Innovative Research & Education Grants Recipients 2015-16

Research Proposals

1. A Pilot Trial to Evaluate the Utility of Integrating Visual and Electrophysiological Measures of Movement to Understand and Reduce Injury Prone Behavior to Promote Healthy Aging

PI: Todd Coleman (JSOE – Bioeng)
Co-PI: Elaine Tanaka (SOM – Surg)

The musculoskeletal system contributes to all voluntary human actions. This system is controlled by nerves that communicate stimuli from the environment back to the brain and spinal cord so that they can coordinate appropriate responses. Chronic pain in these muscles is a growing problem in the workplace. Musculoskeletal disorders resulting from repetitive motion accounted for nearly 380,600 or ¼ of all causes for missing days of work in 2012 [1]. Such injuries obviously lead to a reduced quality of life, but also affect one’s productivity and ability to sustain work throughout the years. This also affects healthy aging and quality of life in later years and retirement. Over the past fifty years, the field of ergonomics has evolved to cope with these workplace injuries by helping to lessen muscle fatigue and increase workplace productivity. The development of an ergonomic system capable of non-invasively monitoring the state of the musculoskeletal system may lead to a better understanding of this chronic pain and associated disorders and may also lead to more effective and targeted therapies. The information gleaned from monitoring of a person’s posture can be used to help train proper musculoskeletal positioning to prevent disabling injuries. Additionally, research has shown that women are at particular risk for developing musculoskeletal problems, perhaps due to their smaller hands and shorter stature than men [2,3].

There is an unmet need to understand when someone is at risk of having injury. Having an opportunity to measure posture as well as electrical activity of individual muscles, in a manner that is unobtrusive, has the potential to revolutionize our understanding of the evolution of injury and prevent injury in the first place with appropriate interventions, reminders, and other decision-support tools. This can also prevent permanent injury and disability which exacerbate the aging process. The unobtrusiveness of the EES and camera will be instrumental in ensuring compliance, ergonomic improvement, and encouraging behavior conducive to healthy aging.

2. Targeting Electrophilic Stress for Healthy Aging

PI: Mohit Jain (SOM – Med Cardiology/Pharmacology)
Co-PI: Jehad Almaliti (SIO/SSPPS)
            Aitor Aguirre (SOM – Med)

Aging is generally distinguished by a continuous loss of physiologic integrity and the current theory of aging implicates a loss of balance from two competing influences – damaging factors that serve to alter cellular function and homeostatic mechanisms that serve to protect against deleterious factors – as the key determinant of aging. The nature of these critical damaging factors and the homeostatic mechanisms responsible for protection from such factors, still remain unknown. Recent work as
implicated both reactive electrophiles as well as the enzymes responsible for their detoxification as critical to biological aging. Work from the Jain laboratory (Departments of Medicine and Pharmacology, UCSD) has developed high throughput mass spectrometry based approaches for probing hundreds of reactive electrophiles from human plasma in large population scale cohorts. Application of these tools in a San Diego community-based cohort of 1089 adults (age range 45-95 yrs) have found distinct reactive electrophile compounds in circulating plasma that are significantly associated with progressive chronologic age. The Gerwick laboratory (SIO / SPPS, UCSD) have recently surveyed a large natural product library for novel modulators of Nrf2 activity, and have uncovered 9 novel, marine natural products that induce Nrf2 activity by over 5 fold. The goal of this UC San Diego Healthy Aging Initiative grant proposal is to forge a unique, cross campus collaboration between Dr. Jain, a junior faculty member and lead-PI, and Dr. Jehad Almaliti, a senior postdoctoral fellow in the Gerwick laboratory and co-PI. Through this funding mechanism, Drs. Jain and Almaliti propose to examine the influence of their recently identified human reactive electrophiles in promoting aging and aging associated disease in an African turquoise killifish (Notobranchius furzeri) model. Moreover, using medical chemistry this collaborative group will examine the effects of their novel Nrf2 inducing agents in protecting against aging in our killifish model.

3. IL-17 Signaling Regulates Age-Related Changes of Liver-Brain Axis

PI: Tatiana Kisseleva (SOM – Surg)
Co-PI: Sheng Zhong (JSOE – Bioeng)
              Cedric Geoffroy (SOM – Neurosci)

As a part of UCSD Healthy Aging Initiative, here we propose to investigate the role of IL-17 signaling on healthy aging and obesity associated aging. Age-related changes affect liver and brain. Hepatic steatosis, inflammation, fibrosis are often observed in aging liver, while neuronal apoptosis and astrogliosis are detected in aging brain. These symptoms are further exacerbated in obese individuals. Furthermore, age related changes in the immune system, such as increased number of Th17 T cells that produce pro-inflammatory cytokine IL-17A, may contribute to pathogenesis of age-related changes in liver-brain axis. There is a growing body of evidence that IL-17 signaling has a detrimental effect on aging. Based on our preliminary data, genetic ablation or pharmacological inhibition of IL-17 signaling protects liver and brain. Here we propose to test if suppression of Th17 cell proliferation attenuates age-related functional changes in brain-liver axis, and improves "healthy aging". For this purpose, aged mice ± high fat diet (HFD) will be treated with RORγt antagonist VP0347 or vehicle. Attenuation of age-related process will be compared to IL-17RA/- r mice, that are devoid of IL-17 signaling. We anticipate to determine if Th17 cells can become a potential target for anti-aging therapy.

4. Regulation of Synapse Function by Septin Rings in Health and Alzheimer’s Disease

PI: Brenda Bloodgood (Bio Sci – Neurobio)
Co-PI: Mark Ellisman (SOM/JSOE - Neurosci/Bioeng)
              Maho Niwa (Bio Sci – Mol Bio)

This proposal aims to investigate the role of Septin proteins in regulating synapse function in the mammalian nervous system. Mutations in Septin proteins have recently been identified in cohorts of people suffering from Alzheimer’s disease (AD), thus understanding their function in neurons will shed new light on the molecular underpinnings of this complex disease. Septins assemble with each other to
form a ring like structure that is essential for yeast cell division. This ring acts as a molecular scaffold at the bud site, create barriers to the diffusion of proteins through the plasma membrane, and regulate the distribution of organelles between the mother and daughter cells. Recently Septin rings have been observed at the base of dendritic spines in mammalian neurons. Spines are small membranous protrusions that enclose synapses and are separated from the parent dendrites by a thin spine neck. We will test the hypothesis that Septin rings are reduced in postmortem tissue from people who had AD, dysregulated in mouse models of AD, and act as molecular scaffolds that support the function of the synapse enclosed within the spine head akin to what is observed in yeast. This series of studies will begin an experimental path that aims to bring new insight into the molecular interactions required for optimal neuronal function and may inspire novel therapies for delaying the onset or slowing the progression of AD in people.

5. Can Acupuncture Decrease Stress and Increase Telomerase Activity to Promote Healthy Cellular Aging?
PI: Amy Non (Soc Sci – Anth)
Co-PI: Laura Redwine (SOM – Psych)
    Nikki Rodney (Jung Tao School of Classical Chinese Medicine)

The goal of the proposed project is to determine if a 3 month intensive trial of biweekly acupuncture can increase telomerase activity in a pilot study of 30 participants. Acupuncture is a cultural practice that originated in China, and is now popular nationwide to treat a variety of illnesses. Acupuncture is hypothesized to have a direct biological effects at the cellular level, and also to potentially act indirectly via reduction of stress. Telomeres are the repetitive DNA elements at the ends of the chromosomes that protect the DNA from degrading, and because they shorten with each replication, they are considered a useful biomarker of cellular aging. Telomerase is the enzyme that can restore the length of telomeres in certain cells by adding DNA back to the ends of the chromosomes, and may be affected by various lifestyle factors. Prior research has shown that a 3-month period of intense meditation was associated with an increase in mean telomerase activity of participants relative to a control group. We expect that we will see a similar effect of acupuncture on telomerase activity following acupuncture. We hypothesize that acupuncture may contribute directly to a biological change at the cellular level by directly increasing the activity of telomerase, or its action may be mediated through stress reduction. We will measure the activity of the telomerase enzyme in DNA extracted from venous blood at 3 time points: 1) baseline, 2) after 3 months without treatment, and 3) after 3 month acupuncture trial, along with psychosocial measures of stress and personality, including an optimism scale, a well-being scale which measures purpose in life and perceived control, and a perceived stress questionnaire. To our knowledge, the association between acupuncture and telomerase has never been assessed. These results will be directly translatable to the study of healthy aging by determining if an easily accessible stress-reducing practice like acupuncture can slow down the process of cellular aging. Findings from this study may be used to contribute to a large scale R01 clinical trial.
Education Proposals

1. Life Course Scholars Program

PI: Leslie Lewis (Soc Sci – USP)
Co-PI: Jeanne Ferrante (JSOE – CSE)
       Mirle Rabinowitz-Bussell (Soc Sci – USP)

The proposed Life Course Scholars (LCS) program will create an interdisciplinary, cross-generational, multi-site learning experience for UCSD undergraduates that will transform their understanding of aging, health, learning & research, as well as connect them more deeply to the “people and places” of surrounding San Diego communities. The program will combine place-based, experiential, and traditional classroom-based learning methods, one-on-one matching with Elder Partners (EPs) living in the community, Learning Exchange Groups (LEGs) comprised of small clusters of EPs and LC Scholars, and both participatory planning and collaborative research activities, on and off campus. The program will culminate in LCS teams designing and implementing community-based Healthy Aging Projects (HAPs) under the guidance and mentorship of an interdisciplinary team of faculty collaborators, with support from interested Elder Partners.

2. Design Competition to Improve the Quality-of-Life for Seniors

PI: Truong Nguyen (JSOE – ECE)
Co-PI: Don Norman (The Design Lab – Calit2)
       Maria Marquine (SOM – Psych)

We propose to organize a year-long design competition with the design theme of “Design a device or platform that improves the quality-of-life of Seniors”. The competition is open to all UCSD students with the requirement that at least one team member is a student or alumni of the ECE Department. During the year, through a series of workshops and one-to-one feedback sessions, the student teams will gain knowledge on aging, the importance of human-centric design as well as understanding product business cycle. The projects will be judged by the attendees, at the annual Alumni Day in June 2016.