

HEALTHY LONGEVITY GLOBAL COMPETITION

2022 Catalyst Awardees

Sponsor: National Academy of Medicine

AI-Based Conversational Agent for Monitoring Cognitive Health of Older Adults

Principal Investigator	Mohammad Mahoor
PI Primary Affiliation	DreamFace Technologies, LLC
Co-Investigator(s)	Abdollahli, Hojjat

PROJECT DESCRIPTION

Due to our seniors' increasing social isolation caused by COVID-19 and projected shortages of caregivers, quality conversations with other human beings will decrease. We will address problems associated with limited human interaction by the design and development of a relatable and caring virtual agent, as a mobile application called MyRyan, featuring emotion recognition, conversation, voice instruction, and the monitoring of cognitive decline and dementia in older adults with MCI. Our multidisciplinary team is essential for an efficacious conversationalist machine and has complementary expertise in computing, machine learning, data science, cognitive rehabilitation, geropsychology, healthy aging research, along insight from caregivers. MyRyan's AI will actively engage individuals in conversation about personalized topics of interest by adapting to the user's language abilities and personal interests. Improvements in the well-being of individuals with MCI through meaningful conversations with MyRyan can reduce mental, physical, and financial burdens, which this study will quantitatively and qualitatively measure. Our invention can lessen the healthcare industry's burdens of limited caregivers and address other pandemic impacts such as loneliness in the elderly population. To date, a conversational agent engaging seniors in open and personalized conversations on topics of interest is beyond the state-of-the-art. The proposed technical advancement will give seniors with MCI a cost-effective opportunity to increase social interaction by communicating, sharing experiences and memories, and laughing with an empathic and intelligent chatbot.

AR Captions Increase Comprehension, Social Connection & Mental Well-Being

Principal Investigator	Alex Westner
PI Primary Affiliation	Spark23 Corp.
Co-Investigator(s)	None

PROJECT DESCRIPTION

Worldwide, about 466 million people experience disabling hearing loss. In the U.S., approximately one in three people between 65 and 74 are impacted by hearing loss and nearly half of Americans 75 and older struggle daily because of hearing impairment. Despite advances in technology, common solutions—hearing aids and cochlear implants—do not completely solve the problem. Even under perfect conditions with well-fitted hearing aids, many patients still struggle to understand speech. Hearing loss has recently been identified as a top risk factor for dementia. The constant strain on the brain to understand speech leads to cognitive decline. Current solutions require sustained concentration that many describe as mentally exhausting. To compensate for the shortcomings of their hearing aid devices, people rely on visual communication methods, including sign language, lip reading and captions/subtitles. Our solution builds on these behaviors. "Speech Glasses" are augmented reality (AR) smart glasses that display real-time captions of what others are saying—like speech

bubbles—in the wearer’s field of view. Speech Glasses enable wearers to use their vision to supplement hearing, making it easier to understand what other people are saying. Speech Glasses promote healthy longevity by improving cognition, mental acuity, and reducing stress on the brain, which can help mitigate cognitive decline. The glasses will help people communicate with others, stay social, be active, go out to restaurants, and engage in family conversations. They can boost confidence and self-reliance, empowering individuals to advocate for themselves and stay sharp when talking to medical professionals.

Bridging the Gap between Postpartum and Primary Care: Novel Approaches to Care Continuity for Women at High Risk for Chronic Disease

Principal Investigator	Jessica Cohen
PI Primary Affiliation	Harvard T. H. Chan School of Public Health
Co-Investigator(s)	Clapp, Mark

PROJECT DESCRIPTION

Primary care providers (PCPs) are essential for prevention and management of chronic diseases across the lifespan. Despite the substantial role of chronic diseases in death and disability in the US, PCP use has been declining. Although chronic conditions are more common in old age, a range of conditions—including diabetes, hypertension, obesity and mental illness—are often detected during pregnancy. Further, certain pregnancy-related conditions increase the risk of developing chronic conditions later in life. The postpartum period is a crucial window for managing these conditions and positioning women toward longer-term health and wellbeing. However, very few postpartum women at risk for long-term disease receive any primary care. Postpartum women with diabetes, obesity, hypertension and mental illness are largely unsupported in transitions to primary care—many are simply told to follow up with their PCP without relevant information, scheduling assistance, or official transfer of accountability across providers. Our project explores the drivers of these postpartum care “cliffs” and tests new approaches to increasing PCP use for postpartum women with high-priority conditions. We will conduct a randomized controlled trial testing a behavioral-science inspired intervention package on PCP use for postpartum women with long-term disease risk. The intervention incorporates best practice from behavioral economics on catalyzing health behaviors, including defaults, nudges and salient, timely information. We will also conduct a longitudinal survey with postpartum women to trace out the barriers and facilitators of primary care use. Our goal is to identify health policy, health system, and provider-level approaches to improving postpartum care continuity.

CARS Silver: Mental Health Screening and Targeted Resources for Older Adults

Principal Investigator	Sarah Nelson
PI Primary Affiliation	Division on Addiction, Cambridge Health Alliance
Co-Investigator(s)	LaPlante, Debi

PROJECT DESCRIPTION

Mental health consists of the absence of mental disorder and the presence of emotional, psychological, and social well-being. It is associated with healthy longevity. Further, whereas mental disorder (e.g., depression and anxiety) is associated with increased risk for mortality, characteristics of well-being (e.g., happiness and life satisfaction) are associated with reduced mortality. These relationships highlight the importance of enabling older adults’ understanding of their mental health risks and strengths. One means of providing such insight and helping to extend healthy longevity is mental health screening and referral to treatment and wellness resources. The purpose of this proposal is to adapt and expand a free, validated mental health screening and referral tool, the Computerized Assessment and Referral System (CARS) for use with older adults on their own or in community-based peer health educator settings. Providing a structured mental health tool with automated

referrals to treatment, community resources, and activities will lead to healthy longevity by facilitating engagement with such resources. Currently, CARS provides DSM-5-based screening and referral for mental illness. This project will add screening for well-being and a specialized module to screen for older adult concerns, such as memory loss, grief, elder abuse, and loneliness. Providing older adults targeted mental health recommendations for resources and experiences will ensure they have the knowledge and support for aging well.

Defining the phenotype-axis of frailty and resilience at single-cell resolution

Principal Investigator	Jude Phillip
PI Primary Affiliation	Biomedical Engineering
Co-Investigator(s)	Walston, Jeremy

PROJECT DESCRIPTION

Age is considered a key risk factor for the development and progression of many diseases. However, person-to-person variations in the way diseases manifest in older adults indicates that this risk is not uniform with chronological age. As such, there is a critical need to develop new approaches that capture underlying biological mechanisms of aging to describe disease susceptibility and resilience. In older adults, frailty and resilience lie at polar extremes of each other. Frailty is defined based on a set of clinical features (e.g. gait speed), and shows strong associations with disease susceptibility and death. Resilience on the other hand is difficult to measure at baseline. Here, resilience describes the ability to recover and rebound after injury or exposure to stressors (e.g. sickness, falls, surgery). In many cases, the only true way to determine resilience is to measure clinical features after-the-fact. As such, clinicians are defaulted to 'trial-and-error' approaches when treating and selecting older adults for invasive medical procedures. Here, we propose to develop a cell-based approach to determine baseline resilience and frailty in older adults. The premise of the idea is that instead of waiting to measure the responses of older adults to stressors after-the-fact, we can stress their cells within engineered microenvironments to predict baseline resilience and frailty. A key goal of this work is to develop precision aging strategies to help guide interventions and shape treatment options. As a result, it could help preserve healthspan, boost longevity, and reduce treatment-associated healthcare costs.

Developing a smartphone app to enhance older drivers' longevity and safety

Principal Investigator	Johnathon Ehsani
PI Primary Affiliation	Johns Hopkins Bloomberg School of Public Health
Co-Investigator(s)	None

PROJECT DESCRIPTION

This catalyst proposal describes a groundbreaking approach to promote older adults' longevity, mobility, and safety. Transportation is a social determinant of health, and extending older adults ability to continue driving is a prerequisite for healthy longevity. Driving cessation is associated with a range of negative outcomes for older adults. In the U.S., driving is a necessity for mobility because of disinvestment in alternative modes of transportation. However, driving poses unique risks for older adults. This population is overrepresented in motor vehicle crash deaths and injuries and have the highest fatality rate per 100 million miles driven. Using a combination of artificial intelligence and epidemiology, I will develop a smartphone application that provides the safest possible route navigation for older drivers, based on individual characteristics, health conditions and risk profile. In addition, the app will monitor driving behavior and detect when an individual's driving behavior declines, flagging the possibility of a health problem which may require assessment and indicate a cessation of driving. The goal is to extend older drivers' mobility for as long as possible, thereby extending their independence, while keeping themselves and other road users safe.

Development of a next-generation pharmaceutical to target oxidized cholesterol and reverse cardiovascular disease

Principal Investigator	Matthew O'Connor
PI Primary Affiliation	Cyclarity Therapeutics
Co-Investigator(s)	None

PROJECT DESCRIPTION

Toxic oxysterols have been tied to numerous age-related diseases. Our team of scientists has engineered a custom cyclodextrin (a cyclic polysaccharide), which is designed to extract these toxic biomolecules from the body. We propose two concise projects to validate our findings that our cyclodextrin can remove oxidized cholesterol, thereby rehabilitating damaged immune cells and allowing them to repair damage such as atherosclerotic lesions. The ultimate goal of our company is to bring one or more of our custom cyclodextrins to the clinic to treat a variety of the world's most deadly diseases, starting with atherosclerosis.

Effects of maternal obesity on oocyte aging in female offspring of the BPH/5 preeclampsic-like mouse

Principal Investigator	Jenny Sones
PI Primary Affiliation	Louisiana State University School of Veterinary Medicine
Co-Investigator(s)	Herzog, Fiona

PROJECT DESCRIPTION

The majority of adults in the United States are overweight or obese often with concurrent cardiovascular disease. The genesis of the cardiometabolic epidemic likely begins with in utero development. Hypertensive pregnancies, as in preeclampsia (PE), greatly increase offspring risk of cardiometabolic diseases later in life. The precise mechanism of this is unknown and the long-term effects on offspring are unclear. To study the transgenerational effect of PE, we utilize the obese female BPH/5 mouse which spontaneously phenocopies PE as seen in women. Our overarching hypothesis is BPH/5 oocytes have premature aging that contribute to cardiometabolic disease in offspring which can be reversed with maternal weight loss before pregnancy. Adult female BPH5 mice are obese with leptin resistance, increased blood pressure, and altered estrogen signaling before pregnancy compared to age-matched lean normotensive control mice. First, oocytes will be evaluated in a time course for signs of reactive oxygen species (ROS), mitochondrial dysfunction, and markers of aging in adult BPH/5 female mice. Our aims are designed to test if BPH/5 female weight loss via pair-feeding before conception would improve offspring cardiometabolic disease by reversing premature oocyte aging. Preliminary data supports our approach that attenuation of BPH/5 maternal obesity via weight loss reduces pregnancy hypertension and in utero fetal death. In the future, we will investigate the epigenetic and in utero programming of maternal weight loss on oocyte markers as predictors of cardiometabolic disease. The findings of this proposal are necessary to understand the effects of PE on offspring into adulthood.

Eliminating mutated mitochondrial DNA with modified nucleic acids

Principal Investigator	Joseph Baur
PI Primary Affiliation	University of Pennsylvania
Co-Investigator(s)	None

PROJECT DESCRIPTION

Mitochondria, the "powerhouses of the cell" contain their own genomes that are present in hundreds of copies per cell and are prone to mutation. Over the course of aging, some cells end up with a high fraction of their mitochondrial genomes ("mtDNA") mutated, leading them to become dysfunctional. Inheriting mutated mtDNA through the germline causes primary mitochondrial disorders - devastating conditions with an array of symptoms that include a shortened life expectancy. Whether the number of cells affected by mtDNA mutation during normal aging is sufficient for it to be a true "driver" of the aging process is debated, but accelerating mutation accumulation shortens mouse lifespan. At present, there is no viable strategy to eliminate mutant mtDNAs, either in disease or during normal aging. We propose that it might be possible to selectively block replication of mutant mtDNAs taking advantage of modified nucleic acids that bind more tightly than natural DNA in a sequence-specific way. By conjugating these nucleic acids to a delivery vehicle that can enter cells and reach the mitochondria, a purifying selection may be imposed to favor wild type mtDNA and restore cell function. We will test this approach in vitro and then in well characterized cell lines containing a mix of wild type and mutant mtDNA. If successful, these experiments would lay the groundwork for efforts to eliminate mutant mtDNA in vivo.

Exercise and Brain Health: Pre-clinical Study of the Energy Transfer Hypothesis of Aging using PET/MRI imaging

Principal Investigator	Lauren Koch
PI Primary Affiliation	College of Medicine and Life Sciences
Co-Investigator(s)	Yu, Xin

PROJECT DESCRIPTION

There is a strong link between high aerobic energy capacity and the increase in resilience to developing complex disease with aging, including Alzheimer's disease and dementia. From this association, we initiated the Energy Transfer Hypothesis of Aging (ETH) that states: Variation in capacity for aerobic energy transfer is the central mechanistic determinant of the divide between aging and longevity. As an unbiased test of the ETH, we performed two large-scale artificial selective breeding experiments in rats for low and high intrinsic (inborn) aerobic treadmill running capacity, and for low and high response to aerobic exercise training. The ETH can be accepted with high confidence given that over 125 published studies performed at ~60 institutions in 11 countries uniformly demonstrate the overall divide for age-related disease risks between low and high exercise capacity rats. We argue that commonly used animal models with induced single gene mutations are too simplistic for understanding features that are driven by multiple gene and environment interactions, such as healthy aging. Rather, our theory-based rat models are thus transformative in the sense of realistically emulating the wide range of exercise capacities as a predictor of the large divide in features underlying healthy aging. Here we will utilize our four exercise rat models to test the medical recommendation of habitual exercise for maintaining brain health. Using PET/MRI imaging, our pre-clinical study will measure for the first time changes in blood flow, metabolism, structural integrity, and waste removal in the brain as a result of habitual exercise across lifetime.

Expanding a Multimodality VR Fitness Platform to Remotely Assess, Monitor, and Report Cognitive and Physical Function for Seniors

Principal Investigator	Jennifer Stamps
PI Primary Affiliation	Rendever, Inc
Co-Investigator(s)	Cote, Theresa

PROJECT DESCRIPTION

As healthcare costs and the aging population increase, preventing the loss of cognitive and physical function is an urgent initiative. Social isolation increases the risk of dementia by 50%, and stroke and cardiovascular disease by 30%, three major causes of loss of function. Equally pressing is the shortage of clinicians to manage the care of this demographic, causing delays between functional changes and effective treatment. While evidence shows exercise as an effective strategy for maintaining independence, preventing cognitive and physical disability, and reducing the healthcare burden of aging populations, compliance is a problem. Interactive video game cycling has shown significant increases in the enjoyment of exercise. Our virtual reality (VR) fitness platform, developed around the neurological and physical needs of seniors, is the first to combine physical exercise with cognitive stimulation and multiplayer social engagement. Scores achieved in similar gaming paradigms have shown correlation with cognitive status, and research in exergaming has demonstrated improvements in cognition and potential efficacy to create a digital diagnostic biomarker. This VR technology may allow for the administration of remote and automated assessments for various use cases, including rehabilitation, patient monitoring, and identifying and alerting to risk factors of cognitive and physical decline. We will determine if the VR fitness platform's performance metrics correlate with clinical tests of cognitive and physical function. This award enables further development of the needed AI capabilities in collaboration with other neurodegenerative clinicians and neurological and orthopedic rehabilitation physical therapists to optimally meet their clinical assessment and reporting needs.

Financial Decision Making: Identification of Financial Vulnerability and Early detection of Cognitive Impairment

Principal Investigator	Eric Chess
PI Primary Affiliation	Knoebel Institute of Healthy Aging
Co-Investigator(s)	None

PROJECT DESCRIPTION

The first sign of cognitive decline is often found in impaired financial decision-making by those who are unaware. This can occur years before any symptoms are noticeable in patients. Research has continued to identify growing independent risk factors regarding vulnerability to financial exploitation and fraud (social isolation, major health events, financial literacy). Currently, despite this research, there exists no accessible validated assessment of financial vulnerability or impaired financial decision-making that may be a precursor to cognitive impairment and dementia. The goal of this project is to create validated, practical and accessible, assessments to detect increased financial vulnerability and the earliest clinical signs of cognitive impairment. This will be achieved through the following three aims: 1) determine whether our practical accessible early screening assessment (ESA) is a valid test that builds on existing research, 2) determine whether the ESA aligns with the Montreal Cognitive Assessment (MoCA) regarding those with cognitive impairment and 3) determine if our financial vulnerability score (FVS) correlates with likelihood of financial fraud and exploitation. Our interdisciplinary team has developed an ESA to detect prodromal cognitive decline by way of impaired financial decision-making as well as FVS to identify increased risk of exploitation and fraud. Our testing takes less than 15 minutes to complete it can be done online (from any location) and without a trained practitioner. An accessible technologic tool to identify signs of financial vulnerability and resources to provide support and protection would alleviate the profound loss related to financial exploitation, fraud and poor/impaired decision-making.

Granulocyte Colony Stimulating Factor: A Novel Agent for Reproductive Longevity and Equality

Principal Investigator	Leslie Appiah
-------------------------------	---------------

PI Primary Affiliation	The University of Colorado Anschutz Medical Campus, Department of Obstetrics and Gynecology, Division Chief of Academic Specialists in Obstetrics and Gynecology
Co-Investigator(s)	Santoro, Nanette

PROJECT DESCRIPTION

Advancements in cancer therapies have resulted in a sharp reduction in cancer mortality rates. However, lifesaving cancer treatments can jeopardize a woman's reproductive longevity and impair her quality of life. It is estimated that 75% of survivors will experience at least one long-term adverse effect following cancer therapy. Infertility is most notably recognized as a common and devastating consequence of cancer treatment. Currently available fertility preservation procedures can mitigate the adverse effects of cancer therapy on reproductive health but are often not feasible due to their invasive nature and cost; thus, creating inequities in access across diverse populations. Recent basic science breakthroughs have identified granulocyte colony stimulating factor (G-CSF) as an effective therapy to preserve ovarian function in animal studies. However, there have been no studies assessing the effectiveness of G-CSF to preserve fertility and hormone function in the human ovary despite its widespread use in clinical practice, ease of administration, and low side effect protocol. We aim to determine the efficacy of G-CSF as an ovarian protective agent in women, and in doing so, equitably restore fertility and hormone function to millions of girls and women with cancer across the world. The timing of this novel proposal is prime as the successful application of this therapy will not only impact cancer survivors but also the increasing population of women who are unable to conceive due to an age-related decline in fertility and women born with a genetic predisposition to premature menopause.

Imaging oxidant production to improve aging and longevity

Principal Investigator	John Chen
PI Primary Affiliation	Massachusetts General Hospital
Co-Investigator(s)	Wang, Cuihua

PROJECT DESCRIPTION

Oxidative stress is postulated to be involved in aging and many diseases. When oxidative species are elevated and overwhelm the antioxidant balance excess oxidants can contribute to aging and disease. However, no currently available method can sensitively and specifically pinpoint the locations/organs where aberrant oxidant production is occurring, critically hampering oxidative stress research and clinical application of antioxidant therapeutics. Thus, there is an unmet need for a marker of excess oxidant production to better understand the role oxidative stress plays in aging and disease. We have accidentally discovered an undescribed relationship between myeloperoxidase (MPO) and normal aging. MPO is a key enzyme involved in generating oxidative stress and produces highly reactive oxygen and nitrogen species that cause protein aggregation, cell signaling interruption, mutagenesis, and tissue damage. We also recently described a positron emission tomography (PET) imaging probe that can specifically and sensitively detect MPO activity, and verified that this probe can cross the blood-brain barrier. We propose to use this imaging probe to track non-invasively MPO activity in the brain over time in normal aging in mice. We hypothesize that this imaging technology can spur antioxidant research and enable personalized treatment plans to improve health and longevity and prevent aging and age-related diseases. Because PET imaging agents are administered at a microdose level, the cost for translation is significantly lower than for other types of drugs. Thus, we anticipate that once validated in animal models, this technology can be quickly translated and applied to study human aging.

Intergenerational Mentoring to Promote Health Across the Lifespan

Principal Investigator	Corey Nichols-Hadeed
PI Primary Affiliation	University of Rochester

Co-Investigator(s)	Van Orden, Kimberly
---------------------------	---------------------

PROJECT DESCRIPTION

Development of an intergenerational mentoring programming will link youth at risk for violence with older adult mentors in their community. Especially important as the community emerges from the COVID-19 pandemic, this approach offers an opportunity to promote health across the lifespan by providing meaningful social connection in older adults while addressing community violence. This collaborative project will leverage strengths from across the community through co-design with a hospital system, local government, and the community, including youth, older adults, and community serving agencies. This work will be accomplished through the following aims:

1. Developing a training manual for guiding mentorship relationships, violence prevention, and health promotion with a focus on self-care, developing and maintaining healthy boundaries, and when to seek additional support;
2. Training a cohort of older adult mentors (n=15) and conducting baseline assessment (surveys and interviews) of risk and resilience for healthy aging, including physical/mental/cognitive/social health/functioning; and 3. Piloting the program with trained older adult mentors paired with youth mentees (n=45) that have experienced violence-related injuries. We hypothesize that participation in an intergenerational mentoring program will increase health and well-being for all participants, both youth and older adults, and promote healthy aging trajectories across the lifespan.

Lifestyle Empowerment Approach for Diabetes Remission (LEADR): A systems-change intervention to achieve diabetes remission for patients and sustainable reimbursement for physicians

Principal Investigator	Micaela Karlsen
PI Primary Affiliation	American College of Lifestyle Medicine
Co-Investigator(s)	Moore, Scott

PROJECT DESCRIPTION

The Lifestyle Empowerment Approach for Diabetes Remission (LEADR) project proposes an intensive therapeutic lifestyle intervention to support patients living with type 2 diabetes (T2D). The foundational component is the use of a low-fat, whole food, plant-based diet—a dietary lifestyle which is adaptable across preferences and cultures and which has been demonstrated to produce T2D remission. Supported by community partnerships in planning and design, a high-quality, randomized controlled trial to document the health benefits of a lifestyle patient intervention will be conducted, reaching 84 families in a Utah community. Serving sustainability and replicability, the intervention will utilize an open-access detailed program curriculum with facilitator scripts, a participant workbook, and planning guides designed to reach majority Hispanic/Latino populations in disinvested communities. The suite of materials will educate and guide health care workers as they address diet, exercise, and stress to target remission (normalized blood glucose without medication) in a meaningful evidence-based departure from the typical disease management approach taken toward patients with T2D. A parallel intervention will be conducted using a version of the curricular resources tailored to a historically Black faith-based community in Missouri. The project will develop and assess a reimbursement pathway utilizing shared medical appointments as part of a systems-change approach to T2D care. Achievement of expected results will provide proof of concept for a lifestyle intervention relevant and adaptable across communities that have historically been furthest from resources, including convenient access to affordable, culturally relevant, nutritious food, that performs better than the standard of care.

Machine Learning-Driven Multimodal Wearable Biosensor for Stress Monitoring

Principal Investigator	Wei Gao
-------------------------------	---------

PI Primary Affiliation	California Institute of Technology
Co-Investigator(s)	None

PROJECT DESCRIPTION

High levels of stress and anxiety can significantly affect human performance and can substantially reduce life expectancy by several years. Early detection and classification of the severity of stress allow for timely intervention and can be used to foster mental wellness proactively. However, current approaches for stress assessment are largely limited to subjective questionnaire-based scales, and to date, there is no existing method that accurately and objectively monitors stress. We hypothesize that molecular biomarker levels monitored continuously by non-invasive sweat analysis along with the key vital sign monitoring, when coupled with a machine learning approach, will provide crucial insight into mental health status and can be used for accurate and dynamic stress and anxiety assessment toward timely intervention. We propose a holistic hardware/software solution based on a multimodal wearable sensing platform to achieve dynamic stress and anxiety assessment. Our strategy is to simultaneously monitor the molecular analytes in human sweat including stress hormones (i.e., cortisol, adrenaline, and norepinephrine), glucose, lactate, uric acid, Na⁺, K⁺, pH, sweat rate, and key vital signs (i.e., temperature, GSR, blood pressure pulse waveforms) using a wearable multimodal sensing platform which can autonomously induce and analyze sweat across activities. We plan to validate this wearable patch in human studies and apply machine-learning data analysis for dynamic stress classification and prediction. We anticipate that the algorithm generated from this study will have a major impact in personalized stress assessment, and potentially many other major health conditions.

Monitoring of Alzheimer's Disease Pathology Through Slow Wave Activity During Sleep in Older Adults

Principal Investigator	Makoto Kawai
PI Primary Affiliation	Department of Psychiatry and Behavioral Sciences, Stanford University
Co-Investigator(s)	Ada Poon

PROJECT DESCRIPTION

It has been suggested that sleep can provide a more affordable, accessible, and less invasive method of monitoring the progression of AD pathology, even in the preclinical period. However, the current sleep assessment methods in the market, including PSG or commercial EEG headbands, are expensive, affect patients' sleep because of discomfort, and lead to intolerability for extended recordings. We propose developing a disposable, miniaturized, wireless, and long-term sleep EEG monitoring system. With the device, we aim to investigate the impact of frontal slow wave activity (SWA) during sleep on cognition and AD pathology in older adults. We will focus on frontal SWA because of its known association with aging and cognition. Our approach focuses on monitoring participants' sleep at home with minimal disruption using a two-channel wireless stamp-sized micro EEG system. We will compare the quality of EEG signal with gold standard polysomnography (PSG). In this project, we propose to investigate 1) the feasibility of our soft, small, flexible sticker-like EEG (SLEEG) to monitor SWA for one week in older adults, 2) validity of machine learning algorithm to detect SWA compared with PSG, and 2) the association of one-week averaged SWA with AD pathology, i.e., Amyloid PET and neuropsychiatric evaluation. Our project consists of three stages: 1) developing the sticker-like EEG sensor, 2) validating it with PSG, and 3) testing its clinical and imaging association in 10 older adults with and without mild cognitive impairment.

Multi-modal Microwave Radar & Electroencephalography-based Brain-Computer Interfaces for Non-Invasive Functional Imaging of the Brain

Principal Investigator	Emily Porter
PI Primary Affiliation	The University of Texas at Austin
Co-Investigator(s)	Millan, Jose del R.

PROJECT DESCRIPTION

Brain-computer interfaces (BCIs) have the potential to revolutionize the way we treat brain-related injuries and diseases. To date, BCIs have been invasive and require surgery to implant into the brain. Developing non-invasive BCIs is critical to improving safety and reducing costs, however the utility of non-invasive BCIs has been hindered by the poor spatial resolution of electroencephalogram (EEG) signals, meaning that fine motor control is not possible. We propose combining microwave radar (MWR) with electroencephalography in a novel multi-modal BCI technology to uniquely enable non-invasive functional imaging of the brain. This technology will harness high-resolution MWR imaging, while maintaining high temporal resolution with a low-cost and wearable nature. Notably, MWR is safe for 24/7 usage with no known side-effects. A joint MWR-EEG platform will result in a powerful technology that allows for non-invasive tracking of the functional activity of small brain regions at the millimeter and millisecond ranges. In this study, we will: i) develop a framework for the integration of MWR and EEG for multi-modal, quantitative functional imaging of the brain; ii) identify the currently undetermined relationship between MWR and EEG signals; and iii) establish the clinical utility of MWR-EEG BCI in rehabilitation of chronic motor stroke patients. Overall, the proposed non-invasive MWR-EEG BCI, will enable decoding of movement attempts well beyond the current state-of-the-art, with great potential to: i) assist, recover and augment people's (lost) abilities through personalized, adaptive treatment strategies, and ii) understand, probe and enhance multimodal brain correlates of human motor and cognitive functions.

Nanomedicine to detect senescence

Principal Investigator	Aditi Gurkar
PI Primary Affiliation	Aging Institute, University of Pittsburgh
Co-Investigator(s)	Balasubramanian, Rama

PROJECT DESCRIPTION

The goal of this project is to develop a specific and sensitive Nanoscale Theranostic (NST) tool that can map senescent cells, provide insight into the mechanisms of aging, and offer novel strategies to promote healthy aging. A hallmark of biological aging is the accumulation of senescent cells. Senescence is a cell-fate decision characterized by permanent proliferation arrest, resistance to apoptosis, and secretion of inflammatory factors collectively termed senescence-associated secretory phenotype. Growing evidence suggests that senescent cells contribute to multiple aging diseases, whereas elimination of senescent cells improves health and delays the onset of several age-related diseases. However, there is a critical lack of knowledge about senescent cell burden, as well as the duration of treatment and efficacy of these senotherapeutics. Senescent cells display varied gene/protein marker expression and hence do not have a universal molecular marker that can be easily tracked. Without tracking the senescent cell burden and understanding the unique characteristics of senescent cells, unlocking the full potential of senotherapeutics will be unattainable. To overcome these challenges, we will develop and validate an NST tool that can identify senescent cells based on mapping of the magnetic field of senescent cells. This unique and innovative approach serves as a 'one-stop-shop platform' for detecting senescence. Development of our NST tool can help with risk stratification and determine the type of intervention needed to minimize the impact of age-related diseases on our society. This transformative approach will be a first step towards developing a personalized medicine practice to promote healthy aging.

Rebuilding the Health Workforce in Africa to Care for an Aging Population

Principal Investigator	Vanessa Kerry
PI Primary Affiliation	Seed Global Health
Co-Investigator(s)	None

PROJECT DESCRIPTION

Africa's elderly population is expected to grow faster than in any other region in the world, with a projected threefold increase by 2050. An aging population is accompanied by a shift in the types of conditions causing illness and disease, with non-communicable diseases the leading cause of mortality and morbidity in older adults around the world. The current health needs, let alone new demands, cannot be met by the current number and distribution of health workers in Africa. Health workers are the prerequisite for strong health systems. Unfortunately, prior efforts to intervene in this space have had limited progress. Timelines have been too short, funding underpowered and planning not ambitious enough. Truly strengthening the health workforce will require a shift in our model of global health aid and strengthened domestic planning; investing in human capacity requires large scale, long-term commitment and planning that encompasses the entire cycle of education, training, employment and retention. We envision a centrally administered African-led compact to provide a framework, targets and metrics to scale up the comprehensive diverse health work-force required to deliver quality primary care and other essential health services needed for the health and wellbeing of the current and future population on the continent. The compact model will critically facilitate the mobilization, consolidation, and alignment of large scale, sustained comprehensive investments and the bespoke programs each country needs for the training and retention of a health workforce required, to care for their respective growing and aging populations.

Systems-Aligned Precision Health for Longevity and Healthy Aging with Type 1 Diabetes

Principal Investigator	Anna Kahkoska
PI Primary Affiliation	Department of Nutrition, University of North Carolina at Chapel Hill Gillings School of Global Public Health
Co-Investigator(s)	Batsis, John

PROJECT DESCRIPTION

As the population of older adults living with diabetes rapidly expands, technologic therapeutics have simultaneously become a central part of evidence-based, high-quality diabetes care. These intersecting trends underscore that we must find innovative and patient-centered ways to promote the effective use of diabetes technology over the lifespan. Despite significant potential benefits, integrating technology for diabetes management into daily routines can be complex for older adults, particularly in the context of unique biopsychosocial needs. Further, the system-level investments necessary to bolster technology use for individuals (i.e., additional provider time, diabetes education, peer support, behavioral health interventions) cannot realistically be made available to all patients due to operational and cost constraints.

Our overarching hypothesis is that providing evidence-based diabetes technology to heterogeneous, complex population of older adults with T1D demands new approaches that consider a breadth of and differences in individual-level needs for patient-oriented onboarding and effective use in daily life. We propose a new approach to tailored diabetes care that leverages precision health analytics, informed by systems thinking and stakeholder engagement, to match patients with the personalized resources or "bolstering" interventions that they need to learn to use technology for diabetes management, integrate it into daily life, and ultimately experience the clinical benefits. We will integrate two scientific methodologies: (1) precision health statistical methods that can assign optimal therapies to individuals, based on their individual real-time data; and (2) systems thinking, a holistic way to investigate the factors and interactions that may contribute to complex outcomes. By using stakeholder-engaged methods, we will work with patients, caregivers, and providers to ensure we develop effective system-level interventions.

We will generate pilot data through an interdisciplinary scientific pipeline, focusing on continuous glucose monitoring, a technologic approach to glucose monitoring with potentially life-saving benefits for older adults, as a case study. If effective, this approach of providing an individualized and optimal, yet feasible, level of support for effective use of existing and emerging therapeutics to older adults with diabetes could transform how we offer evidence-based technology to older adults with diabetes, ensuring that they remain “patient-oriented” for diverse patients and their clinical benefits remain equitable over the lifespan.

Tailoring Tissue Engineering Approaches to the Aging Population

Principal Investigator	Rosalyn Abbott
PI Primary Affiliation	Carnegie Mellon University
Co-Investigator(s)	None

PROJECT DESCRIPTION

Biomaterials can be used to restore or replace tissue function by filling defects, providing physical stability, and allowing cells to infiltrate, expand in number, and form tissue. One of the goals of tissue engineered biomaterial approaches is to design the degradation of the biomaterial to: 1) initially support cells constructing the tissue, and 2) gradually degrade as new tissue replaces the scaffold. In this way, paired tissue in-growth and scaffold degradation can maintain the properties of the tissue through the healing process. However, a major barrier to clinical translation is that patients have differing regenerative tissue capacities due to complex, interacting, and currently unpredictable factors such as age, disease state, nutritional status, lifestyle, and sex. In particular, elderly patients heal at a slower rate than younger patients due to low metabolic reserve and limited repair capacity, that increases the risk of reconstructive failure, repeat surgeries, poor aesthetic outcomes, and patient morbidity. Furthermore, elderly patients frequently have comorbidities, including: malnutrition, diabetes, vasculopathy, hypothyroidism, and cardiopulmonary reserve that affects the healing capacity and rate. To address the highly variable healing environment in the elderly population, and improve overall health longevity, our idea is to design a biomaterial scaffolding system with a slow degradation rate that can be adjusted non-invasively to degrade on-demand to match the healing process in elderly patients. This strategy will ensure that all patients regenerate stable, functional tissue leading to a reduction of repeat surgeries and an improvement in pain, function, and aesthetics over the lifetime of the patient.

The Social-Medical Network: Using a Network-Approach to Examine the Integration of Informal and Formal Care for an Older Adult

Principal Investigator	Catherine Clair
PI Primary Affiliation	Johns Hopkins University, Bloomberg School of Public Health
Co-Investigator(s)	Tobin, Karin

PROJECT DESCRIPTION

Older adults have two care networks, their informal network and their formal network. The informal network consists of family, friends, and neighbors who provide support and care for the older adult. The formal network includes health care professionals involved in the older adult's health care, ranging from primary care providers to specialists (e.g., cardiologist) to direct care workers (e.g., home health aide). The proposed hypothesis is that these two networks (i.e., informal and formal) do not operate within silos and instead form a larger network: The social-medical network. The quality of the social-medical network is dependent on the quality of the individual subnetworks and the integration across the two subnetworks. Subsequently, an older adult's healthy longevity is dependent on the quality of their social-medical network. If one or both subnetworks is weak and/or the integration across the subnetworks is lacking, the health of an older adult may suffer. The social-medical network can be explored for infinite health outcomes: acute service utilization, medication adherence, biomarkers, and

more. The primary objective of this proposal is to measure the social-medical network, examine its relationship to acute service utilization, and explore mechanisms of action within the network to improve its quality and strength. The resulting benefit is not just limited to the improving the human healthspan for an individual but has implications for improving lives of informal caregivers, lowering health care costs, and strengthening care communities.

Uncovering molecular mechanisms of aging clocks with interpretable deep

Principal Investigator	Hong Qin
PI Primary Affiliation	University of Tennessee at Chattanooga
Co-Investigator(s)	None

PROJECT DESCRIPTION

The molecular mechanism of the biological aging clock, such as the DNA methylation clock, remains obscure. We propose developing a knowledge-based neural network (KNN) model to infer the conserved mechanisms for longevity. We plan to first build our KNN using human genomics and phenotype data. We plan to use the multi-view technique to integrate heterogeneous genomic data, and use the DNA methylation sites as a hidden layer of the neural network architecture. The main architecture of the neural network will be based on the hierarchy of functional components within cells. After the development of the neural network for human aging clocks, we will test the conserved mechanisms by applying transfer learning for aging clocks in mice and the naked mole rats. The naked mole rats have exceptional longevity. By comparing trained KNN models in mice and naked mole rats, insights would be gained on how naked mole rats can achieve their exceptional longevity.