TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER™

Garrison Institute on Aging

2017 ANNUAL REPORT

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EXECUTIVE DIRECTOR'S REPORT

I am pleased to report that during 2017, my colleagues and I at the Garrison Institute on Aging have made significant progress in research and in disseminating our research results. In 2017, we published more than 26 peer-reviewed research papers, reviews and book chapters. In addition, I was a guest editor for two special topics in journals: "Neurotransmitters and Alzheimer's Disease" for the Journal of Alzheimer's Disease and "Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases" for the BBA Molecular Basis of Disease. During this past year, I also edited the book Molecular Biology of Aging (Elsevier and Academic Press), which presents 11 articles on healthy aging and several molecular aspects of Alzheimer's disease, written by premier researchers in aging and Alzheimer's disease.

This year also saw the success of the Garrison Institute on Aging Student Scholars Program, as in previous years, and it attracted visiting scholars, summer medical student interns, and masters-level students from science programs across the U.S. Most of these student scholars conducted research with Garrison Institute on Aging researchers and then became authors and co-authors of several research papers they submitted to high-impact factor journals for peer review.

Other activities outside of the Garrison Institute on Aging in which I participated included continuing service on the NIH study section Neuronal Oxidative Stress, Metabolism and Death, and selection to become the Research Committee Chair of the TTUHSC School of Medicine. As Research Committee Chair, I assisted in reviewing School of Medicine grants, The CH Foundation and South Pacific Foundation with NIH review process. In addition, I was invited to become a member of the University Research Council, which involved assisting Dr. Quentin Smith, the TTUHSC Senior Vice President for Research for Strategy Planning, to improve the quality of research at TTUHSC. I also had the honor to become a faculty member in the TTUHSC Public Health Department of Graduate School of Biomedical Sciences, giving me the opportunity to mentor four master's students in the Department of Public Health.

Due to the hard work, cooperation and collaboration of the Garrison Institute on Aging administrative staff and researchers, the institute has received a $1.9 million, five-year R01 grant from the NIH Neurological Disorders and Stroke Institute to study the mitochondrial basis and therapeutics of Huntington's disease. In addition, the institute has received a $100,000 grant from the Garrison Family Foundation and a $35,000 award from Darlene Newby Family to support activities and programs of the Garrison Institute on Aging Brain Bank.

During this past year, the Garrison Institute on Aging has made significant progress in community outreach and educational programs. In addition, through Project Frontier, we actively are working to generate preliminary data for proposals to receive long-term NIH and NSF funding in the field of rural medicine. Project Frontier is being continually developed, and a newly added questionnaire on genetics, diet and culture to collect data on families in rural areas of West Texas. My Garrison Institute on Aging colleagues in community outreach and education and I are excited to continue our participation in the Lubbock Mayor Council Fitness Program, the focus of which is to generate awareness about exercise and diet and to improve the quality of life of Lubbock residents.

In collaboration with colleagues in the Texas Tech University Neuroimaging Institute and School of Medicine Department of Neurology, a proposal was submitted to NIH to study the effects of exercise on cognitive function, brain imaging, and blood-based peripheral biomarkers (microRNAs) in residents from rural West Texas.

I sincerely thank all of the staff, students and colleagues from Garrison Institute on Aging, School of Medicine and the Department of Public Health for their kind support and participation in Garrison Institute on Aging activities. My special thanks to Dr. Scott Trasti and all our colleagues from the TTUHSC Laboratory Animal Resources Center for their support and assistance. Thank you to our colleagues in the TTUHSC Research Integrity Office and Sponsored Research Program for their support and assistance in our continual proposal-submission efforts. Special thanks to TTUHSC President Tedd Mitchell; Dean, Dr. Steven Berk; Provost and Dean, Senior Vice President for Research Quentin Smith, Dr. Vadivel Ganapathy; chair of Cell Biology and Biochemistry, Dr. Volker Neugebauer; chair of Neuroscience/Pharmacology, Dr. John de Toledo, chair of the Department of Neurology, Drs. Theresa Bird and Hafiz Khan, Department of Public Health. I appreciate my administration colleagues – Kathy Stonum, Annette Boles, Ruben Gonzales and Kandi Quesada – for their patience and kind support, and I believe the success of the Garrison Institute on Aging is in large part due to their efforts. I also thank colleagues at the TTUHSC Office of Institutional Advancement for their fund-raising efforts to help support Garrison Institute on Aging research. Special thanks to Mr. Spike Dykes and his family for raising research funds for the Reddy research team, and to Garrison family members for their support of all activities in the Garrison Institute on Aging.

P. Hemachandra Reddy, Ph.D.

PRESIDENT'S REPORT

With the increase in human life expectancy, aging research has become the focus of thousands of laboratories engaged in discovering the mechanisms of aging and age-related diseases. Alzheimer's disease, strokes and diabetes remain widespread among older Americans. In 2017, the Garrison Institute on Aging was a significant contributor to this important body of knowledge. Under the leadership of Dr. P. Hemachandra Reddy, our researchers continue to conduct novel research in these areas with the hope that one day their findings will translate into strategies or treatments to prevent, delay or slow age-related diseases.

Texas Tech University Health Sciences Center is infinitely grateful to the family of Shirley and Mildred Garrison who so boldly placed their faith in us and our ability to advance health aging through research, innovative educational and community outreach programs.

Tedd L. Mitchell, M.D.
President, Texas Tech University Health Sciences Center

FOUNDER OF THE GARRISON INSTITUTE ON AGING

The 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 Allied Health, Medicine, Nursing, and Pharmacy. The GIA is a unique organization, the mission of which 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.

Shirley L. Garrison
Founder of the Garrison Institute on Aging

In 2004, through an endowment funded by Mr. and Mrs. Shirley 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.

RESEARCH AT THE REDDY LABORATORY OF THE GARRISON INSTITUTE ON AGING

The Reddy research team at the Garrison Institute on Aging is involved in lines of research designed to elucidate mechanisms underlying Alzheimer's disease and other neurological diseases, to develop therapeutics to reduce symptoms of Alzheimer's disease and, ultimately, to prevent the onset of Alzheimer's disease. Our research team also has embarked upon a line of research to elucidate mechanisms underlying ischemic stroke and biomarkers for the early diagnosis of ischemic stroke, leading to therapeutics designed to ameliorate symptoms of ischemic stroke.

RESEARCH RELATED TO ALZHEIMER'S DISEASE

1. Hippocampal amyloid beta toxicity and protective effects of reduced dynamin-related protein 1 in Alzheimer's disease.

The purpose of our study was to determine the toxic effects of the mutant amyloid precursor protein (APP) and amyloid beta (A**β**) in the hippocampus of the APP transgenic mouse model, a model used in studies of Alzheimer's disease. Mounting evidence suggests that A**β**-induced dysfunction of mitochondria and A**β**-induced damage of synapses is largely involved in AD. Our test mice were 12-month-old APP mice, and our control mice were 12-month-old, disease-free mice. To assess the cognitive behavior and motor coordination of the APP and control mice, we used the Morris Water Maze test and the rotarod performance test. We used immunoblotting and immunofluorescence, Golgi-cox staining and transmission electron microscopy to measure the levels of multiple mitochondrial fission and fusion proteins, autophagy and mitophagy proteins and to quantify the number and length of mitochondria and characteristics of their dendritic spines. We assessed mitochondrial function by measuring levels of hydrogen peroxide, lipid peroxidation, cytochrome c oxidase activity and mitochondrial ATP.

The Morris Water Maze and rotarod performance tests revealed that cognitive learning and memory, and motor learning and coordination were impaired in APP mice relative to the control mice. The APP mice also had increased levels of mitochondrial fission proteins and decreased levels of fusion, biogenesis, autophagy/mitophagy and synaptic proteins that we studied, compared to levels in the control mice. Golgi-cox staining procedures revealed that the dendritic spines in the APP mice were significantly reduced, and transmission electron microscopy revealed significantly increased numbers and reduced length in the mitochondria of the APP mice. These findings suggest that the accumulation of mutant APP and A**β** in the hippocampus may be responsible for abnormalities found in the APP mice, including defective mitochondrial structure and dynamics, defective biogenesis, reduced dendritic proteins, reduced synaptic, autophagy & mitophagy proteins, malformed dendritic spines, cognitive learning and memory impairments and motor impairments.

Based on earlier studies in the Reddy research laboratory, where abnormal interactions between the mitochondrial fission protein Drp1 and A**β** were found, we studied whether reduced levels of Drp1 provide any protection against the mitochondrial abnormalities and synaptic deficiencies found in the 12-month-old APP mice. We then assessed the impact of the reduced Drp1 on spatial learning and memory, motor learning, the quantity and size of mitochondria and dendritic spines, and the levels of the proteins in the 12-month-old APP mice. We found that a partial reduction of Drp1 correlated with an increase in dendritic spines and reduced A**β** production, which in turn correlated with the maintenance of normal mitochondrial dynamics and the enhancement of mitochondrial biogenesis and synaptic plasticity. These findings suggest that an intervention that reduces Drp1may serve as a therapeutic regimen in slowing disease progression and reducing disease symptoms, possibly resulting in the protection of normal cognitive function and normal protein levels not only in the APP mice but also in patients with Alzheimer's disease.

2. Hippocampal phosphorylated tau toxicity and protective effects of reduced Drp1 in Alzheimer's disease.

The purpose of this study was to characterize the toxic effects of phosphorylated tau in the hippocampus of the tau mouse model with the P301L mutation; this model is used to study disease pathogenesis and progression in Alzheimer's disease. Tau is a protein that plays a key role in regulating microtubule dynamics, neurite outgrowth and the transport of axons. To assess the cognitive behavior, and motor coordination of the test and control mice, we used the Morris Water Maze and rotarod performance tests. We assessed mitochondrial function by measuring levels of hydrogen peroxide, lipid peroxidation, cytochrome oxidase activity, and mitochondrial ATP. Mitochondrial function was assessed by measuring the levels of hydrogen peroxide, lipid peroxidation, cytochrome oxidase activity and mitochondrial ATP.

The Morris Water Maze and rotarod performance tests revealed that learning and memory in the hippocampus and motor learning and coordination were impaired in the tau mice compared to the control mice. Increased levels of mitochondrial fission proteins and decreased levels of mitochondrial fusion and biogenesis proteins were also found in the test mice compared to the control mice, indicating abnormal mitochondrial dynamics in the tau mice with the P301L mutation. Decreased levels of the dendritic protein MAP2 and increased levels of tau were also found in the test mice

relative to the control mice. Mitochondrial function was defective, and dendritic spines were reduced in the tau mice, but not in the control mice. Significantly increased numbers of reduced-length mitochondria were also found in the tau mice, but not in the control mice. These findings suggest that an accumulation of phosphorylated tau in the hippocampus may be responsible for abnormal mitochondrial structure and dynamics, a reduction in the MAP2 protein, a reduction in the number of dendritic spines, and the impairment of cognitive learning and memory in the tau mice.

To determine whether a reduction in the Drp1 protein protects phoshorylated tau in neurons, we developed double mutant (Drp1+/xTau (P301L) mice. Using molecular, biochemical, Golgi-cox staining, and transmission electron microscopy studies, we measured the number and morphology of mitochondria in the hippocampus, mRNA, protein levels in mitochondrial and synaptic genes, and dendritic spines. We also assessed the cognitive behavior of 12-month-old double-mutant mice compared to the tau mice. In the hippocampus of the double mutant mice relative to tau mice, we found significantly increased dendritic spines; significantly reduced, fragmented, and structurally damaged mitochondria; reduced mRNA and protein levels of fission genes; and increased levels of fusion, synaptic autophagy and mitophagy genes. It is noteworthy that we also found ameliorated cognitive deficits in the 12-month-old Drp1+/xTau mice relative to tau mice. These findings suggest that reduced Drp1 may be beneficial to AD-affected neurons and may have a protective, therapeutic value to the double-mutant tau mice that we studied and potentially to patients with Alzheimer's disease.

3. Mdivi1 as therapy drug for AD-affected neurons

The purpose our study was to determine the protective effects of the small molecule drug Mdivi1 (mitochondria division inhibitor 1) in Alzheimer's disease. Mdivi1is hypothesized to reduce excessive fragmentation of mitochondria and mitochondrial dysfunction in Alzheimer's disease neurons. However, very little is known about whether Mdivi1 can confer such effects on mitochondria involved in Alzheimer's disease. In the present study, we sought to determine whether, in Alzheimer's disease-affected neurons, Mdivi1 confers any protective effects against Ab and against excessive fragmentation of mitochondria induced by the mitochondrial fission protein Drp1.

Using real-time RT-PCR and immunoblotting analysis, we then measured mRNA and levels of mitochondrial dynamics, mitochondrial biogenesis, and synaptic gene proteins in cells. We assessed mitochondrial function in Alzheimer's disease -affected neurons by measuring hydrogen peroxide, lipid peroxidation, cytochrome oxidase activity, and mitochondrial ATP; and we also assessed neuronal viability through MTT assays.

We found that Ab42 impairs mitochondrial dynamics and lowers mitochondrial biogenesis, synaptic activity, and mitochondrial function. We found that Mdivi1 enhances mitochondrial fusion, reduces mitochondrial fission, and increases biogenesis and synaptic proteins. Mitochondrial function and neuronal viability were elevated in Mdivi1-treated cells. Interestingly, neurons incubated with Ab before and after they received Mdivi1 treatment showed reduced mitochondrial dysfunction; and they maintained neuronal viability, mitochondrial dynamics, mitochondrial biogenesis, and synaptic activity. The protective effects of Mdivi1 were even stronger in Alzheimer's disease-affected cells (N2a+Ab42) that were pre-treated with Mdivi1, compared to Mdivi1 post-treated cells, suggesting that Mdivi1 works better in preventing mitochondrial structural and functional damage than in treating the damage once begun. Our exciting findings suggest that Mdivi1 may a promising drug molecule to prevent and to treat Alzheimer's disease-related damage in Alzheimer's disease-affected neurons.

4. Mitochondria-targeted SS31 as therapeutic drug in AD mice.

The objective of our study was to better understand the protective effects of the mitochondria targeted antioxidant peptide SS31 against amyloid beta-induced mitochondrial and synaptic toxicities in Alzheimer's disease.

Using intraperitoneal injections, we administered SS31 to an APP mouse model of Alzheimer's disease, beginning when the APP mice were 12 months of age and continuing over a 6-week period. We also studied an APP mouse model of Alzheimer's disease, to which we did not administer SS31. We studied cortical and hippocampal tissues of both mouse groups over the 6-week period. Using biochemical methods, we determined that SS31 crosses the blood brain barrier and reaches mitochondrial sites of free radical production. Measuring H_2O_2, lipid peroxidation, cytochrome c oxidase activity and mitochondrial ATP, we quantified: 1) plasma and brain levels of SS31, 2) mRNA levels and levels of mitochondrial dynamics, biogenesis proteins, and synaptic proteins in APP mice, and 3) levels of soluble Ab. Using immunohistochemistry, we determined the extent of immunoreactivity of mutant APP and Ab levels, and the extent of mitochondrial function and dysfunction.

We found reduced mRNA expression and protein levels of fission genes, and increased levels of mitochondrial fusion, mitochondrial biogenesis, and synaptic genes in the SS31-treated APP mice relative to the untreated APP mice. Immunofluorescence analysis revealed reduced full-length mutant APP and reduced Aβ deposit levels in the SS31-treated APP mice. Sandwich ELISA assays revealed significantly reduced soluble Aβ levels in the SS31-treated APP mice relative to the untreated APP mice. Mitochondrial function was maintained in the SS31-treated APP mice over the 6 weeks of SS31treatment compared to the untreated APP mice. In the SS31-treated APP mice, we found reduced levels of Aβ

production, reduced mitochondrial dysfunction, the maintenance of mitochondrial dynamics, and an enhancement of mitochondrial biogenesis and synaptic activity. Based on these findings, it appears that SS31 may confer protective effects against mutant mitochondrial and synaptic toxicities in APP mice and in patients with Alzheimer's disease.

5. DDQ as a therapeutic drug in the treatment of Alzheimer's disease

   The purpose of our study was to develop a therapeutic agent that can target Alzheimer's disease-affected neurons, reduce A**β** and Drp1 levels, and inhibit abnormal interactions between A**β** and Drp1 in in the AD-affected neurons. To achieve this objective, we designed 82 compounds based on molecular docking. We introduced each of these compounds into Alzheimer's disease-affected neurons and studied inhibitory properties against abnormal A**β**-Drp1 interactions. Among the compounds that we initially designed, we selected DDQ (diethyl (3,4-dihydroxyphenethylamino) (quinolin-4-yl)methylphosphonate) for further investigation because: 1) it received the highest score in terms of the speed and accuracy of its capability to dock with Alzheimer's disease-affected neurons and 2) its capability to dock at specific neuronal sites where Drp1 and A**β** interact.

   Using biochemical, molecular biology, immunostaining, and transmission electron microscopy methods, we studied the effects of DDQ when docked to Alzheimer's disease-affected neurons. We measured the levels of A**β** and Drp1, the frequency and involvement of A**β** and Drp1 interactions, mRNA and protein levels of mitochondrial dynamics, biogenesis and synaptic genes, mitochondrial function, neuronal viability, and the number of DDQ-treated and untreated Alzheimer's disease neurons.

   Our qRT-PCR and immunoblotting analysis of DDQ-treated Alzheimer's disease neurons revealed reduced mitochondrial fission and increased mitochondrial fusion, biogenesis, and synaptic genes. Our immunoblotting and immunostaining analyses revealed reduced A**β** and Drp1 levels and reduced A**β** and Drp1 interactions in the Alzheimer's disease neurons treated with the docked DDQ. The number of abnormally long mitochondria was also reduced following DDQ treatment. Mitochondrial function and neuronal viability were maintained in Alzheimer's disease neurons treated with DDQ. These results indicate that DDQ may be effective in protecting Alzheimer's disease neurons against A**β**-induced mitochondrial and synaptic toxicities by reducing excessive mitochondrial fragmentation and levels of A**β**42, and by enhancing fusion, biogenesis and synaptic activity.

6. Blood-based MicroRNA-455-3p as a potential peripheral biomarker for Alzheimer's disease

   The objective of our study was to identify microRNAs (miRNAs) as early detectable peripheral biomarkers in Alzheimer's disease (AD). To achieve this objective, we assessed miRNAs in serum samples from patients with AD (N=10), patients with mild cognitive impairment (MCI) (N=16), and healthy persons (controls) (N=14). We used Affymetrix microarray analysis to validate differentially expressed miRNAs. We further validated miRNA data with qRT-PCR in postmortem brains from Alzheimer's disease patients, APP transgenic mice and Alzheimer's disease cell lines.

   In this study, we identified a gradual upregulation of four miRNAs: miR-455-3p, miR-4668-5p, miR-3613-3p, and miR-4674. A fifth miRNA, mir-6722, was downregulated in persons with Alzheimer's disease and MCI, compared the mir-6722 in the controls. Validation analysis by qRT-PCR showed significant upregulation of only miR-455-3p (P=0.007) and miR-4668-5p (P=0.016) in Alzheimer's disease patients compared to healthy controls. Further, qRT-PCR analysis of the Alzheimer's disease postmortem brains with different Braak stages also showed upregulation of miR-455-3p (P=0.016). However, ROC curve analysis revealed a significant area under curve (AUC) value only for miR-455-3p in the serum (AUROC=0.79; P=0.015) and brains (AUROC=0.86; P=0.016) of AD patients. Expression analysis of APP transgenic mice also revealed a high level of mmu-miR-455-3p (P=0.004) in the cerebral cortex (Alzheimer's disease-affected) region of brain and a low level in the non-affected areas, such as the cerebellum. Further, human and mouse neuroblastoma cells treated with the amyloid-$\beta_{(1-42)}$ peptide also showed a similarly higher expression of miR-455-3p. Functional analysis of differentially expressed miRNAs via the miR-path indicated that miR-455-3p was associated in the regulation of several biological pathways. Genes associated with these pathways were found to have a crucial role in Alzheimer's disease pathogenesis. An increase in miR-455-3p expression found in Alzheimer's disease patients and A**β** pathologies unveiled its biomarker characteristics and a precise role in Alzheimer's disease pathogenesis.

7. Pharmacophore-based screening and molecular docking probes novel inhibitors against BACE1 in Alzheimer's disease

   The purpose of our study is to identify pharmacophore-based drugs to reduce amyloid beta toxicities in Alzheimer's disease. Pharmacophore-based models are one of the most promising drug targets in Alzheimer's disease. Aspartyl protease inhibitors, like pepstatin, are well-known potent inhibitors designed to reduce the cleavage of proteins, such as the beta amyloid cleavage enzyme 1 (BACE1) protein. The crystal structure of BACE1 contains 2 functional domains: ecto and internal. The ectodomain is the key functional part of catalytic cleavage that is initiated by BACE1. This initiation leads to aggregates of pathological A**β** in Alzheimer's disease neurons. The chief residues involved in the ectodomain

catalytic process are still unknown, and currently, there are no promising BACE1 inhibitors available in the market. In the present study, we constructed a pharmacophore model of BACE1 and pepstatin, using computational screening and molecular docking, and are successfully using the inhibitor-based pharmacophore model of BACE1 to identify new lead molecules that are showing the best potentiation to reduce Aβ formation and the best molecular docking properties. Top-ranking small molecules were studied for their suitability as drugs with minimal or no toxic effects. Three small molecules have been identified as potential therapeutic drug targets for the treatment of Alzheimer's disease. Further, *in vitro* and *in vivo* studies will be conducted to develop new drugs to help reduce toxicity in Alzheimer's disease. Our ongoing efforts will identify new drug targets for Alzheimer's disease.

RESEARCH RELATED TO STROKE

8. Blood-based microRNAs as peripheral biomarkers for ischemic stroke

Ischemic stroke is a common neurological disease that occurs when the blood supply to the brain is interrupted, resulting in a shortage of oxygen and nutrients to brain tissue. Diverse etiologies can lead to stroke, leading researchers to characterize stroke not as one disease but as a syndrome. Stroke is the second leading cause of death globally and third leading cause of disability-adjusted life years worldwide. Identification of early detectable peripheral biomarkers of ischemic stroke could contribute to a better understanding of the etiologies and mechanisms underlying stroke, and ultimately to the development of therapeutics to prevent stroke.

Recent discoveries in molecular biology indicate that miRNAs – short RNAs that regulate gene translation and mediate a large range of biological functions – can detect changes in bodily organs, including the brain, which may lead to ischemic stroke. The long-term goal of our study is to determine whether circulatory miRNAs can serve as early detectable peripheral biomarkers for ischemic stroke. The objective of our initial study was to identify miRNAs that are present in serum samples of persons who have experienced ischemic stroke. To achieve our objective, we took serum samples from patients diagnosed with ischemic stroke (n=34; 43-86 years of age) and from healthy controls (n=11; 51-80 years of age), and then measured expression levels of miRNAs in those samples. We used Illumina deep sequencing (Illumina GAIIx, ACGT101-miR v4.2, LC Sciences) analysis. We selected potential miRNA candidates for stroke biomarkers based on differential expression. We then validated differentially expressed miRNAs sing qRT-PCR.

A total of 484,651,777 raw RNA reads were obtained in our analysis. Seventy percent (341,678,616) of the reads were mapped for miRNAs. A total of 4,656 differentially expressed miRNAs were found in the serum samples from the ischemic stroke, and of these 4,656, only 272 miRNAs were significantly differentially expressed (173 upregulated and 76 downregulated). Sixteen of the most significantly downregulated miRNAs were selected for further validation, using additional serum samples from ischemic stroke patients, serum samples from post mortem brain specimens of ischemic stroke patients, human ischemic stroke lymphoblastoid cells, OGD/R-related human and mouse neuroblastoma cells, and hypoxia and ischemia stroke mouse models. Four miRNA candidates were significantly differentially expressed in these serum samples, post mortem brains, lymphoblastoid cells, OGD/R treated cells and stroke mouse models. We will use these four miRNAs in our studies designed to determine blood-based peripheral markers. In addition, our analysis of the 272 miRNAs revealed that other miRNAs, besides the 4 miRNA candidates, were involved in the regulation of the stroke event. Future studies will focus on determining peripheral biomarkers and therapeutic targets, leading us closer to developing novel therapeutic approaches to prevent stroke and to better understand how miRNAs regulate the stroke event.

RESEARCH RELATED TO DIABETES

9. Oxidative stress and mitochondrial dysfunction in TALLYHO/JngJ mice – A common link across type 2 diabetes, obesity, dementia, and Alzheimer's disease

Recent studies of diabetes have linked the high prevalence of type 2 diabetes mellitus (T2DM) and obesity with the risk of dementia and Alzheimer's disease. However, the molecular mechanisms linking these diseases are unknown. The present study aimed to identify the common link across these diseases through the identification of biochemical and mitochondria/oxidative stress biomarkers in a mouse model of T2DM, TALLYHO/JngJ (TH).

In this research, we studied TH mice at 8, 16, and 24 weeks of age, and age- and sex-matched controls (SWR/j mice) that were nondiabetic and non-obese. The development of T2DM and obesity in male and female TH mice was assessed by measuring body weight, glucose tolerance, insulin tolerance, and triglyceride levels. After T2DM was diagnosed in male and female T2DM and obese mice, oxidative stress and mitochondrial markers were measured. Compared with the control mice, both male and female TH mice diagnosed with T2DM were significantly heavier and hyperinsulinemic without glucose intolerance or hyperglycemia. Hyperinsulinemia was more prominent in the male TH mice diagnosed with T2DM than in the female T2DM TH mice. Plasma glucose levels progressively increased with age in the male T2DM TH mice, while the female T2DM TH mice remained normoglycemic at the different points (ages) of study. Interestingly, male T2DM TH mice demonstrated a significant increase in plasma triglyceride levels in the pre-diabetic stage, and they

maintained this increase throughout the study. Oxidative stress and mitochondrial dysfunction were found in the male T2DM TH mice but not in the female control TH mice. Histopathological examinations showed enlarged pancreatic islets in both male and female T2DM mice compared to the male and female control mice. These findings suggest that insulin resistance, hypertriglyceridemia, and hyperglycemia may cause oxidative stress, which then leads to mitochondrial dysfunction in TH mice. Based on these observations, it appears that TH mice may be a relevant model to study the molecular links between T2DM and Alzheimer's disease.

SUMMER INTERNS' RESEARCH PROJECTS

First-year medical interns conducted research on microRNAs in aging. Summaries of their research are given below:

Justin Williams' Project: "Differential expression of microRNAs in the skeletal muscles of aging mice"

   The purpose of our research is to identify peripheral biomarkers for aging and cellular senescence. Aging processes in many species are regulated by the expression of microRNAs (miRNAs). MiRNAs are 18-25 nucleotide-long, single-stranded RNA molecules that regulate gene expression. Skeletal muscles are key reservoirs of amino acids that maintain protein synthesis, and the loss of muscle mass is considered to be a key determinant of loss of strength in aging. As one of the systems impacted by aging the most, the skeletal muscle system has been heavily researched. However, underlying mechanisms of miRNA regulation in aging are not completely understood. To better understand the regulation of miRNA in aging, we sought to determine the miRNA levels in the skeletal muscles of 2-, 6-, 12-, and 24-month-old C57BL/6 mice. We studied the following miRNAs: mmu-miR-17-5P, mmu-miR-22a-3P, mmu-miR-29a-3P, mmu-miR-133a-3P, mmu-miR-181a-5P, and 101a-3P. These miRNAs were selected, based upon their previous identification as modulators of proliferative and senescent process. In our current study, we measured miRNA levels in the skeletal muscles of 6-month-old (n=6) and 12-month-old (n=6) mice. RNA was extracted from the mouse skeletal muscles, and miRNA expression levels were measured using quantitative real-time RT-PCR. MiR-17-5P was found to be significantly upregulated (P=0.014) in skeletal muscles of 12-month-old mice relative to skeletal muscles of 6-month-old mice. MiR-29a-3P was found to be significantly (P=0.002) upregulated in skeletal muscles of the 12-month-old mice compared to those of the 6-month-old mice. Expression levels of MiR-22a-3P and miR-101a-3P were found to be upregulated in 12-month-old mice, but not significantly. We will continue our miRNA studies of skeletal muscles using 2- and 24-month-old mice in order to critically assess miRNA levels of the skeletal muscles of 6-, 12-, and 24-month-old mice relative to those of 2-month-old mice. The outcome of this time-course miRNA study will provide new insights into aging process.

Flint Smith's Project "Upregulation of microRNAs in the brains of aging mice"

   The overall objective of our study is to identify microRNAs (miRNAs) as peripheral biomarkers in the aging brain. MicroRNAs are small, highly conserved non-coding RNA molecules involved in the regulation of gene expression. MicroRNAs have been identified as candidates that regulate aging process in all species. However, regulation of miRNAs in the aging process, particularly in the brain, is not completely understood. these miRNAs are reported to involve in the processes of brain aging, In the current study, we sought to determine the levels of miRNA in C57BL/6 mice at the ages 2, 6, 12, and 24 months. We focused on the 6 miRNAs known to be involved in the aging process of brains: mmu-miR-17-5p, mmu-miR-22a-3p, mmu-miR-29a-3p, mmu-miR-133a-3p, mmu-miR-181a-5p, and 101a-3p, cellular senescence and cell proliferation. In a preliminary study, we investigated miRNAs levels in the brains of 6- and 12-month-old C57BL/6 mice, using real-time RT-PCR analysis. The levels of miR-29a-3p, miR22a-3p, miR133a-3p, and miR-17-5p were found to be significantly higher in the 12-month-old mice relative to 6-month-old mice. Expressions of miR-101a-3p and miR-181a-5p were also higher in the 12-month-old mice relative to the 6-month-old mice, but not significantly so. Based on these observations, we conclude that microRNAs are the strong indicators of brain aging.

GARRISON INSTITUTE ON AGING TEAMS WITH MAYOR'S OFFICE TO PROMOTE HEALTH

The latest statistics from the Alzheimer's Society point to the severe reality of Alzheimer's disease. Alzheimer's disease affects more than 46.8 million people worldwide, including 5.4 million people in the United States. Currently, there is no cure for this progressive neurodegenerative disease. The annual health care cost worldwide for people with Alzheimer's disease is estimated at $818 billion.

A relatively small number of young adults develop what is called early-onset Alzheimer's disease, which is caused by genetic mutations, but causal factors are still unknown for the vast majority of older patients who develop late-onset Alzheimer's disease. Persons with late-onset Alzheimer's disease have typically been diagnosed with diabetes, obesity, traumatic brain injury or an unhealthy diet before developing Alzheimer's disease. Researchers around the world, including scientists at the Garrison Institute on Aging, note that lifestyle significantly affects the onset and progression of the disease, and that Alzheimer's disease may be preventable — or it may be possible to delay its onset — with regular exercise and a healthy diet.

Lubbock Mayor Dan Pope announced the kickoff of the Mayor's Fitness Council outside Roscoe Wilson Elementary School on Wednesday morning. *Photo by Ellysa Harris/A-J Media*

In Alzheimer's disease, dementia typically progresses from mild, to moderate, to severe. Alzheimer's disease patients — both early-onset and late-onset patients — eventually exhibit dementia, a term that encompasses symptoms affecting memory and thinking abilities and social inabilities that interfere with daily activities of living. In postmortem studies of brains from persons with and without the disease, researchers are identifying abnormalities in the Alzheimer's disease brain, including the loss of synapses in nerve cells and brain tissue. In other words, the Alzheimer's disease brain progressively shrinks, especially in the hippocampus, a brain region that is involved in long-term memory and the formation of new memories. Researchers from the Garrison Institute are finding that abnormalities in Alzheimer's disease brain cells involve reductions in energy output from mitochondria and generate adenosine triphosphate, a source of chemical energy for brain functions, such as storage of long-term memories. Garrison institute researchers are actively working to improve energy levels in brain cells by delivering mitochondria-targeted molecules to the brain.

The Garrison institute's overall mission is to improve the quality of life in older persons through innovative and cutting edge research and the promotion of regular exercise and healthy diets. Consistent with this mission, scientists and health care professionals are investigating the impact of lifestyle and diet on mitochondria in brain cells from persons with and without Alzheimer's disease, in order to identify how late-onset Alzheimer's disease can be prevented or delayed, and how Alzheimer's disease progression can be slowed. Scientists and health care professionals are involved in different approaches to achieve its mission of educating the community about how lifestyle decisions such as exercise and a healthy diet can affect Alzheimer's disease onset and progression, how other conditions, such as diabetes and obesity, can impact Alzheimer's disease onset, researching the identification of biomarkers designed to detect Alzheimer's disease as early as possible in elderly individuals and researching drugs capable of targeting and delivering treatment to Alzheimer's disease-affected.

The Garrison Institute on Aging is partnering with the Lubbock mayor's office to support the Mayor's Fitness Council, the mission of which is to create a healthier Lubbock by showcasing events that promote healthy lifestyles and diets. November is designated Alzheimer's Disease Awareness Month, a perfect time to remind the community of the importance of improving exercise and diet.

While the Garrison institute scientists and health care professionals continue their valuable research, take opportunities to participate in the Mayor's Fitness Council, educational programs and activities to stay healthy.

P. Hemachandra Reddy, Ph.D., is the Executive Director and Chief Scientific Officer of Texas Tech University Health Sciences Center Garrison Institute on Aging.

1. Invited talk 'Synaptic Mitochondrial Damage in Alzheimer's Disease' by Dr. Krishna Bhatt, Professor of Cell Biology and Neuroscience Department, University of Texas Medical Branch, Galveston, TX, December 6, 2017.

2. Invited talk 'Defective Synapses and Mitochondria in Alzheimer's Disease' by Dr. Alvin Terry, Associate Vice President for Basic Science Research, Regents Professor and Chair Department of Pharmacology and Toxicology Medical College of Georgia at Augusta University, September 25, 2017.

3. Invited presentation 'Mitochondrial Fragmentation and Neurodegeneration in Huntington's Disease at Graduate Faculty Retreat, Graduate School of Biomedical Sciences, Texas Tech University Health Sciences Center, Lubbock, TX, September 22, 2017.

4. Invited talk 'Mitochondrial Fragmentation and Synaptic Damage in Alzheimer's disease' by Dr. Asgar Zaheer, Director for Center for Translational Neuroscience, University of Missouri – School of Medicine, Columbia, MO, August 14, 2017.

5. Invited presentation 'Recent Research at Garrison Institute on Aging – Focus on Women's Health' by Ms. Laura Logan, Director Communications, Leadership Women, May 7-9, 2017.

6. Invited talk 'Mitochondria-targeted Molecules and Alzheimer's Disease by Qian Cai, Department of Cell Biology and Neuroscience, Rutgers, The State University of New Jersey, Piscataway, NJ, March 17, 2017.

7. Invited talk entitled 'Synapses and Mitochondria in Alzheimer's Disease by Dr. Anil Kumar, Chair of Pharmacology and Toxicology, UMKC-School of Pharmacy, Kansas City, February 9, 2017.

8. Invited presentation entitled 'Recent Advances in Alzheimer's Disease Pathogenesis: Molecular Basis and Therapeutics, for Korean students of Hallym University, who visited TTUHSC, February 3, 2017.

2017

Manczak M, R Kandimalla, Yin X, Vijayan M, Kuruva CS, Kumar S and Reddy PH (2017) Reduced dynamin-related protein 1 mitigates mitochondrial fragmentation, elevates spatial learning and memory functions and elevates dendritic spines in APP mice. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Kandimalla R, Manczak M, Yin X, Vijayan M, Kuruva CS, Kumar S and Reddy PH (2017) A partial loss of dynamin-related protein 1 enhances dendritic spines, reduces fragmented mitochondria and increases hippocampal based cognitive function in mutant Tau mice. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Kuruva CS, Manczak M, Yin X, Ogunmokun G, Reddy PA and Reddy PH (2017) Aqua-Soluble DDQ Reduces the levels of Drp1 and Amyloid Beta and Inhibits Abnormal Interactions of Amyloid Beta and Dynamin Related protein. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Bhatti JS, Tamarai K, Pradeepkiran AJ, and Reddy PH (2017) Oxidative stress and mitochondrial dysfunction in TALLYHO/JngJ mice - a common link between type 2 diabetes, obesity and Alzheimer's disease. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Vijayan M, Kumar S and Reddy PH (2017) Identification of novel circulatory microRNA signatures linked to patients with stroke. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Kumar S, Vijayan M and Reddy PH (2017) MicroRNA-455-3p as a potential peripheral biomarker for Alzheimer's disease. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Pradeepkiran JA and Reddy PH (2017) Pharmacophore based screening and molecular docking probing the novel inhibitors against BACE1 of Alzheimer's disease. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Reddy PA, Yin X, Manczak M, Ogunmokun G, Bethea C and Reddy PH (2017) Mutant APP and Tau Toxicities in Serotonergic and Non-serotonergic Neurons and Protective Effects of Citalopram. Abstract submitted and poster presented at the Annual Meeting of Society for Neuroscience held at Washington DC, November 11-16, 2017.

Williams J, Smith F, Kumar S, Vijayan M and Reddy PH. Differential expression of microRNAs in the skeletal muscles mice with aging. A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

Smith F, Williams J, Kumar S, Vijayan M and Reddy PH. Upregulation of microRNAs in the brains mice with aging. A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

Bhatti JS, Thamarai K, Reddy PH. Are TallyHo/JngJ mice, a relevant model to study type-2 diabetes, obesity and Alzheimer's disease? A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

Kuruva CS, Manczak M, Yin X, Reddy PH Aqua-soluble DDQ reduces the levels of Drp1 and amyloid beta and protects against amyloid beta-induced mitochondria and synaptic toxicities in Alzheimer's disease. A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

Pradeepkiran JA and Reddy PH. Pharmacophore based on screening and molecular docking probing the novel inhibitors against BACE1 of Alzheimer's disease. A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

Kumar S, Vijayan M and Reddy PH. MicroRNA 455-3p as a potential peripheral biomarker for Alzheimer's disease. A poster presented at the 2nd Annual Research Symposium of Center of Excellence for Translational Neuroscience and Therapeutics. April 27, 2017.

PUBLICATIONS

1. Rajmohan R, Anderson RC, Fang D, Meyer AG, Laengvejkal P, Julayanont P, Hannabas G, Linton K, Culberson J, Khan H, De Toledo J, Reddy PH, O'Boyle MW. Lower Activation in Frontal Cortex and Posterior Cingulate Cortex Observed during Sex Determination Test in Early-Stage Dementia of the Alzheimer Type. Front Aging Neurosci. 2017 May 22;9:156. doi: 10.3389/fnagi.2017.00156. eCollection 2017. PubMed PMID: 28588478; PubMed Central PMCID: PMC5438965.

2. Reddy PH, Manczak M, Kandimalla R. Mitochondria-targeted small molecule SS31: a potential candidate for the treatment of Alzheimer's disease. Hum Mol Genet. 2017 Apr 15;26(8):1597. doi: 10.1093/hmg/ddx129. PubMed PMID: 28419260.

3. Reddy PH. A Critical Assessment of Research on Neurotransmitters in Alzheimer's Disease. J Alzheimers Dis. 2017;57(4):969-974. doi: 10.3233/JAD-170256. PubMed PMID: 28409748.

4. Reddy PH, Manczak M, Yin X. Mitochondria-Division Inhibitor 1 Protects Against Amyloid-β induced Mitochondrial Fragmentation and Synaptic Damage in Alzheimer's Disease. J Alzheimers Dis. 2017;58(1):147-162. doi: 10.3233/JAD-170051. PubMed PMID: 28409745; PubMed Central PMCID: PMC5444307.

5. Rajmohan R, Anderson RC, Fang D, Meyer AG, Laengvejkal P, Julayanont P, Hannabas G, Linton K, Culberson J, Khan HM, De Toledo J, Reddy PH, O'Boyle M. White Matter Deterioration May Foreshadow Impairment of Emotional Valence Determination in Early-Stage Dementia of the Alzheimer Type. Front Aging Neurosci. 2017 Mar 1;9:37. doi: 10.3389/fnagi.2017.00037. eCollection 2017. PubMed PMID: 28298891; PubMed Central PMCID: PMC5331035.

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8. Vijayan M, Kumar S, Bhatti JS, Reddy PH. Molecular Links and Biomarkers of Stroke, Vascular Dementia, and Alzheimer's Disease. Prog Mol Biol Transl Sci. 2017;146:95-126. doi: 10.1016/bs.pmbts.2016.12.014. Epub 2017 Feb 1. PubMed PMID: 28253992.

9. Kumar S, Vijayan M, Bhatti JS, Reddy PH. MicroRNAs as Peripheral Biomarkers in Aging and Age-Related Diseases. Prog Mol Biol Transl Sci. 2017;146:47-94. doi: 10.1016/bs.pmbts.2016.12.013. Epub 2017 Feb 8. PubMed PMID: 28253991.

10. Reddy AP, Reddy PH. Mitochondria-Targeted Molecules as Potential Drugs to Treat Patients With Alzheimer's Disease. Prog Mol Biol Transl Sci. 2017;146:173-201. doi: 10.1016/bs.pmbts.2016.12.010. Epub 2017 Feb 11. PubMed PMID: 28253985.

11. Bhatti JS, Kumar S, Vijayan M, Bhatti GK, Reddy PH. Therapeutic Strategies for Mitochondrial Dysfunction and Oxidative Stress in Age-Related Metabolic Disorders. Prog Mol Biol Transl Sci. 2017;146:13-46. doi: 10.1016/bs.pmbts.2016.12.012. Epub 2017 Feb 1. PubMed PMID: 28253984.

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FUNDING

The 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. 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.

17% Endowment Earnings $374,041

40% Grant Funding $893,844

29% Institutional Funding $638,800

14% Private Donations $325,941
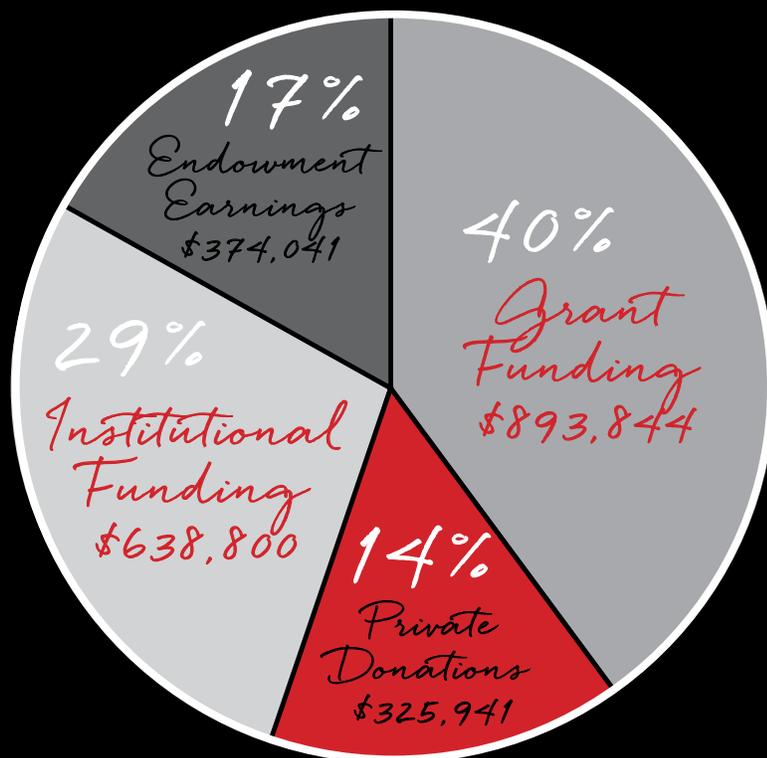
SEPTEMBER 2016 - AUGUST 2017
$2,232,627
Encompasses all of FY2017 • Used Actual Numbers

EVENTS IN PROJECT FRONTIER

(Facing Rural Obstacles to Healthcare Now Through Intervention, Education and Research) Counties:

Project FRONTIER is an on-going longitudinal epidemiological study focused on the health status of adults and elders in Cochran, Bailey, Parmer and Hockley. Over 1000 study participants have been involved in the study during the last eleven years. The study includes more than 2000 data points gathered from physical, mental, and cognitive health tests. Study participants are contacted every three years for follow-up testing.

CARE GIVERS
Coffee Break Workshop
Friona, TX

Monthly Educational Session

2nd Annual HEALTH FAIR
Bovina, TX

BACK TO SCHOOL & Safe Health Fair
Friona, TX

CHRISTMAS IN THE PARK
Bovina, TX

CORDELIA AGUIRRE

Ms. Aguirre has lived in Bailey County since 1968. She worked for Muleshoe ISD for 31 years and retired in 2008. The summer of 2008 she was employed part time for South Plains College as a Facilitator for Long Distance Learning. In June of 2012, she began working for Texas Tech University Health Sciences Center as the Coordinator of Project FRONTIER.

ROCIO CARRASCO

Ms. Carrasco is a graduate from Law School in Mexico with a Juris Doctor Degree. She currently lives in Friona with her family. In 2011, she began working for Texas Tech University Health Sciences Center as the Coordinator of Project FRONTIER for Parmer County. While working with Project FRONTIER, she became a Certified Community Health Worker.

BUILDING CAMP
for Kids and Parents

Friona TX

We collaborated with TYA (Texas Youth Association). This event was sponsored by Friona Chamber of Commerce.

WISE WOMAN
Orientation & Training

Amarillo, TX

WISE Woman & Rural Extension Program is an outreach program of the panhandle for women in need for preventive education and access to screenings services. The Program helps women with no health insurance qualify for mammograms, pap tests, and HPV vaccinations at no cost.

GET FIT FRONTIER NUTRITION Program

FRUIT
GRAINS
VEGGIES
PROTIEN
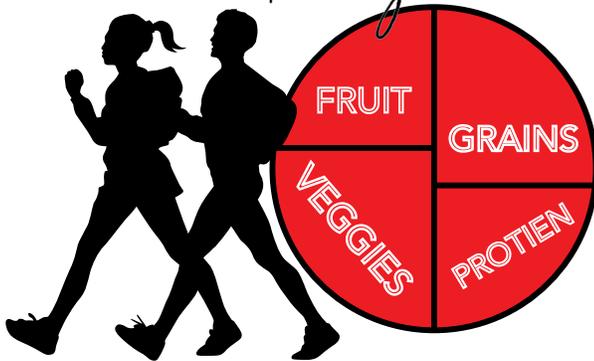
Friona, TX

A healthy plate is comprised of: eating a variety of foods from each of the Myplate food groups; including fruits and vegetables; and limiting portion sizes. Aspects of weight loss and/or weight maintenance are: utilizing small plates and bowls; awareness of emotional eating; behavior modifications; and the two appetite hormones, ghrelin and leptin which regulate our hunger and satiety. Taking a positive approach to healthy eating is most beneficial.

+ DIABETES CHRONIC CLINIC
Friona, TX

Extension Showcase
Bovina, Texas

TEXAS A&M AgriLife EXTENSION
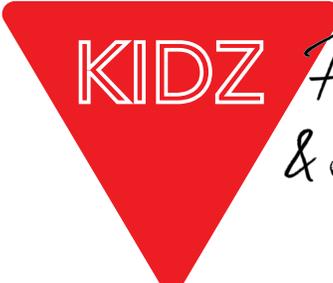
KIDZ Health & Safety Fair

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER RESEARCHER RECEIVES NATIONAL INSTITUTES OF HEALTH GRANT

December 12, 2017 • Written by: Suzanna Cisneros

The National Institutes of Health (NIH) awarded P. Hemachandra Reddy, Ph.D., the executive director and chief scientific officer of Texas Tech University Health Sciences Center Garrison Institute on Aging, a $1.9 million, five-year R01 grant from the Neurological Disorders and Stroke Institute of the National Institutes of Health.

Reddy's grant, "Mitochondrial Fragmentation and Neurodegeneration in Huntington's Disease," will study the protective effects of mitochondria division inhibitor 1 (Mdivi1) that inhibits excessive mitochondrial division in mouse models of Huntington's disease. The research is an extension of Reddy's postdoctoral work he conducted at the National Human Genome Research Institute of the NIH.

Huntington's disease is a fatal genetic disorder that causes the degeneration of brain cells in the motor control regions of the brain. Huntington's disease typically begins between 30 and 50 years of age, and its symptoms progressively worsen. These symptoms include impaired coordination and uncontrolled movements of the limbs (chorea), abnormal body posture, and changes in behavior, emotion, judgment and cognition. People with Huntington's disease also develop impaired slurred speech and difficulty swallowing. Currently, more than 30,000 Americans have the disease.

The Huntington's disease gene was identified in 1993 and was found to carry an expanded polyglutamine repeats or CAG repeats as a dominant mutation in a protein called huntingtin. Since the discovery of the gene, tremendous progress has been made in understanding the biology of huntingtin, which has been found to target neurons in the midbrain region. Research from the Reddy Laboratory at the TTUHSC Garrison Institute on Aging has implicated multiple cellular changes in Huntington's disease-affected neurons during Huntington's disease progression, including abnormal mitochondrial dynamics, defective energy metabolism, abnormal protein-protein interactions, defective axonal transport and synaptic damage.

Reddy and his research team studied the mitochondrial defects in Huntington's disease-affected neurons. Recently, they identified a cause of mitochondrial defects in Huntington's disease-affected neurons and the interaction between the mutant huntingtin and Drp1, a mitochondrial division protein. The research found that an increase in Drp1 leads to excessive fragmentation of mitochondria.

In the newly funded NIH research, Reddy and his research team will determine whether a partial reduction of Drp1 protects Huntington's disease-affected neurons from excessive mutant huntingtin-induced fragmentation of mitochondria, mitochondrial dysfunction and synaptic toxicities. Both genetic and pharmacological approaches to determine the effects of reduced Drp1 in Huntington's disease-affected neurons will be used.

The outcome of Reddy's research will clarify the genetic and pharmacological strategies that may reduce excessive mitochondrial fragmentation and thus increase neuronal survival and synaptic functions in Huntington's disease-affected neurons.

HEALTHY AGING LECTURE SERIES

September 28, 2016
"Healthy Living for a Healthy Heart"
Scott Shurmur, MD
Medical Director and Division Chief
Department of Cardiology
Texas Tech University Health Sciences Center

October 26, 2016
"It's All in Your Head"
Katie Hendley, MD
Neurologist/Movement Disorder Specialist
Covenant Medical Group

November 16, 2016
"The Basics of Alzheimer's"
Hannah Ives
Community Outreach Specialist,
West Texas Chapter
Alzheimer's Association National Organization

January 25, 2017
"Muscle Strength and Aging"
Ty B. Palmer, PhD, CSCS
Assistant Professor, Department of Kinesiology
& Sports Management
Texas Tech University

February 22, 2017
"Nutrition for a Healthy Heart"
Allison Kerin, MS, RD, LD
Director of Employee Wellness & Recognition
Texas Tech University Health Sciences Center

March 22, 2017
"Stroke 101: Prevention is Key"
Sarah Hancock, RN, SCRN
UMC Health System

April 26, 2017
"Stroke: What You Can Do to Prevent and Treat it!"
Yazan Alderazi, MD
Assistant Professor
Department of Neurology
Texas Tech University Health Sciences Center

May 24, 2017
"How to Fix Your Heartburn or Reflux"
Sameer Islam, MD, MBA
Gastroenterologist

GIA RESEARCH SEMINARS

JANUARY 17, 2017
"Global Aging: An unequal distribution of risks later in life"
Hafiz T.A. Khan, Ph.D.
Reader in Statistics,
School of Health Sciences
Faculty of Health,
Education and Life Sciences
Birmingham City University

FEBRUARY 7, 2017
"Infectibesity to anti-diabetic agent: A Translational Journey"
Nikhil Dhurandhar, Ph.D.
Professor and Chair,
Department of Nutritional Sciences
Texas Tech University

MARCH 21, 2017
"Application of MRI and MRSI (Magnetic Resonance Spectroscopic Imaging) using the 3T Skyra at the Texas Tech Neuroimaging Institute (TTNI) in developing quantitative biomarkers for detection of early neurodegenerative processes"
Eric Walden, Ph.D.
Director of the Texas Tech Neuroimaging Institute, Director of Data Science Programs

James C. Wetherbe
Professor, Rawls College of Business,
Texas Tech University

Sunanda Mitra, D.Sc.
Director Emeritus, Texas Tech Neuroimaging Institute (TTNI), P.W. Horn Professor & Director, Biomedical Integrated Devices & Systems (BIDS), Department of Electrical & Computer Engineering,
Texas Tech University

Sai Merugumala
M.D. Candidate, Texas Tech University Health Sciences Center

APRIL 4, 2017
"Mitochondria and Bioenergetics in Alzheimer's Disease"
Russell H. Swerdlow, M.D.
Gene and Marge Sweeney Professor Director, Alzheimer's Disease Center Director, Neurodegenerative
Disease Program
Departments of Neurology, Molecular and Integrative Physiology, Biochemistry and Molecular Biology
University of Kansas Medical Center

MAY 9, 2017
"Mitochondrial dynamic abnormalities contributes to pathogenesis of Alzheimer's Disease"
Xiongwei Zhu, Ph.D.
Professor,
Department of Pathology
Case Western Reserve University

AUGUST 1, 2017
"A Double Whammy: How misfiled tau could hijack immune system to propagate itself and introduce neuroinflammation relevant to Alzheimer's Disease"
Kiran Bhaskar, Ph.D.
Associate Professor,
Department Molecular Genetics
& Microbiology
Department of Neurology
University of New Mexico

SEPTEMBER 12, 2017
"Novecbiomaterials for 3D Culture and Differentiation of Stem Cells"
Havinder S. Gill, Ph.D.
Associate Professor,
Department of Chemical Engineering
Whitacre Endowed Chair
in Science & Engineering
Ed and Linda Whitacre Faculty Fellow
Texas Tech University

OCTOBER 30, 2017
"The lipid peroxidation product 4-hydroxynonenal as a modulator of fat accumulation and aging"
Sharda P. Singh
Associate Professor,
Department of Internal Medicine, Texas Tech University Health Sciences Center

DECEMBER 1, 2017
"Industry-Research Partnership Opportunities through the NSF Cloud and Autonomic Computing Center at Texas Tech University"
Ravi Vadapalli, Ph.D.
Site Director, NSF I/UCRC Cloud and Autonomic Computing Center
Sr. Research Scientist,
High Performance Computing
Adjunct Professor of Petroleum Engineering

AGING & ALZHEIMER'S DISEASE JOURNAL CLUB PRESENTATIONS

09/27/16: Dr. Jasvinder Bhatti...............................Time-Restricted Feeding is a Preventative and Therapeutic Intervention Against Diverse Nutritional Challenges

10/25/16: Dr. Chandra Kuruva Tau ....Derived Hexapeptide 306VQIVYK311 Aggregation Inhibitors: Nitrocatechol Moiety as a Pharmacoperone in Drug Design

11/22/16: Dr. Rui Wang ....Dysfunction of Somatostatin-Positive Interneurons Associated with Memory Deficits in an Alzheimer's Disease Model

12/20/16: Dr. J.A. Pradeepkiran...............................In Silico Modeling of Novel Drug Ligands for Treatment of Concussion Associated Taupathy

01/24/17: Dr. Jasvinder Bhatti.................................Genetic Analysis of a New Mouse Model for Non-Insulin Dependent Diabetes

02/28/17: Dr. Chandra Kuruva.................................Determinants of amyloid fibril degradation by the PDZ protease HTRA1

03/28/17: Dr. Murali Vijayan ....MicroRNA-103-1 Selectively Downregulates Brain NCX1 and its Inhibition by Anti-miRNA Ameliorates Stroke Damage and Neurological Deficits

04/25/17: Dr. Maria Manczak ....Amyloid ß-peptides interfere with mitochondrial pre protein import competence by congregation process

05/23/17: Dr. Hemachandra Reddy ....Deletion of the Mammalian INDY Homolog Mimics Aspects of Dietary Restriction and Protects Against Adiposity and Insulin Resistance in Mice

06/27/17: Dr. Rui Wang ....Dopamine Neuronal Loss Contributes to Memory and Reward Dysfunction in a Model of Alzheimer's Disease

07/25/17: Jake S. Smith, Dr. Subodh Kumar, Dr. Murali Vijayan ....Direct Conversion of Normal Alzheimer's Disease Human Fibroblasts into Neuronal Cells by Small Molecules

08/22/17: Dr. Hemachandra Reddy...........................Hypothalamic stem cells control aging speed partly through exosomal miRNA's

09/26/17: Dr. Josh Lawrence....................................Differential presynaptic ATP supply for basal and high-demand transmission

10/24/17: Dr. Josh Lawrence....................................Silencing of solute carrier family 13 member 5 disrupts energy homeostasis and inhibits proliferation of human hepatocarcinoma cells

11/28/17: Dr. Hemachandra Reddy...........................PINK1 signalling rescues amyloid pathology and mitochondrial dysfunction in Alzheimer's disease

PROJECT FRONTIER & PUBLIC HEALTH JOURNAL CLUB

11/02/16: Dr. Alyce Ashcraft ....End-of-Life Planning in a Rural Elderly Cohort

12/07/16: Dr. Hemachandra Reddy.................Cardiometabolic Risks and Severity of Obesity in Children and Young Adults

01/04/17: Dr. Hemachandra Reddy.................What is Population Health? The Importance of Place of Residence: Examining Health in Rural & Non-Rural Areas

02/01/17: Dr. Hemachandra Reddy.................Neuropsychological Criteria for Mild Cognitive Impairment Improves Diagnostic Precision, Biomarker Associations and Progression Rates

03/01/17: Sarah Mende ....Depression Among People with Type 2 Diabetes Mellitus, US National Health and Nutrition Examination Survey (NHANES), 2005-2012

04/05/17: Alejandro Aquino ....Trends and Disparities in Coronary Heart Disease, Stroke, and Other Cardiovascular Diseases in the United States; Findings of the National Conference on Cardiovascular Disease Prevention

04/26/17: Anthony Anya.................................Weight Loss Predicts Progression of Mild Cognitive Impairment to Alzheimer's Disease

05/03/17: Dr. Hemachandra Reddy ....Alzheimer's Disease: Prototype of Cognitive Deterioration, Valuable Lessons to Understand Human Cognition

07/05/17: Annette Boles ....Clinical and Demographic Predictors of Conversion to Dementia in Mexican Elderly with Mild Cognitive Impairment

10/04/17: Kandi Quesada...............................Racial/Ethnic and Socioeconomic Disparaties in Hydration Status Among US Adults and the Role Tap Water and Other Beverage Intake

SPIKE DYKES CHARITY GOLF TOURNAMENT REMEMBERS TTU LEGEND

July 11, 2017 • Written by: Hope LaFreniere

GIA Staff & HSC Members are thankful to Mr. Spike Dykes for his contributions. He lives in our hearts forever.

The fifth annual Spike Dykes Charity Golf Tournament continued this year in honor of both Texas Tech University (TTU) football coach Spike Dykes and his wife Sharon at the Horseshoe Bay Resort in Horseshoe Bay, Texas, July 14 through 15. Proceeds of the tournament fund Alzheimer's research at the Texas Tech University Health Sciences Center (TTUHSC) Garrison Institute on Aging. The tournament was created to honor Sharon's memory after her battle with Alzheimer's disease and has raised more than $320,000 toward Alzheimer's research since its inception in 2012. "They may have named the tournament after me, but they didn't want to do it for me, they wanted to do it for Sharon," Dykes wrote in "Tales from the Texas Tech Red Raiders Sideline." "When you think about it, she had been the bus driver for our kids to all kinds of practices, including cheerleader practice. If they needed a first baseman, she'd play first base. And never one time in the 44 years I coached did she get on me about not being home. In a way, she was the same with our players." The Garrison Institute on Aging promotes healthy aging by researching age-related diseases such as Alzheimer's. Founded in 1999, the institute identified aging as one of the greatest health priorities of the 21st century. The Garrison Institute on Aging researches potential preventative treatments, brain health maintenance while seeking a cure Alzheimer's disease, which is one of the top 10 leading causes of death in the U.S.

RSVP INFO

Written by: Clay Ament, RSVP Manager

Lubbock RSVP is a grant funded non-profit agency that was established in 1979 and is sponsored by the Garrison Institute on Aging. It was created with the purpose of encouraging adults who are 55 and older, to volunteer and assist the Lubbock community by using the abilities, interest and skills they have acquired throughout their life. The opportunities and rewards are endless with the program. Whether it be delivering meals to seniors through the Lubbock Meals on Wheels program, volunteering at one of the many hospices in Lubbock, or donating homemade pillows, afghans, quilts, and bibs to many of the non-profit agencies around town, our volunteers show how much they care about the community. Since becoming RSVP Manager, it has been very humbling to not only see the amount of time our senior volunteers put into their work, but the enjoyment and satisfaction that they get out of it. It isn't something that I have experienced often before, and the opportunity to be a part of this program has been amazing.

BENEFITS OF MEMBERSHIP:

• Free enrollment to any adult 55 and older
• Supplemental insurance coverage at no cost to volunteer
• Stay active and socialize with other volunteers with same interests
• Free Events throughout year:

Spring Forum – focused on educating and informing seniors on how to age well physically, mentally, emotionally, and financially.

Movie Night – volunteers and friends can enjoy a night of food, fun and fellowship while watching a classic movie!

Recognition Dinner – formal banquet for members and guests to enjoy a free meal and musical entertainment. Volunteers who have reached 4,000 hours are recognized with the Presidential Lifetime Achievement Award.

692 Volunteers
125,000 HOURS
2017 Statistics 65 AGENCIES

Starting Top Row, L-R: Jasvinder Singh Bhatti, Hafiz Khan, PhD, Anthony Anya, Ose Aligbe, Alejandro Aquino, Alexander Jacob, Subdodh Kumar, PhD, Murali Vijayan, PhD, Ruben Gonzales, Chandra Kuruva, PhD, Clay Ament, Kathleen Stonum, Kandi Quesada, Linda Yin, Sarah Mende, Ramesh Kandimalla, PhD, Hemachandra Reddy PhD, Annette Boles, Veronica Lopez