# Regional Healthy Aging and Dementia Research Symposium

*Organized by Garrison Institute on Aging of TTUHSC*

**OCTOBER 24 - 25, 2018**

International Cultural Center, Hall of Nations

601 Indiana Ave | Lubbock, Texas 79409

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| **DAY 1** | **Wednesday, October 24** |
| **8:00 - 8:20 am** | Registration and Continental Breakfast |
| **8:20 - 8:30 am** | Opening remarks<br>*P. Hemachandra Reddy, PhD, Executive Director and Chief Scientific Officer of the Garrison Institute on Aging (GIA), Mildred & Shirley L. Garrison Chair in Aging, Professor of Cell Biology & Biochemistry, Departments of Neuroscience, Pharmacology & Neurology, Adjunct Professor, Department of Speech, Language & Hearing Sciences* |
| **8:30 - 9:15 am** | Reduced Dynamin-Related Protein 1 and Neuroprotection in Alzheimer's disease<br>*P. Hemachandra Reddy, PhD* |
| **9:15 - 10:00 am** | *Mitochondrial Dysfunction and Mitochondrial Cascades in Alzheimer's Disease*<br>*Russell Swerdlow, MD, Professor Neurology, Molecular and Integrative Physiology, and Biochemistry and Molecular Biology University of Kansas School of Medicine* |
| **10:00 am - 10:45 am** | Oral Poster Presentations<br>*Microrna-455-3P as a Potential Peripheral Biomarker and Therapeutic Target for Alzheimer's Disease*<br>*Subodh Kumar*<br>*Novel microRNA PC-5P-12969 as Potential Peripheral Biomarker for Ischemic Stroke*<br>*Murali Vijayan*<br>*Synthesis and Structure-Activity Relationship Studies of AG18051 and Its Analogs in the Treatment of Alzheimer's Disease by Inhibiting Aβ-ABAD Interaction*<br>*Ahmed Morsy* |
| **10:45 – 11:00 am** | Discussion |
| **11:00 -12:00 pm** | Clinical Aspects of Global Aging<br>*John Culberson, MD, TTUHSC Associate Professor of Family and Community Medicine UMC Bernhard T. Mittemeyer, M.D. Endowed Chair in Geriatric Medicine, Program Director, Geriatric Fellowship* |
| **12:00 – 1:15 pm** | Lunch |
| **1:15 – 2:15 pm** | *Molecular Pathogenesis of ADRD: Insights from Proteinopathy and Mitochondria*<br>*David Kang, PhD, Director, Division of Basic Research, Byrd Alzheimer's Institute, Fleming Endowed Chair in Alzheimer's Disease, Professor, Department of Molecular Medicine, USF Health Morsani College of Medicine* |
| **2:15 – 3:00 pm** | Oral Poster Presentations<br>*The Impact of Chronic Diseases on Aging: A Look at Epidemiology, Risk Factors, and Programmatic Efforts for Chronic Disease Prevention*<br>*Gabriela Arandia, PhD* |

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| | *Parvalbumin and Somatostatin Circuitry Dysfunction Differentially Impairs Hippocampal Dg/Ca3 Function During Alzheimer's Disease Pathogenesis*<br>*Josh Lawrence, PhD* |
| **3:00 - 3:30 pm** | Discussion<br>*P. Hemachandra Reddy, PhD* |
| **3:30 - 5:00pm** | Poster Presentation - Hall of Nations |

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| **DAY 2** | **Thursday, October 25** |
| **8:00 - 8:20 am** | Registration and Continental Breakfast |
| **8:20 - 8:30 am** | Opening remarks<br>*P. Hemachandra Reddy, PhD* |
| **8:30 - 9:00 am** | Welcome & Healthcare Update<br>*Tedd Mitchell, MD, President, TTUHSC Interim Chancellor, TTU System* |
| **9:00 - 9:15 am** | HSC Research Update<br>*Quentin Smith, PhD, Senior Vice-President, Dean, Committee Member, TTUHSC Amarillo, School of Pharmacy* |
| **9:15 - 10:15 am** | NIH Research Investigators Funding Opportunities<br>*Sanoj Suneja, PhD, Deputy Director, Health Scientist Administrator, National Institute on Aging* |
| **10:15 – 10:30 am** | Discussion |
| **10:30 – 11:00 am** | Break |
| **11:00 - 12:00 pm** | Reducing Dementia Caregiver Burdens<br>*Marcia Ory, PhD, MPH, Regents and Distinguished Professor, Department of Environmental and Occupational Health, Associate Vice President for Strategic Partnerships and Initiatives. Founding Director, Center for Population Health and Aging, Texas A&M University Health Science Center, School of Public Health* |
| **12:00 – 1:30 pm** | Lunch and Community Awards Presentation<br>*P. Hemachandra Reddy, PhD* |
| **1:30 – 2:30 pm** | *mTOR/S6K1 at the Crossroad Between Aging and Alzheimer's Disease*<br>*Salvatore Oddo, PhD, Associate Professor, Neurodegenerative Disease Research Center, Biodesign Institute, School of Life Sciences, Arizona State University* |
| **3:30 - 4:00 pm** | Expert Panel Q&A<br>*P. Hemachandra Reddy, PhD* |
| **4:00 - 4:20 pm** | Closing Comments<br>*P. Hemachandra Reddy, PhD* |

Welcome to the first Regional Healthy Aging And Dementia Research Symposium organized by Garrison Institute on Aging of the Texas Tech University Health Sciences Center (TTUHSC), October 24 – 25, 2018, at the Texas Tech University International Cultural Center, Hall of Nations 601 Indiana Ave.

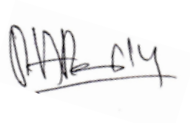
The purpose of this symposium is to bring experts together from educational and research institutions across the United States to discuss the latest developments in research focusing on healthy aging and dementia and public health trends focused on neurodegenerative diseases of aging and community-based research focused on health, nutrition and cognition. Students, postdoctoral scientists, faculty members who are actively involved in dementia research will be presenting at the symposium. In addition, healthcare professionals, from geriatricians to social workers who are involved with patients with dementia, will also be presenting. This two-day symposium is comprised of multiple sessions, each with several presentations by researchers, healthcare professionals, students, and postdoctoral scientists, followed by questions, answers, and discussion.

The Research Symposium will feature experts primarily focused on dementia and neurodegenerative diseases research and healthcare, include Marcia Ory, PhD, MPH, Regents and Distinguished Professor, Texas A&M University Health Science Center; Russell Swerdlow, MD, Director of the University of Kansas Alzheimer's Disease Center; Salvatore Oddo, PhD, Senior Scientist and Associate Professor, Arizona State University; David Kang, PhD, Fleming Endowed Chair in Alzheimer's Disease, Morsani College of Medicine, Director, Byrd Alzheimer's Institute, Division of Basic Research, Professor, Morsani College of Medicine, Molecular Medicine; Sanoj K. Suneja, PhD, Deputy Director, Division of Extramural Activities, National Institute on Aging and P. Hemachandra Reddy, PhD, Executive Director and Chief scientific Officer of the Garrison Institute on Aging. In addition, Dr. Tedd Mitchell, President of TTUHSC, and Interim Chancellor of TTU System; Dr. Quentin Smith, Sr. Vice President for Research and TTUHSC; Dr. John Culberson, Professor of Family Medicine; Josh Lawrence, PhD, Associate Professor of Pharmacology and Neuroscience Department and many others will be speaking at the symposium.

I sincerely thank all of the staff, students, and colleagues from the Garrison Institute on Aging, TTUHSC School of Medicine, and the Public Health Department for their kind support and participation in Garrison Institute on Aging activities. My special thanks to TTUHSC President Tedd Mitchell, MD, and Interim TTU System Chancellor; Dr. Steven Berk, School of Medicine Dean and Provost; Dr. Quentin Smith, Senior Vice President for Research; Dr. Vadivel Ganapathy, Chair of Cell Biology and Biochemistry; Dr. Volker Neugebauer, Chair of Neuroscience/Pharmacology; Dr. John de Toledo, TTUHSC Neurology Chair, for their continuous support with Garrison Institute on Aging activities.

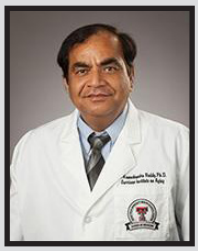
I sincerely thank Annette Boles, Susan Thompson, Ruben Gonzales, Kandi Quesada, Veronica Molinar-Lopez, Clay Ament and Joan Blackmon for their hard work and putting the symposium together. I also thank colleagues at the TTUHSC Institutional Advancement Office for their fundraising efforts to help support Garrison Institute on Aging research. Special thanks to Mr. Spike Dykes and his family for raising research funds for the Garrison Institute on Aging, and to the Garrison family members for their continuous support of all activities in the Garrison Institute on Aging.

Thank you all for your interest and participating in our first Regional Healthy Aging and Dementia Research Symposium.



P. Hemachandra Reddy, PhD
Executive Director and Chief Scientific Officer and Professor of Cell Biology and Biochemistry, Neuroscience/Pharmacology and Neurology, Texas Tech University Health Sciences Center

## October 24
## Presenter Information
*Hemachandra Reddy, PhD*



Dr. P. Hemachandra Reddy is the Executive Director of Garrison Institute on Aging (GIA) and a professor of Cell Biology & Biochemistry, Neuroscience/Pharmacology and Neurology Departments of Texas Tech University Health Sciences Center, Texas. Dr. Reddy has 20 years of research experience working with aging and neurodegenerative diseases, including Alzheimer's, Huntington's disease, Parkinson's disease and multiple sclerosis. He was involved in making and characterizing transgenic animal models of aging and neurodegenerative diseases. He was the first researcher to make full-length cDNA transgenic mice for a study of HD, the findings of which were published in Nature Genetics and Trends in Neurosciences. Dr. Reddy was one of the first researchers who demonstrated the association of amyloid beta, phosphorylated tau with mitochondria in AD progression. Dr. Reddy served in several review panels of NIH, VA Merit Review and currently and is a Chartered Member of Neuronal Oxidative Metabolism and Death NIH Study Section (2013-2019). He was the Chair of SOM Research Executive Committee and a member of University Research Council of TTUHSC and currently he is serving as a Member of Post Tenure Committee, TTUHSC. He received several awards and honors, including Prestigious Bharath Gaurav Award (2016) from Government of India; best mentor award (2003) and Technology innovation award (2007) from Oregon Health and Science University and Alzheimer's Award (2006) from the Journal of Alzheimer's Disease and Fellows Award For Research Award (1999) from National Institutes of Health. Dr. Reddy has a long track record of editorial activities, including: Edited Molecular Biology of Aging Book, Elsevier and Academic Press (2017), and Guest editor for nine special topics - Mitochondrial Drugs for Neurodegenerative Disease, Genes, Mechanisms and Drugs for Asthma in Pharmaceuticals, Current Status of Therapeutics and Preventive Measures for Patients with Thalassaemia and Sickle Cell Disease in Cardiovascular & Hematological Agents in Medicinal Chemistry, Aging and Mitochondria in Alzheimer's Disease in Antioxidants & Redox Signaling, Synaptic Damage in Aging and Neurodegenerative Diseases in Frontiers in Aging Neuroscience, Misfolded Proteins, Mitochondrial Dysfunction, and Neurodegenerative Disease, Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases, Stem Cells and Their Utility to Human Diseases in BBA Molecular Basis of Disease (2018) and Neurotransmitters and Alzheimer's Disease in Journal of Alzheimer's Disease

## October 24
## Presenter Information
*Russell H. Swerdlow, MD*

Dr. Russell Swerdlow is a professor in the Departments of Neurology, Molecular and Integrative Physiology, and Biochemistry and Molecular Biology at the University of Kansas School of Medicine. He directs the NIH-funded University of Kansas Alzheimer's Disease Center, the Kansas University Medical Center's Neurodegenerative Disorders Program, the Heartland Center for Mitochondrial Medicine, and staffs the Kansas University Medical Center's Memory Disorders Clinic. He received his undergraduate and doctor of medicine degrees from New York University, and trained as a neurologist and Alzheimer's specialist at the University of Virginia.

He currently holds the Gene and Marge Sweeney Chair at the University of Kansas and is a recipient of an S. Weir Mitchell Award from the American Academy of Neurology, a Cotzias Award from the American Parkinson's Disease Association, a Scholarly Research Award from the University of Kansas, and a Chancellor's Club Research Award from the University of Kansas. He served as the Research Committee Chair of the CurePSP Foundation; Chaired the Commonwealth of Virginia's Alzheimer's Disease Commission; currently sits on the National Institute on Aging's Board of Scientific Counselors; and is on the editorial board of several journals. Dr. Swerdlow's research focuses on brain energy metabolism, the role brain energy metabolism plays in Alzheimer's disease and other neurodegenerative diseases, and how to manipulate brain energy metabolism.

## October 24
## Presenter Information
*John Culberson, MD*

Dr. Culberson received his MD degree from New Jersey Medical School, and completed training in Geriatric Medicine at Baylor College of Medicine. He is currently an Associate Professor of Family and Community Medicine, with a Joint Appointment with the Department of Pharmacology and Neuroscience at the Texas Tech University Health Sciences Center, Lubbock Texas. Dr. Culberson holds the Mittemeyer Endowed Chair for Excellence in Geriatric Medicine, is Program Director of the Geriatrics Fellowship, and is a collaborator at the Garrison Institute on Aging. He is a clinician-educator with a large geriatrics practice, and was Physician of the Year at the DeBakey VA Medical Center in Houston, Texas. He has received a Geriatric Academic Career Award, and has served as Chairman of the Aging, Alcohol, and Addictions group at the Gerontological Society of America. His research interests include neuroimaging in Alzheimer's Disease, medication reduction in long-term care, sarcopenia in post-menopausal women, and clinical manifestations of Vitamin D deficiency.

## October 24
## Presenter Information
*David Kang, PhD.*

In my laboratory, we focus on the mechanisms of neurodegeneration in Alzheimer's disease (AD) and related disorders such as Frontotemporal dementia (FTD) and Amyotrophic Lateral Sclerosis (ALS). We utilize various molecular, biochemical, cell biological, advanced imaging, and animal modeling (mouse & C. elegans) tools to answer important questions pertinent to healthy vs. pathological brain aging. I have been actively engaged in neurodegeneration and Alzheimer's disease (AD) research for the past 22 years. Specifically, we are currently interested in 1) the mechanisms of Abeta production and neurotoxicity, 2) signal transduction mechanisms between Abeta and tau, 3) interplay between pathogenic proteins such as tau and the UPR and chaperone systems, 4) mechanisms underlying mitochondrial dysfunction in AD and FTD/ALS, 5) role of selective autophagy and mitophagy in the accumulation of toxic components, and 6) the study of extracellular vesicles (i.e. exosomes) as disease biomarkers and agents of neurodegeneration. Of interest, we have shown that the Slingshot-cofilin activation plays a key role in both Abeta-mediated neurodegenerative changes. We are currently working on a series of Slingshot inhibitors that antagonize this pathway of Abeta-induced neurotoxicity. We have recently shown that a scaffolding protein RanBP9, which is elevated in brains of AD patients and promotes Abeta production, also positively regulates tauopathy via its direct interactions with tau and Hsp90/Hsc70 complexes. Our studies with the novel FTD/ALS gene CHCHD10 showed that CHCHD10/har-1 plays an essential role in mitochondrial function, longevity, and movement behavior in C. elegans. Wild type human CHCHD10 but not the ALS/FTD CHCHD10 mutants rescued all of these phenotypes in har-1 KO C. elegans, activities which were mirrored in mammalian cells and mouse brains. We also discovered a link between CHCHD10 and a canonical ALS-associated protein, Tar DNA Binding Protein 43 (TDP-43), which is usually nuclear but often found cytoplasmically mislocalized and aggregated in ALS/FTD. We found that CHCHD10 binds to TDP-43, that reduction of CHCHD10 or expression of ALS mutants induced cytoplasmic mislocalization of TDP-43, and that wild-type but not mutant CHCHD10 is protective against TDP-43-induced apoptosis and synaptic impairment. Finally, we are conducting on studies of extracellular vesicles (exosomes & microvesicles) as both biomarkers and agents of neurodegeneration, in which neural-derived exosomes are isolated from human serum samples and neural cell cultures to perform proteomic analysis.

## October 25
## Presenter Information
*Tedd L. Mitchell, MD*

Tedd L. Mitchell became the eighth president of the Texas Tech University Health Sciences Center on May 17, 2010. As its longest serving president, Mitchell has successfully led a period of record growth in enrollment, academic excellence, and physical expansion on all campuses. Texas Tech University Health Sciences Center now graduates more health care professionals than any other health related institution in Texas.

Dr. Mitchell has launched initiatives for interprofessional concentration around the university's five schools – Biomedical Sciences, Health Professions, Medicine, Nursing, and Pharmacy – and promoted programs to support novel research and creative endeavors such as the Department of Public Health which will eventually become the School of Public Health. Under his leadership, the university remains financially strong while maintaining low tuition rates.

Dr. Mitchell is an Ashbel Smith Distinguished Alumnus of the University of Texas Medical Branch, where he received his Doctor of Medicine degree in 1987. After graduation he pursued training in Internal Medicine. In 2012, Dr. Mitchell was honored as a distinguished alumnus of the Department of Internal Medicine. He is a Fellow of the American College of Physicians and the American College of Sports Medicine. From 1988 to 1996, he served as a captain in the U.S. Army Reserves (Medical Corps).

Prior to coming to Texas Tech University Health Sciences Center, Mitchell served as president and chief executive officer of the Cooper Clinic in Dallas, an internationally recognized center of excellence in preventive and sports medicine.

Dr. Mitchell is a member of the faculty. His research interest is focused on the effects of activity and life style on health, and he has authored or co-authored dozens of scientific papers, abstracts and book chapters. He is a frequent lecturer, both nationally and internationally, on the physiology of exercise and the effects of exercise on aging, fitness, and overall quality of life.

As health editor and a weekly columnist for USA Weekend from 1998 to 2010, Dr. Mitchell published more than 600 articles. He received the 2006 Clarion Award and the 2008 Walter C. Alvarez Award for Excellence in Medical Communication from the American Medical Writers Association. His writings led to collaborative efforts with other health experts, culminating in the publication of the books Fit to Lead (2004 St. Martin's press), Move Yourself (2008 Wiley Press) and Fit to Lead 2 (2012).

In 2002, Dr. Mitchell was appointed by President George W. Bush to the President's Council for Physical Fitness and Sports and served until 2009. During his term, he was engaged in efforts that changed the President's test from one that was fitness based to one that is health based.

Dr. Mitchell is married to Dr. Janet Tornelli-Mitchell. They met while in medical school and practiced together for nearly two decades. The Mitchells have three children, Katherine, an assistant district attorney in Dallas, Charlie, a petroleum engineer in Houston, and Chris, an undergraduate student at Texas Tech University.

## October 25
## Presenter Information
*Quentin Smith, PhD, BA*

Quentin Smith's primary research interests are focused on assessing and ultimately improving drug delivery across the blood-brain barrier for the treatment of brain tumors, stroke, and neurodegenerative disease. He has established highly sensitive, regio-specific methods to map the distribution of low levels of bound and free drug in brain and brain metastases of breast cancer following systemic drug administration in animals. His lab is dissecting the roles of key BBB transporters in controlling brain and brain metastasis exposure of drugs. Also, he is working on developing and evaluating modified drugs that are specifically designed to circumvent the BBB. Both novel carrier vectors to deliver conventional drugs and rational design of drug modifications that retain chemotherapeutic activity while circumventing the transporters that limit brain access are being investigated. Research is funded by the Cancer Prevention Research Incentive of Texas (CPRIT), DoD, NIH, and numerous collaborations with industry.

## October 25
## Presenter Information
*Sanoj Suneja, Ph.D.*

Dr. Sanoj K. Suneja joined the National Institute on Aging (NIA) in 2006 as Research Program Analyst and currently serves the institute as Health Scientist Administrator. Dr. Suneja is responsible for extramural research grants referral and analyses in the NIA Division of Extramural Activities (DEA). As a Supervisory Scientist in his academic career at the Univ. Conn. Health Center (UCONN) from 1988-2006, he had researched on neuro-biochemical behavior of the auditory system after hearing damage for managing the goals of the NIH-funded research project(s).

Before joining UCONN, Dr. Suneja was a Scientist with Government of India from 1986-1988. He received his Master (1982) and Doctorate (1986) degrees in Biochemistry from Haryana Agricultural University, Hisar, India. Dr. Suneja has published over 40 peer reviewed scientific research articles. Dr. Suneja has served as a reviewer for various scientific journals in neurosciences such as European Journal of Neuroscience, Neurochemical Research, Brain Research, and Ear and Hearing.

## October 25
## Presenter Information
*Marcia G. Ory, PhD, MPH*

Regents and Distinguished Professor, Department of Environmental and Occupational Health
Associate Vice President for Strategic Partnerships and Initiatives
Founding Director, Center for Population Health and Aging
Texas A&M University Health Science Center, School of Public Health

Marcia G. Ory, PhD, MPH, is a regents and distinguished professor in the Department Environmental and Occupational Health at the Texas A&M School of Public Health. She also serves as Associate Vice President for Strategic Partnerships and Initiatives at the Health Science Center, directing Healthy Texas, a system-wide effort to examine strategies for promoting health and wellness at the Texas-Mexico border, as well as throughout Texas. Dr. Ory is the founding director of the university-wide Center for Population Health, chair of the Health and Wellness Committee and academic partner for the Community Research Center for Senior Health with Baylor Scott and White Health. In her many roles, she is working with an interdisciplinary cross-campus group to develop innovative research projects across public health, medicine, engineering and computer sciences. Her passion is ensuring the scalability and sustainability of evidence-based programming and policies designed to improve the health and well-being of older adults.

Prior to coming to Texas A&M University, Dr. Ory spent 20 years in federal service as chief of Social Science Research on Aging in the Behavioral and Social Research Program at the National Institutes of Health's National Institute on Aging.

Dr. Ory received her Bachelor of Arts in sociology and psychology from the University of Texas, Master of Arts in sociology and human development from Indiana University, doctorate in family studies and human development from Purdue University and Master of Public Health in chronic disease epidemiology and behavioral sciences from John Hopkins University Bloomberg School of Public Health.

## October 25
## Presenter Information
*Salvatore Oddo, Ph.D.*

Dr. Oddo received his undergraduate degree in Molecular Biology from the University of Catania, Italy, and his graduate degree in Neurobiology of Learning and Memory from the University of California, Irvine. Dr. Oddo's research focuses on understanding the molecular mechanisms underlying memory deficits in Alzheimer's disease. Using animal models, he showed that dysfunction signaling transduction pathways that are critical for learning and memory play a pivotal role in the cognitive decline associated with Alzheimer's disease. Currently, he is the Principal Investigator of a grant from the National Institute of Health, which is focused on elucidating the role of the mammalian target of rapamycin on the pathogenesis of Alzheimer's disease. Dr. Oddo has published more than 70 research articles in international peer-reviewed journals. In recognition of his contribution to the aging and Alzheimer's disease fields, he has been the recipient of several national and international awards.

**Title:** **Can Healthy Diets, Regular Exercise and Better Lifestyle Delay the Progression of Dementia in Elderly Individuals?**

**Elizabeth George, Darryll Oliver, P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Elizabeth George**

**Abstract:**

The purpose our study is to assess the impact of healthy diets and regular exercise on dementia in elderly individuals and patients with early Alzheimer's disease (AD). Our presentation identifies various modifiable and non-modifiable risk factors, and also outlines the evidence for lifestyle changes associated with the reduced risk of dementia. Currently, over 50 million people are living with Alzheimer's and other forms of dementias worldwide. Annual estimated health care cost is about $818 billion and are projected to be $2 trillion by 2050. Currently, there are no drugs that can delay and/or prevent the progression of disease in elderly individuals and in patients with Alzheimer's. Extracellular amyloid deposits and intracellular neurofibrillary tangles are the major pathological hallmarks. Loss of synapses and synaptic damage are the best correlates of cognitive decline in Alzheimer's disease patients. Two thirds of women and one third of men are at lifetime risk for AD. Multiple sites are affected by disease, including entorhinal cortex, temporal cortex, fronto-parietal cortex, hippocampus and subcortical nuclei. Synaptic damage and mitochondrial dysfunction are early events in disease progression. Causal factors are known for about 1-2% of total AD patients. Mutations in amyloid precursor protein (APP), presenilin 1 (PS1), presenilin 2 (PS2) genes are involved in early onset AD. Several risk factors have been identified, including Apolipoprotein E4 genotype, type 2 diabetes, traumatic brain injury, depression and hormonal imbalance and these are reported to associate with late-onset sporadic AD. Recent research revealed that antioxidants enriched diets and regular exercise reduces toxic radicals, enhances mitochondrial and synaptic functions, and improve cognitive health in elderly individuals. Presently available data on the use of antioxidants in transgenic mouse models of AD and antioxidant(s) supplements in diets of elderly individuals were critically assessed. We also assessed the use of antioxidants in randomized clinical trials in AD patients. Overall, our presentation discusses the current status of healthy diets and regular exercise on dementia in elderly individuals.

**Title:** **Mitochondria Targeted Molecules as Therapeutic Agents against Alzheimer's Disease**

**Darryll Oliver, MS and P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Darryll Oliver, MS**

**Abstract:**

The purpose of our study is to explore the protective effects of mitochondria-targeted small molecules in Alzheimer's disease (AD). Mitochondrial dysfunction is a hallmark characteristic of AD as well as numerous neurodegenerative diseases. Quality of mitochondria is important to maintain cellular ATP and function. Damaged mitochondria yield impairment to bioenergetics and mitochondrial dynamics, which result in defective synaptic function, neuronal damage and loss of cognition. Drugs, which have included cholinesterase and glutamate inhibitors, augment neurotransmitters and help curtail loss of cognition, but fail to address mitochondrial damage. Increasing evidence suggests that daily exercise (both mental and physical) and healthy diets can improve cognitive function and alleviate AD pathology in elderly individuals and patients with AD. Several naturally occurring antioxidants, such as vitamin C & E, beta-carotene, glutathione and others tested for their efficacies to delay the progression of dementia in AD patients. However, these natural antioxidants are unable cross the blood brain barrier and reach the sites of free radicals, mitochondria. Recently, there has been a breakthrough where researchers have been able to promote the uptake of certain antioxidants/molecules to mitochondria using positively charged lipophilic phosphonium cation. These mitochondria-targeted molecules include MitoQ, MitoVitE, MitoTempo, Mitoalpha-lipoic acid, MitoPBN, MitoPeroxidase. Their accumulation in mitochondria with their cationic and hydrophobic moiety greatly improves free-radical scavenging ability and maintain mitochondrial function. Further, recently, several mitochondria-targeted, cell permeable, tetra-peptide molecules such as Szeto-Schiller 31 (SS31) have been developed and currently are being tested in cell and mouse models of AD. This presentation discusses the benefits and limitations of these small molecules and their ability to reduce amyloid beta-induced damage, improve mitochondrial and synaptic functions, and protect cognitive function in patients with AD.

**Title:** **Whole transcriptome analysis dissecting the differential gene expression profiles of Alzheimer's disease samples with next generation sequencing method - RNA-Seq**

**Pradeepkiran JA and P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Pradeepkiran JA, PhD**

**Abstract:**

The purpose of our study is to understand gene expression profiles of different brain regions of postmortem Alzheimer's disease (AD) brains. RNA sequencing (RNA-Seq) expansions enabled the transcriptome analysis of lethal genes in Alzheimer's disease (AD) condition with an unbiased manner. The RNA-Seq data analysis underlying functional heterogeneity of the genes in disease and normal states may provide the better information in order to understand the disease mechanisms in AD. However, the probabilistic methods of gene expression profiles influence probability with robust models may allow critical analysis of the gene expression data, protein localizations and pathway interactions to dissect the disease/normal states in a systemic way. Results from our RNA-Seq data showed that among six genes from frontal (FITM1, NFKBIA, SLC25A29, RPPH1, IFI27, AHSA1), seven genes from temporal (HOMEZ, LINC01550, ESR2, EFCAB11, GPR65, OTX2-AS1, and DHRS4L2) and three genes from other regions (LOC101927045, LINC01551 and IFI27) were upregulated in Ad brains relative to age-matched control brains. Gene ontologies of all up regulated genes may have compensatory response disease toxicity. The upregulated genes involved in signal transduction, gene regulation and neuro-inflammatory responses. Furthermore pathway interaction network analysis was performed with these upregulated genes. The analysis revealed highly connected functional networks with NFKBIA and Akt pathways. These genes can be recommended as some of the potential drug targets for AD. Overall, the AD Seq data provides the better understanding of differentially expressed genes and physiological relevance in normal and diseased condition.

**Title:** **Structure Based Design and Molecular Docking Studies for Phosphorylated Tau Inhibitors in Alzheimer's Disease**

**Pradeepkiran JA and P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Pradeepkiran JA, PhD**

**Abstract:**

The purpose of our study is to identify phosphorylated Tau (p-Tau) inhibitors. P-Tau has recently received great interest as a potential drug target in Alzheimer's disease (AD). The continuous failure of Aβ-targeted therapeutics recommends an alternative drug targets to treat AD. There is an increasing evidences and growing awareness of tau, plays a centric role in AD pathophysiology, including tangles formation, higher activation of phosphatases/kinases, leads p-Tau aggregation in AD neurons. In the present study, we performed computational pharmacophore-based models, molecular docking and simulation studies for p-tau in order to identify hyperphosphorylated sites. We found multiple Serine and Tyrosine sites that alter the R1/R2 repeats in tau protein. The ligand molecules exhibiting the p-O ester scaffolds with inhibitory and/or blocking actions against Serine and Tyrosine of p-tau. Our molecular docking screening revealed five ligands with high docking scores and optimal protein-ligand interactions of p-tau. These five ligands showed the best pharmacokinetic and physicochemical properties, including good absorption, distribution, metabolism, and excretion (ADME) and admetSAR toxicity. The p-tau pharmacophore drug discovery approach provides the comprehensive and rapid drug interventions in AD and tauopathies are expected to be the prospective future therapeutic approach in AD.

**Title:** **Protective Effects of BACE1 Inhibitory Ligand Against Amyloid Beta-Induced Synaptic and Mitochondrial Toxicities in Alzheimer's Disease**

**Poster Presenter:** **Pradeepkiran JA, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

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**Abstract:**

Amyloid-β peptides (Aβ) are the major drivers of Alzheimer's disease (AD) and formed by successive cleavage of the amyloid precursor protein (APP) by the beta and gamma secretases. Mounting evidence suggests that Aβ and mitochondrial structural and functional abnormalities are critically involved in the loss of synapses and cognitive decline, in patients with AD. The crystal structure of the beta amyloid cleavage enzyme 1 (BACE1) protein contains the two functional domains, external and internal. The external domain is the key functional part of catalytic cleavage of c-terminal part of APP that results 38 to 42 amino acid Aβ peptide(s). In the present study, we constructed a pharmacophore BACE1 with pepstatin ligand-based screening through computational drug discovery and molecular docking. We found 3 potential ligands in our molecular docking analysis of BACE1 inhibitory ligands, and we tested all 3 BACE1 inhibitory ligands for APP processing and Aβ inhibition in AD neurons. Using biochemical, molecular, transmission electron microscopy and immunoblotting analyses, we studied ligand 1 protective effects against Aβ-induced synaptic and mitochondrial toxicities in mouse neuroblastoma (N2a) cells that express mutant APP. We found physical interaction between ligand 1 and BACE1 and this interaction decreased abnormal APP processing, reduced BACE1 activity and Aβ40 and 42 levels. We also found increased mitochondrial biogenesis, mitochondrial fusion and synaptic activity and reduced mitochondrial fission. Based on these results, we cautiously conclude that ligand 1 reduces Aβ-induced mitochondrial and synaptic toxicities, and maintains mitochondrial dynamics and neuronal function in AD.

**Title:** **Ignored Brain Region 'The Brainstem' in the Progression and Pathogenesis of Alzheimer's Dementia: Gender-Based Data From Human and Rhesus Macaques**

**Arubala P Reddy, PhD1 and P. Hemachandra Reddy, PhD2**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **P. Hemachandra Reddy, PhD**

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**Abstract:**

The purpose of our study is to understand the role of brainstem in the progression and pathogenesis of Alzheimer's disease. Normal aging of the brain is governed by adaptive cellular degeneration, the rate of synaptogenesis and decreased neurogenesis. Inceasing evidence suggests that the levels of neurotransmitters are reduced with aging, but differently expressed in males and females. Most of the neuronal degeneration thus far studied in the telencephalic region consists of the prefrontal cortex, hippocampus, temporal cortices. Brainstem nuclei are involved in the progression and pathogenesis of several neurodegenerative diseases, including Alzheimer's, Parkinson's, Fronto-temporal dementia. However, brainstem was poorly investigated area of neurodegenerative diseases. Brainstem harbor many neurons and the nuclei which synthesize neurotransmitters and neurotrophic factors. The importance of serotonin, dopamine, norepinephrine has not been investigated at protein, cellular and molecular level in the rhombencephalic region. Hypothesis: We hypothesize that isodendritic core of the brainstem is important to define disease pathology of neurodegenerative as well as neuropsychiatric diseases may also have a gender dimorphism in progression as well as the outcome of the treatment. Methods: In the current study, we investigated global gene expression analysis using healthy control human and rhesus raphe tissues of the isodendritic core. Brain tissues were obtained from Neuro-Biobank Tissue Repository and Oregon National Primate Research Center Tissue Bank. RNA was isolated from raphe region of 4 groups (5 males and 5 females human DRN, 5 males and 5 females rhesus macaques DRN). In experiment 1, rhesus raphe RNA samples were hybridized to the rhesus specific chip (TAQ4.1 Affymetrix). Data were analyzed using transcriptome analysis console software between male and female rhesus macaques. In experiment 2, human raphe RNA samples were hybridized to Clariom D human chip and rhesus chip. Data were analyzed between males and females and also between humans and rhesus macaques. In experiment 3, differentially expressed genes were verified using Eva-Green chemistry based real-time qRT-PCR. Results: Gene expression data revealed that electron transport chain (OXPHOS) and olfacotry receptor genes were upregulated in humans relative to rhesus macaques. On the other hand, genes related to copper & zinc homeostasis, EGFR, VEGF, BDNF, MAP K, NRF2 signalling, monoamine transport and signalling were upregulated in rhesus macaques relative to humans. MicroRNAs related to muscles, lymphocytes, and epithelium were upregulated in rhesus macaques relatve to humans. The genes related to focal adhesion, Alzhiemrs disease, electron transport, insulin signalling, BDNF, acin cytoskeleton, VEGF, circadian rhythm, G-protien, leptin, WNT signalling are upregulated in males relative to females in both humans and rhesus. Further, genes related to olfactory receptor, immune interection witt lymphoid and non lymphoid cells, TNFR2, DNA synthesis and replication were regulated in females relative to males in both humans and rhesus macaques. Overall, our study provides gender- and species-specific based fundings in the brainstem of humans and rhesus macaques.

**Title:** **Expression Level of Novel Mirna Pc-5P-12969 in Two Different In Vivo Stroke Models**

**Murali Vijayan, PhD1, Subodh Kumar, PhD1, Pelin Cengiz, MD2, Vardan T. Karamyan, PhD3, P. Hemachandra Reddy, PhD1**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Waisman Center and Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA**

**Center for Blood Brain Barrier Research, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX, USA**

**Poster Presenter:** **Murali Vijayan, PhD**

**Abstract:**

MicroRNAs (miRNAs) are involved in growth, development, and occurrence & progression of many diseases. Circulating miRNAs have been used effectively as biomarkers and mechanistic targets for diseases such as stroke, Alzheimer's and cancer. MiRNA mediated post-transcriptional regulation is poorly understood in vascular biology and pathology. The purpose of this study is to determine circulatory miRNAs as early detectable peripheral biomarkers in patients with ischemic stroke (IS). In our recent global microRNA expression study, we found two previously unreported miRNAs in serum samples from patients with ischemic stroke (Vijayan et al 2018). Further validation of differentially expressed miRNAs, we found miRNA PC-5P-12969 up-regulated in serum IS samples, postmortem IS brains, lymphoblastoid IS cell lines, oxygen-glucose deprived human and mouse neuroblastoma cells (Vijayan et al 2018). In the present study, we sought to determine miRNA PC-5P-12969 expression levels, using quantitative real-time PCR assay (qRT-PCR) in 4 different brain regions, including hippocampus, striatum, cerebral cortex and cerebellum from 1) hypoxic-induced (HI) neonatal and control naive mice, 2) IS-affected and unaffected regions of a photothrombotic stroke model at day 1, 3, and 7 post-stroke group. Expression levels of miRNA PC-5P-12969 were significantly upregulated (P=0.0005) in the hippocampi of HI mice relative to naïve control mice. In the photothrombotic stroke model, there was a significant upregulation of the miRNA PC-5P-12969 expression level on day 1 post-stroke compared to the control brains. In the cerebellum, there was no change in the miRNA PC-5P-12969 expression level in HI and photothrombotic stroke models, indicating that PC-5P-12969 miRNA is specific to hippocampal and cortical tissues. Our silico analysis revealed that PC-5P-12969 is associated with the regulation of the stroke-related gene(s). To the best of our knowledge, this is the first study identified/validated potential novel candidate miRNAs in ischemic stroke. Based on these observations, we conclude that MiRNA PC-5P-12969 is potential biomarker for ischemic stroke.

**Title:** **MicroRNA-455-3p regulates amyloid precursor protein processing, mitochondrial biogenesis and synaptic activity in Alzheimer's disease**

**Subodh Kumar1 Murali Vijayan1 Arubala P Reddy2, Xiangling Yin1 and P. Hemachandra Reddy1,2**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Pharmacology & Neuroscience Department, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Subodh Kumar, PhD**

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**Abstract:**

The purpose of our study is to understand the role of MicroRNA-455-3p (MiR-455-3p) in APP processing, amyloid beta levels, mitochondrial biogenesis and synaptic activity in AD progression. Using molecular, cellular and biochemical assays, double/triple immunofluorescence analysis and transmission electron microscopy, we studied the protective effects of miR-455-3p against 1) abnormal APP processing, 2) defective mitochondrial biogenesis and mitochondrial morphology, 3) synaptic pathology and 4) defective cell viability in neurons that express mutant APP and amyloid beta. We transfected mouse neuroblastoma (N2a) cells with mutant APP cDNA (with Swedish/Indiana mutations) and further cells were transfected with miR-455-3p (mimics and inhibitors). The N2a cells transfected with the miR-455-3p mimics exhibited healthy cell morphology and increased cell proliferation compared to the N2a cells that were transfected with the miR-455-3p inhibitor. In-silico analysis of microRNAs has identified the APP gene as a putative target of miR-455-3p, and our luciferase assay confirmed the binding of miR-455-3p at the 3'UTR of APP gene, and luciferase activity was found to be significantly suppressed by miR-455-3p (P=0.002). MiR-455-3p expression was significantly modulated by mimics (225-fold increase, P=0.0001) and inhibitors (-5.23-fold decrease) compared to controls. Full-length mutant APP was reduced in mutant APP cells that were transfected with the mimics and was upregulated by 2.6-fold in the N2a cells transfected with the inhibitors. Our cell viability assay showed a significantly higher population (91.35%) (P=0.014) of viable N2a cells transfected with miR-455-3p vector compared to miR-control vector. Immuno-blotting and immunostaining analysis also confirmed the downregulation of the mutant APP by miR-455-3p. We also found the reduced levels of mitochondrial biogenesis genes (PGC1α, NRF1, NRF2, and TFAM) and synaptic genes (synaptophysin and PSD95) in mutant APP cells; on the other hand, mutant APP cells that express miR-455-3p showed increased mRNA and protein levels of biogenesis and synaptic genes. Additionally, transmission electron microscopy analysis showed a decrease in the number of mitochondria and an increase in the average size of mitochondria in the N2a cells transfected with miR-455-3p. Given our findings, that the miR-455-3p decrease abnormal APP processing and increase mitochondrial biogenesis and synaptic activity. Based on these observations, we cautiously conclude that miR-455-3p could be an effective therapeutic target for AD.

**Title: Alzheimer's disease and other Dementias: Review of Epidemiological Data and Promising Interventions**

**Gabriela Arandia, PhD and P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter: Gabriela Arandia, PhD**

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**Abstract:**

**Background:** Alzheimer's disease (AD) and other dementias are neurodegenerative diseases characterized by loss of memory, cognitive impairment, and physical inability. The purpose of this presentation is to highlight prevalence and mortality data on dementia in the U.S., an overview of modifiable and non-modifiable risk and protective factors of dementia, and promising interventions that aim to maintain or improve cognitive health.

**Findings:** Nearly 5.7 million individuals in the U.S. have AD. AD is the 6th leading cause of death in the U.S. Risk factors include age, genetics, family history, sex (women at higher risk than men), and race and ethnicity. Modifiable risk and protective factors include: education, healthy diet, and physical activity (protective factors), as well as smoking, diabetes, obesity, and traumatic brain injury (risk factors). Community-level risk factors (lack of access to healthy foods and parks, increased air pollution, and rural residence) are highlighted as well. Lastly, physical activity programs (e.g., walking, yoga, swimming) and dietary interventions (e.g., Mediterranean diet, antioxidant-enriched diet) have been shown to improve cognitive function among elderly people and with mild cognitive impaired subjects.

**Discussion:** Dementia is complex and not fully understood, though scholars have identified an array of modifiable and non-modifiable risk and protective factors of dementia. As the prevalence of dementia is expected to rise with a growing aging population, further research into potential prevention strategies and treatments is warranted. Large-scale, longitudinal studies are needed to track cognition and associated risk factors over the life course in rural settings. Moreover, randomized controlled trials are needed to test the efficacy of lifestyle interventions (i.e., dietary and physical activity programs) that aim to improve or maintain cognitive function among older adults.

**Title:** **Abnormal Mitochondrial Dynamics and Defective Synapses: Protective Role of Reduced Dynamin-related protein 1 in Alzheimer's Disease**

**Ramesh Kandimalla1, Maria Manczak1, Xiangling Yin1 and P. Hemachandra Reddy 1,2,3,4,5,6**

**1. Garrison Institute on Aging, 2. Cell Biology & Biochemistry, 3.Pharmacology/Neuroscience, 4. Neurology, 5. Department of Public Health and 6. Speech, Language and Hearing Sciences Departments, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, Texas 79430Sciences Center, 6630 S. Quaker Ste. E, MS 7495, Lubbock, Texas 79413Lubbock, Texas 79430**

**Poster Presenter:** **Maria Manczak, PhD**

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**Abstract:**

Synaptic pathology and mitochondrial oxidative damage are early events in Alzheimer's disease (AD) progression. Loss of synapses and synaptic damage are the best correlates of cognitive deficits found in AD patients. Recent research on amyloid beta (Aβ), tau mitochondria and synapses in AD revealed that Aβ and tau accumulates in synapses and synaptic mitochondria, leading to abnormal mitochondrial dynamics and synaptic degeneration in AD neurons. Further, recent studies using live-cell imaging and primary neurons from amyloid precursor protein (APP) transgenic mice revealed reduced mitochondrial mass, defective axonal transport of mitochondria and synaptic degeneration, indicating that Aβ is responsible for mitochondrial and synaptic deficiencies. We recently found that abnormal physical interaction between mitochondrial fission protein, dynamin-related protein 1 (Drp1) and Aβ and Drp1 and phosphorylated tau (p-Tau), leading to excessive mitochondrial fragmentation, reduced mitochondrial fusion and defective mitochondrial function in AD (Manczak et al 2011 Hum Mol Genet and Manczak and Reddy 2012 Hum Mol Genet). Based on these observations, we hypothesized that a partial reduction of Drp1 inhibits and Drp1and Aβ and Drp1-pTau interactions and protects neurons from pTau-induced mitochondrial and synaptic toxicities, and maintains neuronal function in AD progression. To test our hypothesis, we created double mutant (Drp1+/-xTau) mice. Using molecular, biochemical, Golgi-cox staining and transmission electron microscopy studies, we investigated mRNA, protein levels of mitochondrial dynamics, biogenesis and synaptic genes, dendritic spines, mitochondrial number and morphology and Morris Water Maze based cognitive behavior in 12-month-old Drp1+/-xTau mice. We found significantly increased dendritic spines, significantly reduced fragmented and structurally damaged mitochondria and reduced mRNA and protein levels of fission genes and increased levels of fusion, biogenesis and synaptic genes in the brains of 12-month-old Drp1+/-xTau mice relative to age-matched Tau mice. Importantly, we also found ameliorated cognitive deficits in 12-month-old Drp1+/-xTau mice relative to age-matched Tau mice. These observations strongly suggest that reduced Drp1 is beneficial to AD neurons and may have a therapeutic value to AD patients.

**Title:** **Reduced Dynamin-Related Protein 1 Mitigates Mitochondrial Fragmentation, Elevates Spatial Learning and Memory Functions and Elevates Dendritic Spines in App Transgenic Mice**

**Maria Manczak1,4 , Ramesh Kandimalla1,3, Xiangling Yin1, , Murali Vijayan1, Chandra Sekhar Kuriva1, Subodh Kumar1, P. Hemachandra Reddy 1,2,3,4,5,6**

**1. Garrison Institute on Aging, 2. Cell Biology & Biochemistry, 3.Pharmacology/Neuroscience, 4. Neurology, 5. Department of Public Health and 6. Speech, Language and Hearing Sciences Departments, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, Texas 79430; 6. Garrison Institute on Aging, South West Campus, Texas Tech University Health Sciences Center, 6630 S. Quaker Ste. E, MS 7495, Lubbock, Texas 79413**

**Poster Presenter:** **Maria Manczak, PhD**

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**Abstract:**

The purpose of our study is to understand the protective effects of reduced levels of mitochondrial fission protein Drp1 against amyloid beta (Aβ) induced mitochondrial abnormalities and synaptic deficiencies in Alzheimer's disease (AD) pathogenesis. Mounting evidence suggests that Aβ-induced mitochondrial dysfunction and synaptic damage are largely involved in AD progression and pathogenesis. We recently found that abnormal physical interaction between Drp1 and Aβ, leading to excessive mitochondrial fragmentation, reduced mitochondrial fusion In the current study we continued to explore the reduced Drp1 biological functions in lieu of spatial learning and memory, synaptic numbers and mitochondrial number/size along with the expression of mitochondrial division/fusion proteins, synaptic proteins, and biogenesis proteins in 12-month-old APPXDrp1+/- relative to the 12-month-old APP mice. Our findings suggest that a partial reduction of Drp1 increased dendritic spines (Golgi-cox) may potentially be effective in ameliorating cognitive function (Morris-water maze). In addition, reduced Aβ production in APPXDrp1+/- mice eventually reduced mitochondrial dysfunction, and maintains mitochondrial dynamics, enhances mitochondrial biogenesis and synaptic plasticity. Based on these observations, we conclude that a partial reduction of Drp1 may serve as therapeutic traget in preventing Alzheimer's disease.

**Title:** **Protective Effects of DDQ Against Mutant Huntingtin-induced Mitochondrial and Synaptic Toxicities in Huntington's Disease Striatal Neurons**

**Joshua Willms, Bhagavathi Ramasubramanian, Neha Sawant and P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Joshua Willms**

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**Abstract:**

Huntington's disease (HD) is a progressive, fatal neurodegenerative disease, characterized by chorea, seizures, involuntary movements, dystonia, cognitive decline, intellectual impairment and emotional disturbances. HD has an autosomal dominant pattern of inheritance and an age-dependent penetrance. HD is a rare disease, occurs in 4–10 per 100,000 persons, mainly of Caucasian origin. HD caused by polyglutamine (polyQ) repeat expansion within the exon 1 of HD gene, that encodes an expanded polyQ stretch in the huntingtin (Htt) protein. Although both wild-type and mutant Htt proteins are expressed ubiquitously in the peripheral and central nervous systems, medium spiny neurons (MSNs) in the basal ganglia of selectively affected. The precise reasons for this selective neurodegeneration are not completely understood. Cellular changes occur in MSNs as the disease progresses, including the formation of inclusion bodies, calcium dyshomeostasis, impairment of axonal transport, and mitochondrial fusion/fission imbalance. Further, there are no drugs/agents that prevent disease progression in patients with HD. Recently, we designed and synthesized DDQ [diethyl (3,4-dihydroxyphenethylamino)(quinolin-4-yl) methylphosphonate] based on the structure of dopamine and tested it in Alzheimer's disease (AD) cell models and found reduced mitochondrial fission and increased fusion and synaptic activity. Based these data, we hypothesize that DDQ will reduce mitochondrial fragmentation and increase synaptic activity in HD neurons. In the current study, we propose to investigate mitochondrial dynamics, biogenesis, autophagy/mitophagy and synaptic activity in both WT (STHDhQ7/Q7) and mutant striatal (STHDhQ111/Q111) neurons treated and untreated with DDQ. We will use biochemical, molecular, immunoblotting/immunofluorescence, transmission electron microscopy and confocal microscopy techniques. Preliminarily, we tested five concentrations of DDQ in both WT and mutant striatal neurons and found significantly increased cell viability at 250 nM concentration. In the current presentation, we will discuss the effect of DDQ on mitochondrial dynamics, biogenesis, autophagy/mitophagy and synaptic activity.

**Title:** **Protective Role of Citalopram Against Amyloid Beta-induced Mitochondrial, Autophagy and Synaptic Toxicities in Alzheimer's Disease**

**Xiangling Yin[1], Arubala P Reddy[2], Subodh Kumar[1] and P. Hemachandra Reddy[1,2]**

**1. Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**2. Pharmacology & Neuroscience Department, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Xiangling Yin**

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**Abstract:**

Alzheimer's disease (AD) is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and eventually the ability to carry out the simplest tasks. AD is also associated with synaptic loss and mitochondrial damage, selectively in learning and memory regions of the brain, including hippocampus and cortical regions of the brain. According to Alzheimer's Association, more than 50 million people, including 5.7 million Americans suffer from AD. Currently, there are no drugs that can delay and/or prevent the progression of disease in patients with Alzheimer's. Researchers found that up to 38 percent less serotonin in mild cognitive impaired subjects than cognitively healthy, age-matched counterparts. Serotonin is a hormone that transmits messages between nerve cells, and serotonin may play a key role in AD and other mental disorders. Citalopram is used to treat depression, anxiety, eating disorders and obsessive-compulsive disorder among other mood disorders. Citalopram selectively inhibits the neuronal reuptake of the neurotransmitter serotonin (5-HT) in presynaptic cells in the central nervous system, thereby increasing the levels of serotonin within the synaptic cleft and enhancing the actions of serotonin on its receptors. However, there are no studies that investigate the role of citalopram on mitochondrial dynamics, biogenesis, and autophagy/mitophagy activities in AD. In the current study, we investigated the protective effects of citalopram against amyloid beta (Aβ)-induced mitochondrial, autophagy and synaptic toxicities in AD using mouse primary hippocampal (HT22) neurons. We transfected HT22 cells with human mutant APP (with Swe/Ind) mutations and treated with citalopram and assessed mitochondrial dynamics, biogenesis, and autophagy/mitophagy activities. We found decreased levels of mitochondrial fission genes Drp1 and Fis1, increased levels of fusion genes Mfn1, Mfn2 and OPA1, increased levels of mitochondrial biogenesis genes PGC1α, Nrf1, Nrf2, TFAM, and increased levels of synaptic genes synaptophysin and PSD95 in mutant APP cells treated with citalopram relative to untreated mutant APP cells. Interestingly, we also found increased levels of mitophagy genes PNK1, TERT and autophagy genes ATG5, ATG7, LC3B and P62 in mutant APP cells treated with citalopram relative to untreated mutant APP cells. Importantly, we also found reduced levels of C-terminal fragment C99, and Aβ42 levels in mutant APP cells treated with citalopram relative to untreated mutant APP cells. Further, we also found mitochondrial number significantly decreased and average mitochondrial length significantly increased in mutant APP cells treated with citalopram relative to untreated mutant APP cells. Based on these observations, we conclude that citalopram is protective against amyloid beta-induced toxicities.

**Title:** **Analysis of Blood-based Biomarkers to Detect Cognitive Decline Among The Residents of Rural West Texas – Project FRONTIER Data**

**Bhagavathi Ramasubramanian, Divya Burugu, Xiangling Yin, Annette Boles and P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Bhagavathi Ramasubramanian, PhD**

**Abstract:**

The purpose of this study is to determine the blood-based biomarkers as indicators of cognitive decline in the residents of rural west Texas. Alzheimer's disease (AD) is a slow progressive neurodegenerative disorder that destroys mental function. According to CDC over 5 million Americans are living with AD and this is expected to increase to 14 million by the year 2060. The neuropathological state of AD includes amyloid beta (Aβ) containing plaques and cytoskeletal protein, Tau containing neurofibrillary tangles in learning and memory regions of the brain. AD is of a serious public health concern. Since no cure exists for the disease, the current treatment includes effective medical management. Early diagnosis of the disease has been shown to be more effective and provide better treatment options. One of the ways to detect the presence of the disease is to measure the levels of early detectable biomarkers. Increasing evidence has been focused on studying the levels of Aβ and Tau in cerebrospinal fluid (CSF). However, reliable methods to determine the biomarkers in blood is still being explored and more practical. Therefore, in the current study, we investigated serum samples obtained from the residents of rural West Texas, as a part of ongoing study – Project FRONTIER. In an attempt to optimize the ELISA test, we initially analyzed 80 serum samples from participants in project FRONTIER. These are either healthy controls or few people with history of depression and anxiety, in the age group 45-85 in both males and females. We tested for nine different AD biomarkers, including Aβ 40 and 42, phosphorylated Tau, soluble APP-α, soluble APP-β, BACE-1, BDNF, and the neurotransmitters serotonin and dopamine. We found detectable levels of 7 markers, including Aβ 40 and 42, phosphorylated Tau, sAPP-α, BACE-1, BDNF and serotonin in serum samples that we studied. We also found huge variation in the levels of Aβ42, and moderate variability in the levels of Phosphotau-181 and serotonin. The levels of sAPP-β and dopamine could not be detected for any of these subjects at the given sensitive range of the kit used. These findings will provide us the basis to validate and establish a cutoff value for the blood-based biomarkers for healthy, non-demented subjects versus cognitively impaired individuals. We will discuss our findings of blood-based biomarkers in relation to cognitive/demographic status of all 80 serum samples from participants of rural West Texas.

**Title:** **An Assessment – Texas Healthy Communities Program.**

**Veronica Lopez, Annette N. Boles, MS, P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA**

**Poster Presenter:** **Veronica Lopez**

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**Abstract:**

The purpose of the Texas Healthy Communities grant is to assess Lubbock County has policies and environments that promote chronic disease awareness and education and promote healthier worksites, schools, and communities. The Garrison Institute on Aging staff assesses nine specific indicators that were identified by the Department of State Health Services.

Texas Healthy Communities Program promotes public health practices to reduce the risks factors for cardiovascular disease and stroke disease. Communities assess their existing environment. Environmental, policy and system changes at the local level are evaluated using nine community-based policy, systems and environmental change indicators.

In the poster presentation, we will discuss the current state of the Lubbock community, the assessment that was conducted and future directions of the program.

**Title:** **Project FRONTIER: Study Protocol**

**Annette N. Boles, MS, P. Hemachandra Reddy, PhD, Veronica Lopez, Gabriela Arandia, PhD, Rocio Carrasco, Cordelia Aguirre**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA.**

**Poster Presenter:** **Annette Boles, MS**

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**Abstract:**

Project FRONTIER (Facing Rural Obstacles to Healthcare Now Through Intervention, Education & Research) is an ongoing longitudinal epidemiological study exploring the natural course of chronic disease development and its impact on longitudinal cognitive, physical, social, and interpersonal functioning in a multi-ethnic sample of adults and elders living in rural communities of West Texas.

There are eleven aims of Project FRONTIER and the GIA staff is working on projects associated with these aims. The first aim is to evaluate the prevalence of cardiovascular disease and associated risk factors using self-report and objective assessments of risk factors. Project FRONTIER also seeks to evaluate the prevalence of cognitive dysfunction and dementia syndromes in this rural cohort using medical, neuropsychological, and functional assessments. Another aim is to examine the link between cardiovascular disease and associated risk factors and cognitive functioning as well as the risk conveyed for dementia associated with these factors. There is also a need to evaluate the link between alcohol and substance use on cognition and healthcare status. The staff also examines healthcare disparities between ethnic groups residing within the county (primarily Mexican American and non-Hispanic white), and investigates gender differences in healthcare status. Dr. Reddy's lab staff also evaluates the link between inflammation (via C-Reactive Protein) and cognition and the potential mediating role of this protein in the link between cognitive dysfunction and cardiovascular disease. The research lab staff also assesses blood-based microRNAs as peripheral biomarkers in aging and neurological diseases, and evaluates coronary heart disease in males and females. Another aim is to evaluation how depression and/or anxiety impact physical and mental health; and the link between sleep apnea and cognition will be evaluated. We will discuss the protocol of Project FRONTIER, measures that are assessed, and descriptive findings.

**Title:** **Healthy Lubbock Workshops**

**Veronica Lopez, Susan Thompson, Annette N. Boles, MS, Rocio Carrasco, Cordelia Aguirre, Joan Blackmon, P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA.**

**Poster Presenter:** **Veronica Lopez**

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**Abstract:**

Garrison Institute on Aging (GIA) has been involved with the multiple agencies and organizations, such as the Area Agency on Aging, the City of Lubbock Health Department, the City of Lubbock Park and Recreation, Texas Tech University Health Sciences Center Worksite Overall Wellness Program, Texas A&M Center for Population Health and Aging and experts in the field, such as John Culberson, MD. These collaborative efforts enable the GIA to establish workshops that are evidence based and provide an educational service to community members that need information on self-care.

The GIA is a unique organization whose mission is to promote healthy aging through cutting-edge research in Alzheimer's disease and other diseases of aging, and through innovative educational and community outreach programs that target students, clinicians, researchers, health care professionals and the public. The vision of the institute is to become nationally and internationally recognized as a center of excellence for the creation and application of new knowledge about healthy aging through research, innovative interdisciplinary education and collaborative community outreach efforts.

The purpose of the poster presentation is to explain the multiple workshops the GIA provides as a service to the community. In the presentation, we will discuss the current status of Healthy Lubbock workshops.

**Title:** **TTUHSC Garrison Institute on Aging – Community Outreach Programs Healthy Lubbock Programs**

**Annette N. Boles, MS, Veronica Lopez, Clay Ament, Joan Blackmon, Susan Thompson, P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA.**

**Poster Presenter:** **Annette N. Boles, MS**

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**Abstract:**

Healthy Lubbock is a program of the Texas Tech University Health Sciences Center (TTUHSC) Garrison Institute on Aging (GIA). The community outreach division aims to provide health information and services about healthy aging by collaborating with local, state and national organizations to foster healthy lifestyles.

Programs that have been implemented by GIA staff provide and promote healthy activities and options for everyone in Lubbock and the surrounding communities. They also educate individuals about healthy behavioral choices for themselves and for their families in a positive and affirming manner. The GIA staff plays a leadership role in developing, implementing, tracking, and evaluating various health initiatives. The GIA staff values each relationship that is established with community organizations and individuals.

We will discuss the long-standing efforts of the GIA and the importance of community outreach programs for Lubbock and surrounding communities.

**Title:** **Lubbock Retired & Senior Volunteer Program**

**Clay Ament, Annette Boles, MS, Joan Blackmon, P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA.**

**Poster Presenter:** **Clay Ament**

**Abstract:**

Lubbock Retired & Senior Volunteer Program (RSVP) is a grant funded non-profit agency sponsored by the Texas Tech University Health Sciences Center's (TTUHSC) Garrison Institute on Aging (GIA). The program was established in 1979 and is under the umbrella of the Corporation for National and Community Service (CNCS) and Senior Corps. RSVP was established with the purpose of encouraging adults, who are 55 and older, to volunteer and assist the Lubbock community by using the abilities, skills, and interests they have acquired throughout their life. The program engages seniors in a wide array of community service projects that help non-profit and community-based organizations working in health, nutrition, human services, education, community, and economic development and public safety.

The poster presentation will highlight how the RSVP program improve lives, strengthen communities, and foster civic engagement through service and volunteering.

**Title:** **Region- and Circuit-Specific Changes in Somatostatin and Parvalbumin Interneuron Networks in Novel Alzheimer's Disease Mouse Models: Insights Into Seizure-Induced Circuit Remodeling**

**Rui Wang[1], Emily R Stephens[1,2], Brittney Hoang[1,2], and J. Josh Lawrence[1]**

**[1]Department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center, 3601 4th St, Lubbock, TX 79430**

**[2]Honors College, Texas Tech University, 2500 Broadway, Lubbock, TX 79409**

**Poster Presenter:** **Rui Wang**

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**Abstract:**

Hippocampal hyperexcitability during Alzheimer's disease (AD) pathogenesis causes spatial memory deficits and seizure susceptibility. During memory formation, spatial information is routed through the dentate gyrus (DG) and CA3 region. The DG separates patterns by sparse coding of incoming sensory input to the hippocampus, whereas the CA3 region completes patterns by recruiting internally stored memory traces. Intact parvalbumin (PV)-positive feedforward and somatostatin (SOM)-positive feedback circuits are required for both pattern separation and completion operations. Moreover, hippocampal rhythms rely on the integrity of long-range PV and SOM circuits. Despite increased appreciation of the importance of these inhibitory circuits in normal DG/CA3 function, their roles during AD have yet to be determined. In this study, we investigated the differential contributions of specific PV and SOM circuits to the etiology of AD using the J20 mouse transgenic model that overexpresses a mutant form of human amyloid precursor protein (hAPP). We generated novel triple transgenic (3Tg) $J20^{+/-}$ AD mouse models, which enable CRE recombinase-dependent expression of the red fluorescent protein tdTomato in PV or SOM circuits, and we found significant differential expression of tdTomato in PV/SOM cells in a region- and time-specific manner. Particularly, in 7-month-old 3Tg mice, SOM-CRE; tdTomato expression revealed a massive upregulation of SOM circuits, including a *de novo* SOM circuit targeting DG inner molecular layer (IML). The appearance of this *de novo* circuit coincides with published reports of memory deficits and was absent from 2-month-old $J20^{+/-}$ mice and age-matched $J20^{-/-}$ sibling littermate controls. In contrast, PV-CRE; tdTomato expression was reduced in DG and CA3 principal cell layers in $J20^{+/-}$ mice at both 2 and 7 months of age compared to $J20^{-/-}$ littermate controls, suggesting an earlier global impairment of PV signaling. These novel findings indicate differential alterations of PV and SOM circuitry in the etiology of AD, suggesting that disruption of PV and SOM circuits impairs spatial memory formation through divergent synaptic mechanisms. For future directions, we aim to further identifying PV and SOM neuron subpopulations that cause aberrant synaptic connections, determine synaptic consequences and cellular mechanisms of PV/SOM dysfunction in 3Tg AD mouse models, and investigate the behavioral impact of PV and SOM dysfunction on hippocampal memory tasks.

**Title:** **The lysosomal-mitochondrial axis and neurodegeneration in Alzheimer's disease: dissecting molecular mechanisms**

**Kevin Bass and P. Hemachandra Reddy**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9424, Lubbock, TX 79430, United States**

**Poster Presenter:** **Kevin Bass, MD/PhD Student**

**Abstract:**

Endosomal-lysosomal network (ELN) dysfunction and mitochondrial fragmentation are the twin cellular bioenergetic hallmarks of Alzheimer's disease (AD) and other neurodegenerative states. For instance, many neurodegenerative lysosomal storage diseases (LSDs)—for which ELN dysfunction is a core feature—also exhibit mitochondrial dysfunction. ELN and mitochondrial dysfunction are each characteristic of many neurodegenerative and other diseases, and many of the genetic risk factors for these diseases modulate either ELN or mitochondrial function and impact both. Recent experimental evidence manipulating ELN and mitochondrial function frequently demonstrates a close relationship between the two. For instance, deleting autophagy genes causes mitochondrial fragmentation, and overexpressing autophagic genes rescues mitochondrial functionality in disease models. Similarly, inducing and rescuing mitochondrial dysfunction induces and rescues ELN dysfunction, respectively.

Dynamin-related protein 1 (Drp1) is a mitochondrial fission protein whose activity has been shown to be upregulated in neurodegenerative diseases. In mutant APP and mutant tau overexpression models, reducing Drp1 activity via genetic knockout or pharmacological inhibition by Mdivi-1 rescues both mitochondrial function and autophagy gene expression. However, the impact of these changes on ELN function is not well-characterized. Likewise, as noted above, exactly why autophagy induction (via overexpression of Beclin-1, ATG5, ATG7, TFEB, and others) rescues neurodegeneration is not clear. In part, this is because of crosstalk between these autophagy genes and other critical signaling pathways.

In *in vitro* and *in vivo* model systems for AD, we propose to investigate the relationship between autophagy and mitochondrial function in relation to neurodegeneration. We will use transient and stable gene overexpression, RNA interference, immunoblotting, immunohistochemistry, ELISA, transmission electron and confocal microscopy, and other techniques. We will characterize *in vitro* cellular function changes that occur when ATG7 and other autophagy-inducing proteins are overexpressed in mutant APP and Tau HT-22 models. We will also characterize changes in autophagy that occur after Drp1 overexpression and knockdown. We will also conduct experiments in mutant APP transgenic mice that have hippocampus-specific floxed-in and floxed-out ATG7 alleles. These experiments will begin to "dissect" the cellular mechanisms responsible for observed improvements to AD models. Since AD model pathology has been improved through interventions that operate through entirely different mechanisms, the above approach may identify the extent to which different interventions correcting different cellular dysfunctions provides separate or overlapping benefits. This will give insight into whether and how each pathway might plausibly be multiply activated or inhibited to provide additive or synergistic therapeutic benefit in AD. This is particularly pertinent in AD, because AD pathology seems to involve multiple feed-forward systems that may need to be multiply and simultaneously reversed to achieve therapeutic success.

**Title:** Age- and Gender-Based MicroRNA Levels in C57BL6/J mice

**Christopher Hornback[1], Subodh Kumar[1], Murali Vijayan[1], C. Breann Williams[1], Pratibha Kottapalli[2], Rao Kottapalli[2], P. Hemachandra Reddy[1]**

**1. Garrison Institute on Aging, Texas Tech University Health Sciences Center, 3601 4th Street, MS 424, Lubbock, TX, 79430, United States**

**2. Center Biotechnology and Genomics Core Facility, Texas Tech University, Canton & Main Experimental Sciences Building, Room 101, Lubbock, TX 79409, United States**

**Poster Presenter:** Christopher Hornback

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**Abstract:**

The purpose of this study is to determine the age and gender differences in expression of microRNAs (miRNAs) in mice. MicroRNAs are short stranded, non-coding, RNA molecules that are approximately 22 base-pairs in length. Mature miRNA help regulate gene expression through complementary base paring with messenger RNA (mRNA). In mammalian organisms, miRNA base pairing is not completely complementary to the mRNA strand, and a single miRNA can have many targets. MicroRNA levels were reported to differentially expressed in a large number of human diseases, including cancer, neurodegenerative diseases, Alzheimer's, Parkinson's, Huntington's, ALS and multiple sclerosis. In most of these diseases, aging plays a key role in disease progression and pathogenesis. Age-dependent differential expression of miRNAs in mammals, including rodents, humans are not completely understood. Further, gender plays a large role in some of these diseases, including Alzheimer's and multiple sclerosis. Currently, we do not have base-line gender-based miRNA profiles in rodents and humans. Therefore, it is important to establish age- and gender-based miRNA profiles in mice. Hence, in the current study, we propose to investigate age- and gender-based miRNA levels in C57BL6/J mice. Using Illumina/RNA-Seq approach, we studied miRNA levels in brain and skeletal muscle tissues from 2-, 6-, 12- and 24-month-old male and female C57BL6/J mice. We analyzed the data 2 months to 6 months, 2 months to 12 months and 2 months to 24-month-old mice in order to understand the impact of aging. We also analyzed the data between male and female mice to determine gender-based changes, if any. The outcome of our findings will provide age- and gender-related base-line miRNA levels.

## Oral Abstracts

**Title: MicroRNA-455-3p as a potential peripheral biomarker and therapeutic target for Alzheimer's disease**

**Subodh Kumar, PhD and P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center**

**Oral Presenter: Subodh Kumar, PhD**

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**Abstract:**

The purpose of our study was to identify microRNAs (miRNAs) as early detectable peripheral biomarkers in Alzheimer's disease (AD). To achieve our objective, we assessed miRNAs in serum samples from AD patients, mild cognitive impairment (MCI) subjects and healthy controls by using Affymetrix microarray. Our global microRNA analysis showed a gradual upregulation of four miRNAs: miR-455-3p, miR-4668-5p, miR-3613-3p and miR-4674. A fifth miRNA, mir-6722, was down-regulated in persons with AD and MCI compared with controls. We further validated these miRNA in AD postmortem brains, APP transgenic mice, AD cell lines, fibroblasts and B-lymphocytes obtained from AD patients. Our qRT-PCR validation analysis identified significant upregulation of only miR-455-3p in different AD sources. Receiver operating characteristic (ROC) curve analysis of miR-455-3p in AD serum, AD postmortem brains, fibroblasts and B-lymphocytes showed a significant AUC values for miR-455-3p. We also studied the role of miR-455-3p in amyloid precursor protein (APP) processing and amyloid-β(1-40) and Aβ(1-42) levels and mitochondrial biogenesis and synaptic activity. We found that the miR-455-3p decrease abnormal APP processing and increase mitochondrial biogenesis and synaptic activity. Based on these observations, we cautiously conclude that miR-455-3p could be an effective therapeutic target and potential peripheral biomarker for AD.

**Title:** **Novel microRNA PC-5P-12969 as Potential Peripheral Biomarker for Ischemic Stroke**

**Murali Vijayan, PhD and P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center, Lubbock, TX, USA.**

**Oral Presenter:** **Murali Vijayan, PhD**

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**Abstract:**

The purpose of this study is to determine circulatory microRNAs (miRNAs) as early detectable peripheral biomarkers in patients with ischemic stroke (IS). MicroRNAs are involved in growth, development, and occurrence & progression of many diseases. Circulating miRNAs have been used effectively as biomarkers and mechanistic targets for neurodegenerative diseases, including such as stroke, Alzheimer's and Parkinson's. MiRNA mediated post-transcriptional regulation is poorly understood in neurodegenerative diseases and vascular biology. In the current study, microRNA expression levels were measured in IS serum samples and healthy controls using Illumina deep sequencing analysis and identified differentially expressed miRNAs. Differentially expressed miRNAs were further validated using SYBR-green-based quantitative real-time PCR (qRT-PCR) assay in postmortem IS brains, lymphoblastoid IS cell lines, oxygen and glucose deprivation/reoxygenation -treated human and mouse neuroblastoma cells, and mouse models of hypoxia and ischemia (HI)-induced stroke. A total of 4656 miRNAs were differentially expressed in IS serum samples relative to healthy controls. Out of 4656 miRNAs, 272 were found to be significantly deregulated in IS patients. Interestingly, we found several novel and previously unreported miRNAs in IS patients relative to healthy controls. Further analyses of previously unreported miRNA PC-5P-12969 and their functional relevance to ischemic stroke using in vitro and in vivo models will be discussed.

**Title:** **Synthesis and Structure-Activity Relationship Studies of AG18051 and Its Analogs in the Treatment of Alzheimer's Disease by Inhibiting Aβ-ABAD Interaction**

**Ahmed Morsya, Paul C. Trippier**

**1. Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, School of Pharmacy, Amarillo, Texas 79106, USA.**

**2. Center for Chemical Biology, Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409, USA.**

**Oral Presenter:** **Ahmed Morsya**

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**Abstract:**

Alzheimer's disease (AD) is the most common form of dementia affecting around 20 million people worldwide. The disease pathology starts by formation and aggregation of amyloid beta protein (Aβ), in which the oligomeric form has been identified to be the neurotoxic form. Mitochondrial dysfunction is a hallmark for Aβ neurotoxicity. This is due in part to the interaction between Aβ and mitochondrial enzyme amyloid-binding alcohol dehydrogenase (ABAD). This enzyme is an important energy regulator in the mitochondria that acts by oxidizing and reducing substrates with a NAD molecule as a co-factor.

Estradiol, a substrate for ABAD, plays a vital function in the mitochondrial system and its levels are an important determinant of neuronal survival. The role of ABAD is to maintain the balance of estradiol/estrone in neurons. However, Aβ-ABAD interaction disrupts this balance and leads to reduction in the levels of estradiol. Thus, leading to an increase in ROS levels, DNA fragmentation and apoptosis. Two other ABAD substrates have been identified to date: peroxiredoxin-2, which functions as an antioxidant and has been shown to be inactivated in AD. Second, endophilin-1, a member of a family of proteins that are responsible for synaptic vesicle endocytosis mitochondrial function, and receptor trafficking. Its activity has been shown to be diminished in AD. Thus, ABAD represents a novel target for the development of pharmacological inhibitors to treat AD.

Several groups targeting the Aβ-ABAD interaction identified inhibitors, that are still in their nascent stages of development and require further optimization. The most potent inhibitor identified to date is AG18051, (IC50 = 92 nM), containing a pyrazolo[3,4-d]pyrimidine-4(1H)-thione backbone. The compound binds in the active-site cavity of the enzyme and reacts with the NAD+ cofactor to form a covalent adduct. Despite its promising activity AG18051 has not been studied further. We have synthesized and characterized a library of AG18051 analogues possessing structural diversity. Assaying our library of compounds for neuroprotective action to ameliorate Aβ-induced toxicity in human SH-SY5Y cells has identified derivatives with increased protective effect and simpler more 'drug-like' structures.

**Title:** **mTOR/S6K1 at the crossroad between aging and Alzheimer's disease**

**1. Arizona State University-Banner Neurodegenerative Disease Research Center at the Biodesign Institute, Arizona State University, Tempe, AZ, 85287**

**2. School of Life Sciences, Arizona State University, Tempe, Arizona, 85287.**

**Oral Presenter:** **Salvatore Oddo**

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**Abstract:**

Aging is the major risk factor for Alzheimer' disease (AD); however, little is known as to how the aging process facilitates the development of AD. Changes that occur in the brain as a function of age may facilitate the development of AD. Reducing the activity of the mammalian target of rapamycin (mTOR), and its downstream target S6K1, increases lifespan and healthspan in several genetically different species. mTOR is a protein kinase that plays a key role in regulating protein translation (via S6K1) and degradation. Therefore, mTOR is key in controlling protein homeostasis, a process that is altered in AD and other proteinopathies. Using several mouse models of AD, we employed multidisciplinary approaches to dissect the role of the mTOR/S6K1 signaling in AD. We will show that genetic and pharmacologic reduction of mTOR and S6K1 signaling reduced amyloid-β and tau pathology and rescued memory deficits. We will also show that reducing mTOR signaling rescues some of the gene expression dysregulation associated with AD. Given that mTOR and S6K1 regulate lifespan and healthspan, the data presented here have profound clinical implications for aging and Alzheimer's disease and provide the molecular basis for how aging may contribute to AD pathology. Our results implicate hyperactive mTOR/S6K1 signaling as a previous unidentified signaling pathway underlying gene expression dysregulation and cognitive deficits in Alzheimer's disease.

## Abstract for Oral Presentation

**Title: The Impact of Chronic Diseases on Aging: A Look at Epidemiology, Risk Factors, and Programmatic Efforts for Chronic Disease Prevention**

**Gabriela Arandia, PhD and P. Hemachandra Reddy, PhD**

**Garrison Institute on Aging, Texas Tech University Health Sciences Center**

**Oral Presenter: Gabriela Arandia, PhD**

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**Abstract:**

Aging is the major risk factor for many chronic diseases. With a growing aging population, the burden of chronic diseases, including heart disease, stroke, cancer, diabetes, and Alzheimer's disease, stands at the forefront of public health concerns. These long-term conditions give rise to morbidity and mortality risks later in life. The objectives of this oral presentation are to: 1) present epidemiological data on chronic diseases, 2) highlight modifiable and non-modifiable risk factors and protective factors, and lastly, 3) present an overview of policy and programmatic efforts at the global, national, state, and local levels that aim to address and reduce chronic diseases. Local efforts include the Garrison Institute on Aging of TTUHSC, which spearheads research, community outreach, and health education initiatives for Lubbock and surrounding rural West Texas communities. This presentation discusses with currently available evidence on chronic diseases and public health initiatives.

**Title: Parvalbumin and somatostatin circuitry dysfunction differentially impairs hippocampal DG/CA3 function during Alzheimer's disease pathogenesis**

**Rui Wang[1], Emily R Stephens[1,2], Brittney Hoang[1,2], and J. Josh Lawrence[1]**

**[1]Department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center, 3601 4th St, Lubbock, TX 79430**

**[2]Honors College, Texas Tech University, 2500 Broadway, Lubbock, TX 79409**

**Oral Presenter: J. Josh Lawrence**

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For future directions, we aim to further identifying PV and SOM neuron subpopulations that cause aberrant synaptic connections, determine synaptic consequences and cellular mechanisms of PV/SOM dysfunction in 3Tg AD mouse models and investigate the behavioral impact of PV and SOM dysfunction on hippocampal memory tasks.