PILOT AWARDS – FISCAL YEAR 2020

Institute on Aging Pilots

1. Evaluating the use and outcomes of post-acute care for individuals with dementia

PI: Robert Burke, MD, MS

Abstract: Over 3 million Medicare beneficiaries currently carry a diagnosis of dementia, and this number is expected to increase to more than 14 million by 2050. These individuals, like many Medicare beneficiaries, receive post-acute care in nursing homes (called skilled nursing facilities, SNFs) or at home supported by a home health agency after they are hospitalized. Post-acute care delivered by home health agencies and SNFs has received national attention because it is so common (40% of beneficiaries receive post-acute care after hospitalization), so expensive (Medicare spends more than $60 billion on this care annually), and associated with such poor outcomes. In fact, one in four Medicare beneficiaries is readmitted to the hospital during their post-acute care stay, and only about half of beneficiaries in SNF return to the community by 100 days following hospital discharge. Despite the increasing focus on dementia and post-acute care in the United States, very little is known about how individuals with dementia – as a particularly vulnerable cohort – currently receive post-acute care, nor what their outcomes are. Understanding this care is not just important for the reasons above. It is particularly pressing because payment reforms that drive patients towards less expensive forms of post-acute care are being implemented now and could create a disparity in care for vulnerable populations. For example, health systems may doubt that patients with dementia will benefit from more intensive rehabilitation provided in a SNF and limit this care unfairly. Alternatively, individuals with dementia could benefit more from being in a familiar environment during their rehabilitation and exhibit better outcomes in home health. Our analysis describes the use and outcomes of post-acute care in individuals with dementia compared to those without this diagnosis in a propensity-matched analysis, and then uses an instrumental variable approach to help establish whether home health or SNF provides better outcomes for post-acute care in patients with dementia. This analysis is essential to support a larger R01 proposal to NIH to evaluate the effect of new payment reforms for post-acute care in vulnerable populations.

2. 'Post-biotic' interventions to ameliorate age-related inflammation

PI: Maayan Levy, PhD

Abstract: Aging is a diverse and complex process which is associated with the development of chronic diseases that have been shown to enhance inflammation. While inflammation is a common denominator for a broad range of age-associated diseases, such as inflammatory bowel disease, cancer, heart disease and Alzheimer disease, the underlying causes are poorly understood, thus hampering the development of effective preventive or therapeutic approaches. This proposal is based on a new strategy to counteract age-related inflammatory processes. This new strategy is based on small molecules produced by a rich but largely unknown endocrine system of the mammalian body: the intestinal microbiome. The microbiome comprises numerous species of bacteria, fungi, parasites, and viruses, most of which are still uncharacterized. We hypothesize that the endocrine function of the microbiome contributes to age-associated disease. Specifically, the microbiome is producing a large range of molecules that cannot be synthesized by the host but are estimated to be a major component of host physiology in homeostasis and disease. We will explore the interconnection between the intestinal microbial ecosystem, the gastrointestinal milieu, and the molecules that are exchanged between host and microbiome.
We will use a newly devised functional metabolomics approach to detect microbiome-derived metabolites whose abundance is altered in an aged host and which are causatively involved in age-associated inflammation. Our vision is to mechanistically characterize specific microbial metabolites that can be used for modulatory interventions against age-associated diseases. The ultimate goal of this project is to define strategies for the restoration of intestinal homeostasis at old age through modulation of metabolite abundances.

3. The impact of the microbiome on sarcopenia

PI: Christoph A. Thaiss, PhD and Karthikeyani Chellappa, PhD

Abstract: Sarcopenia, the progressive loss of muscle mass in the elderly, is a major cause of immobility and frailty in aged individuals. It frequently leads to major complications associated with reduced muscle strengths, including increase in risk for bone fractures and metabolic diseases. Our understanding of the causes of sarcopenia and the currently available treatment options are limited. In this pilot project, we will explore the hypothesis that the endocrine activity of the intestinal microbiome, the community of commensal microorganisms colonizing the human gut, is involved in the pathophysiology of sarcopenia. We hypothesize that the community of intestinal bacteria undergoes changes in composition and function over the host's lifetime, and that signals derived from the activity of intestinal bacteria influence the loss of muscle mass and function in aged individuals. To address this question, we will combine technologies from the fields of microbiome and aging research. This pilot study will establish proof-of-concept evidence for an involvement of the microbiome-muscle axis in the development and manifestations of age-associated loss of muscle function. The goal of this study is to catalyze the systematic exploration of microbiome-derived signals that can be harnessed for therapeutic interventions against sarcopenia in the future.

4. Restoring Sleep in the Aging Brain
PI: Franz Weber, PhD

Abstract: A major health concern for older adults is poor sleep. Frequent awakenings throughout the night and problems maintaining long and deep sleep periods are common in older adults. The resulting disruption of non-rapid eye movement (NREM) sleep has been linked to impairments in memory, attention and learning, severely impacting life quality. Therefore, it is crucial to understand the mechanisms by which the maintenance of NREM sleep is impaired in older adults and to identify novel therapeutic targets to restore healthy sleep. Previously, we discovered a population of neurons in the midbrain of the mouse that powerfully maintain NREM sleep. Opto- or chemogenetic activation of GABAergic neurons in the ventrolateral periaqueductal gray (vlPAG) maintains NREM sleep. We hypothesize that the activity of NREM sleep-maintaining neurons in the vlPAG is altered with aging and that normalizing their activity through opto-, chemogenetic or pharmacological approaches will restore healthy sleep in old mice and alleviate related neuropathological symptoms such as memory impairments. First, we will perform in vivoelectrophysiological recordings to examine whether the neural dynamics of vlPAG GABAergic neurons is changed in aged mice. Next, we will examine whether opto- or chemogenetic activation of vlPAG GABAergic neurons restores consolidated NREM sleep in old mice and remedies memory deficits. Finally, we will generate transcriptional profiles from vlPAG neurons of young and old mice to identify differentially regulated genes, in particular of G-protein coupled receptors (GPCRs), and test whether pharmacological manipulation of identified GPCRs can restore NREM sleep. This research effort employs a paradigm-shifting strategy to discover novel targets for therapeutic interventions to prevent sleep circuits from becoming dysfunctional with aging. Restoring NREM sleep by targeting a specific population of neurons in older adults will potentially also alleviate other health problems associated with the decline in sleep quality.

Alzheimer's Disease Core Center Pilots

5. Post-surgical acceleration of neurodegeneration
PI: Krzysztof Laudanski, PhD

Abstract: Surgery and anesthesia induce severe stress to the body, and the brain in particular. Until recently, the debate about the importance of these surgery-induced changes was very inconclusive while technical means did not allow for the practical study of the brain function and damage after surgery. Recently, a team of investigators showed an increase in neurodegeneration markers in blood up to seven days after elective, non-cardiac surgery. Our work showed that patients undergoing elective heart surgery had elevated tau protein serum level up to 3 months in some subjects. Both groups used ultra sensitive techniques to detect neurodegeneration markers in serum. These data suggest that elective surgery impose stress on the body beyond what is commonly believed. Therefore, it is fascinating to explore if we can predict which elderly patients will develop an abnormal elevation of neurodegeneration markers after elective heart surgery.
Furthermore, by predicting first which subjects will develop the rise in neuro-degeneration markers we can open a window for precisely targeting these individuals for an intervention. Since the majority of the data suggest that neuroinflammation plays the critical role, we suggest that studying the early dynamic of neurodegeneration markers in combination with measuring activation of monocytes to allow for identification of vulnerable population among patients undergoing elective heart surgery. We will focus on the aspect of monocyte function previously linked to increasing in tau protein – M-CSF production. Since M-CSF production is regulated by several epigenetic mechanisms, sustained expression of this molecule can be present long-term after inciting heart surgery and accelerate neurodegeneration in vulnerable elderly subjects. The potential implication of our findings may result in a change of the surgical practice or introduction of personalized measures to curb the inflammation in vulnerable individuals susceptible to accelerated neurodegenerative processes in the aftermath of surgery.

6. Evaluating Time Out: An intergenerational respite, training and mentorship program
PI: Lauren Massimo, PhD, CRNP

Abstract: Five million people currently live with Alzheimer's disease (AD) in the United States. AD takes a physical, emotional, and financial toll on patients and their caregivers. Family and friends provide an estimated 18 billion hours of unpaid care to those with AD at an estimated cost of $230 billion annually. Therefore, it is important to create effective strategies to support family caregivers so that they can continue to perform their demanding role. Respite care is a supportive service often provided in the home to give the caregiver a temporary break from caregiving duties. The Time Out program is a nationally recognized program that trains students to provide respite for older adults living in the community. The overall goal of this project is to determine if the Time Out program can be extended to individuals living with AD and their caregivers to reduce caregiver burden and behavioral symptoms in the patient that often occur as a result of low patient engagement. Finally, we will determine if student participation in the Time Out program increases student interest to pursue a career in the field of aging.