SA Pepper OAIC Annual Directory Outline

Section I. Description of Center

The central premise of the San Antonio Claude D. Pepper Older Americans Independence Center (SA OAIC) is that basic aging research has advanced to the point where scientifically validated, aging-modulating approaches are ready to be tested and translated into human therapies. Our Center was conceived as an Intervention Program that will advance discoveries obtained in rodents into the pre-clinical arena using a non-human primate model, the common marmoset, and from the pre-clinical arena into humans through clinical studies. To fulfill this goal, our Center provides investigators with the scientific infrastructure and services that are requisite to translate innovative interventions that target the aging process and age-related diseases into humans. Initially, our major focus is pharmacological interventions; however, regenerative and gene transfer interventions also will be tested as they become available.

The Specific Objectives of the SA OAIC are:

1. To provide, through Resource Core (RC-1—Pre-clinical Research Core), functional assessment (health span) services, and determine the effect of interventions on lifespan. This Core also supports pharmacokinetic, pharmacodynamics, safety, and tolerability assessment of aging-modulating interventions.
2. To provide human clinical research and pharmacology services to studies of interventions aimed at preventing physiological decline and age-related diseases through Resource Core (RC-2 – Clinical Research Core). Services provided by this core include study design, subject recruitment, subject retention, and procedures to assess physical performance, cognition, glucose metabolism, vascular function, atherosclerosis, exercise tolerance, gait, balance, imaging, and specimen (blood, muscle, fat) processing. This core also performs pharmacokinetic studies in humans.
3. To provide, through the Biostatistics Core (RC3), expertise in data entry systems, data quality control, data security, and state-of-the-art quantitative and qualitative analytic and medical informatics strategies.
4. To provide assistance to faculty for developing research programs in gerontology and geriatrics, the Research Career Development Core (RCDC) provides protected research time, research training, and mentorship to SA OAIC Scholars. All scholars will have research projects, mentoring teams and specific short and long-term career goals.
5. The Pilot and Exploratory Studies Core (PESC) funds pilot projects to gather preliminary data that may guide the design of future studies.

Section II. Research, Resources and Activities

A. Cores

LEADERSHIP AND ADMINISTRATIVE CORE (LAC)
Core Leader: Nicolas Musi, MD
Co-Leader: Randy Strong, PhD

This core oversees the overall coordination, monitoring, compliance, evaluation, and reporting functions of the SA OAIC. It promotes institutional interactions and external relationships. The LAC supports the Executive Committee, the Institutional Advisory Committee, and the External Advisory Board.

The LAC co-sponsors a weekly seminar series with our on-campus partners, an annual retreat, visiting professor series, topical workgroups, grant planning meetings, and national conferences.

RESEARCH CAREER DEVELOPMENT CORE (RCDC)
Core Leader: Michael Lichtenstein, MD
Co-Leader: Peter Hornsby, PhD

This core promotes the career development of early-stage investigators. Accessing the research education, training and career development resources of UTHSCSA's Institute for Integration of Medicine and Science (IIMS) and the robust and unique aging research resources and research education programs in South Texas, our Mentored Research Career Development Scholars are trained in the mechanisms that govern the aging process, and in the design of pre-clinical and clinical interventions for diseases and conditions that affect older adults. All SA OAIC Scholars will have research projects, mentoring teams, and specific short- and long-term career goals. The RCDC also will sponsor various training and mentoring research experiences.

The UTHSCSA and its partners offer a rich pool of available trainees and mentors, additional sources of career funding, laboratories, and multiple opportunities for didactic coursework. SA OAIC scholars also are eligible for pilot support from the PESC.

PILOT AND EXPLORATORY STUDIES CORE (PESC)
Core Leader: Robert Clark, MD
Co-Leader: Alfred L. Fisher, MD, PhD

This core seeks to draw investigators into aging research relevant to the theme of the SA OAIC and to promote early stage research that will set the stage for the development of both larger definitive studies and successful grant applications to continue the research project. To advance these goals the core leadership seeks the creation of novel aging research, and manages the application, review, selection, monitoring, and subsequent tracking of pilot proposals.

RC1: PRE-CLINICAL RESEARCH AND ANALYTICAL PHARMACOLOGY CORE (PRAP)
Core Leader: Suzette Tardif, PhD
Co-Leader: Randy Strong, PhD

This core supports pre-clinical (animal) projects that explore the basic biology of aging and evaluate interventions that target the aging process to enhance healthy aging, as well as to prevent and better treat aging-related diseases. To this end, the Core conducts research in a nonhuman primate model (marmoset) to investigate the mechanism of action, pharmacokinetics, toxicity, and efficacy of drugs that might prolong healthspan, facilitating translation of potential aging-modulating drugs to the clinical setting.

RC-2: CLINICAL RESEARCH CORE (CRC)
Core Leader: Dean Kellogg, MD, PhD
Co-Leader: Sara Espinoza, MD, MPH

This core assists basic and clinical investigators in developing rigorous and appropriately powered clinical studies and trial concepts that will lead to innovative approaches to improve healthspan and lifespan, and facilitates implementation and execution of translational human studies and clinical trials by investigators.

The Core provides expertise and coordinated access to resources and technology in both our Pepper Center and facilities throughout our institution to maximize the depth of phenotypic characterization relevant to aging in trial outcomes. Training in clinical research for early-stage faculty and those new to clinical research is also available. This Core is also available to provide research project consultation and planning, assistance with safety and regulatory compliance processes, facilitates research subject recruitment and retention, and coordinates relationships with relevant SA OAIC Cores and other Core facilities of our institution.

RC-3: BIOSTATISTICS AND DATA MANAGEMENT CORE (BDMC)
Core Leader: Jonathan Gelfond, MD, PhD
Co-Leaders: Alfredo Tirado-Ramos, PhD; Alex Bokov, PhD

This core provides expertise in study design and development of database applications. Services include comprehensive biostatistical support, data quality control, and data security. This Core also provides assistance related to grant proposals (e.g. study design, statistical methods, power and sample size calculations) and manuscript preparation, and will play an active role in the KL2 program, tailored to the focus of the SA OAIC BDMC provides biostatistical and data management support to all SA OAIC Developmental Projects, Pilot Studies, and research projects from KL2 Scholars, and will support the other center cores in reporting and regulatory functions through the IDEAS data management system used for quality improvement processes across the SA OAIC. Services are also available to external projects.

B. Research

SA OAIC resources contributed to a successful R01 proposal and two publications.

Adam Salmon, PhD, an Assistant Professor of Research in UTHSCSA's Department of Molecular Medicine and the Barshop Institute, received a $2.7 million R01 award from the National Institute on Aging to study the role of mTOR inhibition in longevity and aging in a nonhuman primate. During this five-year study, Dr. Salmon's lab will test whether mTOR inhibition through chronic administration of rapamycin delays aging in a non-human primate, the common marmoset, as an important step towards translational approaches to delay age-related disease in humans. While inhibition of the mTOR signaling pathway has been shown to extend both lifespan and healthspan in mice, the implications of these findings for improving normal, healthy aging in humans is largely unknown. Dr. Salmon's study is a promising step towards bridging this knowledge gap.

In one published study, SA OAIC investigators found that long-term treatment of marmoset monkeys with orally-administered encapsulated rapamycin resulted in no overall effects on body weight and only a small decrease in fat mass over the first few months of treatment. Moreover, the study demonstrated that marmosets offer an interesting alternative animal model for future intervention testing and translational modeling. See Ross C, Salmon A, Strong R, Fernandez E, Javors M, Richardson A, Tardif

S. Metabolic consequences of long-term rapamycin exposure on common marmoset monkeys (*Callithrix jacchus*) – Aging (Albany NY). 2015 Nov;7(11):964-73

In another published report, SA OAIC investigators provided the first description of dosing procedures, pharmacokinetics, biochemical action, and general tolerability of the antiaging drug rapamycin in the common marmoset. Tardif S, Ross C, Bergman P, Fernandez E, Javors M, Salmon A, Spross J, Strong R, Richardson A. Testing efficacy of administration of the anti-aging drug rapamycin in a non-human primate, the common marmoset. J Gerontol Biol Sci. J Gerontol A Biol Sci Med Sci. 2015 May;70(5):577-587

C. Pilots

2015 Pilots:

"Evaluating pharmacokinetics and tolerability of metformin and acarbose in the marmoset", Elizabeth Fernandez, PhD, Investigator

"Methylene blue enhancement of fMRI brain activity, memory, and cognition in healthy aging and MCI", Peter Fox, MD and Pavel Rodriguez, MD, PhD, Co-Investigators

"Metformin for preventing frailty in high-risk older adults", Sara Espinoza, MD, MPH, Principal Investigator

"Exploration of GDF11 as a rejuvenation factor in a non-human primate", Senlin Li, PhD, Principal Investigator

"RAPA & Acarbose / Effect of mTOR Inhibition and other Metabolism Modulating Intervention on the Elderly: Immune, Cognitive, and Functional Consequences" , Dean Kellogg, MD, PhD and Ellen Kraig, PhD, Co-Investigators

These projects are ongoing as of the date of this report.

2016 Pilots:

Pending administrative approvals, the following projects have been selected for funding in response to our 2016 PESC RFA:

"A novel gene therapy to retard motor neuron degenerative disease and sarcopenia",Qitao Ran, PhD and Corinna Ross, PhD, Co-Investigators

"Feasibility of using the iron-chelator deferiprone in Mild Cognitive Impairment (MCI)", Donald Royall, MD and Dean Kellogg, MD, PhD, Co-Investigators

"NAD Modulation to Improve Cognition in Mild Cognitive Impairment (MCI)", Becky Powers, MD and Miranda Orr, PhD, Co-Investigators

"Effect of Stress-Busting Program on Caregivers' Quality of Life, Immunology/Stress Biomarkers and Cellular Aging", Lyda Arevalo-Flechas, PhD and Chih-Ko Yeh, DDS, Co-Investigators

An RFA to recruit the next cohort of pilot projects will be released in Fall 2016.

Section III. Career Development: Provide names and funding subsequent to Pepper pilot funding.

The first three SA OAIC career development scholars have just begun Year 2 of their two-year scholar positions. Our current scholars are:

Sukeshi Patel, MD

Research Project: A study to evaluate proteostasis modulation with histone deacetylase (HDAC) inhibitors as potential aging modulating agents in cancer patients.

Dr. Patel's research focus in on the effects of proteostasis modulation with histone deacetylase (HDAC) inhibitors as aging modulation agents in cancer patients. Her research takes advantage of an active on-going phase II study of Vorinistat, a pan-DHAC inhibitor and hydroxycholoroquine in colorectal cancer patients. In animal models, Vorinistat plus hydroxycholorquine enhance apoptotic activity. In her time as a KL2 scholar, Dr. Patel has been collecting and banking specimens from research subjects. She has developed a budget and will be evaluating the drug effects on pro-inflammatory factors produced by senescent cells (e.g., IL-1, IL-6, TNFα).

Kelly Reveles, PharmD, PhD

Research Project: Comparison of gut microbiota composition and inflammation in elderly proton pump inhibitor-users and non-users.

In this prospective study, Dr. Reveles will determine the changes in the microbiome of older adults before and after exposure to PPI, investigating alterations in (a) fecal microbiota, (b) systemic inflammatory markers, and (c) IGF-1 levels. Dr. Reveles has obtained IRB approval for her protocol, finalized a budget for recruitment of research volunteers, and specimen processing. She is working in conjunction with our Clinical and Translational Science Award (CTSA) to utilize the out-patient clinical research center to evaluate subjects and obtain specimens.

Corinna Ross, PhD

Research Project: The effects of chronic rapamycin treatment on motor and cognitive function in a nonhuman primate model of aging, common marmosets.

In the fall, Dr. Ross moved her marmosets from the Southwest National Primate Center to the UTHSCSA Barrier facility at the STCBM. There they will first be subject to collection of baseline physiological and behavioral data prior to beginning rapamycin dosing. This stage is ongoing. Animals will be trained in this time to accept the rapa dose orally, move into testing cages, target an object and weigh. Baseline physiological data to be collected will include metabolic assessments (fasting glucose, fasting insulin, response to glucose challenge, respirometry, and blood pressure). Baseline behavioral data will focus upon initial training ability and response to handling and restraint. Animals will be divided into two cohorts (rapa and control). After this initial phase of the experiments, Dr. Ross will begin collecting data on these animals to assess the effects of rapa on health status.

An RFA to recruit the next class of scholars will be released in Fall 2016.

Section IV. Publications: Provide only those that are a direct result of Pepper Center resources and list publications published in the 2015-2016 years only.

Ross, Corinna; Salmon, Adam; Strong, Randy; Fernandez, Elizabeth; Javors, Marty; Richardson, Arlan; Tardif, Suzette Metabolic consequences of long-term rapamycin exposure on common marmoset monkeys (Callithrix jacchus). Aging. 2015 Nov; 7 (11):964-73

Section V. External Advisory Board Members Names, Institutions and Years of service

James L. Kirkland, MD	Mayo Clinic	1 year of service
Stephen Kritchevsky, PhD (Chair)	Wake Forest School of Medicine	1 year of service
Stephanie Studenski, MD, MPH	National Institute on Aging	1 year of service
Douglas Seals, PhD	University of Colorado, Boulder	1 year of service

University of Texas Health Sciences Center, San Antonio Pepper Center
2015-2016
Recognition and Awards

Robert Clark, MD – Core Leader, Pilot and Exploratory Studies Core, San Antonio Pepper Center – Elected President of the Society for Leukocyte Biology, a position that he will hold throughout 2016 and 2017