

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTE HEALTH SCIENCES CENTER

Garrison Institute on Aging

Annual Report 2015 - 2016







TABLE OF CONTENTS

- 2 Garrison Institute on Aging
- 3 Executive Director's Report
- 5-6 Garrison Institute on Aging Staff
- 7 Research The Molecular Basis
- 11 Research Drug Discovery Unit
- 14 Research Biomarker Development Unit
- 14 Spike Dykes Charity Golf Tournament
- 15 Research Research Collaborations
- 15 Research Collaborations with Department of Public Health
- 15 Research Student Scholars and Visiting Scientists
- 17 Aging and Alzheimer's Disease Journal Club
- 17 Funding
- 18-19 Community Outreach and Education Project FRONTIER
- 20 Healthy Aging Lecture Series
- 20 Research Seminar Series
- 21 Community Outreach and Education Healthy Lubbock
- 21 The Project FRONTIER and Public Health Journal Club
- 22 Community Outreach and Education Marathon for Kids
- 22 Community Outreach and Education Retired Senior Volunteer Program
- 23 Community Outreach and Education Bike Fix It Station
- 23 Community Outreach and Education Healthy Lubbock Events Website
- 23 Community Outreach and Education -Community Gardens
- 24-25 Publications
- 26 Invited Talks/Presentations at Local, National and International Conferences of GIA Scientists
- 27 Poster Presentations
- 28 Grants

Mission of the GIA

The Garrison Institute on Aging is a unique organization whose mission is to promote healthy aging through cutting-edge research on Alzheimer's disease and other diseases of aging, and through innovative educational and community outreach programs that target students, health care professionals and the public.



TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Garrison Institute on Aging



Shirley L. Garrison Founder of the Garrison Institute on Aging

he Garrison Institute on Aging (GIA), formerly the Institute for Healthy Aging, was established in 1999 by the Texas Board of Regents to meet Texas Tech University Health Sciences Center's (TTUHSC) strategic priority on aging and as a collaborative initiative with the TTUHSC Schools of Health Professionals, Medicine, Nursing, and Pharmacy. The GIA is a unique organization, whose mission is to promote healthy aging of the populace through cutting-edge research on Alzheimer's disease (AD) and other diseases of aging, through the development of innovative educational opportunities for students, clinicians, researchers, health care professionals, and the public. The vision of the GIA 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.

In 2004, through an endowment funded by Mr. and Mrs. Shirley L. Garrison and by private donations, the GIA was created to support aging research and education programs. Multiple programs were established, including: 1) education and community outreach programs and activities, and 2) Geriatric Education and Training Academy of Certified Nurse Aides (CNA). The CNA program focused on training health care professionals who assist elderly populations. In 2007, researchers designed a collaborative, multidisciplinary study known as the Cochran County Aging Study, which researches cognitive decline and dementia syndromes of the elderly in rural Texas. The GIA also developed the first multidisciplinary, multi-school program – the Student Scholars Program – that trains university-level seniors from Texas Tech University (TTU) and TTUHSC in health care issues of the elderly. The community outreach division has grown from providing health fairs through the Healthy Lubbock program to providing new programs that focus on self-management of chronic diseases, healthy eating, and active living.

In the GIA research laboratories, academic professionals develop and perform cutting-edge research projects aimed at understanding AD and other diseases of aging, as well as developing novel therapeutic approaches to cure or prevent age-related disorders and diseases.

Vision of the GIA

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.

EXECUTIVE DIRECTOR'S REPORT

he Garrison Institute on Aging (GIA) has enjoyed a productive and exciting 2015-2016. With strong support from colleagues at the GIA and leadership from Texas Tech University Health Sciences Center, GIA colleagues and I expanded the GIA on several fronts: Research, Project FRONTIER and Students Scholars and Visiting Scientists Program. Previously from the F. Marie Hall Institute for Rural and Community Health, Project FRONTIER is now a part of the GIA. I started the Aging and Alzheimer's Disease Journal Club and the Project FRONTIER and Public Health Journal Club. The Student-Scholars program is expanded and running well, now covering medical, public health, graduate and high school students at GIA.

I expanded the research arm of the GIA into three units: Molecular Basis, Drug Discovery, and Biomarker Development. The major objectives of the Molecular Basis Unit are to elucidate factors that promote healthy aging of the brain, to prevent and/or delay the progression of Alzheimer's disease, stroke, Huntington's disease and Parkinson's disease and to identify conditions that accelerate dementia in elderly individuals, including Type 2 diabetes mellitus and obesity. The objective of the Drug Discovery Unit is to develop drug molecules capable of reducing the impact of mutant proteininduced neuronal toxicities in Alzheimer's and Huntington's disease neurons. The Biomarker Development Unit was formed to develop peripheral biomarkers capable of identifying early detectable biomarkers for dementia. With this new unit, the Reddy Lab scientists are actively working to identify peripheral biomarkers – referred microRNAs for Alzheimer's disease, and related conditions such as stroke, vascular dementia and diabetes.

Colleagues at Outreach/Education and I have expanded Project FRONTIER to better understand conditions that impact the local health care system that serves minorities in rural West Texas and to use this information to inform the West Texas residents of what they can do to improve overall health in their community. The expanded focus of Project FRONTIER has received strong support from TTUHSC President Tedd L. Mitchell, M.D. Other projects expanded under the GIA auspices include GET FiT Lubbock and West Texas, Retired Senior Volunteers Program, Texas Healthy Communities and Community Outreach/Education.

Student-Scholars Program has been expanded to admit visiting scientists, medical, public health, graduate and high school students during the academic year. These interns will be drawn from local high schools, Texas Tech University, TTUHSC and other Texas institutions. I am glad to say that the Reddy Lab interns are authors and/or co-authors in publications from high-impact factor journals.

A high **P Hemachandra Reddy, Ph.D.** Executive Director and Chief Scientific Officer of the Garrison Institute on Aging Mildred and Shirley L. Garrison Chair in Aging Professor of Cell Biology &

Professor of Cell Biology & Biochemistry, Departments of Pharmacology/Neuroscience and Neurology

Adjunct Professor, Department of Speech, Language and Hearing Sciences





continued on next page

Executive Director's Report...continued

I am glad to report that I have received funding from the CH foundation to develop peripheral biomarkers in patients with Alzheimer's dementia and this study is based on ongoing Project FRONTIER. I also received support from Alzheimer's Association (a 3-year grant) to understand the molecular basis of women's increased risk for both depression and Alzheimer's disease. Using brain tissue collected from humans and non-human primates, we will measure the gene expressions associated with brain's serotonin network, which impacts mood, anxiety and depression. This ongoing project is in collaboration with Arubala P. Reddy, Ph.D. from the TTUHSC Department of Internal Medicine. In addition, we have received continuous support from National Institutes of Health, the state of Texas and the Garrison Family Foundation.

In 2015-2016, the GIA research and outreach/education staff and scientists, published over 20 peerreviewed articles in journals considered high-impact. In addition, I edited the book Molecular Biology of Aging, which presents 11 chapters on different topics of biology relating to aging and Alzheimer's disease. In addition, I am bringing 2 special topics as a guest editor focusing on aging and Alzheimer's disease – one in *Journal of Alzheimer's Disease* 'Neurotransmitters and Alzheimer's Disease' and second one in *BBA Molecular Basis of Disease* 'Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases.'

I appreciate and thank all of the GIA staff, including research, outreach and Project FRONTIER and also my colleagues in the School of Medicine Departments and the TTUHSC leadership and staff at Research Integrity Office and Sponsored Research Programs for all of their support to GIA. My sincere thanks to GIA administrative staff, Annette Boles, Kathy Stonum, Ruben Gonzales and Kandi Quesada. My special thanks to President Mitchell, Dean and Vice Provost Steven Berk, M.D., Senior Vice President for Research, Michael Conn, Ph.D., Cell Biology Biochemistry Chair, Vadivel Ganapathy, Ph.D. Pharmacology/Neuroscience Chair Volker Neugebauer, Ph.D., and Neurology Chair, John De Toledo, M.D., for their kind support with GIA programs. I also extend my special thanks to the TTUHSC Office of Institutional Advancement, particularly Kendra Burris. And special thanks to Mr. Spike Dykes and his family for raising funds for research at the GIA Reddy Lab.

P. Hemachandra Reddy, Ph.D.

BOOK PUBLICATION:

Editor: P. Hemachandra Reddy, Ph.D.

'Molecular Biology of Aging' (with Elsevier). The focus of this book is Biological Aspects of Aging. The tentative publication date of this Volume is March 1, 2017.

Authors List:

- 1. John Culberson, M.D., TTUHSC, Lubbock
- 2. Subodh Kumar, Ph.D., TTUHSC, Lubbock
- 3. Murali Vijayan, Ph.D., TTUHSC, Lubbock
- 4. Jasvinder Bhatti, Ph.D., TTUHSC, Lubbock
- 5. Arubala Reddy, Ph.D., TTUHSC, Lubbock
- 6. Sharma Prabhakar, M.D., TTUHSC, Lubbock
- 7. Russell Swerdlow, M.D., University of Kansas Medical School, Kansas
- 8. ShiDu Yan, M.D., University of Kansas, School of Pharmacy, Kansas
- 9. Peter Rabinovitch, M.D., Ph.D., University of Washington, Seattle
- 10. Subbiah Pugazhenthi, Ph.D., University of Colorado, Denver
- 11. P. Hemachandra Reddy, Ph.D., TTUHSC, Lubbock



Ruben Gonzales Director, Alzheimer's DNA Bank and GIA Brain Bank

STAFF

Rui Wang, Ph.D. Senior Research Associate



Kandi Quesada Assistant Director of Finance Chandra Kuruva, Ph.D. Post-doctoral Research Associate



Kathleen Stonum Coordinator Murali Vijayan, Ph.D. Post-doctoral Research Associate



Maria Manczak, Ph.D. Senior Research Associate Subodh Kumar, Ph.D. Post-doctoral Research Associate



Linda Yin Senior Research Associate

Ramesh Kandimalla, Ph.D.

Professor, Department of Pharmacology/Neuroscience

Research Assistant

and GIA

Jasvinder Singh Bhatti, Ph.D. Post-doctoral Research Associate

> Carrah Osborn Medical Research Intern











5

2015-2016 Annual Report



STAFF...CONTINUED

Gilbert Ogunmokun Volunteer

Annette Boles, M.S. Director, **Community Education** and Outreach

Mary Katherine Grady Medical Research Intern

Cindy Hale Manager, **Retired Senior and** Volunteer Program

Flint Smith Medical Research Intern Veronica Molinar-Lopez Unit Manager





Justin Williams Medical Research Intern

Vani Thirumala

(UT Austin)



Sahil Tonk **High School Research Intern** (Lubbock High)

Undergrad Research Intern

Clay Ament Coordinator

Ose Aligbe Coordinator

Emily Street Intern















The Texas Tech University Health Sciences Center (TTUHSC) Garrison Institute on Aging (GIA) has expanded its research since 2014. P. Hemachandra Reddy, Ph.D., has initiated three research units including the Drug Discovery, Biomarker Development and the Molecular Basis.

THE MOLECULAR BASIS research includes the following projects:

1). To elucidate the biology underlying aging, particularly in terms of the aging brain and to identify factors that promote healthy aging of the brain.

2). To conduct research aimed at ultimately preventing or delaying the progression of agerelated neurological diseases, including Alzheimer's disease, stroke, Huntington's disease and Parkinson's disease. The Reddy Lab is also investigating conditions that accelerate dementia in elderly individuals, including Type 2 diabetes mellitus in aging.

Alzheimer's disease

The most common forms of dementia can be seen throughout elderly populations worldwide. Phenotypically, dementia associated with Alzheimer's disease is characterized by the impairment of cognition, abnormal behavior and personality changes. Cellular changes that are known to occur in Alzheimer's disease progression include mitochondrial fragmentation, loss of synapses, microglial activation, neuronal loss and the formation and accumulation of amyloid beta (A β) and phosphorylated tau (p-Tau). Currently, 47 million people worldwide live with dementia, including 5.4 million Americans. As populations advance in age, this number is projected to increase to more than 131 million by 2050. The worldwide cost of dementia has been estimated at \$818 billion, and Alzheimer's disease-associated dementia is anticipated to become a trillion-dollar disease by 2018. There are no drugs or agents that can delay and/or prevent Alzheimer's disease and its dementia, and there are no definitive early detectable peripheral biomarkers that can indicate its presence or likely development, thus eliminating any opportunity for early

intervention even if drugs are available. The Reddy Lab is actively working to determine early biomarkers and to improve the basic understanding of the Alzheimer's disease process.

In research funded by the National Institutes of Health (NIH), brain neurons were studied from Alzheimer's disease patients and Alzheimer's disease mice that express mutant APP and A β . The Reddy Lab reported the mitochondria fission protein Drp1 (dynamin-related protein 1) interacts with A β and p-Tau, and this interaction increases in Alzheimer's disease progression (*Human Molecular Genetics*, 2011). Increased Drp1 levels correlated with elevated levels of GTPase enzymatic activity and caused excessive mitochondrial fragmentation and abnormal mitochondria distribution, leading to defective mitochondrial function. The loss of mitochondrial integrity and function are factors known to mediate synaptic loss and to drive neurodegeneration and cognitive decline in Alzheimer's disease patients. Based on these findings, the research hypothesized a partial deficiency (i.e., reduction) in Drp1 is capable of inhibiting Drp1-A β and Drp1-p-Tau interactions, protecting A β -induced and p-Tau mitochondrial and synaptic toxicities and maintaining mitochondrial dynamics and neuronal function in Alzheimer's disease neurons.

To understand the protective effects of reduced Drp1 in Alzheimer's disease mice that express mutant APP and A β , this research used genetic approach and crossed mice that express reduced Drp1 (Drp1+/-) mice with APP transgenic mice (Tg2576 line), resulting in the development of double mutant (APPXDrp1+/-) mice. Messenger RNA expressions and protein levels of genes related to mitochondrial dynamics and mitochondrial biogenesis were measured. Using biochemical methods, mitochondrial function and measured soluble A β in brain tissues from all lines of the mice were studied. Preliminary results showed a decrease in mRNA expression and in Drp1 protein levels and an increase in fusion, biogenesis and synaptic proteins in the 6-monthold APPXDrp1+/- mice relative to the APP mice. Functional assays of mitochondria revealed a reduction in mitochondrial dysfunction. Sandwich ELISA assays revealed that soluble Aβ levels were significantly reduced in the APPXDrp1+/- mice. These findings suggest that a partial reduction in Drp1 can reduce A β production and mitochondrial dysfunction, which ultimately results in the maintenance of mitochondrial dynamics and the enhancement of mitochondrial biogenesis and synaptic activity in APP mice. These observations have been published in 2016 Human Molecular Genetics paper. The Reddy Lab is currently extending this research to determine the beneficial effects of reduced Drp1 in 12- and 20-month old APP mice.

To better understand the effects of a partial reduction of Drp1 on Alzheimer's disease in mutant tau mice, the Reddy Lab crossed Drp1+/- mice with mutant tau mice, produced double mutant (TauXDrp1+/-) mice and characterized these mice at 6 months of age. Research found decreased mRNA expressions and protein levels, and increased fusion, biogenesis and synaptic proteins in the 6-month-old TauXDrp1+/- mice. Mitochondrial function was normal in the TauXDrp1+/- mice, which was defective in Tau mice. Synaptic activity was increased in the TauXDrp1+/- mice, suggesting that a partial reduction in Drp1 protects against p-Tau toxicity. These initial results were published in a separate *Human Molecular Genetics* in 2016. Currently, this research will be extended to determine the beneficial effects of reduced Drp1 in older mutant Tau mice.

In another NIH funded project, the Reddy Lab is investigating the mitochondrial, outer-membrane protein VDAC1 (voltage-dependent anion channel protein 1) and its involvement in Alzheimer's disease progression. The research team demonstrated that VDAC1 physical interacts with p-Tau and soluble $A\beta$ physically interacts with VDAC1, blocked mitochondrial pores, leading to abnormalities in mitochondrial structure and function and neuronal damage. Using cell and mouse models of VDAC1, mutant APP and tau, researchers are continuing to investigate the physiological relevance of the abnormal interactions between VDAC1 and mutant APP/soluble

8

A β , and VDAC1 and mutant tau, in Alzheimer's disease neurons. Researchers also are investigating whether a partial reduction of VDAC1 in mutant APP and tau mice lines results in or is associated with reduced VDAC1.

Currently, the Reddy Lab is studying the physiological relevance of A β and p-Tau interactions with Drp1 and VDAC1 proteins in Alzheimer's disease progression. Using postmortem brain tissues from Alzheimer's disease patients and control subjects and also brain tissues from APP and Tau transgenic mice and *in vitro* assays, such as GST fusion proteins, researchers will determine precise interacting domain(s) of Drp1 with A β and p-Tau and also interacting domains of VDAC1 with A β and p-Tau. Researchers also will determine the physiological relevance of abnormal interactions between Drp1 and A β , and between Drp1 and hyperphosphorylated tau by measuring GTPase Drp1 enzymatic activity and mitochondrial morphology and distribution.

Huntington's disease

The Reddy Lab is also conducting research on Huntington's disease, a rare autosomal neurological disease that is fatal. Chorea, seizures, involuntary movements, dystonia, cognitive decline, intellectual impairment and emotional disturbances characterize Huntington's disease. In Huntington's disease patients, selective neuronal loss has been observed in the caudate and putamen of the striatum, cortex and hypothalamus. Mutant huntingtin (Htt) protein aggregates have been found in pathological sites in the postmortem brains from Huntington's disease patients. Currently, there are no drugs or agents available to treat or to prevent Huntington's disease. Multiple lines of evidence suggest that abnormal mitochondrial bioenergetics, impaired dynamics, defective axonal transport and defective function are involved in Huntington's disease progression.

To determine the molecular links between mutant Htt and mitochondria, the Reddy Lab studied abnormal mitochondrial dynamics in tissues from postmortem brains of Huntington's disease patients (at HD3 and HD4 stages), primary neurons and brain tissues from BACHD transgenic mice and control subjects. Higher levels of Drp1 and Fis1 in the HD4 brain tissues compared to the HD3 brain tissues were found, and decreased levels of Mfn1, Mfn2, and Opa1 in the HD4 brain tissues compared to the HD3s brain tissues from the striatum and the cortex (HD-affected brain regions). Researchers did not find such levels in the cerebellum (a non-HD-affected brain region), indicating that abnormal mitochondrial dynamics may be related to Huntington's disease. These observations were published in 2011 *Human Molecular Genetics* paper.

Using a recently developed BACHD mouse model that expresses a full-length (170 kb DNA) human Htt gene with 97 CAA and CAG, the effects of mutant Htt and mitochondrial and synaptic genes on 2-month-old BACHD mice relative to age-matched wild-type mice were investigated. Significantly increased mRNA levels of the fission genes were found as well as decreased levels of the fusion genes, suggesting that abnormal mitochondrial dynamics is an early event in Huntington's disease progression. To determine whether the interaction between Drp1 and mutant Htt increases as Huntington's disease progresses, the Reddy Lab performed co-immunoprecipitation analysis of Drp1 and mutant Htt in Huntington's disease brains and BACHD mice. Researchers found an 82 kDa and 40 kDa mutant Htt proteins in Huntington's disease patients. Significantly increased levels of Dp1 enzymatic activity (critical for mitochondrial division) in the cortex of Huntington's disease patients relative to the control subjects also were found. Researchers elevated levels of Drp1 enzymatic activity in the cerebral cortex and striatum in the BACHD mice relative to the wild-type mice. These observations were published in 2012 *Human Molecular Genetics* paper.

The Reddy Lab continues its research into molecular mechanisms underlying synaptic damage associated with the interaction between mutant Htt and mitochondria in Huntington's disease

neurons. The lab also investigated the protective effects of reduced Drp1 levels in Huntington's disease neurons from Huntington's disease mice and the beneficial effects of mitochondrial division inhibitors against mutant-Htt induced mitochondrial and synaptic activities.

Parkinson's disease

The Reddy Lab has investigated molecular basis of Parkinson's disease for the last six years. Parkinson's disease is the second most common neurodegenerative disease, characterized by disabling motor abnormalities, such as tremors, muscle stiffness, a paucity of voluntary movements and postural instability. Its main neuropathological features are the loss of nigrostriatal dopamine neurons, cell bodies in the substantia nigra pars compacta (SNpc), and nerve terminals in the striatum. Lewy bodies also have been found in the SNpc.

The etiology of Parkinson's disease is complicated and ultimately remains unknown. However, mitochondrial dysfunction is known to play a key role in the development of Parkinson's disease, with the disease recognized as a putative mitochondrial disease. Interestingly, sporadic and familial Parkinson's disease seems to converge at the level of mitochondrial integrity. Since mitochondria are the major source of reactive oxygen species and play a crucial role in cellular bioenergetics and apoptosis, mitochondria-related therapeutics may open new avenues to treat Parkinson's disease. Recently, the Reddy Lab found that brain-rich neuropeptide CART (cocaine-and amphetamine-regulated transcript) is preferentially localized to mitochondrial (especially complex I) dysfunction and oxidative stress have been strongly implicated in Parkinson's disease. The neurotoxin, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) impairs mainly the complex I and produces oxidative damage in the substantia nigra, resulting in dopamine neuronal degeneration and parkinsonian symptoms in several species, including humans, non-human primates, and mice.

After administering MPTP to a Parkinson's disease mouse model (C57BL/6J) and performing motor behavioral tests on the mice, the Reddy Lab determined the effects of CART on tyrosine hydroxylase-labeled neurons in the substantia nigra pars compacta. CART protects against Parkinson's disease toxicity in the MPTP mouse model, which mimics the main features of Parkinson's disease. Given the unique molecular structure of CART and its and biological features, we conclude that CART is an antioxidant peptide. The research was published in PLOS ONE (2012) and in *Pharmaceuticals* (2013).

In collaboration with scientists from postgraduate medical sciences in Chandigarh, India, the Reddy Lab is investigating molecular links between pesticide exposure and Parkinson's disease. The underlying cellular and molecular mechanisms for neuronal degeneration in sporadic Parkinson's disease remains unknown, but we hypothesize that mitochondrial dysfunction, oxidative stress and proteasomal dysfunction are contributing factors. Pesticides, including rotenone, paraquat and dieldrin have been reported to cause degeneration of dopaminergic neurons and linked to Parkinson's disease. Although the majority of Parkinson's disease patients with sporadic onset do not have a familial history of Parkinson's disease, these genetic studies of Parkinson's disease patients have resulted in important insights into pathogenic mechanisms of the disease. Recent experimental evidence has revealed that aberrant cell cycle progression plays an important role in Parkinson's disease pathogenesis. The abnormal expression of cell cycle markers and cell cycle reentry has been found in post-mitotic neurons of the central nervous system in Parkinson's disease patients. Thus, recent findings suggest that neurodegeneration in Parkinson's disease may be associated with the activation of cell cycle machinery in post-mitotic neurons. Cell-cycle analysis of DDVP exposed cells revealed a reduction of cells in the G0/G1 phase of the cell cycle and a concomitant increase of cells in the S phase and the G2/M phase compared to control PC12 cells. These findings concluded that the exposure of DDVP might generate oxidative stress, which may activate cell cycle machinery, leading to apoptotic cell death via cytochrome c release from mitochondria and subsequent caspase-3 activation. This research was published in the *BBA Molecular Basis of Disease* (2016). The Reddy Lab currently is investigating whether pesticide exposure renders persons susceptible to early Parkinson's disease onset in rural areas of West Texas.

Diabetes and Alzheimer's disease

Type 2 diabetes mellitus is a condition in which a high level of blood glucose results in increased hepatic glucose production, impaired insulin production by pancreatic β -cells, and insulin resistance. Type 2 diabetes mellitus is associated with a variety of genetic and environmental risk factors, including age, family history of diabetes, poor diet, obesity and physical inactivity. The disease, which accounts for 90 to 95 percent of the total number of diabetic cases, is a major public health problem that places substantial personal, social and economic burdens on the society. Currently, there are 415 million people with Type 2 diabetes mellitus worldwide, and this number is expected to increase to 642 million by 2040. India, China and the U.S. are the countries most affected by Type 2 diabetes mellitus.

Improved health care for diabetes-related complications has extended the lives of people with Type 2 diabetes mellitus, leading to questions about complications that may result when persons with the disease also develop Alzheimer's disease. Over the past three decades, numerous epidemiological studies have shown a clear association between Type 2 diabetes mellitus and an increased risk of developing Alzheimer's disease. (Recently, estimates show people living with Alzheimer disease-related dementia will increase from 35.6 million worldwide in 2010 to 115.4 million in 2050.) In addition, Type 2 diabetes mellitus is known to increase the risk of Alzheimer's disease-related dementia by 50 to150 percent. Further, Type 2 diabetes mellitus-related conditions, including obesity, hyperinsulinemia and metabolic syndrome also increase the risk of Alzheimer's disease. The molecular mechanisms linking Type 2 diabetes mellitus and Alzheimer's disease are poorly understood.

Current research in the Reddy Lab also focuses on identifying potential molecular mechanisms linking Type 2 diabetes mellitus and its related conditions to Alzheimer's disease, ultimately for a rational development of improved preventative and therapeutic strategies. Researchers use primary neurons and different tissues from polygenic mouse models of Type 2 diabetes mellitus (TALLYHOJngJ and NONcNZO10) to elucidate these underlying molecular mechanisms, including oxidative stress and mitochondrial dysfunction, insulin resistance and deficiency and impaired insulin receptors.

Research staff includes Maria Manczak, Ph.D., Ramesh Kandimalla, Ph.D., David Fry, B.S., Rui Wang, Ph.D., Murali Vijayan, Ph.D., XiangLing Yin, M.S., Carrah Osborn, Vani Tirumala, Jasvinder Bhatti, Ph.D., and P. Hemachandra Reddy, Ph.D.

DRUG DISCOVERY UNIT

A major interest of the Reddy Lab is to design, synthesize and test the efficacies of drug molecules against mutant proteins induced in Alzheimer's disease, Huntington's disease, Multiple Sclerosis and stroke. Another interest is to extend the lifespan of cells and to promote healthy aging of the brain. The Reddy Lab uses cell and mouse models of aging, Alzheimer's disease, Parkinson's disease,

Huntington's disease and Multiple Sclerosis. An update of this drug testing, which has focused on curcumin, SS31 and MitoQ is provided.

Curcumin and Alzheimer's disease

Using the natural curcumin and human neuroblastoma (SHSY5Y) cells, the Reddy Lab has studied the protective effects of curcumin against $A\beta$ toxicity in Alzheimer's disease neurons. Very little research has been reported about the effects of curcumin on mitochondrial biogenesis, dynamics, function and synaptic activities. Using SHSY5Y cells, curcumin and the A β peptide, researchers studied protective effects of curcumin against A β , the preventive (curcumin+A β) and its intervention (A β +curcumin). Using real-time RT-PCR, immunoblotting and immunofluorescence analysis, we measured mRNA, protein levels of mitochondrial dynamics, mitochondrial biogenesis and synaptic genes. Researchers also assessed mitochondrial function. Cell viability studied using MTT assay. A β was found to impair mitochondrial dynamics, to reduce mitochondrial biogenesis, and to decrease synaptic activity and mitochondrial function. In contrast, curcumin enhanced mitochondrial fusion activity, reduced fission machinery and increased biogenesis and synaptic proteins. Mitochondrial function and cell viability were elevated in curcumin-treated cells. Interestingly, cells that were pre- and post-treated with curcumin and then were incubated with $A\beta$ showed reduced mitochondrial dysfunction, and showed cell viability and mitochondrial dynamics, mitochondrial biogenesis and synaptic activity. Further, the protective effects of curcumin were stronger in SHSY5Y cells pretreated with curcumin compared to SHSY5Y cells that were posttreated with curcumin, suggesting that curcumin works better in the prevention of disease rather than in the treatment of disease in Alzheimer's disease-like neurons. These findings suggest that curcumin is a promising drug molecule for the treatment of Alzheimer's disease. These results were published in *Journal Investigative Medicine*, December 2016.

Molecular Inhibitors and Alzheimer's disease

The Reddy Lab also seeks to determine whether molecular inhibitors that reduce and/or prevent abnormal interactions of A β and mitochondrial proteins and of p-Tau and mitochondrial proteins also reduce A_{β}- and p-Tau-induced mitochondrial and synaptic toxicities. To achieve this objective, a number of molecular structures and conducted molecular docking studies were designed using these Alzheimer's disease-related proteins, which came from the Protein Data Bank. Only those molecular structures from all crystal structures that exhibited the best-binding capability and that received the highest docking score were selected. Researchers synthesized the selected drug molecules using retro-synthesis analysis to analyze the structure spectrally. These drug molecules are water soluble. A cell viability assay was conducted and determined the dosage levels of each drug molecule. Researchers currently are conducting research to determine whether small molecule reduces A β , p-Tau and Drp1 in Alzheimer's disease neurons. In this research, experiments are conducted at three different stages. In stage one (*in vitro*), researchers will determine whether synthesized drug (small molecule inhibitors) exhibit protective properties in Alzheimer's disease neurons; determine whether small molecules reduce abnormal interactions between A β and Drp1 and p-tau and Drp1; and whether our molecule reduce levels of A β , p-Tau, and Drp1. Based on results from stage one, stage 2 experiments (*in vivo*) will begin to determine the protective effects of molecules against neuronal toxicities at different stages of Alzheimer's disease progression. Six- and 12-month-old mice, will be treated with a molecule to determine whether the molecule resulted in reduced abnormal interactions, similar to the methods of stage one. Researchers also conduct blood brain barrier crossing studies and pharmacokinetic studies of molecules.

Other neurodegenerative diseases exhibit pathological conditions similar to Alzheimer's disease. Therefore, in future studies, the Reddy Lab will seek to determine whether their molecules exert protective effects against mutant protein toxicities in neurons from persons who had Huntington's or Parkinson's disease and Amyotrophic Lateral Sclerosis or ALS.

Inhibitors of Mitochondria Division and Huntington's disease

The Reddy Lab studies the protective effects of Mdivi1 (mitochondrial division inhibitor 1) in striatal neurons that stably express mutant Htt (STHDhQ111/Q111) and wild-type Htt (STHDhQ7/Q7). Researchers treated mutant and wild-type Htt neurons with Mdivil molecules. Using gene expression analysis, biochemical methods, transmission electron microscopy and confocal microscopy methods, it was determined that mitochondrial and synaptic activity by measuring mRNA and protein levels of mitochondrial and synaptic genes; mitochondrial function; and ultra-structural changes in mutant Htt neurons relative to wild-type Htt neurons.

Increased expressions of mitochondrial fission genes, and decreased expression of fusion genes and synaptic genes in the mutant Htt neurons relative to the wild-type Htt neurons were found. Electron microscopy of the mutant Htt neurons revealed a significantly increased number of mitochondria, suggesting that mutant Htt fragments mitochondria. Biochemical analysis revealed defective mitochondrial functioning.

In the Mdivil-treated mutant Htt neurons, fission genes were down-regulated, and fusion genes were up-regulated, suggesting that Mdivil decreases fission activity. Synaptic genes were up-regulated, and mitochondrial function was normal in the Mdivi1-treated mutant Htt neurons. Immunoblotting findings of mitochondrial and synaptic proteins agreed with mRNA findings. The electron microscopy studies revealed that increased numbers of structurally intact mitochondria were present in Mdivi1-treated mutant Htt neurons. The Reddy Lab found increased synaptic and mitochondrial fusion genes and decreased fission genes in the Mdivi1-treated wild-type Htt neurons, indicating that Mdivi1 beneficially affects healthy Htt neurons. Taken together, these findings suggest that Mdivi1 is protective against mutant Htt-induced mitochondrial and synaptic damage in Huntington's disease neurons and that Mdivi1 may be a promising molecule for the treatment of Huntington's disease neurons.

Mitochondria-Targeted Molecules and Huntington's disease

The Reddy Lab sought to determine the protective effects of the mitochondria-targeted molecules MitoQ and SS31 in striatal neurons that stably express mutant Htt (STHDhQ111/Q111) in Huntington's disease. To determine the effects of MitoQ and SS31 on mutant Htt neurons, researchers treated the neurons with both molecules. Using gene expression analysis, biochemical methods, transmission electron microscopy and confocal microscopy methods, mRNA were measured and the protein levels of mitochondrial and synaptic genes, mitochondrial function and ultra-structural changes in the MitoQ- and SS31-treated neurons. In the MitoQ- and SS31-treated mutant Htt neurons, fission genes were down-regulated, and fusion genes were up-regulated, suggesting that MitoQ and SS31 reduce fission activity. Interestingly, the mitochondrial biogenesis genes were up-regulated in the MitoQ- and SS31-treated neurons. The synaptic genes were upregulated, and mitochondrial function was normal in the treated neurons. Immunoblotting findings of MitoQ and SS31were in agreement with the mRNA findings. Transmission electron microscopy studies revealed decreased numbers of structurally intact mitochondria in the MitoQ- and SS31treated mutant Htt neurons. These findings suggest that MitoQ and SS31 are protective against mutant Htt-induced mitochondrial and synaptic damage in Huntington's disease neurons and these molecules are potential therapeutic molecules for the treatment of Huntington's disease neurons.

Research staff includes Chandra Sekhar Kuruva, Ph.D., Maria Manczak, Ph.D., Ramesh Kandimalla, Ph.D., XiangLing Yin, M.S., Mary Catherine Grady, Andrew Mitchell and P. Hemachandra Reddy. Ph.D.

BIOMARKER DEVELOPMENT UNIT

The Reddy Lab works to identify peripheral biomarkers for aging, stroke, vascular dementia and Alzheimer's disease. A biomarker, such as a protein, nucleic acid or a metabolite, is the quantification of a definite biological state, typically relevant to the risk, occurrence, severity, prognosis or projected therapeutic response of a particular disease. Identification of biomarkers of a disease can contribute to a better understanding of the etiologies and mechanisms underlying particular diseases and can inform the development of early detectable peripheral biomarkers. Recent discoveries in molecular biology have revealed that circulatory microRNA (miRNAs) are potential candidates for biomarkers because they are stable in peripheral circulation, and the level of a particular miRNA appears to change with the progression of Alzheimer's disease, stroke and vascular dementia. Recently, the Reddy Lab undertook a global microarray analysis of serum samples from Alzheimer's disease patients, individuals who were mildly cognitively impaired and healthy control subjects. Researchers found significant alteration in five miRNAs in the serum samples from the Alzheimer's disease patients relative to healthy subjects. Similarly, the Reddy Lab conducted global miRNA sequencing of serum samples from stroke cases and control cases to identify potential miRNA biomarkers

The Reddy Lab will conduct miRNA analysis from T2DM and obese mice and humans to determine the relationship between mRNAs and parameters of insulin sensitivity and adiposity in young adults. Findings from this research may reveal miRNAs that could function as biomarkers and also provide a better understanding of the role of miRNAs in insulin sensitivity and obesity and the identification of blood-based early detectable miRNAs could contribute to a better understanding of the etiologies and mechanisms underlying Alzheimer's disease, stroke, VaD and Type 2 diabetes mellitus.

Research staff includes Subodh Kumar, Ph.D., Murali Vijayan, Ph.D., Justin Williams, Flint Smith, Sahil Tonk and P. Hemachandra Reddy, Ph.D.

SPIKE DYKES GOLF TOURNAMENT

The Spike Dykes Charity Fund was founded in honor of Sharon Dykes, who passed away in 2010 after a long battle with Alzheimer's disease. Since it's creation in 2012, the Spike Dykes Charity Fund has invested over \$320,000 to support Alzheimer's research thanks to the success of the Charity Golf Tournament. This year the annual event benefitted the TTUHSC Garrison Institute on Aging. It was held in Horseshoe Bay on July 15-16. There were over 160 participants that played on Ram Rock and Apple Rock courses at the Horseshoe Bay Resort.



RESEARCH COLLABORATIONS

The Reddy Laboratory of GIA is actively collaborating with investigators at Texas Tech University (Vijay Hegde, Ph,D., Department of Nutritional Sciences), School of Health Professions (Yang-Soo Yoon, Ph.D.) and the TTUHSC-School of Medicine (Leslie Shen, Ph.D.), and investigators from outside TTUHSC, including Johns Hopkins University (Hiromi Sesaki, Ph.D., Department of Cell Biology) and Baylor College of Medicine (William Craigen, M.D.) and Postgraduate Medical Institute, Chandigarh (Kiran Dip Gill, Ph.D.) and Department of Biotechnology and Bioinformatics, Sri Guru Gobind Singh College, Chandigarh (Jasvinder Singh Bhatti), India.

COLLABORATIONS WITH DEPARTMENT OF PUBLIC HEALTH

Dr. Reddy is involved with the Master of Public Health (MPH) students by mentoring for their practicum and giving guest lectures to MPH students. And MPH students, particularly Sarah Mende, Alejandro Aquino, Anya Anthony and Anthony Jacob are actively involved with Project FRONTIER. Dr. Hafiz Khan is actively assisting with statistical analysis of the Project FRONTIER.

STUDENT SCHOLARS AND VISITING SCIENTISTS

The GIA participates in multiple student training programs

- 1) The Student Scholars in Geriatrics
- 2) The SOM Student Summer Research Program
- 3) The High School Student Scholars Research Program.

The Student Scholars in Geriatrics (SSG) is an inter-professional program that offers students from TTUHSC and TTU exposure to the geriatric field. Students attend lectures, clinical practicum, community service and an inter-professional geriatric service event. Students participate in the program for one academic year with the option to re-apply for additional terms in the program. Select students will have the opportunity to attend regional and national meetings of the American Geriatrics Society and the Gerontological Society of America.

The purpose of the SSG Program is to develop a cadre of students from multiple disciplines who have a long-term commitment to advancing geriatric healthcare and are actively engaged in inter-professional projects designed to extend the years of active, healthy life for older adults. Creating leaders in geriatrics is key to the long-term success of this program; therefore, the students are charged with developing learning activities for themselves and others.

The goals of the project include 1) providing hands-on opportunities to work with the geriatric population in academic, community service and clinical care settings; 2) provide exposure to the field of Geriatrics in classroom- and practice-based environments; 3) provide an opportunity to participate in a longitudinal clinical project; and 4) provide students with the experiences that will help them to become leaders who promote geriatrics to their fellow students and the community-at-large.

R E S E A R C H

The SOM Student Summer Research Program

The GIA also participates in the SOM Student Summer Research Program, an 8-week program designed to help students gain experience in an area of research interest. First-year medical students in Lubbock are encouraged to coordinate with interested faculty members on project proposals that are to be submitted for approval to the Office of the Dean. A stipend in the amount of \$2,240 will be paid to each participating student in accordance with this guideline, and students are required to present information regarding summer research activities during the Student Research Week in Spring 2017. Justin Williams and Flint Smith, medical summer interns 2016, are working in the Reddy Laboratory of GIA. Justin is focusing on the role of microRNAs in aging and cellular senescence using skeletal muscle tissues from 2-, 6-, 12- and 20-month-old C57BL6 mice. Flint is studying the role of microRNAs in aging and cellular senescence using cerebral cortex tissues from 2-, 6-, 12- and 20-month-old C57BL6 mice. Overall, the Reddy Lab is interested to identify peripheral biomarkers of aging and cellular senescence.

The Undergraduate Summer Research Program

Similar to medical interns' program, the GIA is participating in an 8-week program to train undergraduate summer interns in aging and Alzheimer's disease. In 2016 summer, Ms. Vani Tirumala, a secondyear undergraduate from University of Texas, Austin participated in our undergraduate summer research program. Vani focused on the role of synaptic damage, oxidative stress/mitochondrial dysfunction in relation to amyloid beta and phosphorylated tau in the progression and pathogenesis of Alzheimer's disease.

The High School Student Scholars Research Program

The High School Student Scholars Summer Research Program is a new initiative by Dr. Reddy, to help high school students gain experience in the research areas of aging and neurodegenerative diseases. It is an 8-week program, supported by GIA. Currently, Sahil Tonk, 10th grader from Lubbock High School is working in the Reddy Laboratory of GIA to understand the molecular basis of microRNAs in Alzheimer's Disease.

Goals

- Provide a hands-on opportunity to work with the geriatric population in academic, community service and clinical care settings.
- Provide exposure to the field of Geriatrics in classroom- and practice-based environments.
- Provide an opportunity to participate in faculty advised research.
- Provide students with the experiences that will help them to become leaders who promote geriatrics to their fellow students and the community-at-large.

Aging and Alzheimer's Disease Journal Club

1/26 Subodh Kumar, Ph.D.

- Genome-Wide Serum microRNA Expression Profiling Identifies Serum Biomarkers for Alzheimer's Disease
- 2/23 **Chandra Sekhar Kuruva, Ph.D.** Multi-target Drug Discovery for Alzheimer's Disease: Triazinones as BACE-1 and GSK-3b Inhibitors
- 3/29 Rui Wang, Ph.D.
 Aβ induces astrocytic glutamate release, extrasynaptic NMDA receptor activation, and synaptic loss
- 4/26 **Murali Vijayan, Ph.D.** Selective astrocytic endothelin-1 overexpression contributes to dementia associated ischemic stroke by exaggerating astrocyte-derived amyloid secretion
- 5/31 **John Lawrence, Ph.D.** Accelerated aging of the GABAergic septohippocampal pathway and decreased hippocampal rhythms in a mouse model of Alzheimer's Disease
- 6/28 **Subodh Kumar, Ph.D.** microRNA-33 Regulates ApoE Lipidation and Amyloid-β_ Metabolism in the Brain
- 7/26 **Ramesh Kandimalla, Ph.D.** Silencing of CDK5 Reduces Neurofibrillary Tangles in Transgenic Alzheimer's Mice
- 8/30 **Linda Yin** Meta-Analysis of Peripheral Blood Apolipoprotein E Levels in Alzheimer's Disease
- 9/27 **Jasvinder Bhatti, Ph.D.** Time Restricted Feeding Is a Preventative and Therapeutic Intervention
- 10/25 **Chandra Sekhar Kuruva, Ph.D.** Tau-Derived Hexapeptide 306VQIVYK311 Aggregation Inhibitors: Nitrocatechol Moiety as A Pharmacoperone in Drug Design

FUNDING



he Garrison Institute on Aging is primarily funded by competitive grants. Previously funded NIH grant awards constitute the bulk of the grant funding, with continuing plans to apply and receive additional grant funding. In 2016, Dr. Reddy has received a 3-year grant from Alzheimer's Association to study the molecular basis of women's increased risk for both depression and Alzheimer's disease. Additionally, through an endowment provided by the Garrison family, the Garrison receives a secure flow of income from the earnings on the endowment. The earnings alone are not enough to operate the GIA but do provide a steady income for operation. Without the support of the Texas Tech University Health Sciences Center administration, the GIA would find it difficult to continue operating. It goes without saying that the funds received by our generous donors are well appreciated and allow the GIA to operate programs such as the GIA Brain Bank and RSVP program.

In keeping with the GIA vision, Dr. Reddy and his research team are working to unlock the needed research results to submit for additional grant funding. As the new fiscal year for TTUHSC begins, Dr. Reddy will receive additional collaborative and competitive grant awards, with several big awards and additional programs on the horizon that are not included in the timeframe represented by this report.

FRONTIER PROJECT STAFF

18

P. Hemachandra Reddy, Ph.D. Principal Investigator

Hafiz Khan Ph.D. Associate Professor, Public Health Department

Annette Boles M.S Director, Community Education and Outreach

Catherine Hudson M.P.H. Research Director, Rural and Community Health

Robby McCasland, M.Ed., CISA Managing Director, Information Technology

Chip Shaw M.P.H. Vice President, Information Technology

Brian Nordstrom Enterprise Programmer Analyst V Information Technology

Kandi Quesada Assistant Director of Finance

Kathleen Stonum Unit Coordinator

Veronica Molinar-Lopez Unit Manager

Ose Aligbe Coordinator

Cordelia Aguirre Coordinator

Rocio Carrasco Coordinator

Anthony Anya Student focused on dementia

Sarah Mende Student focused on cancer

Alexander Jacob Student focused on cardiovascular disease

Alejandro Aquino Student focused on stroke

COMMUNITY OUTREACH AND EDUCATION

PROJECT FRONTIER:

he objective of Project FRONTIER (Facing Rural Obstacles to health care Now Through Intervention, Education & Research) is to determine the feasibility of creating a rural, communitybased cohort in rural West Texas. The TTUHSC Garrison



Institute on Aging created the Project FRONTIER as Cochran County Aging Study to generate pilot data about the cognitive functioning, CVD-factors, and the link between these constructs in a rural, multi-ethnic sample.

History, Development and Current Status

Project FRONTIER began in 2006 at the TTUHSC Garrison Institute on Aging under the original name, Cochran County Aging Study, and ran successfully until 2010. The Project FRONTIER, then moved to F. Marie Hall Institute for Rural and Community Health in 2010 and ran until 2015. Due to administrative and research convenience, it was moved back to GIA.

Project FRONTIER is an epidemiological study to explore the natural course of chronic disease development and its impact on longitudinal cognitive, physical, social and interpersonal functioning in a multi-ethnic adult sample from rural communities of West Texas. Information from this study can then be used to develop programs for effective disease management, preservation of cognitive functioning throughout the lifespan and improvement of the overall health of individuals living in rural West Texas. Currently, Project FRONTIER is collecting data from participants in Cochran, Bailey, Parmer and Hockley counties. Since its beginning, the data from the Cochran County Aging Study and Project FRONTIER have been analyzed by over eighty researchers affiliated with thirteen different institutions. This has resulted in numerous publications in peer-reviewed journals and presentations at national, regional and university scientific meetings.

Who can participate?

Any person who is 40 and older and lives in one of the participating counties is eligible to participate. Project FRONTIER currently has participants in Cochran, Parmer, Bailey and Hockley Counties.

Mission

The mission of Project FRONTIER is to explore the natural course of chronic disease development and its impact on longitudinal cognitive, physical, social and interpersonal functioning in a multi-racial adult sample from rural communities of West Texas. Such exploration will be used to develop programs for effective disease management and preservation of cognitive functioning throughout the lifespan and improvement of the overall health of individuals living in rural West Texas.

Despite the fact that 21 percent of the total U.S. population resides in rural communities, very few studies have examined the factors that contribute to health status and population health outcomes in rural communities, especially using the power of a community-based participatory research approach and a longitudinal cohort.

Objectives and Health Related Issues

The proposed research is designed to provide information on rural health, by determining answers to the following questions:

- 1. What does it mean to live in a rural community in terms of health and illness?
- 2. In rural areas, how is community health different from public health?
- 3. Are rural residents more at risk for chronic diseases, including cardiovascular disease, stroke, diabetes mellitus, Alzheimer's disease, asthma, allergies and other diseases?
- 4. What is the natural history of health risks, trajectories of diseases and other issues pertaining to health in rural communities?
- 5. What is the impact of culture and lifestyle on chronic diseases?
- 6. What is the impact of genetics and epigenetics on chronic diseases?
- 7. How does gender affect health?

Study Variables

Medical Examination:

- Standardized medical exam completed by local M.D., Nurse Practitioner or physician's assistant
- Review of systems general, dermatology, HEENT (head, eyes, ears, nose, throat), breast, respiratory, cardiovascular, gastrointestinal, genitourinary, endocrine, hematologic, musculoskeletal, neurological, psychiatric and functional
- Neurological assessment

Interviews

- Portions of the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System (BRFSS) questionnaire diabetes, hypertension, cholesterol, cardiovascular disease, cancer, women's and men's health, physical activity
- Demographics, education, residential and occupational history
- Medical history (self and family)
- Cultural information
- Medication use and dosage (prescription, over-the-counter, vitamins and supplements)
- Affective screenings (Geriatric Depression Scale and Beck Anxiety Inventory)
- Substance use history (tobacco, alcohol)
- Informant report of participant's cognition, memory and daily functioning
- Objective measures:

Blood pressure and pulse (3 readings each) Height and weight Body Mass Index (BMI) Abdominal and neck circumference Blood oxygen saturation Body impedance (body fat percentage) Heel scan (bone density – Parmer County only)

Research Seminar Series

Healthy Aging Lecture Series	January 5, 2016	"It is all about delivery" Ravikumar Majeti, Ph.D. Professor of Pharmaceutical Sciences Texas A&M Rangel College of Pharmacy
	February 9, 2016	"The Spaghetti Conundrum - Our journey to a detailed understanding of the intracellular domain of pentameric ligand-gated ion channels"
September 28, 2016		Michaela Jansen, PharmD, Ph.D. Associate professor, Department of Cell Physiology and Molecular Biophysics
"Healthy Living for a Healthy	March 29, 2016	Center for Membrane Protein Research TTUHSC "Besource allocation and message organization in persons with
Heart" Scott Shurmur, M.D. Medical director and division Chief TTUHSC	March 29, 2010	chronic severe Broca's Aphasia: informing clinical decisions related to the use of assistive technology" Rajinder Koul, Ph.D. Professor and Chair, Department of Speech, Language and Hearing Sciences Associate Dean of Research for School of Health Professions TTUHSC
···· October 26, 2016	May 17, 2016	"Balancing age-related hormonal dysregulation to combat age-related memory loss in AD development" Gemma Casadesus-Smith, Ph.D. Associate Professor, Department of Biological Sciences Kent State University
"It's All in Your Head"	June 14, 2016	"Pre-clinical studies on alcohol disorder" Susan E. Bergeson, Ph.D. Associate Professor, Department of Pharmacology and Neuroscience TTUHSC
Katie Hendley, M.D. Neurologist/ Movement Disorder Specialist Covenant Medical	August 2, 2016	"The aging pituitary-gonad-bone axis: how does FSH act on ovary & bone?" T. Rajendra Kumar, Ph.D., Edgar L. Makowski Endowed Professor Associate Vice-Chair of Research Division of Repro- ductive Sciences, Department of Obstetrics & Gynecology University of Colorado Denver-Anschutz Medical Campus
Group -\$*	September 6, 2016	"Novel mechanisms of progesterone-induced brain protection: implications for Alzheimer's disease" Meharyan Singh, Ph.D. Dean, Graduate School of Biomedical
November 16. 2016		Sciences, Professor, Center for Neuroscience Discovery Institute for Healthy Aging, University of North Texas Health Science Center
"The Basics of Alzheimer's"	October 11, 2016	"From bench to bedside: regulators expectations" Mansoor Khan, Ph.D., Professor and vice dean, College of Pharmacy Texas A&M Health Sciences Center
Hannah Ives Community Outreach Specialist, West Texas Chapter	October 14, 2016	"Why bones age: implications for hip fractures in the elderly" Sudhaker Rao, M.D. Section Head, Bone & Mineral Metabolism director, Bone & Mineral Research Laboratory Henry Ford Hospital
Association National Organization	December 6, 2016	"Clinical aspects of glucose metabolism and chronic disease" John W. Culberson, M.D. Associate Professor of Family and Community Medicine and director of Geriatric Medicine Programs TTUHSC

COMMUNITY OUTREACH AND EDUCATION

Healthy Lubbock:

Texas Healthy Communities

The GIA obtained funding from Texas Healthy Communities. The Healthy Community initiatives, as determined by the Centers for Disease Control and Prevention are designed to focus on:

- 1. Promoting physical activity and nutrition
- 2. Reducing tobacco use and exposure
- 3. Building capacity to implement policy, system, and environmental and organizational changes related to chronic disease risk factors
- 4. Fostering improved access to care
- 5. Reducing/eliminating health disparities
- 6. Reducing complications and incidence of chronic diseases

For Lubbock, the GIA is focused on physical activity. A Physical Activity Committee has been organized and works diligently to promote physical activity programs to ensure that the Lubbock community has an opportunity to improve their health through physical activity. The ultimate goal of the Physical Activity Committee is to prevent disease and disability, and enhance quality of life. Biological



THE PROJECT FRONTIER AND PUBLIC HEALTH JOURNAL CLUB

In collaboration with the Graduate School of Biological Sciences, Department of Public Health, Laura W. Bush Institute for Women's Health, Clinical Research Institute, F. Marie Hall Institute for Rural & Community Health, TTUHSC School of Medicine and Texas Tech University, the Texas Tech University Garrison Institute on Aging started a journal club titled "The Project Frontier and Public Health Journal Club." The first meeting was held on November 2nd, 2016. The title of the paper was *End-of-life planning in a rural elderly cohort* and presenter was Alyce Ashcraft, Ph.D., School of Nursing. Areas covered were public health, geriatrics, aging, Alzheimer's Disease, obesity/diabetes, stroke, cancer, asthma/ allergy and cardiovascular diseases.

Date 11/2/2016 12/7/2016

Presenter

Alyce Ashcraft, Ph.D. P. Hemachandra Reddy, Ph.D.

Title

End-of-life planning in a rural elderly cohort Cardiometabolic Risks and Severity of Obesity in Children and Young Adults

COMMUNITY OUTREACH AND EDUCATION

Community Outreach Spotlight Program: Marathon Kids

Marathon Kids is a free running/walking and nutrition program for kindergarten-5th grade students in the Lubbock Independent School District (LISD). Marathon Kids participants ran or walked at least one marathon (26.2 miles) and/or up to four marathons (104.8 miles) over a six-month period. They ran in increments of 1/4-1/2 mile at a time and tracked their progress by coloring in a Marathon Kids Mileage Log. They also were challenged to eat healthy fruits and veggies and colored a "food log". Children participated in the program at school and at home, tracking their miles and healthy eating choices with the help of their parents and teachers. Children were able to see their progress. They were rewarded for beginning the program at the "Kick-Off" ceremony and for completing the program at the "Finisher" celebration. All children who completed the program received a Marathon Kids t-shirt and finisher medal.

Lubbock Independent School District (LISD) Wide

Terry Dalton, Healthy Lubbock Physical Activity Committee member, is the organizer for the LISD wide Marathon Kids. Dalton has been the organizer for several years and says that each year it continues to grow beyond his expectation. The program started with only 12 schools participating and now has 20 schools participating with more than 7,000 students.

Last summer Dalton received the 2014-2015 Texas Classroom Teachers Association's Friend of Education. He has contributed many volunteer hours and brought Marathon Kids to the LISD elementary schools. Terry enjoys promoting and encouraging children in leading a healthy lifestyle through running and eating right.

Retired Senior Volunteer Program

Lubbock RSVP is sponsored by the Institute and promotes volunteerism for adults 55 and older while assisting to meet the needs of the Lubbock community. Lubbock RSVP began in 1979.

Program Focus

- Promote volunteerism and service for adults 55 and older and seek opportunities in the Lubbock community to be a positive catalyst.
- Utilize the lifetimes of experience, skill, and talents and interests of senior citizens to meet community needs through volunteer service.
- Assist the Lubbock community to 'age in place' with a healthy physical and mental approach.

Benefits of Program

- Enrollment is free and open to all adults 55 and older.
- Lubbock RSVP provides a supplemental insurance for volunteers at no cost to volunteers.
- We host two community events: Spring Forum – designed to educate and provide seniors with resources defined for their needs. Movie Night – members and community guests meet and enjoy a classic movie and share a meal with others.
- Annual Recognition Event a banquet for members and guests to meet and be recognized for their service and achievements. Members who have served 4,000 or more hours are awarded the 'Presidential Lifetime Achievement Award'.

2016 Statistics

Over 600 volunteers served over 110,000 hours for an economic impact of over 2.4 million dollars to the Lubbock Community.



Bike Fix It Station

With funding provided by a state grant from the Department of State Health Services (DSHS) Texas Healthy Communities, GIA purchased a Bike Fix It Station. With a collaborative effort from the City of Lubbock Parks and Recreation, the new Bike Fix It Station was installed at the entrance of the Martin Luther King Jr. Mountain Bike Trail at the Dunbar Historical Lake in June 2016.

The Bike Fix It Station is an attempt from the Healthy Lubbock Physical Activity Committee to help promote healthier, more active and sustainable lifestyles for the Lubbock community.

The Bike Fix It Station is a repair stand with an air pump and hand tools, including screwdrivers, wrenches and a tire leveler. Many cyclists are enjoying the addition to the Mae Simmons Bike Trails because they don't need to carry extra tools with them. They can use the station to fix their bikes at no charge and in no time get back to riding again.

COMMUNITY OUTREACH AND EDUCATION

Healthy Lubbock Events Website

Healthy Lubbock Events website: www.healthylubbockevents.org

was established as a central clearinghouse of healthy events for the citizens of Lubbock and the surrounding community. The events website is a "one-stop" shop to finding out about fun, active events taking place around the Lubbock community. The website has information on fun runs, exercise classes, Healthy Aging Lectures, diabetes classes, farmers' markets and health fairs. Many events are submitted daily so the website can be viewed on a daily basis. Lubbock has over 80 parks. The website highlights 17 of the parks with walking trails.

Community Outreach Spotlight Program: Community Gardens

The Heart of Lubbock Community Garden was developed in 2014 by the Community Transformation grant. It is located at Ave. X and 21st Street.

The Heart of Lubbock Community Garden is overseen by Elizabeth Roesler. Monthly meetings are held every 1st Thursday of each month for those wanting to participate in planting their produce and making art. The garden grows herbs, okra, tomatoes, peppers and many more great veggies and fruits. There is a monthly Taste Testing on the 3rd Tuesday of each month so that attendees can try foods grown at the community garden, learn new recipes, and hear about different produce varieties.

Booker T. Washington Community Garden was also developed in the Summer of 2014 by the Community Transformation Grant. It is located at 2109 Cedar Ave. and is overseen by Eric Strong and the Lubbock Roots Historical Arts Council. They encourage the community to come out and grow with them. They grow squash, tomatoes, watermelon, melons, strawberries and beautiful West Texas flowers. Contact the Lubbock Roots Historical Arts Council if you would like to volunteer at their garden.







Publications 2016

Williams J, Smith F, Kumar S, Vijayan M, Reddy PH. Are microRNAs true sensors of ageing and cellular senescence? Ageing Res Rev. 2016 Nov 27. pii: S1568-1637(16)30168-4. doi: 10.1016/j.arr.2016.11.008. [Epub ahead of print] Review. PubMed PMID: 27903442.

Bhatti JS, Bhatti GK, Reddy PH. Mitochondrial dysfunction and oxidative stress in metabolic disorders - A step towards mitochondria based therapeutic strategies. Biochim Biophys Acta. 2016 Nov 9. pii: S0925-4439(16)30292-7. doi: 10.1016/j. bbadis.2016.11.010. [Epub ahead of print] PMID: 27836629.

Kuruva CS, Reddy PH. Amyloid beta modulators and neuroprotection in Alzheimer's disease: a critical appraisal. Drug Discov Today. 2016 Oct 27. pii: S1359-6446(16)30388-9. doi: 10.1016/j.drudis.2016.10.010. [Epub ahead of print] Review. PubMed PMID: 27794478.

Manczak M, Kandimalla R, Fry D, Sesaki H, Reddy PH. Protective Effects of Reduced Dynamin-related Protein 1 Against Amyloid Beta-induced Mitochondrial Dysfunction and Synaptic Damage in Alzheimer's Disease. Hum Mol Genet. 2016 Sep 27. pii: ddw330. [Epub ahead of print] PMID: 27677309.

Wang R, Reddy PH. Role of Glutamate and NMDA Receptors in Alzheimer's Disease. J Alzheimers Dis. 2016 Sep 23. [Epub ahead of print] PMID: 27662322.

Kandimalla R, Manczak M, Fry D, Suneetha Y, Sesaki H, Reddy PH. Reduced Dynaminrelated Protein 1 Protects Against Phosphorylated Tau-induced Mitochondrial Dysfunction and Synaptic Damage in Alzheimer's Disease. Hum Mol Genet. 2016 Sep 15. pii: ddw312. [Epub ahead of print] PMID: 27634647.

Kandimalla R, Thirumala V, Reddy PH. Is Alzheimer's disease a Type 3 Diabetes? A critical appraisal. Biochim Biophys Acta. 2016 Aug 25. pii: S0925-4439(16)30215-0. doi: 10.1016/j.bbadis.2016.08.018. [Epub ahead of print] PMID: 27567931.

Rajmohan R, Reddy PH. Amyloid-Beta and Phosphorylated Tau Accumulations Cause Abnormalities at Synapses of Alzheimer's disease Neurons. J Alzheimers Dis. 2016 Aug 26. [Epub ahead of print] PubMed PMID: 27567878.

Vijayan M, Reddy PH. Stroke, Vascular Dementia, and Alzheimer's Disease: Molecular Links. J Alzheimers Dis. 2016 Sep 6;54(2):427-43. doi: 10.3233/JAD-160527. PubMed PMID: 27567871.

Reddy PH, Tonk S, Kumar S, Vijayan M, Kandimalla R, Kuruva CS, Reddy AP. A critical evaluation of neuroprotective and neurodegenerative MicroRNAs in Alzheimer's disease. Biochem Biophys Res Commun. 2016 Aug 12. pii: S0006-291X(16)31324-9. doi: 10.1016/j.bbrc.2016.08.067. [Epub ahead of print] PMID: 27524239.

Reddy PH, Manczak M, Yin X, Grady MC, Mitchell A, Kandimalla R, Kuruva CS. Protective effects of a natural product, curcumin, against amyloid β induced mitochondrial and synaptic toxicities in Alzheimer's disease. J Investig Med. 2016 Aug 12. pii: jim-2016-000240. [Epub ahead of print] PubMed PMID: 27521081.

Vijayan M, Reddy PH. Peripheral biomarkers of stroke: Focus on circulatory microRNAs. Biochim Biophys Acta. 2016 Oct;1862(10):1984-93. doi: 10.1016/j.bbadis.2016.08.003. PMID: 27503360.

Kumar S, Reddy PH. Are circulating microRNAs peripheral biomarkers for Alzheimer's disease? Biochim Biophys Acta. 2016 Sep;1862(9):1617-27. doi: 10.1016/j. bbadis.2016.06.001. PMID: 27264337.

Wani WY, Kandimalla RJ, Sharma DR, Kaushal A, Ruban A, Sunkaria A, Vallamkondu J, Chiarugi A, Reddy PH, Gill KD. Cell cycle activation in p21 dependent pathway: An alternative mechanism of organophosphate induced dopaminergic neurodegeneration. Biochim Biophys Acta. 2016 Jun 2. pii: S0925-4439(16)30130-2. doi: 10.1016/j. bbadis.2016.05.014. [Epub ahead of print] PMID: 27262357.

Boles AN, Khan H, Lenzmeier TA, Molinar-Lopez VA, Ament JC, TeBrink KL, Stonum K, Gonzales RM, Reddy PH. Impact of Exercise and Education in Adults of Lubbock, Texas: Implications for Better Lifestyle. Front Aging Neurosci. 2016 May 10;8:85. doi: 10.3389/fnagi.2016.00085. PMID: 27242507; PubMed Central PMCID: PMC4861719.

Pugazhenthi S, Qin L, Reddy PH. Common neurodegenerative pathways in obesity, diabetes, and Alzheimer's disease. Biochim Biophys Acta. 2016 May 6. pii: S0925-4439(16)30097-7. doi: 10.1016/j.bbadis.2016.04.017. [Epub ahead of print] PubMed PMID: 27156888.

Yin X, Manczak M, Reddy PH. Mitochondria-targeted molecules MitoQ and SS31 reduce mutant huntingtin-induced mitochondrial toxicity and synaptic damage in Huntington's disease. Hum Mol Genet. 2016 May 1;25(9):1739-53. PMID: 26908605; PubMed Central PMCID: PMC4986329.

2015

Kandimalla R, Reddy PH. Multiple faces of dynamin-related protein 1 and its role in Alzheimer's disease pathogenesis. Biochim Biophys Acta. 2016 Apr;1862(4):814-28. PubMed PMID: 26708942.

Blackmon J, Boles AN, Reddy PH. Garrison Institute on Aging-Lubbock Retired and Senior Volunteer Program (RSVP) Provides Services to South Plains, Texas. Front Aging Neurosci. 2015 Dec 8;7:215. PMID: 26696877; PubMed Central PMCID: PMC4672082.

Manczak M, Reddy PH. Mitochondrial division inhibitor 1 protects against mutant huntingtin-induced abnormal mitochondrial dynamics and neuronal damage in Huntington's disease. Hum Mol Genet. 2015 Dec 20;24(25):7308-25. PMID: 26464486; PubMed Central PMCID: PMC4664169.

Invited Talks/Presentations at Local, National and International Conferences of GIA Scientists

P. Hemachandra Reddy, Ph.D.

- 1. Invited seminar entitled 'Mitochondria-Targeted Molecules As Potential Therapeutic Targets' at the Alzheimer's Association International Conference, July 24-28, 2016, Toronto, Canada.
- 2. Invited seminar entitled 'Oxidative Stress, Mitochondrial Dysfunction and Defective Synapses in Alzheimer's Disease, on January 22, 2016 at NSM Biological Sciences 2016 Spring Seminar Series, University of Texas, Dallas.
- 3. Invited presentation entitled 'Is Mitochondrial Impairment A Key Factor For Aging and Alzheimer's Disease? January 11, 2016 at Sri Venkateswara University, Tirupathi, India.
- 4. Invited seminar entitled 'Advances in Alzheimer' Neurology & Epilepsy Grand Round Series on Wednesday, December 2nd, 2015 at the Overton Hotel & Conference Center in Lubbock, TX.
- 5. Invited Healthy Aging Seminar entitled 'Can Healthy Diets, regular exercise and better lifestyle delay progression of dementia in elderly individuals? Garrison Institute on Aging Healthy Aging Lecture Series, November 18, 2015.
- 6. Plenary Lecture entitled 'Mitochondrial division inhibitor 1 protects against mutant huntingtin-induced abnormal mitochondrial dynamics and neuronal damage in Huntington's disease' at 33rd Indian Academy of Neurosciences, Chandigarh, India October 30-November 2, 2015.
- 7. Invited talk entitled 'Is Impaired Mitochondria Dynamics A Key Factor For Aging and Alzheimer's Disease?' at International Brain Research Organization School, Chandigarh, India. October 26 30, 2015.
- 8. Invited talk entitled 'Stress, Dysfunction & Aging: Culprit Affecting Our Cells.... Garden & Art Center at 44th St. and University Ave. Lubbock, September 22, 2015.
- 9. Invited talk entitled 'Defective Synapses and Mitochondrial Dysfunction' at Faculty Retreat, TTUHSC, Lubbock, September 11, 2015.
- 10. Invited Guest Lecture entitled 'Molecular Mechanisms of Aging and Alzheimer's disease' for neuroscience course for speech and hearing science seniors, Department of Speech, Language & Hearing Sciences, Texas Tech University Health Sciences Center, September 13, 2015.

Ramesh Kandimalla, Ph.D.

1. Invited presentation entitled 'Protective Effect of Reduced Dynamin-Related Protein 1 in Alzheimer's Disease at Pharmacology/Neuroscience Faculty Seminar, Texas Tech University Health Sciences Center, Lubbock, Texas August 18, 2016.

Annette Boles, M.S.

- 1. Invited presentation entitled 'Exercise & Diet in Alzheimer's Disease' for Neurology & Epilepsy Grand Round Series, Covenant Hospital, Lubbock, Texas, December 2, 2015.
- 2. Invited presentation entitled 'Life is a Highway: Finding Your Way to Healthy Living' for Healthy Aging Lecture Series, Texas Tech University Health Sciences Center, Lubbock, Texas February 2015.

Poster Presentations

Presenters - Andrew Mitchell and Mary Catherin Grady

Mitchell A, Grady MK, Yin X, Manczak M and Reddy PH (2016) Glycogen Synthase Kinase 3β Inhibitor, IM-12 Protects Against Amyloid Beta, Synaptic and Mitochondrial Toxicities in Alzheimer's Disease Neurons. Poster presented to the 28th Annual Student Research Week, March 8-11, 2016.

Presenter – Taylor Lenzmeier

Boles AN, Khan H, Lenzmeier TA, Molinar-Lopez VA, Ament JC, TeBrink KL, StonumK, Gonzales RM, Reddy PH. Impact of Exercise and Education in Adults of Lubbock, Texas: Implications for Better Lifestyle. Poster presented to the 28th Annual Student Research Week, March 8-11, 2016.

Presenters - P. Hemachandra Reddy and Arubala P. Reddy

Reddy PA, Manczak M, Yin X, Reddy PH (2016) Protective Effects of Selective Serotonin Reuptake Inhibitors and Neurosteroids Against Alzheimer's Disease Neurons. Abstract submitted to Alzheimer's Association International Conference, July 24-28, 2016, Toronto, Canada.

Presenter - P. Hemachandra Reddy

Reddy PH, Manczak M, Kandimalla R, Yin X, Pandey AK, Kuruva CS, (2015) Synaptic Gene Expression Analysis of Autopsy Brains From Garrison Institute on Aging Brain Bank: Eva-Green Biochemistry Based Real-time RT-PCR Detects mRNA levels Better Than Sybr-Green. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.

Presenter - XiangLing Yin

Yin X, Manczak M, Kandimalla R, AK Pandey, CS Sekhar, S Yeguvapalli, and Reddy PH (2015) Mitochondrial Division Inhibitor 1 and Mitochondria-Targeted Molecules MitoQ and SS31 Protects Against Mutant Htt-induced Mitochondrial toxicities in Huntington's Disease Neurons. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.

Presenter – Maria Manczak

Manczak M, R Kandimalla, Pandey AK, Yin X, Kuruva CS, Yegavapalli S, Fry D, Osborn C and Reddy PH (2015) Reduced Dynamin-related Protein 1 Protects Against Amyloid Beta, Mitochondrial Toxicities and Synaptic Damage in Alzheimer's Disease. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.

Presenter – Ramesh Kandimalla

Kandimalla R, Manczak M, Pandey AK, Yin X, Kuruva CS, Yegavapalli S, Fry D, Osborn C and Reddy PH Reduced Dynamin-related Protein 1 Protects Against Phosphorylated Tau, Mitochondrial Dysfunction and Synaptic Damage in Alzheimer's Disease. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.

Grants

Alzheimer's Association - SAGA grant

Title: Gender Difference in Human and Primate Serotonin Network

In collaboration with Arubala P. Reddy, Ph.D. from the Internal Medicine Department of TTUHSC, Dr. Reddy has received a 3-year grant from the Alzheimer's Association to study the gender-based serotonin network in the progression and pathogenesis of Alzheimer's disease.

This funded project is an Alzheimer's Association's Initiative exploring why more women than men are living with the disease. The first-ever Alzheimer's Association Sex and Gender in Alzheimer's (SAGA) research grant awarded \$2.2 million to nine projects to advance understanding of the disproportionate effect of Alzheimer's disease on women.

Each of the SAGA grant-funded projects received \$250,000. The majority of the investigations are examining relationships between hormones, genetics and the development of Alzheimer's. Other key themes include differences in men's and women's brains that may contribute to the development or progression of the disease, and sex-specific response to Alzheimer's risk factors.

CH Foundation Grant

Title: Circulatory microRNAs and Alzheimer's Disease - FRONTIER Data

This proposal seeks to secure funding for the continuation of data collection for Project FRONTIER and to determine microRNAs as peripheral biomarkers for Alzheimer's disease (AD). Project FRONTIER is a rural-based research study looking at the health conditions of adults and elders living in rural communities. Study participants from Cochran, Parmer, Bailey and Hockley counties are followed over time to test for changes in physical, mental, and cognitive health and the factors that may influence those changes. There are currently over 1300 West Texas residents participating in the study, with over 1500 data points collected from each participant. Based on physical, mental, and cognitive health factors, a large number of individuals were identified as AD patients, individuals with mild cognitive impairment (MCI) and nondemented control subjects. Using serum samples from individuals with MCI, AD patients and non-demented control subjects, we will identify AD-specific circulating microRNAs as peripheral biomarkers for AD. The outcome of our proposed research will determine the early peripheral diagnostic markers for AD, and also provide new information for the development of drug targets to reduce AD risk in elderly individuals and ameliorate cognitive decline in AD patients. The overall goal of the proposed research is to determine miRNAs as peripheral biomarkers in the development and progression of AD.



Bottom Row: Ramesh Kandimalla, Ph.D., Hemachandra Reddy, Ph.D., Annette Boles, Veronica Molinar-Lopez



