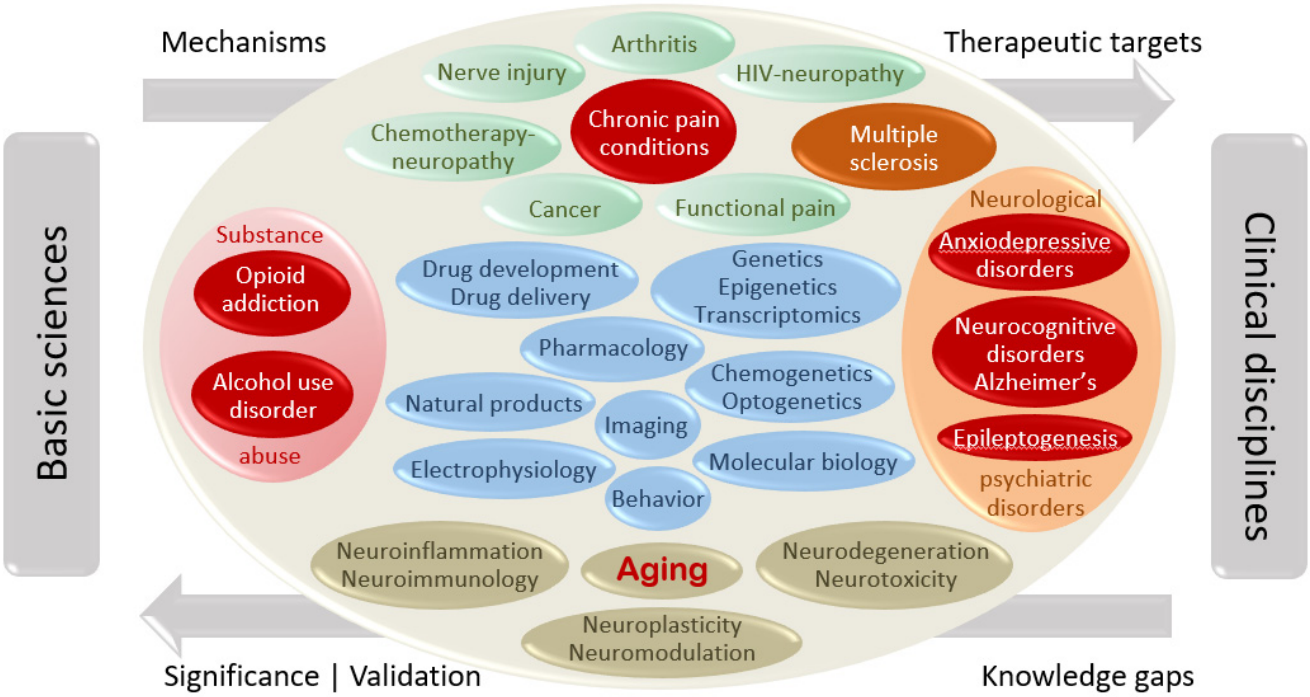
Seed funds awarded for collaborative basic science-clinical research projects proposed by CTNT members: 3 in 2020 (13 since 2015)

Grant applications by CTNT members related to CTNT activities (research club presentations, translational research funds, and other collaborative interactions):
39 (13 NIH, 1 USDA) grants in 2020

Current funding of CTNT members:
34 grants for a total of $22,121,182

Patents:
1 international patent published, several US patents submitted

Collaborative Translational Research Areas – CTNT and GIA



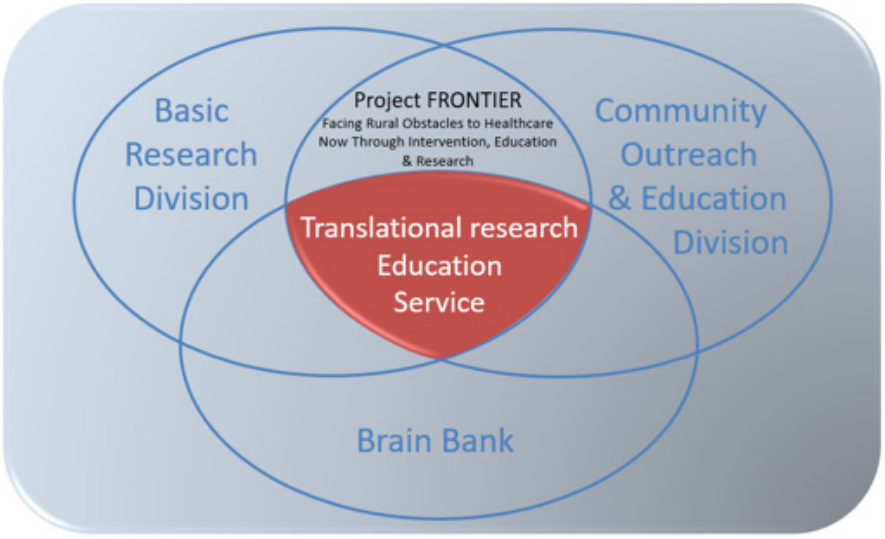
GIA Factsheet

Established in 1999 the Institute for Healthy Aging was remained the Garrison Institute on Aging (GIA) in 2005 in honor of Mildred and Shirley L. Garrison. The GIA promotes healthy aging through cutting-edge research in aging-related health issues, such as Alzheimer's disease, and through innovative educational and community outreach programs. The GIA team investigates causes of neurodegenerative diseases and educates the community on preventative medicine and challenges impacting the geriatric population.

The GIA vision is to serve as the central hub within TTUHSC to stimulate and accomplish collaborative initiatives in research, education and community outreach related to healthy aging and aging-related disorders. Through a combination of GIA based programs and collaborative initiatives with colleagues across TTUHSC, the GIA seeks to provide a unique platform for the creation and application of new knowledge about healthy aging through research, interdisciplinary education and community outreach efforts.

https://www.ttuhsc.edu/centers-institutes/garrison-aging/default.aspx

GIA Organization and Activities



- GIA Team (4 faculty, 10 staff members): Research laboratories (molecular biology, electrophysiology, behavior, imaging), Brain Bank, Community Outreach and Education Division
- Research Collaborators (6, TTUHSC Pharmacology and Neuroscience, Cell Biology and Biochemistry, Immunology, TTU Nutritional Sciences/Obesity Research Institute)
- Clinical Collaborators (4, TTUHSC Neurology, Family and Community Medicine, Nursing)
- Project Frontier Collaborators (2, TTUHSC Public Health)

Activities

- Research collaborations (6 GIA-based projects; also Seed Fund Program)
- Collaborative community-based participatory research (2 projects)
- Co-sponsor of the Translational Neuroscience and Pharmacology Lecture Series and Annual Symposium
- National Alzheimer's Disease Awareness Month
- Opioid Misuse Prevention in Older Adults Symposium (with Texas Health and Human Services/Aging Services Coordination)
- Healthy Aging Lecture series (monthly, at the Carillon Senior Living Center)
- Diabetes Self-Management and Chronic Disease Self-Management programs (6-week workshop; endorsed by CDC)
- Dementia Friendly Lubbock (with Mayor's Council, City of Lubbock; support and education for people with dementia, caregivers and families)
- Care Partner Academy (bi-weekly workshops to discuss common issues and resources)
- RSVP Retired and Senior Volunteer Program (established in 1979, under the umbrella of the Corporation for National and Community Service, CNCS, now AmeriCorps Seniors)

Eliezer Masliah, MD

Director, Division Neuroscience (DN)
National Institute on Aging
National Institutes of Health

Eliezer Masliah, M.D., joined the National Institute on Aging (NIA) as Director of the Division of Neuroscience in the summer of 2016. Before joining NIA he held joint appointments as tenured track Professor at the Departments of Neurosciences and Pathology and as Director of the Autopsy Service at UCSD-Medical Center. His laboratory investigates the mechanisms of synaptic damage in AD/ADRD and developed novel animal models of neurodegeneration, as well as new gene therapies, small molecules, and experimental immunotherapies for Alzheimer's disease and Parkinson's disease for which 4 are in phase II clinical trials. He is a prolific author with approximately 800 original research articles and dozens of patents. As Director of the Division of Neuroscience at NIA, Dr. Masliah is responsible for providing leadership on NIH-sponsored programs dedicated to better understanding brain aging and Alzheimer's disease. The division plays a key role in developing the implementation research milestones targeting the ultimate goal of the National Plan to Address Alzheimer's Disease, which calls for the nation to identify effective ways to treat or prevent Alzheimer's disease and related dementias by 2025. Dr. Masliah also participates in the NIA Intramural Research Program as an investigator in the Laboratory of Neurogenetics.

Maria Manczak, PhD
Research Assistant Professor, Department of Neurology
Garrison Institute on Aging
Texas Tech University Health Sciences Center

Dr. Maria Manczak received M.S. in biochemistry and Ph.D. in immunogenetic from Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Poland. She obtained postdoctoral training at Morgan School of Biological Sciences, University of Kentucky (USA). For over 15 years at Oregon Health Sciences University Dr. Manczak studied mechanisms of neurodegenerative disorders such as Alzheimer's disease (AD), Parkinson's disease, Huntington's disease (HD) and Multiple Sclerosis (MS). She published over 100 peer-reviewed papers in these areas. Her research has mainly focused on mitochondria dysfunction which is a major contributor to age-related processes and neurodegeneration diseases. Her major discovery is detection of β-amyloid inside the mitochondria and finding abnormal interaction between mitochondrial fission protein (Drp1) with β-amyloid and hyperphosphorylation Tau in Alzheimer's disease neurons. Dr. Maria Manczak joined TTUHSC in 2014 where her research area continues to be mitochondrial dysfunction and autophagy/mitophagy signaling in aging brain and Alzheimer's disease. Mechanistic studies of autophagy/mitophagy may not only improve our understanding of the mechanism of aging, neurodegeneration and other diseases but also can help to develop a novel therapeutic strategy for treatment. Her research is supported by NIH and GIA seed grants.

Dysfunctional Mitochondria and Mitophagy in Tau pathology of Alzheimer's disease.
Alzheimer's disease is the form of neurodegeneration in aging population that is characterized by memory loss and progressive cognitive decline. Senile plaques, neurofibrillary tangles, inflammation process, dysfunctional mitochondria and deficit in autophagy-mitophagy system are pathological hallmarks of Alzheimer's disease. Abnormal phosphorylated Tau is unable to bind to the microtubules, microtubules begin to disintegrate and block transport of important substances from one part of the neuron to another. Mitochondria plays a key role in energy production, calcium homeostasis, cell survival, and death. The accumulation of damaged mitochondria in AD brains contributes to aberrant synaptic structure and function, leading to loss of synapses, dendritic spines, synaptic proteins, and disruption of synaptic transmission. Mitophagy, an important process in cell survival and health as a global regulator of mitochondria homeostasis. Mitophagy is a specialized form of autophagy, critical for neuronal health because regulates the clearance of damaged and dysfunctional mitochondria.
Our study explored: 1. if overexpression of mitophagy proteins in mutant-Tau SH-SY5Y cells can promote induction of autophagy/mitophagy process? 2. If overexpression of mitophagy proteins can improve mitochondrial function? 3. If overexpression of mitophagy proteins can decrease the level of hyperphosphorylated Tau protein. We overexpressed mitophagy proteins, Pink1 (serine/threonine kinase), Parkin (E3 ligase) and Pink1, Parkin together in the human neuroblastoma cells (SH-SY5Y) transfected with the human normal-Tau and human (P301L) mutant Tau. After overexpression of mitophagy proteins we determined expression of Tau gene and level of hyperphosphorylated Tau protein. We examined the function of mitochondria by measured energy production (ATP) and ROS production by determined hydrogen peroxide (H_2O_2) and lipid peroxidation level. We investigated the autophagy/mitophagy process by determined expression of mitophagy, mitophagy receptors, autophagy adaptors and autophagosome receptor genes expression.

Gabriela Ashworth, PhD
Research Assistant Professor, Pharmacology and Neuroscience
Co-Director, Project Frontier
Texas Tech University Health Sciences Center

Dr. Gabriela Ashworth is a faculty member in the Department of Pharmacology and Neuroscience and the Garrison Institute on Aging at the Texas Tech University Health Sciences Center. She holds a PhD in Public Health from the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill. She has been actively involved in healthy aging research and community outreach programs, and serves as Co-Principal Investigator of Project FRONTIER, a longitudinal cohort study collecting aging-related health data from rural West Texas communities to identify risk and protective factors of Alzheimer's disease and cognitive decline. Dr. Ashworth's work on human studies and interventions has so far resulted in 10 publications and numerous oral and poster presentations, and provides an important avenue for translational work in the Department and Institute. Moreover, she mentors several health professions students on their research projects. Dr. Ashworth has developed numerous grant applications that aim to improve healthy aging in Lubbock and West Texas. Importantly, she added a COVID-19 component to Project FRONTIER that will provide valuable information to guide disease management in rural settings. Lastly, her work to raise awareness about Alzheimer's Disease was featured in a Tech Doc piece in the Lubbock Avalanche Journal and in an interview with Mrs. Karin McCay on KCBD's HealthWise.

Biopsychosocial Predictors of Mild Cognitive Impairment, the Precursor to Alzheimer's Disease and Other Dementias: A Project FRONTIER Study

The etiologies of Alzheimer's disease and related dementias (ADRD) are multifaceted, complex, and not well understood. Few studies have explored the impact of biopsychosocial (biological-psychological-social) determinants on mild cognitive impairment (MCI), the precursor to ADRD, using large longitudinal cohorts. Even fewer studies have been conducted in rural settings with large Hispanic/Latino populations, though ADRD prevalence varies across urban vs. rural landscapes, and Hispanics/Latinos face elevated risks for developing ADRD compared to non-Hispanic Caucasians. Project FRONTIER (Facing Rural Obstacles to Healthcare Now Through Intervention, Education & Research) is an ongoing longitudinal cohort study on cognitive aging based in rural West Texas. Project FRONTIER enrolls residents, aged 40 and over, living in Cochran, Parmer, Hockley, and Bailey counties. Participants are followed every 3 years and complete an interview (survey), medical examination by a health care provider, neuropsychological and functional tests, and blood work. In this presentation, links between biopsychosocial factors and MCI from baseline to 3-year follow-up are examined. A better understanding of biopsychosocial factors that are associated with MCI could yield important knowledge for ADRD public health surveillance and prevention research.

Andrey L. Karmyshev, PhD
Assistant Professor, Cell Biology and Biochemistry
Texas Tech University Health Sciences Center

Dr. Andrey Karamyshev received PhD in biochemistry from the Russian Academy of Sciences. He obtained extensive postdoctoral training at the Institute of Medical Science, University of Tokyo (Japan), and at the Texas A&M University Health Sciences Center, then he studied protein misfolding disorders at the UT Southwestern Medical Center. Dr. Karamyshev joined TTUHSC in 2016. His research interests are connected with molecular mechanisms of neurodegenerative diseases, protein quality control, post-transcriptional regulation of gene expression, and protein folding/transport. Dr. Karamyshev is an author of more than forty publications, including papers in *Cell, Mol. Cell, Cell Rep., PNAS, NAR, JMC, JBC,* etc. His major accomplishment is a discovery of a novel pathway of translational regulation and protein quality control termed RAPP (Regulation of Aberrant Protein Production). This discovery was highlighted in *Nature Rev. Genet.* and *Trends Biochem. Sci.* Studies from the Dr. Karamyshev lab demonstrate that many human diseases are resulted from the involvement of the pathway. His research is supported by the CTNT, South Plain Foundation and the NIH.

Deciphering Molecular Mechanisms of Neurodegenerative Diseases

Neurodegenerative disorders are the biggest burden of the 21st century. With aging population in the developed countries the human and economic costs of the diseases are dramatically increasing every year. About 50 million people suffer from dementia worldwide, and more than 6 million Americans are affected by Alzheimer's Disease, 1 million by Parkinson's, and many suffer from other neurodegenerative disorders. Numerous neurodegenerative diseases are associated with accumulation of protein aggregates or change in expression of specific proteins. Alzheimer's, Parkinson's and Huntington's diseases, amyotrophic lateral sclerosis and others are caused by the aggregation of aberrant proteins. Some forms of Frontotemporal Dementia are associated with decreased expression of granulin. Connections between these processes and diseases are well documented. However, mechanisms are poorly understood. Our study is based on a novel concept that co-translational interactions of the proteins associated with neurodegenerative disorders play a crucial role in their biogenesis, and rearrangement of these interactions leads to protein misfolding or expression change and finally to a disease. In our research, we combine unique technologies, site-specific photo-crosslinking and iPINCH, with cell and molecular biology techniques and with a power of bioinformatics to identify interacting partners in normal conditions and in a disease state. The first set of partners identified include proteins involved in protein targeting, quality control and mRNA stability. The data suggest that these proteins may play a crucial role in protein biogenesis and in molecular basis of neurodegenerative diseases.

Round Table Attendees
CTNT Director and Steering Committee

Volker Neugebauer, M.D., Ph.D.
Professor and Chair,
Department of Pharmacology and Neuroscience
Executive Director and Chief Scientific Officer of the Garrison Institute on Aging
Director, Center of Excellence for Translational Neuroscience and Therapeutics (CTNT)
Giles McCrary Endowed Chair in Addiction Medicine
Mildred and Shirley L. Garrison Chair in Aging

Neuroplasticity in higher brain functions and dysfunctions related to clinically relevant conditions (e.g., chronic pain, anxio-depressive comorbidities, substance/alcohol use disorder, neurodegenerative diseases, epileptogenesis)

Vadivel Ganapathy, Ph.D.
Grover Murray Professor and Chair
Welch Endowed Chair in Biochemistry
Department of Cell Biology and Biochemistry
Center for of Excellence Translational Neuroscience and Therapeutics
Center for Membrane Protein Research

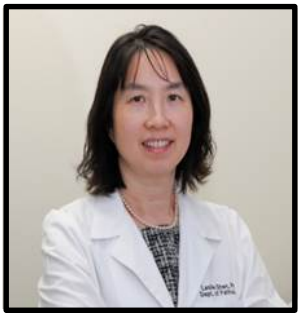
Amino acid transporters, GPCR for bacterial/endogenous metabolites, and ketogenesis in human diseases

Susan E. Bergeson, Ph.D.
Kayla Weitlauf Endowed Professor for Women's Health
Department of Cell Biology and Biochemistry
Director of Biotechnology
Center of Excellence for Translational Neuroscience and Therapeutics

Medications development for Alcohol Use Disorder

Josee Guindon, DVM, Ph.D.
Associate Professor
Department of Pharmacology and Neuroscience
Center of Excellence for Translational Neuroscience and Therapeutics
Garrison Institute on Aging

Sex differences and endo-cannabinoid modulation in acute, inflammatory, chronic and cancer pain models



Chwan-Li (Leslie) Shen, Ph.D.
Professor
Department of Pathology
Associate Dean for Research
Director, Center of Excellence for Integrative Health
Center of Excellence for Translational Neuroscience and Therapeutics

Mind-body exercise and bioactive compounds in chronic disease management

George Henderson, Ph.D.
Professor
Department of Pharmacology and Neuroscience
Center of Excellence for Translational Neuroscience and Therapeutics

Alcohol, environmental toxins, neurons, glia, apoptosis and oxidative stress

Round Table Attendees
GIA Research Collaborators

Diyya Burugu, M.S.
Research Scientist
Garrison Institute on Aging

Association of trans synaptic complex with neurodegenerative disorders

Gail A. Cornwall, Ph.D.
Professor
Department of Cell Biology and Biochemistry
Garrison Institute on Aging

Functional amyloids in the reproductive tract and brain

Andrey Karamyshev, Ph.D.
Assistant Professor
Department of Cell Biology and Biochemistry
Garrison Institute on Aging

Posttranscriptional regulation of gene expression, protein transport and molecular mechanisms of human diseases

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

Nutritional deficiencies in regulating hippocampal learning, excitation/inhibition balance, and oxidative stress in aging/Alzheimer

Maria Manczak, Ph.D.
Research Assistant Professor
Department of Neurology
Garrison Institute on Aging

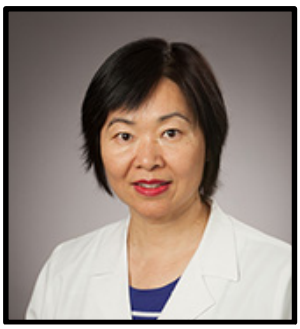
Dysfunction mitochondria and mitophagy impartment in aging and neurodegenerative disorders such Alzheimer's disease

Igor Ponomarev, Ph.D.
Associate Professor
Department of Pharmacology and Neuroscience
Center of Excellence for Translational Neuroscience and Therapeutics
Garrison Institute on Aging

Interplay between genetic, epigenetic and environmental causes in controlling brain gene expression and behavior in Alcohol Use Disorder (AUD)

Kevin Pruitt, Ph.D.
Associate Professor
Childers-Fralick Chair in Basic Cancer Research
Department of Immunology and Molecular Microbiology
Garrison Institute on Aging

Wnt signaling and epigenetics in models of disease



Xiangling Yin, M.S.
Senior Research Associate
Garrison Institute on Aging

In vivo and in vitro models of Alzheimer's and related neurodegenerative diseases

Round Table Attendees
GIA Community/Clinical Collaborators

Gabriela Ashworth, Ph.D.
Research Assistant Professor
Department of Pharmacology and Neuroscience
Garrison Institute on Aging

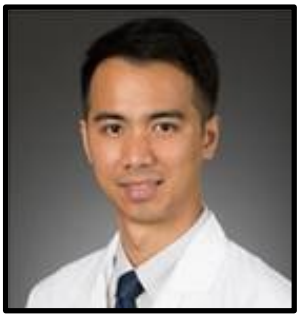
Risk and protective factors of Alzheimer's disease and other dementias; community-based health promotion for healthy aging

Annette Boles, M.S.
Director
Garrison Institute on Aging
Community Outreach and Education

Duke Appiah, Ph.D.
Assistant Professor
Department of Public Health
Garrison Institute on Aging

Etiology and prevention of chronic diseases, specifically cardiovascular disease, diabetes and obesity with emphasis on women, reproductive health, and, minority as well as underserved populations

John W. Culberson, M.D.
Associate Professor
Department of Family and Community Medicine
UMC Bernhard T. Mittemeyer, MD, Endowed Chair in Medical Excellence in Geriatric Medicine
Program Director, Geriatric Fellowship
Director, Garrison Institute on Aging
Clinical Geriatric Programs



Parunyou Julayanont, Ph.D.
Assistant Professor
Corinne Payne Wright Regent Endowed Chair in Alzheimer's Disease
Department of Neurology
Garrison Institute on Aging

Clinical behavioral neurology and neuropsychiatry of dementias and other neurologic disorders

Theresa Byrd, Ph.D.
Professor
Associate Dean and Chair
Julia Jones Matthews
Department of Public Health
Garrison Institute on Aging

Behavioral sciences and public health with a focus on cancer screening and prevention

Institutional

Darrin D'Agostino, D.O., MPH, MBA
Provost and Chief Academic Officer

Min H. Kang, Ph.D.
Professor
Interim Senior Vice President for Research
Department of Pediatrics

Tom Tenner, Ph.D.
Professor
Department of Medical Education
Department of Pharmacology and Neuroscience

Poster Judges

Susan Bergeson, PhD
Cell Biology and Biochemistry
TTUHSC, Lubbock

Michael Blanton, PhD
Pharmacology and Neuroscience
TTUHSC, Lubbock

Josee Guindon, DVM, PhD
Pharmacology and Neuroscience
TTUHSC, Lubbock

J. Josh Lawrence, PhD
Pharmacology and Neuroscience
TTUHSC, Lubbock

Volker Neugebauer, MD, PhD
Pharmacology and Neuroscience
TTUHSC, Lubbock

Michael O'Boyle, PhD
Human Development and Family Studies
TTU, Lubbock

Igor Ponomarev, PhD
Pharmacology and Neuroscience
TTUHSC, Lubbock

Leslie Shen, PhD, MS
Pathology
TTUHSC, Lubbock

Poster Presentation Times

1. Basic Science – Graduate/Undergraduate

Time	Presenter	Judges
3:15-3:30	Blanton, Henry	Dr. Susan Bergeson/ Dr. J. Josh Lawrence
3:30-3:45	Hernandez, Sarah M.	Dr. Susan Bergeson/ Dr. J. Josh Lawrence
3:45-4:00	Kisby, Brent R.	Dr. Susan Bergeson/ Dr. J. Josh Lawrence
4:00-4:15	Presto, Peyton	Dr. Susan Bergeson/ Dr. J. Josh Lawrence
4:15-4:30	Shahi, Sadisna	Dr. Susan Bergeson/ Dr. J. Josh Lawrence
4:30-4:45	Mazzitelli, Mariacristina	Dr. Susan Bergeson/ Dr. J. Josh Lawrence

2. Basic Science – Medical Student

Time	Presenter	Judges
3:15-3:30	Karen Casteneda	Dr. Michael Blanton/ Dr. Volker Neugebauer
3:30-3:45	Albin John	Dr. Michael Blanton/ Dr. Volker Neugebauer
3:45-4:00	Ray, Nandini	Dr. Michael Blanton/ Dr. Volker Neugebauer
4:00-4:15	Sheladia, Shyam	Dr. Michael Blanton/ Dr. Volker Neugebauer

3. Basic Science – Postgraduate

Time	Presenter	Judges
4:15-4:30	Castro-Piedra, Isabel	Dr. Michael Blanton/ Dr. Volker Neugebauer

Poster Presentation Times

4. Clincial – Graduate/Undergraduate

Time	Presenter	Judges
3:15-3:30	Driskill, Jackosn	Dr. Igor Ponomarev/Dr. Leslie Shen
3:30-3:45	Shahbazi, Siayash	Dr. Igor Ponomarev/Dr. Leslie Shen

5. Clinical – Medical Student

Time	Presenter	Judges
3:15-3:30	Jonathan Abrham	Dr. Josee Guindon/Dr. Michael O'Boyle
3:30-3:45	George, Asher	Dr. Josee Guindon/Dr. Michael O'Boyle
3:45-4:00	Holder, Katherine	Dr. Josee Guindon/Dr. Michael O'Boyle
4:00-4:15	Payberah, Daniel	Dr. Josee Guindon/Dr. Michael O'Boyle
4:15-4:30	Pourghead, Omhammed	Dr. Josee Guindon/Dr. Michael O'Boyle
4:30-4:45	Swinney, Seth	Dr. Josee Guindon/Dr. Michael O'Boyle

6. Clinical – Postgraduate

Time	Presenter	Judges
3:45-4:00	Sarangi, Ashish(1)	Dr. Igor Ponomarev/Dr. Leslie Shen
4:00-4:15	Sarangi, Ashish(2)	Dr. Igor Ponomarev/Dr. Leslie Shen

Abstracts

1. Basic Science – Graduate/Undergraduate

Blanton, Henry

The G protein coupled estrogen receptor agonist G1 antagonizes the anti-allodynic effects of the cannabinoid receptor agonist CP 55,940 in a cisplatin model of chemotheraphy-induced neuropathic pain using ovariectomized female mice.

Henry Blanton, Melissa Mchann, Josée Guindon
Department of Pharmacology and Neuroscience, TTUHSC, Lubbock

Among states with the legalized medical use of cannabis, pain relief is the most common reason for use among both men and women (Boehnke et al., 2019). Sex has consistently been demonstrated to be a contributing factor to both pain and response to analgesics, however, the impact of sex on cannabinoid pharmacology is still a relatively new field of study, especially in humans. Previous studies in rodent models have generally suggested that females may be more sensitive to cannabinoid-mediated analgesia than males and that this sensitivity may be mediated by female sex hormones, particularly estrogen (Blanton et al., 2021). This study sought to address the hypothesis that estrogen-mediated effects on cannabinoid actions may be mediated in part by the G-protein coupled estrogen receptor (GPER). To test this hypothesis C57BL6J female mice were ovariectomized and allowed to recover for thirty days prior to testing. A neuropathic pain state was induced through weekly delivery of the chemotherapeutic agent cisplatin, for a total of four injections. Pain hypersensitivity (allodynia) in the hind paws of the mice was evaluated through von Frey and acetone modalities of mechanical and cold allodynia. The anti-allodynic effects of a GPER agonist (G1) and a cannabinoid receptor agonist (CP 55,940) were evaluated alone, and in combination, for four weeks of daily administration to evaluate both the acute and chronic effects of these drugs. The cannabinoid receptor agonist CP 55,940 relieved mechanical and cold allodynia, but tolerance to this analgesic effect developed over the course of the experiment. Conversely, the GPER agonist G1 potentiated mechanical and cold allodynia when delivered alone, and antagonized the anti-allodynic effects of CP 55,940 when the two drugs were co-administered. These results suggest that in states of high estrogen, the analgesic effects of cannabis, or cannabinoids, may be diminished via activity at the G-protein coupled estrogen receptor (GPER).

Hernandez, Sarah M.

Regulation of alpha-Synuclein Biogenesis Through the RAPP Pathway

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Synucleinopathies are a group of neurodegenerative disorders that are characterized by the presence of intracellular inclusions known as Lewy bodies. These include Parkinson's disease (PD), Lewy body dementia, and Multiple System Atrophy. Lewy bodies are composed of aggregated protein alpha-Synuclein (aSyn). Understanding why aSyn is aggregating is a crucial step in developing preventative therapies for PD and other neurodegenerative disorders. Our hypothesis is that alterations of aSyn interacting partners during translation leads to its misfolding and aggregation, causing disease. In PD, these alterations in interacting partners can be due to a mutation in aSyn itself (familial PD) or by defects in the interacting partners (sporadic PD). aSyn

clinical mutations present in familial PD (A30P, E46K, H50Q, G51D, A53E, and A53T) are all present within N-terminus, the region of the protein where early co-translational interaction events take place. The major goal of this study is to identify possible interacting partners of aSyn during its translation. Site-specific photo-crosslinking experiments show that aSyn interacts with multiple factors during its synthesis on the ribosome. Using predictive examination through Ingenuity Pathway Analysis (IPA), we also demonstrate the existence of a complex network consisting of more than a hundred potential aSyn interacting partners. They include chaperones, chaperonins, modifying factors, and others. To experimentally test the involvement of some of these factors, as well as components of the RAPP protein quality control pathway, in aSyn biogenesis, we selectively knocked down these proteins in cultured human cells. The data demonstrate that members of the RAPP pathway, SRP54 and AGO2, are involved in the regulation of aSyn expression.
In this project we focused on studying NMDAR-mediated synaptic transmission and intracellular signaling cascades that are altered by stress. One such molecule is the brain-derived neurotrophic factor (or BDNF), known to be involved in cell growth and proliferation, and synaptic plasticity. Using an animal model of chronic stress in rodents (21-day chronic stress) we studied changes occurring in the hippocampus of stressed mice using a combination of behavioral examination, in vitro electrophysiology and virus-mediated gene manipulation. Our results show that field recordings from CA3 region in the hippocampus decrease in response to multiple pulse stimulation in slices from stressed mice, while NMDAR-isolated responses showed the opposite effect, increasing in stressed mice. Furthermore, our behavioral studies showed that mice subjected to stress spent significant more time in the periphery of the open field and the closed arms of the elevated plus maze, indicating a heightened level of anxiety. Similarly, mice chronically stressed moved less in the forced swimming test, showing depressed-like behaviors. Finally, using a virus-mediated strategy we probed the role of hippocampal BDNF on behavior. Our results show that reducing BDNF recapitulates some of the behavioral effects of stress.
In summary, our results link alterations in excitatory synaptic transmission in the CA3 area of the hippocampus with specific behavioral deficits and BDNF reduction. Understanding the physiological mechanisms affected by stressful conditions could provide important clues of possible therapeutic avenues. Considering that stress is one of the leading causes of neuropsychiatric disorders, elucidating its mechanisms of action could be extremely beneficial for the general population and specific groups that may be more vulnerable.

Kisby, Brent R.
Effects of Repeated Administration of the TLR3 Agonist, Poly(I:C) on Alcohol Consumption and Brain Expression of Immune Related Genes in Male and Female Mice with Mixed Genetic Background
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Excessive alcohol (ethanol) consumption is a hallmark of alcohol use disorder (AUD). Innate immune activation by repeated injections of the TLR3 agonist, Poly(I:C) (PIC) results in escalation of alcohol consumption in C57BL/6J (B6J) male mice and a decrease or no change in consumption of female mice. These behavioral responses are associated with differences in the time course of immune gene expression in males and females. The effects of sex and genotype on the immune modulation of alcohol intake are not well understood. Here, we tested the effects of innate immune activation by PIC on ethanol consumption and brain expression of immune genes in male and female mice with mixed genetic background.
Female *Camk2a-Cre* (https://www.jax.org/strain/005359) and male *Sun1-sfGFP-Myc* (https://www.jax.org/strain/021039) mice were crossed in house to produce F1 animals. This cross on a mixed genetic background contains a GFP tag expressed in a cell type-specific manner and has been used to study cellular responses to perturbations. Male and female F1 animals were randomly assigned into either saline or

10 mg/kg PIC injection group and allowed 24-hour free access to 15% ethanol and water (2-bottle choice) every other day. Mice were injected with either saline or PIC every 4 days for a total of 13 injections. 3, 6, 24 or 48 hours after the 13th injection, animals were sacrificed, prefrontal cortex (PFC) was dissected, and total RNA extracted and analyzed using qPCR for 9 immune-related genes (*Ccl5, Ccl2, Il6, Il1b, Myd88, Tnf, Ticam1, Tlr3,* and *Tlr4*).
Female F1 mice showed a moderate decrease in alcohol consumption after repeated PIC injections (ANOVA main effect of Treatment p=0.04), and there was a similar trend in the males (ANOVA main effect of Treatment p=0.16). All genes except for *Ticam1* were up-regulated after the last PIC injection at the 3 and/or 6 hr time point, and expression of all genes except for *Ccl5* returned to the baseline at the 48 hr time point. There was no main effect of Sex and no Sex x Treatment interaction for any gene. Taken together with published data, these findings suggest that immune modulation of alcohol consumption in mice is strongly influenced by sex and genotype and that the sex- and genotype-specific effects may depend on the time course of immune activation. Funded by AA027096

Presto, Peyton

Sex differences in brain neuroimmune signaling related to pain: Molecular and behavioral outcomes

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Chronic pain is a prevalent national healthcare issue, yet many knowledge gaps exist in regard to brain mechanisms of pain, particularly neuroimmune signaling and sexual dimorphisms. Although alterations in neuroimmune signaling have been linked to chronic pain at the spinal cord level, including strong evidence for sex-specific immune involvement, the molecular mechanisms of neuroimmune responses in the brain in a pathological pain state are poorly understood. The amygdala is a limbic brain center that plays a key role in the emotional-affective dimensions of pain and pain modulation. The main goal of the present study was to determine the effects of exogenously induced neuroimmune response within the amygdala on pain-related behaviors and mRNA expression levels. Polyinosinic-polycytidilic acid (poly I:C) is a potent immunostimulant (toll-like receptor TLR3 agonist) and known viral mimetic. Here we tested the hypothesis that direct poly I:C administration into the amygdala will induce a neuroimmune response that causes significant and potentially sexually dimorphic behavioral and molecular changes. The rationale was that comparison of the poly I:C effects with those of a neuropathic pain model would provide insight into the role of neuroimmune signaling in amygdala pain mechanisms, as similar patterns may suggest involvement of this neuroimmune signaling pathway in neuropathic pain. Identification of brain mechanisms of pain will aid in the development of sex-specific therapeutic strategies of chronic neuropathic pain relief.

Shahi, Sadisna

Urea-based dopamine transporter inhibitors as a therapeutic option for neurodegenerative diseases

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[7]Multiple Sclerosis and Demyelinating Diseases Clinic; Department of Neurology, Texas Tech University Health Science Center.
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Neurodegenerative diseases, such as amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's, Alzheimer's, and Huntington's diseases, are characterized by the loss of neurons' structure and function or by neuronal death in the advanced pathological stage. One of the underlying reasons is an imbalance of dopamine in the CNS, a neurotransmitter responsible for mood, movement, behavior, cognition, memory, and attention. Further, it was proposed that restoration of dopamine levels may inhibit neuroinflammation of the brain tissue. Thus, restoration of dopamine levels in the CNS can provide an advantage in treating certain neurodegenerative disorders.
Recently, our lab has reported a novel class of urea analogs capable of inhibiting Dopamine Active Transporter (DAT) with a high degree of selectivity and potency. To evaluate DAT inhibitors' effect on CNS-induced inflammation, we have tested our lead compound with the optimal pharmacokinetic profile in the experimental autoimmune encephalomyelitis (EAE) mouse model mimicking clinical signs of multiple sclerosis. We observed that this compound has statistically significant anti-inflammatory effects and attenuates motor deficits and pain behaviors. Here we present the project's current status, providing more insights into the structural features of the molecule responsible for the observed activity.

Mazzitelli, Mariacristina
Optogenetic stimulation of CRF neurons in the amygdala modulates pain- related behaviors in neuropathic pain model
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The amygdala is a limbic area critically involved in pain-related emotional-affective disorders and pain modulation. The central nucleus of amygdala (CeA) serves as a major output nucleus of the amygdala. CeA activity is increased and mechanistically linked to pain-related behaviors in different pain conditions. One of the CeA cell types contain corticotropin releasing factor (CRF). The CRF system is critically involved in the modulation of pain and affective disorders. Hence, we focused on the effects of optogenetic activation or silencing of CeA-CRF neurons on pain related behaviors under normal and neuropathic pain conditions. Anxiety-like behavior (elevated-plus maze), emotional responses (audible and ultrasonic vocalizations evoked by innocuous and noxious stimuli of the hind paw) and mechanical withdrawal thresholds were measured in adult normal and neuropathic rats (4 weeks after spinal nerve ligation, SNL). For optogenetic activation or silencing of CRF neurons, a Cre-inducible viral vector (DIO-AAV) encoding light sensitive molecules (channel rhodopsin 2, ChR2 or enhanced Natronomonas pharaonis halorhodopsin, eNpHR3.0) was injected stereotaxically into the right CeA of transgenic Crh-Cre rats. Animals were allowed to recover for channel expression. For wireless optical stimulation of ChR2 or eNpHR3.0 expressing CRF-CeA neurons, an LED optic fiber delivering blue (473 nm) or yellow (590 nm) light was stereotaxically implanted into the right CeA.

Optical activation of CeA-CRF neurons increased vocalizations and mechanical sensitivity and induced anxiety like-behaviors under normal conditions, whereas optical silencing of CeA-CRF neurons decreased vocalizations and ameliorated anxiety-like behaviors, but had no effects on withdrawal thresholds, in the neuropathic pain model.
These findings provide evidence for an important role of CeA-CRF neurons in the formation and modulation of pain-related behaviors.

2. Basic Science – Medical Student

Casteneda, Karen

All-trans retinoic acid deficiency in Alzheimer's disease: evidence from human transcriptomics and a novel mouse model

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TTUHSC School of Medicine[1]

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Excessive activity in the hippocampus is associated with impaired novelty detection in early stages of Alzheimer's disease (AD). Causal upstream signaling mechanisms occurring within hippocampal circuits early in AD pathogenesis remain poorly understood. The Mitochondrial Free Radical Theory of Aging proposes that mitochondria, through the production of excess reactive oxygen species (ROS), cause oxidative damage to proteins, lipids, and DNA — a process termed oxidative stress (OS). Antioxidants (AOs) counteract this process by scavenging excess ROS, thereby preventing OS. The antioxidant all-trans retinoic acid (ATRA), the active form of retinol, plays a dual role as a ROS scavenger and transcriptional regulator of synaptic/neuronal proteins via its function as a retinoic acid receptor (RAR) agonist. Recent evidence from rodents has demonstrated an age-dependent depletion in hippocampal ATRA levels due to liver dysfunction. We propose that ATRA depletion in the hippocampus is an early event in AD pathogenesis, leading to excess ROS-induced damage, mitochondrial dysfunction, and reduced occupancy of RARs, accelerating amyloidosis, network hyperexcitability, and cognitive dysfunction. To investigate whether ATRA deficiency occurs in the hippocampus of human AD, we performed a secondary analysis of human hippocampal transcriptomic data from both AD and control brains. We found that genes involved in ATRA synthesis, catabolism, and transport (ADLH1A3, CYP26A1, CYP26B1, RBP1, and RBP4) were downregulated, consistent with ATRA deficiency. Interestingly, RAR co-repressors that inhibit RAR-dependent transcription (NCOR1, PML, ZBTB16, and TNIP1) were significantly upregulated, consistent with disruption of ATRA/RAR binding to retinoic acid response elements (RAREs) in AD. ATRA-responsive genes present at hippocampal synapses were also downregulated (NGRN, GAP43, and CALB1). Finally, changes in ATRA-responsive genes were accompanied by the upregulation of the ROS sensors Nrf1/Nrf2 (NFE2L1/NFE2L2), consistent with antioxidant depletion. Collectively, this human hippocampal transcriptomic data reveals a number of genes essential for ATRA synthesis, transport, RARE binding, and AO activity to be dysregulated in the hippocampus of post-mortem AD brains. The dual function of ATRA in minimizing ROS and avoiding Aβ accumulation is reduced, resulting in mild cognitive impairment (MCI) and the acceleration of AD pathogenesis. In the J20 AD mouse model crossed with a somatostatin-CRE:tdTomato reporter mouse, we tested the hypothesis that ATRA administration delays or prevents AD-related behavioral, circuit, and transcriptional abnormalities in the hippocampal dentate gyrus (DG; 3-9 mice per group, 4.8 ± 0.8 months of age, M/F sexes, 31 mice total). We administered ATRA intraperitoneally (IP; RA, 20 mg/kg) or vehicle (corn oil) 3 x/week for 8 weeks, followed by behavioral testing in the Y-maze and open

field maze (OFM). Consistent with the hyperactivity phenotype of J20 mice, vehicle-treated (VT) mice traveled a greater distance compared to WT mice (U = 5.000, p = 0.009). In contrast, ATRA-treated (RT) AD and WT mice did not vary in their overall distance traveled, indicative of a normalization of phenotype (U = 16.000, p = 0.727). In the OFM, a similar pattern of results was observed. One week after the last behavioral test, each mouse brain was cut into separate hemispheres to enable correlative histological and molecular analyses. Through tdT visualization, we found that DG SOM microcircuits were aberrantly targeted to the DG inner molecular layer of $J20^{+/-}$ AD but not $J20^{-/-}$ WT mice. However, treatment with ATRA prevented this aberrant SOM circuit from forming in 6/6 males but not in 3/3 female mice. Finally, we conducted a transcriptomic RNA-Seq analysis from DG tissue of WT and J20 mice. Pairwise comparison of VT WT and VT AD groups indicated that many molecular pathways were disturbed, including Synaptogenesis, Protein Kinase A, and Calcium Signaling. Pairwise comparison of ATRA-treated WT and AD groups revealed that ATRA administration partly normalized these signaling pathways. Therefore, chronic treatment with ATRA normalized behavior, prevented the formation of aberrant inhibitory circuits in the DG, and normalized a number of molecular pathways. Collectively, these observations support the hypothesis that ATRA deficiency occurs in AD and ATRA replacement therapy can mitigate AD-related behavioral, circuit, and molecular abnormalities.

John, Albin

Can healthy lifestyle reduce disease progression of Alzheimer's during a global pandemic of COVID-19

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The novel coronavirus disease 2019 (COVID-19) has pushed the medical system to its breaking point. While the virus does not discriminate, the elderly and those with comorbidities, including hypertension severe obesity, diabetes mellitus, coronary disease, pneumonia and dementia, are at a greater risk for adverse outcomes due to COVID-19. While many people navigate their new normal, the question of what the long-lasting effects of the pandemic may be, lingers. To investigate how vulnerable populations are affected by the pandemic, we focused on Alzheimer's disease, a vector to understanding how the virus has impacted AD progression and risk. By assessing the effect of COVID-19 on AD patients, we explore genetics, metabolism, and lifestyle factors in both COVID-19 and Alzheimer's disease that can work synergistically to precipitate adverse outcomes. This article also discusses how age-related conditions and/or comorbidities susceptible to COVID-19. We also discuss possible healthy lifestyle factors reduce and/or combat COVID-19 now and in the future.

Ray, Nandini

Structural and Physiological Changes of the Aging Kidney: A Focus on COVID-19

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Globally, individuals aged 65 and older are part of the fastest expanding population demographic, and as a result, a greater number of older patients are receiving diagnoses of impaired renal function. The purpose of this study is to summarize recent findings of the structural and functional differences between the normal and aging kidney, exhibit evolutionary changes in kidney structure and function, and demonstrate the role of aging in conditions such as diabetes, chronic kidney disease, and hypertension. Recent studies have shown that age-related loss of kidney function is associated with a host of hemodynamic, structural, and physiologic changes. Some of these changes include hemodynamic changes such as decreases in renal blood flow, glomerular filtration rate, and afferent arteriolar resistance; structural changes such as decreased renal mass, hyalinosis of arterial walls, increased sclerotic glomeruli, and tubulointerstitial fibrosis; and physiologic changes such as enhanced responses to vasoconstriction and impaired responses to vasodilation. Many of these age-related changes affect the ability of the kidney to withstand and recover from injury and may predispose individuals in these populations to more progressive renal diseases. Several studies conducted around the world at the height of the COVID-19 pandemic have demonstrated parallels in the age demographic being most affected, and these individuals have a greater risk of infection, severe complications, and even death. As a result, the direct and socioeconomic effects of the pandemic may potentially increase the prevalence and contribute to a poor prognosis for those with kidney disease. The purpose of our study is to discuss known structural and functional changes associated with the aging kidney and their role in chronic conditions along with their impact on SARS-CoV-2. We also discuss the potential therapeutic strategies to treat aged individuals with kidney health issues and how the impact of a healthy lifestyle, diet, and exercise can improve health conditions with aged kidneys

Sheladia, Shyam

Age-Related Chronic Diseases and Alzheimer's Disease in Texas: A Hispanic Focused Study

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The emergence of age-related chronic diseases in the United States has led to the direct increase of Alzheimer's disease (AD) prevalence, which ultimately contributes to the development of dementia. Age-related chronic diseases such as cardiovascular disease, high cholesterol, diabetes, and kidney disease contribute to the advancement of dementia. Furthermore, unmodifiable risk factors such as advancing age and genetics as well as modifiable risk factors such as socioeconomic status, educational attainment, exercise, diet, and access to healthcare further contribute to the development of dementia. The purpose of our study is to determine the molecular links between age-related chronic diseases/risk factors and cognitive decline within the Hispanic population of Texas and rural West Texas.
We collected data associated with the prevalence of AD within the Hispanic population of the United States, Texas, and rural West Texas. We also collected data related to the prevalence of age-related chronic diseases, unmodifiable risk factors, and modifiable risk factors which lead to the development of AD in the Hispanic population. The data collected was previously published data from reputable sources such as the Alzheimer's Association, American Heart Association, National Kidney Foundation, U.S. Department of Health and Human

Services, Centers for Disease Control and Prevention, National Institutes of Health, United States Census Bureau, and Texas Demographic Center.
Our analysis showed that Hispanics face the greatest burden of dementia due to the increase in the prevalence of overall population age, predisposing genetics, age-related chronic diseases, low socioeconomic status, low educational attainment, as well as poor lifestyle choices. Additionally, Hispanics living within rural West Texas face the added challenge of finding appropriate healthcare services.
Although it is difficult to provide a solution to certain factors such as socioeconomic status, steps can be taken to provide education to the Hispanic population regarding lifestyle changes that can be made in order to significantly reduce the risk of developing age-related chronic diseases which lead to the development of AD. Furthermore, a sincere effort by the Texas government and major hospital systems should be made to provide adequate healthcare resources to the counties of rural West Texas.

3. Basic Science – Postgraduate

Castro-Piedras, Isabel
Role of aberrant Wnt/Ca^{2+} signaling in Alzheimer's disease and cancer
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Cancer and Alzheimer's disease (AD) are among the leading causes of death in the United States. Low-cost prophylactic modifications that concurrently act to mitigate both cancer and AD risk could save billions of dollars per year in health care costs, boost quality of life, and reduce premature death. Increasing evidence indicates that diet is a modifiable risk factor for both cancer and AD. Nutrient-poor diets elevate both cancer and AD risk. By contrast, the nutrient-rich Mediterranean diet (MeDi) can mitigate both cancer and AD risk, suggesting common protective signaling mechanisms. One distinguishing feature of MeDi is the pairing of vegetables and oils, collectively enhancing the bioavailability of lipid-soluble vitamins such as Vitamin A. Consistent with this idea, obesity, which causes sequestration of lipid-soluble vitamins in adipose tissue, increases AD and cancer risk, presumably through oxidative stress/antioxidant depletion mechanisms. Furthermore, our own preclinical data point to overlapping molecular mechanisms between AD and cancer. We recently performed a transcriptomic screen of total RNA from hippocampal tissue in the J20 AD mouse model. Surprisingly, Ingenuity Pathway Analysis (IPA) software revealed cancer-related pathways and genes to be the most significantly dysregulated in mouse AD tissue. A secondary analysis of published RNA-seq human hippocampal AD tissue also revealed a similar dysregulation of cancer-related pathways and genes, further corroborating overlapping molecular mechanisms of cancer and AD. Wnt signaling is one pathway that is dysregulated in both human AD and AD mouse models. Aberrant Wnt signaling has been implicated in age- and AD-related synaptic dysfunction. Six genes in the Wnt/Ca^{2+} signaling pathway (*ATF4*, *DVL2*, *FZD8*, *PLCB1*, *PLCL1*, and *PPP3CA*) were found to be significantly dysregulated in the J20 AD mouse model (p=0.0178), with the DVL2 gene being most dysregulated (p=2.53E-4). Interestingly, intraperitoneal treatment of J20 AD mice with retinoic acid (RA) normalized Wnt-Ca^{2+} signaling and AD-related behaviors, suggesting that stimulation of nuclear RA receptors restores Wnt-Ca^{2+} signaling. To further explore Wnt/Ca^{2+} signaling pathway genes in AD, RT-qPCR analyses were performed for genes that are key regulators of the Wnt pathway including, *DVL2*, *FZD8* and *CTNNB1* (β-catenin). In addition, we were able to cross-validate *DVL2* and *FZD8* mRNA and protein expression in the hippocampus using publicly available HPA Mouse Brain RNA-seq and Allen Mouse Brian ISH data sets, which appear specifically enriched in the hippocampal dentate gyrus (DG). The incidence of AD is

higher in women than men. Interestingly, in our model we discovered a possible sex-specific difference for both genes. For both *DVL2* and *CTNNB1*, mRNA expression was lower for females than males. In conclusion, we have developed tools that will further examine the roles of Wnt signaling genes, their dysregulation in AD, and therapeutic interventions that can potentially counteract this dysregulation. Future experiments will examine protein expression using Western blot and immunocytochemistry.

4. Clincial – Graduate/Undergraduate

Driskill, Jackson

Development of a Pre-Health Professions Student Volunteering/Mentorship Program Provide Positive Exposure, and Address the Economic Challenge of the Caregiver-Patient Ratio in Geriatric Memory Units

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The Garrison Geriatric Care and Education Center was established in 2005 as a teaching nursing home at Texas Tech University, (TTU), focused on memory care. Pre-health profession students run a volunteer group and have created a progressive learning platform to perform dementia caregiving tasks, including emotional support, managing behavioral symptoms, feeding, and structured activities. Our objectives were to provide experiential learning for pre-health students in a memory care unit, and to provide supportive care for dementia patients without increasing financial burden. Students are given opportunities for innovation, interprofessional collaboration, and leadership experience. Experiential learning of future health care professionals in this setting may produce healthcare teams that are more empathetic, anticipatory of patient needs, and who value an integrated health care system. Additionally, pre-health students receive volunteer hours in a healthcare setting which improve their professional school applications. Unpaid caregivers provided 18.6 billion hours of care to patients with age-related dementias in 2019.[1] Despite this, the lifetime cost to a patient diagnosed with dementia for skilled care, medical attention, and housing is $357,297.[1] Over the past four years through spring 2020, TTU volunteers contributed ~1700 hours of unpaid care. We estimated the value of this care to be ~$5,355 per year. The COVID-19 Pandemic has provided an opportunity to implement and evaluate innovative and collaborative education models in long-term care. The TTU Clinical Council has recently developed a work group, reporting to the Office of the President, based upon the success and passions of our student-run group. Undergraduate pre-health students are an untapped resource that could decrease the financial burden on families and the healthcare system, and serve as a powerful driver for change in the care of memory patients.

1. Alzheimer's Association. "2020 Alzheimer's Disease Facts and Figures." Alzheimer's & Dementia (2020);16(3):391+.

Shahbazi, Siayash

Design and syntesis of novel KOP receptor antagonists, a treatment option for neuropathic pain

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Using the structure of dehidrogliotoxin (fungal metabolite) as a starting point, we have prepared novel diketopiperazine-based ligands with a varying degree of selectivity between opioid subtypes. Selected

compound with the preferential binding to KOR was tested *in vivo*, using the neuropathic pain model in rats. It showed the ability to modulate sensory and emotional pain-related behaviors in animals when administered 3 mg/kg intraperitoneally. These findings are in line with the existing data on the role of KOR-mediated signaling in the development of chronic pain conditions. Here, we report continuing work on pharmacophore's evaluation for this class of agents. Our compounds' chemical novelty, their favorable drug-likeness profile, and observed in vivo activity provide a platform for further developing these chemical agents as potential candidates for pain therapy.

5. Clincial – Medical Student

Abraham, Jonathan

O-arm guided Femoral Osteotomy with Cannulated Screw Fixation in Severe Chronic Slipped Capital Femoral Epiphysis: A report on Two Cases

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Slipped capital femoral epiphysis (SCFE) is the most common hip disorder in adolescents roughly occurring in 10-11 per 100,000 children. This condition involves displacement of the femoral epiphysis through the growth plate due to stress from excessive weight or bony weakness secondary to an endocrinopathy. If the deformity is not addressed it can lead to increased slippage, worsening pain, decreased range of motion, and predisposes to early onset osteoarthritis. The treatment of SCFE involves surgery of some level depending on the classification and severity of the SCFE. In severe chronic SCFE, there is controversy in what is considered the optimal approach for correction. The modified Dunn procedure has recently gained popularity for addressing this deformity. Despite better correction compared to in-situ fixation, modified Dunn osteotomy still comes with similar risks including joint instability, increased slippage, early onset osteoarthritis, and avascular necrosis.

We describe a novel technique for treating severe chronic SCFE with O-arm guided femoral osteotomy followed by cannulated screw fixation. This technique utilizes intraoperative navigation, a recent innovation in surgery that is widely used in minimally invasive spine surgery and hip trauma. This technology has not yet been adopted in pediatric orthopedics. Applying intraoperative navigation in the treatment of SCFE allows for correction of the deformity with
preservation of the femoral head vasculature. This is done in a minimally invasive manner reducing risk of early onset arthritis, and avascular necrosis.

We highlight two cases who both presented with severe chronic SCFE and were treated with O-arm guided femoral osteotomy and cannulated screw fixation. We report our initial experience with this technique and demonstrate favorable follow-up outcomes in both cases.

George, Asher

Incidental Neuroendocrine Tumor in Ileal Conduit Following Ileal Bladder Augmentation

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Gastrointestinal neuroendocrine tumors have increased in incidence in the United States, and almost half of these occur in the jejunum and ileum of the small intestine. We report a case of a 35-year old male, with a history of spina bifida and end-stage renal disease, who underwent removal of an ileal bladder augmentation

that occurred at a young age. Subsequent pathology reports following this surgery reveal an incidental neuroendocrine tumor in the ileal conduit. The staging of the tumor is pT2N1cMx, but the patient did not show clinical symptoms of carcinoid syndrome nor did radiology show signs of metastasis on post-operative care. After extensive discussion and opinions from multiple institutions, the patient has tolerated chemotherapy with carboplatin and etoposide, and currently undergoes stereotactic body radiation therapy for consolidation treatment. To date, the neuroendocrine tumor has not recurred.

Holder, Katherine

The Effect of COVID-19 on Immunity, Inflammation, and Mitochondrial Function in Aging Patients

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Introduction

In the last months of 2019, a novel coronavirus now known as COVID-19 spread from Wuhan, China and engulfed the globe causing illness, economic collapse, and almost 1.5 million deaths to date. Data from the global outbreak supports that COVID does not affect all patient populations equally, causing asymptomatic infection in some and leading to critical illness with respiratory failure, shock, and multiple organ dysfunction in others[1]. This study examines the impact of COVID-19 on immunity and mitochondrial function and provides a possible mechanism for disease severity in the immunocompromised.

Methods/Results

Strict procedures were followed to ensure a comprehensive, high-quality literature review was performed over all available data. First, a comprehensive search of peer reviewed papers was performed based on broad key terms including: COVID-19, ACE-2, coronavirus, mitochondria, inflammation. Second, the references for each article were inspected and reviewed for integrity and usefulness to this investigation. In total, the search uncovered 42 articles relevant to this study all published between 2012 and 2020.

Discussion/Conclusion

COVID-19 mortality rates increase with patient age and chronic diseases, making the sick and elderly most susceptible to severe infection. Chronic inflammation is prevalent in patients with age-related diseases, contributing to the relationship between severe COVID-19 infection and comorbidities[2,3]. Aging itself is associated with chronic, baseline inflammation, sometimes called inflamm-ageing[4]. Elevated baseline inflammation may aggravate or cause intrinsic defects in T cells and B cells via mitochondrial disinhibition, decreasing the body's ability to respond to infection[4].

At the cellular level, COVID-19 can invade and critically inhibit mitochondria via the ACE-2 receptor, contributing to disease progression and severity[5,6]. Mitochondria perform crucial functions in regulating innate and adaptive immune response, development, and differentiation[7]. Mitochondrion alter cellular respiration to effectively adapt macrophage response between proinflammatory and anti-inflammatory phenotypes[7]. Since mitochondria are the chief cellular regulators of oxidative homeostasis, increased inflammation may lead to platelet damage and apoptosis as a result of mitochondrial dysfunction[6].

In healthy patients, mitochondrial turnover through mitophagy, an auto-phagocytic process, is critical for maintaining proper cellular functions[5]. Mitochondria are constanly undergoing fusion and fission in a process of dynamic equilibrium[6,8]. Fusion and fission, which involve mitochondria merging and dividing respectively, maintains mitochondrial number, morphology, and function[30]. In healthy patients, fusion and fission occur at similar rates[9]. In COVID-19 patients, new and compelling evidence suggests that mitochondrial fission is inhibited while fusion is promoted, causing mitochondrial elongation and providing a receptive intracellular environment for viral replication[9]. COVID induced disruption of mitochondrion dynamic equilibrium effectively inhibits mitochondrial autophagy[9]. This increases oxidative stress, promotes mitochondrial dysfunction and

can impair the body's immune response to COVID-19[6]. This study offers a possible mechanism for the increased severity of COVID-19 infections in patients with pre-existing age-related diseases and inflammation. This information may be useful in developing targeted therapies for COVID-19.

Payberah, Daniel

The Effectiveness of Botulinum Toxin in the Prevention and Treatment of Tension Type Headaches A Systematic Review and Meta Analysis

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Background: Tension-type headache (TTH) is the most common primary headache, with a life-time prevalence up to 78%. Management of chronic TTH that is resistant to analgesics remains a challenge. Botulinum toxin type A (BTX-A), a paralytic used in treating migraines, remains an uncertain treatment for TTH. This study aimed to investigate the efficacy of BTX-A on treating isolated TTH in a systematic review and meta-analysis.
Methods: PRISMA guidelines were followed. PubMed, Scopus, Web of Science, and ProQuest databases were searched to collect records on BTX-A and TTH, without language or date restrictions. Two independent reviewers used predetermined eligibility criteria to systematically screen records for randomized, controlled clinical trials testing the efficacy of BTX-A on treating TTH. Eligible articles were assessed for risk of bias per the Cochrane handbook. Pre- vs. post-intervention intensity and frequency of TTH and the proportion of responders to treatment were extracted from intervention and control groups. DerSimonian Liard random-effects meta-analyses were performed using the meta package in R (4.0.2).
Results: Eight trials were included, totaling 564 participants. Overall risks of bias were mixed, with most studies being low risk. Compared to placebo, BTX-A treatments showed improvement in headache intensity (Cohen's d = -0.81 [-1.56, -0.07], n = 262, I^2 = 86%), decrease in headache frequency (Δ = -2.92 days/month [-4.43, -1.41], n = 205, I^2 = 51%), 64% greater probability of observing improvement in TTH (RR = 1.638 [1.075, 2.495], n = 308, I^2 = 15%; ARR = 0.137 [0.018, 0.256], n = 308, I^2 = 27%; NNT = 8 [4, 56]).
Conclusion: While the results on the efficacy of BTX-A on TTH are promising, our results are limited by the high between-study heterogeneity, limited sample sizes, and the limited number of high-quality controlled trials. Future well-designed, adequately-powered, multi-center randomized controlled trials are warranted.

Pourghaed, Mohammed

Associations between Vitamin D Levels with Hispanic/Latino Ethnicity, General Health Status, and Co-Morbid Conditions among Older Rural West Texans: A Project FRONTIER Study

Mohammed Pourghaed, Felipe Ramirez Velandia, Ashish Sarangi, Gabriela Ashworth, John Culberson, Hafiz Khan, Annette Boles, Volker Neugebauer, and J. Josh Lawrence

Sufficient levels of Vitamin D (VD), an antioxidant and hormone-like transcriptional regulator, are increasingly associated with healthy aging. In contrast, Vitamin D (VD) deficiency (VDD; ≤20 ng/mL) and insufficiency (VDI; 21-29 ng/mL) have been linked with deleterious health outcomes. Dysfunction in two major pathways lead to VDD/VDI: 1) failure to consume, absorb, and/or transport VD through the digestive system, and 2) failure to produce calcitriol (1,25-dihydroxy-vitamin D_3) via ultraviolet B irradiation in the skin and subsequent reactions in the liver and kidney. VD supplementation in only certain foods such as fish and milk make it subjected to cultural and diet restrictions; moreover, UV light is dependent on external and internal elements such as season, latitude, skin pigmentation, outdoor activity, and even use of sunscreen. Using a cohort of 299 participants from Project FRONTIER (Facing Rural Obstacles to Health Care Now Through Intervention, Education, and Research), we investigated relationships between VD levels with self-reported measures of general health, history of co-morbid conditions, VD supplementation, and disease-related blood-based biomarkers. We analyzed the sample using descriptive statistics and assessed for correlations using Spearman's correlation, logistic regression, and linear regression. Of 299 people, the demographic distribution had a mean age of 62.6 (±11.7), female gender of 70.9% (n=212), and Hispanic/Latino ethnicity (HL) of 40.5% (n=121). Nearly 61.5% of the population fell into VDD (25%) or VDI (36.5%) serum levels categories. VD levels were significantly lower in HL (22.93 ng/ml, n=121) compared to non-HL (32.36 ng/ml, n=178, Mann-Whitney U = 5280, p<0.0001) populations. Significant differences between VD subcategories were found across varying levels of self-reported health (p<0.0001). Logistic regression analysis revealed a significant association between VD level and self-reported health assessment as fair or poor (AUC = 0.693 ± 0.033, p<0.0001). HLs rated themselves as being categorically worse in general health (p<0.0001), only 3/121 (2.5%) HLs relative to 38/178 (21.4%) non-HLs rated themselves in fair health. Conversely, 60/121 (49.6%) of H/L compared to 30/178 (16.9%) of non-HL rated themselves as having fair or poor health. These results highlight ethnic health disparities in VD levels and self-reported general health. We also examined relationships between VD levels and existing consensus diagnosis (CD) variables for available medical and psychological conditions using a Spearman correlation matrix. We included (each condition scored as a binary outcome 0 or 1, for absence vs. presence of conditions, respectively), as well as their relationships with vitamin D level, age, and HL ethnicity. Significant correlations between VD level and CD variables were found for obesity (p=0.020), diabetes (p=0.0018), depression (p=0.025), and nicotine use (p<0.0001). Additional blood-based variables and objective measures supported and validated co-morbid conditions. An inverse significant relationship was seen between VD level with body mass index (R2 = 0.0497, p=0.0001) and abdominal circumference (R2 = 0.0520, p<0.0001). Another linear regression method found significant positive associations between VD with fasting blood glucose level (R2 = 0.041, p=0.0004) and HbA1c level (R2 = 0.040, p = 0.0005). Logistic regression revealed VD level was negatively associated with nicotine use (AUROC = 0.735 ± 0.49, p=0.0002) and having diabetes (AUROC = 0.643 ± 0.037, p=0.0003), with the inclusion of pre-diabetes status (>110 mg/dL) further strengthening the negative association (AUROC = 0.646 ± 0.032, p<0.0001). HL ethnicity was associated with significantly higher HbA1c levels (6.27 ± 0.13%) compared to non-HLs (5.83 ± 0.067%; Mann Whitney U = 8207, p = 0.0006). Similarly, fasting glucose levels were higher in HLs (114.5 ± 3.2 mg/dL vs 105.9 ± 2.4 mg/dL; Mann-Whitney U = 8621, p = 0.0034). A positive significant association between VD level and VD supplementation (AUC: 0.83 ± 0.39, p <0.0001) was found. Finally, a multiple linear regression model consisting of 15 parameters was chosen to determine VD level predictability and showed to adequately fit the model (adjusted R^2 = 0.649, F(15,275) = 36.79, p<0.0001). Those with the highest association were HL ethnicity (p<0.0001) and

VD supplementation (p<0.0001). In conclusion, VD levels were negatively associated with obesity, diabetes, nicotine use, positively associated with VD supplementation, and differentially associated with HL ethnicity. These co-morbid conditions are associated with oxidative stress and inflammation. Sufficient or high sufficient VD levels achievable through VD supplementation may improve general health, reduce the severity of co-morbid conditions, and improve the overall quality of life of adults, especially among HLs at heightened health risks.

Swinney, Seth
COVID-19 and Acute Encephalopathy in a Patient with Dementia: A Case Report
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A novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected in Wuhan, China in December 2019. Since then, SARS-CoV-2 has been identified as the COVID-19 pandemic. It has challenged the health care system, disrupted the norms of society, and, most importantly, placed individuals with Alzheimer's disease or related dementias in vulnerability. The risk of contracting COVID-19 targets the population with dementia in different ways. Individuals with severe dementia are often unable to follow recommendations, such as maintaining hand hygiene or physical distance from others. Many of those with milder forms of dementia have depression or apathy and, thereby, unwilling to follow the general guidelines that the public health authorities recommend.
The typical presentation of a respiratory virus, such as SARS-CoV-2, involves fever, cough, and shortness of breath. Morbidity and mortality rates are highly associated with the patient's age and comorbid medical conditions. In the dementia patient population, age is one of the factors that is most highly associated with dementia. On top of the age factor, morbidity and mortality is increased in this population as comorbidities are also associated with older age. Large-scale studies have demonstrated that the mortality rate from COVID-19 pneumonia has been reported to be twice as high in individuals with dementia compared to that of those without dementia.
While flu-like symptoms are the most classical presentation of upper respiratory viral infections, prior studies have demonstrated extensively that the initial presentation of COVID-19 infection is variable. We present a case report of a patient with Alzheimer’s dementia who presented with acute decline in functional and mental status.

6. Clincial – Postgraduate

Sarangi, Ashish(1)
Associations between Vitamin D Levels, Depression, and Hispanic/Latino Ethnicity among OlderRural West Texans: A Project FRONTIER Study
Ashish Sarangi[1,2], Mohammed Pourghaed[3,4], Felipe Ramirez Velandia[3], Gabriela Ashworth[3], John Culberson[4], Hafiz Khan[5], Annette Boles[3], Volker Neugebauer[2,3,6], and J. Josh Lawrence[2,3,6]
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Vitamin D (VD), a dietary antioxidant and hormone-like transcriptional regulator, plays an essential role in body and brain function. Accumulating evidence indicates that VD deficiency (VDD) and insufficiency(VDI) are

associated with health disparities that heighten risks for numerous chronic conditions among underserved rural populations. Following up on published pilot study that explored the relationship between VD and depression using a cohort of 68 participants recruited in Project FRONTIER (Facing Rural Obstacles to Health Care Now Through Intervention, Education, and Research), we assessed whether VDD or VDI was significantly and positively associated with depression using a larger cohort of 298 Project FRONTIER participants. We calculated descriptive statistics on the sample and employed logistic regression to assess correlations between vitamin D levels and depression (measured using Geriatric Depression Scale, a well validated screening tool for depression in the elderly population).Specifically, we assessed associations between VD levels and GDS total scores for depression, along withthe four GDS subfactors: apathy, cognitive impairment, dysphoria, and meaninglessness. Of 299 people, the demographic distribution had a mean age of 62.6 (±11.7), female gender of 70.9% (n=212), and Hispanic/Latino ethnicity (HL) of 40.5% (n=121). Nearly 61.5% of the population fell into VDD (25%) or VDI (36.5%) serum levels categories. Most (83.9%, n=250) participants had GDS total scores that fell in the Normal category (GDS 1-9), whereas (13.8%, n=41) were classified with Mild Depression (GDS 10-19), and (3.2%, n=7) had Severe Depression(GDS 20-30). Consistent with the previous pilot study, we found a significant negative correlation betweenVD level and GDS total scores ($r = -0.1333$, $p=0.021$). Similarly, logistic regression revealed a significant negative association between VD level and the consensus diagnosis for depression (ROC area = 0.59 ± 0.042, $p=0.0091$). Among those clinically depressed, those reporting use of antidepressant medications had significantly higher VD levels (31.5 ± 1.9 ng/ml vs 23.2 ± 1.6 ng/ml, $p=0.0025$). GDS scores were significantly lower in the antidepressant group (8.8 ± 1.0, vs 13.9 ± 0.8, $p<0.0001$). In regard to GDS subfactors, significant negative associations were found between VD level and Dysphoria ($R^2 = 0.038$, $p=0.0007$) and Meaninglessness ($R^2 = 0.018$, $p=0.020$). The overlap in VD sensitivity between these subfactors led us to further examine variability within the GDS. We found that 6/11 Dysphoria and 3/7 Meaninglessness GDS questions were sensitive to VD level, enabling us to create a new VD-sensitive GDSsubfactor (VD-sensitive scores were summed into a new subfactor) that was highly associated with VD level (Spearman $r = -0.281$, $p<0.0001$). Finally, using logistic regression analysis, we examined the relationship between VD level and Hispanic/Latino ethnicity. VD levels were lower in Hispanics/Latinos compared to non-Hispanics (22.93 ng/ml vs 32.36 ng/ml, n=178, Mann-Whitney U = 5280). In addition, Hispanic/Latino ethnicity and GDS total scores were positively associated (ROC area = 0.601, $p<0.0001$). Furthermore, Hispanics/Latinos had significantly higher Dysphoria (2.79 ± 0.26 vs 1.32 ± 0.13, Mann- Whitney U = 7472, $p<0.0001$) and Meaninglessness score (0.98 ± 0.13 vs 0.49 ± 0.07, Mann-Whitney U =8615, p=-0.0012). Finally, an investigation was conducted whether Hispanics/Latinos and non- Hispanics/Latinos were differentially stratified across VD levels. It was found that VD stratification significantly differed between Hispanics/Latinos and non-Hispanics/Latinos ($p<0.0001$). A greater proportion of Hispanics/Latinos occupied VD deficient and insufficient categories than non- Hispanics/Latinos. Conversely, a greater proportion of non-Hispanics/Latinos occupied VD sufficient and high sufficient categories. The largest difference was observed in the VD deficient category, whereby 48/121(39.7%) of Hispanics/Latinos were deficient, compared to only 27/178 (15.2%) of non-Hispanics/Latinos. Moreover, 43/178 (24.1%) of non-Hispanics/Latinos but only 5/121 (4.1%) of Hispanics/Latinos were in the VD high sufficient category. In summary, the negative significant association between VD status and depression, originally described in the published pilot study, was confirmed in a larger sample of Project FRONTIER participants. Overall, these data underscore troubling disparities in VD-related health status and depression among Hispanic/Latino and non-Hispanic/Latino populations that need to be addressed while performing a clinical or metabolic evaluation.

Sarangi, Ashish(2)

A descriptive study evaluating the impact of COVID-19 on delivery of care and mental health of geriatric nursing home staff in a community nursing home

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Background T*his study aims to explore the consequences of COVID-19 on geriatric care, including the impact on mental health in a nursing home setting, in order to determine approaches to efficiently deliver care by nursing home staff.*

Participants (nursing home staff), in direct contact with nursing home residents, were identified from a nursing home in Lubbock, Texas. An online survey was distributed to agreeable staff via Qualtrics. The survey assessing various aspects relating to the consequences of COVID-19 *was made available for a duration of one month. Data from the surveys was then collected and analyzed.*

Results *Significant mental health burden was identified among staff members secondary to the ongoing COVID-19 pandemic and this included feeling excessively stressed, overwhelmed and experiencing difficulty with handling personal issues. Overall mood was during the pandemic reflected increase in irritability and anger and reasons included too many work hours, watching patients decline and not having adequate mental health support. Staff response to utility of technology interventions was less than optimistic.*

Conclusion*: The COVID-19 pandemic has added significant stress and burden to the mental health of staff members working in the geriatric nursing home setting and this has not been fully offset by utilization of technological measures as previously hoped. More mental health support and optimizing staffing and other resources may be needed to augment current policies.*

Key Words: Elderly Pandemic , COVID-19 Burnout, Geriatric Nursing Home