

HEALTHY LONGEVITY GLOBAL COMPETITION

2022 Catalyst Awardees

Sponsor: Ministry of Health of Singapore

Ageing in Solitude: Perception and Health among Older Adults

Principal Investigator	Peter Tay
PI Primary Affiliation	Singapore Institute of Technology
Co-Investigator(s)	Nadya Patel

PROJECT DESCRIPTION

Being alone can be a negative or positive experience and little is known about the health benefits associated with solitary experiences involving positive emotions, spiritual or mental renewal. This research aims to delineate solitary and loneliness experiences among older adults in the context of eating, working, physical and recreational activity participation. Effectiveness of health messaging relating to solitary and social activities will also be investigated. Approximately three hundred older Singaporeans will be recruited for a survey eliciting the amount of time they spent alone and with others for the activities. In addition, they will report whether they have any medical conditions and mental disorders, their satisfaction with life and quality of life. They will then be randomised into one of four experimental conditions to determine which method of health messaging aimed to promote solitary and social activities is most effective. Each health promotional advertisement is rated for affective quality, meaningfulness, and persuasiveness. Multiple linear regression analyses will be conducted to examine the correlations between perceived solitude and loneliness, and the health correlates; and the effectiveness of varied health messaging will be examined. The findings provide insights on the qualitative differences between solitude and loneliness experiences among older adults and their health outcomes. The effectiveness of health messaging through visual advertisement will also be assessed. Findings can inform policymakers, and healthcare and social care professionals in terms of the activities that could support and promote positive solitude experiences and potentially better health.

An evaluation of the validity, reliability and acceptability of a virtual reality system in assessing cognitive function using mixed methods.

Principal Investigator	Tan Ngiap Chuan
PI Primary Affiliation	SingHealth Polyclinics
Co-Investigator(s)	Ng Chirk Jenn, Lim Jie En, B.Eng, SingHealth Polyclinics Koh Yi Ling Eileen

PROJECT DESCRIPTION

Introduction

Dementia is increasingly prevalent in aging populations. Early identification of cognitive impairment is important, so that interventions can be initiated to retard the decline of cognitive function. However, current paper-and-pencil-based cognitive tests like the Montreal Cognitive Assessment (MoCA) may not adequately predict the cognitive function of individuals in real-life environments. Virtual reality (VR) is a potential alternative, but existing VR systems are limited in evaluating all cognitive domains. We have developed a novel fully-immersive

VR system (CAVIRE) to assess all six cognitive domains: perceptual-motor function, executive function, complex attention, social cognition, learning and memory, and language.

Aims

This study aims to evaluate the validity, reliability and acceptability of CAVIRE among older individuals. We hypothesise that CAVIRE is a valid and reliable screening tool for cognitive impairment, and the participants are acceptable towards its use in primary care.

Methods

The study will be conducted at two polyclinics in Singapore. Participants aged 55-84 years old will be recruited. In Visit 1, an assessor will conduct the CAVIRE assessment for the participants. Subsequently, a second assessor, blinded to the participants' CAVIRE score, will conduct the MoCA. Participants will return for Visit 2 to repeat the CAVIRE assessment, followed by an interview and questionnaire to capture their feedback.

Validity will be evaluated via Receiver Operating Characteristic analysis of the CAVIRE scores, and Pearson correlation of the CAVIRE and MoCA scores. Reliability will be assessed via Cronbach alpha and Intraclass Correlation Coefficients. Acceptability will be evaluated using mixed methods via interviews and feedback questionnaires.

Artificial Intelligence modelling approach to Comprehensive Geriatric Assessment for Haematology-Oncology patients

Principal Investigator	Clarice Choong Shi Hui
PI Primary Affiliation	National University Hospital (NUH)
Co-Investigator(s)	Francis Ho Cho Hao, Co-I (NUH) Melissa Ooi Gaik Ming, Co-I (NUH) Leo Hwa Liang, Co-I (NUS) Matthew Chen Zhixuan, Co-I (NUH) Nesaretnam Barr Kumarakulasinghe, Co-I (NUH) Pang Shien Ling Angela, Co-I (NUH) Jia Li Low, Co-I (NUH) Ling Mun Wai Natalie, Co-I (NUH) Liu Zhanhong, Collab (NUS) Ng Yean Shin, Collab (NUHS)

PROJECT DESCRIPTION

Our ageing population will be the key demographic change that will impact our country for the next 50 years and there will be a concurrent increase in the number of older adults being diagnosed with cancer. We already have in place a geriatric oncology service with provision of care for older cancer patients. These patients will undergo comprehensive geriatric assessment (CGA) which can identify impairments and gaps that may contribute to vulnerability and adverse outcomes. The ability to identify patients that are fit, pre-frail or frail is of paramount importance as we do not want to short-change our older cancer patients. The correct identification of this group of vulnerable patients will enable the oncologist to use a non-intensive regimen and avoid excessive toxicity whilst the patient can still enjoy a stable quality of life (QoL). We aim to develop an artificial intelligence (AI) model based on machine learning (ML) algorithms to assess the medical fitness of geriatric oncology patients as a replacement to the traditional CGA. This AI model will be designed to perform at least, as well as current CGA tool but utilising significantly less resources in terms of manpower and time.

Can Gait Parameters Obtained Through 3D-printed Smart Insole/Footwear Predict Mild Cognitive Impairment?

Principal Investigator	Reshma Aziz Merchant
PI Primary Affiliation	National University of Singapore (NUS)
Co-Investigator(s)	Chia Lye Peng, Chia Lye Peng, Ho Pei

PROJECT DESCRIPTION

By 2050, 135 million will be suffering from dementia and there is no cure to date. Mild cognitive impairment (MCI) is a transitional phase of cognitive decline between normal aging and dementia, and a known precursor of dementia. MCI is prevalent in 20-30% of adults where more than 60% of the individuals will progress to dementia in their lifetimes. While dementia may be irreversible, progression of MCI to dementia can be delayed or prevented through lifestyle modification such as diet, exercise, lifelong learning, hearing and vision restoration and chronic disease management.

Gait and cognition share a common neural pathway, and any neurodegenerative processes will affect both simultaneously. The crux of our idea is to assess gait and balance variability for healthy and those with MCI through smart 3D-printed insole/footwear with an embedded pressure sensor layer. Identification of these signature hallmarks may enable early identification of those at risk, and with appropriate preventive efforts, possibility of preventing or delaying the onset of dementia.

While it is known that gait speed decline can precede dementia by 10 years, progression of gait pattern and balance changes in older adults with MCI has been under investigated. The personalised 3D-printed smart insole/footwear has the potential to be used at population level for early identification of MCI, and other related conditions such as frailty and sarcopenia where all are precursors for dementia and disability. Our hypothesis being MCI and healthy controls can be differentiated through gait pattern variability and postural control.

Cross-species drug screening for sarcopenia

Principal Investigator	Tang Hong-Wen
PI Primary Affiliation	Duke-NUS Medical School
Co-Investigator(s)	None

PROJECT DESCRIPTION

Sarcopenia, as characterized by the progressive decline in muscle mass, function and quality, commonly occurs with aging and is associated with increased risks of falls, morbidity, and mortality. Increased aging populations, coupled with the adverse effects of sarcopenia, further underscores the importance of identifying therapeutics to prevent muscle weakness. Age-related loss of skeletal muscle mass and strength is associated with the progressive accumulation of protein aggregates, and alleviation of protein aggregates has been shown to improve lifespan. To identify potential inhibitors against sarcopenia in vivo, we will 1.) screen compounds with therapeutic potential in sarcopenia by using the Drosophila as an in vivo drug screening tool, followed by verifications in mice; and 2.) functionally characterize the effect of candidate drugs in mice. Our results will establish a new drug screening platform for sarcopenia combining two model systems, Drosophila and mice. Drosophila is an efficient and effective animal model for large-scale drug screens. Subsequent verification and characterization in mice and mouse myocytes can further confirm that the candidate drugs apply to mammals. Together, our cross-species drug screening approach will provide a genetic and mechanistic basis for sarcopenia and contribute to an effective treatment for sarcopenia patients.

Developing modelling infrastructure to establish the population at risk of frailty and the effectiveness of nationwide interventions until 2050

Principal Investigator	Borame Sue Lee Dickens
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PI Primary Affiliation	National University Singapore (NUS)
Co-Investigator(s)	Alexander Richard Cook, Ken Wei Tan, Tan Ken Wei

PROJECT DESCRIPTION

The aim of this study is to create an individual based model designed to test the efficacy of interventions which reduce frailty among older individuals, including resistance-based exercise, nutrition supplementation and hormone supplementation, which can allow for small scale studies to be tested at a national scale to ascertain health burden savings. The model utilises censuses and clinical cohort data to establish risk factors and scale up estimations for the whole population. At the base, we already have a model framework called DEMOS, which operates as a synthetic yet realistic representation of Singapore's population in terms of its sociodemographics, epidemiology, behaviour and environmental heterogeneities. We will build on this to incorporate frailty with a greater focus on the wellbeing of the older population where different suites of interventions will be applied. Similar efforts have been conducted for other public health problems spanning both the infectious and chronic disease domains, exploring the effects of interventions at a national scale. The project is therefore feasible and able to be successfully carried out as the core team members have a wealth of experience in the creation of such individual based models. The scientific merits of this project are in its novelty, as individual based modelling with frailty interventions have not yet been carried out for an ageing population, and its potential to be carried out for more ageing related illnesses and in other locations outside of Singapore.

Development of a personalized medicine strategy for age-related macular degeneration (AMD) therapeutic

Principal Investigator	Simon Nusinovi
PI Primary Affiliation	Singapore Eye Research Institute
Co-Investigator(s)	Tham Yih Chung, Zhou Lei, Teo Yi Chong Kelvin

PROJECT DESCRIPTION

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the elderly, yet treatments are lacking. Statin has been thought to be of possible interest for AMD therapeutic, however, studies have shown discrepant results. Therefore, this question does not have yet a clear answer despite the important clinical implications. Based on recent findings regarding the pathophysiology of the disease, we hypothesize that the effect of statin on the risk of AMD depends on the genetic characteristics. Preliminary analyses conducted in the Singapore Epidemiology of Eye Diseases (SEED) cohort indicated that the effect of statin medication could vary according to a gene. In this grant, we first propose to replicate these analyses in two external cohorts (Australia and Ireland). Secondly, we will measure the levels of proteins coded by the gene previously identified. This will allow us to investigate the underlying biological mechanisms. If successful, this will open up the avenue for a possible personalized AMD treatment based on genotype profile.

Nanoscale Nuclear Patterning to Detect Nuclear Envelope Remodeling During Skin Cell Aging

Principal Investigator	Wenting Zhao, PhD Assistant Professor (Appear as Dr. Wenting Zhao)
PI Primary Affiliation	Nanyang Technological University, Singapore

Co-Investigator(s)	Oliver Dreesen Isabella Saggio,
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PROJECT DESCRIPTION

A significant hallmark of aging is the deterioration of the nucleus in cells. A better understanding of how aging-related genetic and epigenetic alterations is triggered by or leads to the physically mis-organized nuclear morphology is important for the discovery and evaluation of anti-aging therapeutics. However, a reliable and quantitative detection of the abnormal nuclear morphology is technically challenging. Here, we propose to introduce nanofabrication-enabled nuclear patterning to quantify abnormal nucleus in aged and senescent cells. The success of this proposal will establish nanostructure-based nuclear patterning as a new strategy to detect cellular aging and open a new angle to develop anti-aging therapeutics.

Peptide-based eye drop as non-invasive treatment of age-related macular degeneration (AMD)

Principal Investigator	Wenqian Chen
PI Primary Affiliation	National University of Singapore
Co-Investigator(s)	Lakshminarayanan Rajamani

PROJECT DESCRIPTION

This project develops the first topical non-invasive formulation (in the form of eye drop) to treat age-related macular degeneration (AMD), which is one of the major causes of avoidable blindness for people aged 50 and above, affecting 1.8 million people per year globally. New therapeutics are needed urgently to address the challenges faced by the current anti-VEGF therapy, namely low patient compliance to the monthly intravitreal injection for a prolonged period, and limited efficacy (i.e. 30-50% of patients do not respond or have poor response, while ~51% of patients still have active disease after 2 years). Our eye drop is based on the therapeutic peptide developed by the co-investigator, A/P Rajamani Lakshminarayanan that has shown effective inhibition of multiple angiogenesis pathways in mice. This therapeutic peptide is modified in the current project to be multi-targeting long-acting, cell penetrating and highly bioavailability to achieve better sequela. The composition of the eye drop is optimised to prolong the storage stability at temperatures that can be conveniently achieved in normal households (i.e. 4 - 25 °C).

Reducing Inflammatory Syndrome In Surgery - Colorectal (RISIS-CR) Trial

Principal Investigator	Ti Lian Kah
PI Primary Affiliation	National University Hospital (NUH)
Co-Investigator(s)	Loh Ne-Hooi Will, Sophia Chew Tsong Huey, Tan Ker Kan, Andrea Britta Maier

PROJECT DESCRIPTION

After 60 years of age, our immune system dramatically changes in a process called “immunosenescence”. In some of us, we gradually lose the ability to fight infections and our wounds take longer to heal. Conversely in others, the immune system is over-active. In surgery, the immune response is essential to help fight off infections and promote wound healing. However, the immune system cannot differentiate surgery (ideally eliciting a modest response) from infections and cancer, which produces an exaggerated response that can potentially damage organs and slow recovery. In patients undergoing colorectal cancer surgery, an exaggerated immune response increases the risk of infection and failure of the intestine to heal.

We intend to recruit 80 patients scheduled to undergo surgery for colorectal cancer and test their blood to see if they are likely to have this exaggerated immune response. If they are, we will then randomize them to receive

either a supplement that reduces the immune response or placebo before surgery. We will measure their immune response after surgery using biomarkers. With this, we hope to show that by identifying the patients at risk of an exaggerated immune response, we can selectively treat them and prevent this potentially harmful response.

Screening for therapeutic targets of NOTCH2NLC gene non-coding CGG repeat expansions associated neurodegeneration

Principal Investigator	Zhou Zhi Dong
PI Primary Affiliation	National Neuroscience Institute (NNI)
Co-Investigator(s)	Tan Eng King

PROJECT DESCRIPTION

Recently, pathogenic non-coding CGG repeat expansions in the neuroblastoma breakpoint family member 19/ notch 2 N-terminal like C (NOTCH2NLC) gene are found to be the cause of Neuronal Intranuclear Inclusion Disease (NIID). Furthermore the non-coding CGG repeat expansions in the NOTCH2NLC gene can be the pathogenic factor of comprehensive neurodegenerative conditions, including dementia and Parkinsonism. However, the pathophysiological mechanism of non-coding CGG repeat expansion diseases remains to be elucidated. No therapeutic targets have been identified and no therapies have been developed. In our current study, we will perform high throughput single cell sequencing (SCS) of neurons from transgenic (Tg) NOTCH2NLC gene CGG expansion mice to search for therapeutic targets of non-coding CGG expansion associated neurodegeneration. SCS analysis of transcriptome (mRNA sequencing, scRNA-seq), translome (ribosome profiling sequencing, scRibo-seq) and methylome (epigenetic sequencing, scMT-seq) will be performed. Potential therapeutic target identified from SCS study will be further validated in our NOTCH2NLC gene CGG expansion patient cells derived human neuron models. Our study aims to enhance clinical diagnosis, treatment and prognosis assessment of CGG expansion neurodegeneration and finally improve our life quality.

Variable Stiffness Wrist Brace for Parkinson's Tremor Suppression

Principal Investigator	Wang Yifan
PI Primary Affiliation	Nanyang Technological University
Co-Investigator(s)	Chung Lau Ha, Wei Tech Ang

PROJECT DESCRIPTION

In Singapore, three out of every 1000 individuals aged 50 and above have Parkinson's disease (PD). This number is expected to go up with the rapidly ageing population. Statistically, about 80% of PD patients suffer from tremor, which is manifested by unconscious shaking of the hands or arms at rest and is aggravated during emotional stress. In this proposal, we present a novel wrist brace to suppress hand tremors for PD. The brace is composed of a 3D printed fabric with variable stiffness which can be controlled by pneumatic pressure. In the soft state, the brace offers very little resistance to the daily movements of their wrist. When the embedded sensors detect shaking movements, the brace rapidly stiffens and provides additional damping to the wrist, thus suppressing the tremor. Then, the patient's normal activity can be performed.