

HEALTHY LONGEVITY GLOBAL COMPETITION

2021 Catalyst Awardees

Sponsor: Ministry of Health of Singapore

A molecular prevention strategy for cancer-free ageing

Principal Investigator	Prof Kanaga Sabapathy
PI Primary Affiliation	National Cancer Centre Singapore
Co-Investigator(s)	Prof Suresh Mathivanan

PROJECT DESCRIPTION

Ageing results in increased propensity for cancer development, due to the accumulation of mutations over the life-time. Not surprisingly, cancer incidence is on the rise globally. If left unchecked, the outlook is dismal. Treatment modalities alone will be insufficient to tackle the impending “cancer tsunami”. This proposal is therefore driven by the need of the hour, and is aimed at establishing the concept of “molecular cancer prevention” to reduce cancer incidence in the ageing population. It is based on the idea of enhancing one’s own tumor-suppression mechanisms to prevent damaged cells from turning malignant. p53 is the master tumor-suppressor gene that prevents cancer development. Using mice expressing additional p53, we have shown that elevating p53 levels can indeed significantly delay the development of cancers. To translate these initial findings, we are proposing to provide exogenous p53 using extracellular vesicles (EVs) that we have developed, to increase an individual’s tumor-suppression capabilities. This, in essence, constitutes a prophylaxis model whereby the exogenous p53 will enhance the body’s vigilance against cancers. We will evaluate the efficacy of the p53EVs for their ability to induce a p53 response, establishing the proof-of-concept for a molecular cancer prevention strategy to keep the aged cancer-free.

Advocating CPAP for Taxi drivers to Improve Vigilance and Employability (ACTIVE)

Principal Investigator	Chi-Hang Lee
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PROJECT DESCRIPTION

There has been an increasing number of elderly taxi drivers in Singapore. Elderly people are more likely to suffer from obstructive sleep apnoea (OSA) which is a common cause of malaise and sleepiness. We believe treatment for taxi drivers with OSA will improve their sleep quality and vigilance. This will in turn improve road safety. This approach replaces punishment-based accident preventive measures with prevention.

ACTIVE (Advocating CPAP for Taxi drivers to Improve Vigilance and Employability) is an applied science project to improve attention and blood pressure of taxi drivers. A total of 50 taxi drivers above the age of 60 will be recruited for a sleep study. We estimate that 60% of the taxi drivers (n=30) will be eligible for OSA treatment, and CPAP therapy will be provided for a duration of 6 months. During the 6-month study period, they will be under the care of an accredited sleep specialist. The taxi drivers are encouraged to continue using the CPAP after the 6-month study period.

AI and Healthy Ageing: Developing AI-based Computational Framework and Approaches to Define Healthy Ageing in the Singapore Longitudinal Ageing Study (SLAS) Cohort

Principal Investigator	Dr. ZHONG Xin
PI Primary Affiliation	Institute of High Performance Computing
Co-Investigator(s)	Dr. YANG Feng (Ph.D. Senior Scientist, Co-Innovation Lead for Knowledge-driven AI, Computing & Intelligence Department, Institute of High Performance Computing, A*STAR) Assoc Prof NG Tze Pin MBBS (S'pore), PhD, FAFOEM (Australia), FAMS (OM), MFPHM (Public Health) (UK) Associate Professorial Fellow & Research Director, Department of Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore)

PROJECT DESCRIPTION

The improvements of the health care systems, wealth, and major advances in medical sciences leads to extended human lifespan. The current challenge is the increasing number of elderly visiting healthcare institutions. Older adults are expected to prolong their healthspan and maintain the productivity. As 70% of the older population is living in the community, we are greatly promoting ageing-in-place in Singapore. However, poor understanding of healthy ageing may plague efficient health program/service designs. We aim to develop AI-based computational framework and approaches to help formulate novel ways of defining healthy ageing in the Singapore Longitudinal Ageing Study (SLAS) Cohort. Our hypothesis is that healthy elderly will display specific determinants from non-healthy agers and that gradation of determinants will follow the progression of age-related conditions. Our data already possesses more than 10 years longitudinal samples from elderly Singaporean (n>3000; 55-94 years), including nutritional, socio-economic, cognitive, physical, medical history, lifestyle, activities, medication, hospitalization, comorbidities, frailty, mortality which would allow the most meaningful study of Asian elderly. In contrast to traditional theory-based and hypotheses-driven approaches, the AI-based approaches are innovative by selecting markers and predicting health outcomes without any prior assumptions in a train-test manner to formulate novel phenotypes of healthy ageing.

Community Based and Participant-led Initiatives to Increase Civic Engagement Among Older Adults

Principal Investigator	Professor Paulin Straughan
PI Primary Affiliation	Singapore Management University
Co-Investigator(s)	Associate Professor William Tov

PROJECT DESCRIPTION

This proposal adopts an asset-based approach to enabling civic engagement among older adults in Singapore by positioning them as both the drivers and beneficiaries of ground-up initiatives aimed at keeping older adults integrated in their communities. It is hypothesized that such an intervention will improve overall well-being for older adults based on findings from the Singapore Life Panel® (SLP). A pilot program is proposed to assess the efficacy of such an approach. 50 older adult residents of an estate will participate by developing and implementing various initiatives in their community under the broad themes of 'rediscovering Singapore', 'cultural exchanges', 'volunteering', 'physical activities', and 'collective purchasing initiatives'. The themes are targeted at specific quadrants of well-being (economic, social, psychological, and physical). We will conduct pre and post intervention surveys to track the overall well-being. If successful, the project will be proposed to be run in additional neighbourhoods. The particular intervention model can be easily replicated in different communities across Singapore, largely due to the fact that it is a community driven initiative and can be easily adapted.

Conglomerating the Effects of Physical Activity on Cardiovascular Longevity in Ageing

Principal Investigator	ANGELA KOH SU-MEI
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PROJECT DESCRIPTION

Physical activity is frequently prescribed as an important lifestyle modifier that promotes health and well-being. Among older adults, activity promotes muscle strength and overall fitness. However, ageing is associated with complex changes in bodily structure such as reduction in muscle mass and altered metabolism. These changes imply that measurements of body mass index (BMI), for instance, are inadequate for assessing response to physical activity. We have found that circulating metabolite markers in the blood may represent the sum of activity and ageing processes among older adults. In this study, we propose to advance this finding by measuring the changes in metabolite markers in relation to cardiovascular ageing health outcomes, in comparison to traditional targets such as BMI. This proposal will provide new targets for physical activity outcomes in promoting healthy longevity.

Development of miobiotics to maintain healthy ageing gut microbiota

Principal Investigator	Guan Shou Ping
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PROJECT DESCRIPTION

The human gut consists of both good bacteria that provide nutrients from indigestible sources and bad bacteria, which could lead to inflammatory and various disease states. The number of bad bacteria, however, increases as we age, leading to chronic low-level inflammation and age-related diseases. Both probiotics and prebiotics have been widely used to increase good bacteria, but the effect on bad bacteria is minimal. Antibiotics while effective also kill other good bacteria and select for resistant bacterial strains. To overcome these limitations, we propose to develop “miobiotics”, a novel food supplement that could specifically reduce the factor that drives the selection for bad bacteria in the ageing gut. We propose that an increase of gut urea due to ageing kidneys will preferentially select for bad bacteria, which have an energy-efficient pathway to incorporate ammonium, which is a by-product of urea breakdown. Alpha-ketoglutarate (AKG) is a safe dietary constituent that could reduce gut ammonium levels, which is a good miobiotic candidate. Hence, we propose to study the effects AKG in lowering the number of bad bacteria in both preclinical and clinical settings. The development of miobiotics could potentially improve health and productivity in ageing populations.

Enhancing cognitive reserve in the community: Exploring the effects of Sensory Environment and Playfulness on Depression and Cognition (SEPDC) among older adults

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PROJECT DESCRIPTION

In view of sensory and cognitive declines that advance with ageing, this interdisciplinary study aims to explore effects of Sensory Environment and Playfulness on Depression and Cognition (SEPDC) among older adults, and their capacity to enhance cognitive reserve in the community. While sensory environment refers to capacity to engage through all environmental stimuli, playfulness is the tendency to engage in play, a personality trait that enables people to render activities as playful. Our hypothesis is that sensory environment and playfulness are valuable interrelated mechanisms to reduce depression and cognitive decline.

This study employs quantitative survey and path analysis to examine direct and indirect effects of exposure (sensory environment, playfulness) on outcome variables (self-rated memory, cognition) through intermediates (depression, loneliness). Cross-sectional surveys will be conducted in 20 public housing neighbourhoods in Singapore, involving 400-500 participants. Additional verification study with 20 representative participants will include biospecimen collection (saliva to measure interleukin levels as indicators of stress and depression) and eye-tracking data (associated with mild cognitive impairment, personal traits, emotional arousal, etc.).

Establishing the empirical validity of these pathways in the population will identify the relevant focal variable(s) for intervention development, which will be piloted and tested in the future.

Gamification in eHealth intervention to enhance learning and self-care management for post-stroke care

Principal Investigator	Associate Professor Elaine Siow Kee Chen
PI Primary Affiliation	Singapore Institute of Technology
Co-Investigator(s)	▪ Professor Alan Wong, SIT ▪ Ms Jade Soh Gek Sang, SIT ▪ Dr Jocelyn Koh Mei Lin, AMK-THKH ▪ Associate Professor Jeannie Lee Su Ann, SIT ▪ Dr David Tan Wee Lit, AMK-THKH ▪ Associate Professor Agnes Xue Lishan, SIT ▪ Associate Professor Yar Kar Peo, SIT ▪ Dr Loh Yong Joo, TTSH ▪ Ms Lam Siu Lin June, AMK-THKH ▪ Ms Sathya Sambandam, AMK-THKH

PROJECT DESCRIPTION

Gamification is the method of applying game elements to motivate people to engage in targeted behaviors. There is limited application of gamified electronic health (eHealth) for stroke care to enhance learning and self-care management. The use of novel approaches to enhance learning and self-care management may help promote healthy living and aging among stroke survivors. Informal caregivers make important contributions by promoting self-care management to stroke survivors. When stroke survivors and informal caregivers are more knowledgeable about stroke care, the self-care management by stroke survivors will be more effective. The stroke survivors' quality of life can be enhanced by preventing the complications associated with stroke through the early recognition and prompt response of stroke symptoms. We plan to conduct a mixed-methods study. Eligible stroke survivor and caregiver dyads will be recruited to use the eHealth intervention for one month in a community hospital. Quantitative data will be collected at the time of hospital discharge. Qualitative data and usage statistics will be collected one-month after hospital discharge to explore how users are adapting at home. The study findings may inform how stroke survivors can be reintegrated back to the community using innovative approaches in stroke care education.

Gamified fitness for healthy living

Principal Investigator	Yeo Joo Chuan
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PROJECT DESCRIPTION

Sedentary lifestyle is the major risk factor for non-communicable diseases. While member states of World Health Organization have agreed to a 10% relative reduction in the prevalence of insufficient physical activity by 2025, recent survey has shown that this target is unlikely to be met. A key reason for the physical inactivity is owing to the lack of motivation to adhere to sustained workouts. To overcome this, we propose a gamified fitness programme that utilizes a smart sleeve to monitor joint movement and muscle activity. We believe that the feedback of the fitness profile will ensure higher user engagement and adoption.

Healthy living through personalized monitoring of eyelid care

Principal Investigator	Professor Louis Tong
PI Primary Affiliation	Singapore Eye Research Institute
Co-Investigator(s)	Dr Ong Wai Sing, Ngee Ann Polytechnic

PROJECT DESCRIPTION

A lot of people with dry eye have significant discomfort, healthcare spending and time off work. A lot of this dry eye can be improved by unblocking the eyelid oil glands through daily eyelid warming. However, it is difficult to ensure that this is done. We use a method of digital monitoring that helps people to remember to do this preventive measure, even to be motivated through other linked incentives

Identification of microRNA biomarkers in women predictive of reproductive senescence and longevity

Principal Investigator	Huang Zhongwei
PI Primary Affiliation	National University Hospital (NUH)
Co-Investigator(s)	Cheong Jit Kong PhD, Department of Biochemistry, Precision Medicine Programme and NUS Centre for Cancer Research, Yong Loo Lin School of Medicine, National University of Singapore

PROJECT DESCRIPTION

Infertility affects ~15% of Singapore's population. The number of couples in Singapore seeking assisted reproductive technology (ART) to help them conceive more than doubled from 2005-2013. With the median age at first marriage and first birth rising, demand for ART treatment is set to increase but ART success rate hovers around 30–40%; it rapidly drops with increasing maternal age due to the inevitable decrease in oocyte numbers and quality. Yet, effective therapeutics to combat reproductive ageing in woman is sorely lacking. In current clinical practice, a woman's reproductive lifespan and health-span is only determined by her age and one serum ovarian reserve marker, Anti-mullerian hormone (AMH), which is far from ideal. We thus hypothesise that miRNAs can be accurately quantified in follicular fluid and cumulus/granulosa cells and these molecular footprints coupled with the woman's demographic characteristics can be used together to build a framework, via machine learning, to provide predictive power to infer true ovarian age and oocyte quality that will inform

accurately on reproductive senescence. Having a robust predictive framework, based on accurate miRNA expression profiling, will aid clinicians in their decision-making process, allowing a precise, holistic and robust assessment of a woman's true reproductive potential and longevity.

Laser spatiotemporal photoplethysmogram and computational method for extended chronic cardiometabolic therapeutic care

Principal Investigator	Dr. Eddie NG Yin-Kwee
PI Primary Affiliation	Nanyang Technological University
Co-Investigator(s)	Dr. Bi Renzhe Dr. Huang Weiting, MBBS, MRCP, MMed, MCI, NHCS Dr. Ee Ying Hui Dina, MBBS, MRCP, NUHS Dr. Ken Lee, PhD, NTU Mark Wong Kei Fong, B.Eng. NTU Dr. Suchitra Kataria, MD, MBBS, Salveo-Therapeutics Dr. Tan Hong Chang, MBBS, MRCP, MMed, MCI, SGH

PROJECT DESCRIPTION

Sensors in modern smartwatches and fitness trackers can measure resting heartrate, which has proven to be an important indicator of cardiovascular health. Unfortunately, the absence of sufficient computational power to analyze biosignal waveforms in situ on a wearable prevents the full potential of wearables to be realized for clinical applications. Today, 25% of adults suffer from hypertension and associated secondary pathologies, and by 2050, Singapore projects that there will be 1 million sufferers of diabetes, accounting for 10% of the disease burden in Singapore. This problem is especially pertinent in our aging population. Unfortunately, today's blood pressure and blood glucose meters are obtrusive and inconvenient, leading to poor compliance and resurgence of the disease in chronic sufferers. In previous work, we have accomplished Blood Pressure (BP) and Blood Glucose Level (BGL) estimation without the compressing the arm or blood sampling with a novel sensor and signal computing method. Although our technology provides good assessment of BP and BGL changes, this novel modality has not yet been validated on everyday individual lifestyles and the goal of this proposal is to enhance our existing technology for everyday use.

Novel AI-driven ageing biomarker based on retinal photos for mortality risk stratification

Principal Investigator	Professor Ching-Yu Cheng
PI Primary Affiliation	Singapore Eye Research Institute
Co-Investigator(s)	Assistant Prof. Tyler Hyungtaek Rim, MD, PhD, MBA Assistant Prof. Yih Chung Tham, PhD Dr. Simon Nusinovici, PhD Dr. Xinxing Xu, PhD (Institute of High Performance Computing, A*STAR, Singapore; Adjunct Assistant Prof., Duke-NUS Medical School)

PROJECT DESCRIPTION

Globally, the number of persons aged 80 years or over is projected to increase more than threefold in the next 30 years. This aging population is likely to result in an increased burden of cardiovascular and chronic diseases with significant healthcare associated costs. In this context, early identification of individuals at risk of dying from these diseases would allow early health interventions such as lifestyle modifications. The retina of our eyes represents a unique window into the systemic health status and is amenable to rapid non-invasive imaging. We

propose to develop a novel aging biomarker predicted from retinal photographs via artificial intelligence. This aging biomarker may capture physiological changes associated with aging process in human bodies and thus can help identifying people who have a higher risk of mortality. Recent advances in artificial intelligence technologies provide opportunities to extract relevant information from the retinal photographs to estimate this new aging biomarker. This project thus aims to develop an easily accessible screening tool to help early identify individuals with a faster physiological deterioration, possibly leading to diseases and mortality.

Systematic identification and functional analysis of synergistic small molecule combinations targeting aging

Principal Investigator	Dr. Mohammad Alfatah
PI Primary Affiliation	Bioinformatics Institute
Co-Investigator(s)	Dr. Frank Eisenhaber

PROJECT DESCRIPTION

The world's aging population is growing dramatically. Aging is associated with progressive degeneration of physiological integrity, impaired morphological and essential functions. Most importantly, aging is the major risk factor for chronic diseases, including cancer, diabetes, cardiovascular and neurodegeneration. The prevalence of age-related diseases affect life quality and threaten a wide range of sectors, such as health care systems and economic growth. We will identify small molecules, both drugs and natural products that target aging. Since aging is controlled by many biological processes, we will identify small molecule combinations that simultaneously target different aging processes. We will identify synergistic combinations targeting aging for effective therapy to increase the healthy lifespan. We will develop a novel "Pair to Pool" (PTP) high-throughput method to identify the small molecule combinations. We will screen small molecules in budding yeast *Saccharomyces cerevisiae* which is the powerful model system to identify interventions for human post-mitotic cells aging. We will perform functional profiling to identify the mechanism of synergy. We will validate anti-aging effect of synergistic combinations in human cell lines. This project will provide effective anti-aging synergistic combinations and may uncover hitherto uncharacterized genes functions, which is an important goal to understand the biology of complex aging.

Targeting SPTLC3-generated d16:1 sphingolipids for healthspan extension

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PROJECT DESCRIPTION

Age is the single most important factor that predicts risk of death due to diseases such as cancer, diabetes, and dementia. However, current medical approaches are designed to treat diseases after they have occurred, without addressing the underlying inflammatory processes that increase with age and lead to the disease state. We have identified a metabolic process that changes with age and is responsible for regulating chronic

inflammation. We will evaluate this process to determine whether modulating this metabolic pathway can slow age-related decline.