

MEDIA RELEASE

Prolonging healthspan by delaying ageing -- NUHS opens Singapore's first Centre for Healthy Longevity to increase healthy lifespan of Singapore population by five more disease-free years

The National University Health System (NUHS) establishes the NUHS Centre for Healthy Longevity – a world's first integrated pre-clinical and clinical ageing research institute that is poised to lead the Longevity Medicine field with clinical research to prolong healthspan by delay ageing.

- The NUHS Centre for Healthy Longevity (NUHS CHL) will initiate, for the first time in a South-East Asian population, clinical research based on 'longevity medicine' or 'geroscience' to target the biggest risk factor for chronic disease, namely, biological age.
- The Centre will focus on key geroscience projects, and develop and validate ageing 'clocks' in the Singapore population, and to test the efficacies of novel geroprotectors in delaying biological ageing and enhancing healthspan.
- The Centre will develop an integrative pre-clinical laboratory model and clinical human research pipeline that focuses on identifying, and treating biological hallmarks of disease.
- Lien Foundation gifts S\$5 million to the Centre's research partner, the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), for these research efforts.

Singapore, 7 September 2022 – Ageing is the climate change in medical science, where global societies are experiencing a sharp rise in the number of older adults relative to the rest of the population. Singapore will be the fastest country by 2025, with 25% of its population estimated to be above 65 years old by 2030. Although medical advancement has improved life expectancy among Singaporeans by 8.7 years to 84.8 years, one of the longest in the world; our healthy life expectancy, or healthspan, increased by only 7.2 years to 74.2 years. The grim reality is that Singaporeans are spending about 10 years of their twilight years in poor health. As the gap between life expectancy and health adjusted life expectancy increases, healthcare and caregiving costs will represent an unsustainable socioeconomic burden for society.

2 NUHS CHL has one clear mission: *to enhance healthspan by five years in the Singapore population by slowing biological ageing*. Its strategy is to embark on geroscience and longevity medicine-based approaches to achieve this mission. Geroscience and longevity medicine are paradigm-shifting concepts in research and medicine, that acknowledge species-conserved pathways of biological ageing, and view biological ageing as the greatest risk factor for chronic, age-related diseases. Proponents of geroscience/ longevity medicine also advocate the implementation of the use of biomarkers and interventions with the use of artificial intelligence to enhance healthspan.

3 Pre-clinical model organisms have traditionally been used in early pharmaceutical trials, but do not always translate successfully to human trials. NUHS CHL will use age-appropriate models for discovering mechanistic pathways that respond well to novel interventions, called geroprotectors. These treatments will then be translated into clinical human studies of CHL. Both clinical and pre-clinical divisions in the centre work iteratively to identify, refine and implement promising geroprotectors. The South-East Asian population has been traditionally understudied in clinical research. With the three major races, Chinese, Malay and Indian, numbering about 2.5 billion people and accounting for more than a quarter of humanity, results gleaned from the CHL's research will have significant global impact, particularly in Asia.

4 NUHS CHL is also the clinical and translational partner of the Healthy Longevity Translational Research Programme (TRP) at NUS Medicine, whose research to slow ageing, and improve healthspan for the broader population has received generous funding (\$5 million) from the Lien Foundation. Termed 'Hacking Ageing', the research initiative comprises three broad themes, which will contribute to the creation of an integrated biomarker-artificial-intelligence (AI) platform that will be the

world's first in testing supplements and repurposed drugs combined with lifestyle interventions in the Asian population. This will allow for better early detection, risk stratification and development of personalised, preventive and therapeutic strategies to improve healthspan. Lee Poh Wah, CEO, Lien Foundation said, "Through the 'Hacking Ageing' initiatives, we hope to contribute to the national agenda to shift the healthcare paradigm from the present state of reactive 'sick care' towards a population health prevention approach. Socioeconomic factors are often at the root of health inequalities. As a society, we have a moral duty to ensure anti-ageing therapeutics are not confined to the realm of the rich and exacerbate existing disparities. Developing biomarkers and interventions that are accessible to all in the community, is necessary towards narrowing this gap and democratising healthy longevity. A takeaway from our Gym Tonic programme is that seniors want, and can, get strong on their own terms. Healthspan encompasses not just the physical but the cognitive and emotional dimensions too. We need to mainstream longevity science, and arm everyone with the knowledge and tools to extend the period of life spent in good health."

5 The first research theme funded under the 'Hacking Ageing' initiative is a series of clinical studies to test novel nutritional supplements and repurposed drugs to slow ageing in middle-aged adults (40-60 years). The second research theme is to use deep omics data to personalise these supplements and repurposed drugs and other interventions for optimal healthspan extension in middle-aged participants. The third research theme focuses on extending healthspan in older adults through strength training exercise, harnessing the Foundation's Gym Tonic community of seniors.

6 Professor Brian Kennedy, internationally recognised for his research into the biology of ageing and for his work to translate research discoveries into new ways of delaying, detecting, and preventing human ageing and its associated diseases, is helming the Centre with co-director, Professor Andrea Maier, an internal medicine specialist renowned for translational research in ageing and age-related diseases diagnostics and pharmacological and non-pharmacological interventions in ageing humans. The 1,600 square feet Centre for Healthy Longevity (CHL) located at Alexandra Hospital, will conduct trials and execute validation studies with healthy participants from the age of 30 years. The Centre will also develop and test these interventions using newly identified biomarkers of human ageing. Once approaches are validated, the Centre will develop strategies that integrate a combination of nutritional and exercise approaches together with supplements and (repurposed) drugs for personalised adoption in the Singapore population. The ultimate goal is to bring the individual closer to his/her state of optimal peak performance during the entire lifespan (e.g. screening to start from 30 years of age).

7 CHL will be looking at blood-based biomarkers, probably the most investigated group due to a large amount of data accumulated in clinical trials.

- Genetic markers, meanwhile, reflect predispositions to certain ageing phenotypes, characterised by the prevalence of specific pathological processes and age-related diseases.
- One biomarker CHL is looking at is DNA methylation or a DNA methylation "clock", which measures the degree of chemical modification in the human genome to predict biological age.
- CHL is also measuring ageing using inflammation markers, metabolomics, and other novel parameters like facial ageing analysis.

8 "The hundred year life may well be the norm for children born in developed countries, if the current trends continue. Such a development will fundamentally change societies and how we individually lead our lives. What matters more than absolute longevity, is whether we live actively, age purposefully, and stay in relative good health. Healthy longevity ensures that the additional years are a boon, rather than a grim millstone of disease burden and fiscal cost. This is particularly salient for Singapore and many parts of the world, where our populations are rapidly ageing. The new NUHS Centre for Healthy Longevity has much to contribute. You have set yourselves an ambitious mission to enhance healthspan by five years in Singapore by slowing ageing. I look forward to your ground breaking research work on geroscience and longevity medicine, which can be a valuable contribution not just for Singapore but the world. I am also glad that Lien Foundation has generously supported this cause. Together, we can turn ageing into a positive force and enable seniors to age gracefully", said Deputy Prime Minister and Coordinating Minister for Economic Policies, Mr Heng Swee Keat on the opening of CHL.

9 “Developing new interventions to slow ageing and developing new biomarkers to measure ageing, are what we are trying to do here in Singapore through the new Centre,” says Prof Kennedy, “and then, we can recommend inventions to see if they can slowly reverse aspects of ageing in the Asian population.” Co-director, Professor Andrea Maier added, “The body’s ability to fight diseases reduces dramatically with age. If we can address the physiological changes of ageing, we may be able to slow or stop the onset of disease. In three to five years, healthy longevity will not only exist as a lab-proven concept, but will become part of everyone’s life.”

She elaborated, “The aim of geroscience is to prevent age-related diseases like the occurrence of dementia, cancer, lung diseases, osteoarthritis or sarcopenia, all the diseases we know of. So next time, tell your GP, your biological age, not your chronological age, for a more targeted, customised and precise prognosis and treatment or intervention plan. This also gives the physician a better association with risk of outcomes one will not want to have like impairment and death.”

Anyone who is keen to participate in the above various studies can contact healthy_longevity@nus.edu.sg for more information.

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Three Participant Profiles:

Mr Kelvin Lee, 32, a microbiology student and tutor with a BMI of 29, is slightly obese and exercises once a week. He loves his food, especially meat. He has witnessed premature deaths, ahead of time, for his loved ones. He participated in NUHS CHL’s research studies on biological vs. chronological ageing tests, in order to ‘*contribute in his small way to humanity and help scientists crack the code of how to live healthier lifespans, earlier and for longer.*’

Ms Suzana Binte Abou Bakar, 56, is an operations manager. A participant of the Centre’s ABIOS study, ‘*I want to see if what I have now in my regime is sufficient? Are there any changes I should make to my lifestyle and diet, nutrition, exercise, so that I can prevent illnesses early enough to find remedy, and reduce my exposure to genetic diseases.*’ Seeing family members and loved ones suffer from chronic conditions at young ages and a younger brother who had passed away from cancer, Suzana hopes to be more prepared financially, psychologically and mentally with early intervention.

Another participant is **Mr Roslan Bin Maarof**, 55, in IT sector, who suffers from high cholesterol. He is keenly aware that ‘*in a high-strung stressed society, people are getting sick sooner. He takes regular long and brisk walks and hits the gym a few times a week.*’ He left his sedentary job recently and was pleased that the test said he is younger than he is. ‘*My biological age is 35. I am surprised because I am 55 experiencing the normal ageing process, with aches in joints, and I don’t really control my diet. My dad and brother had cancer and my elder brother is obese. And so I don’t know whether it will affect me eventually and whether I can change the course with an improved lifestyle. Is there anything hereditary or is this something you need to work hard to become healthy?*’ All these and more are the common questions in the minds of some 400 participants in a pilot study conducted by NUHS CHL since last year and more are asked to step forward to help in the validation.

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NUHS Centre for Healthy Longevity

The Centre for Healthy Longevity is a Centre of Excellence under the National University Health System (NUHS) and serves as the clinical and translational partner of the Healthy Longevity Translational Research Programme (TRP) at the NUS Yong Loo Lin School of Medicine.

The multi-disciplinary Centre promotes not only lifespan, but healthspan extension through the integration of research and clinical care. From identifying and developing novel biological signatures of human ageing, to conducting personalised interventions with cutting-edge technologies, the Centre's vision is to change the paradigm that ageing is immutable. By recognising and promoting a preventive health approach, society can embrace a future where older adults are empowered and continue to lead independent and vibrant lives.

About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

For more information on NUS, please visit www.nus.edu.sg.

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2022 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2022).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>

About Lien Foundation

The Lien Foundation is a Singapore philanthropic house noted for its model of radical philanthropy. It breaks new ground by investing in innovative solutions, convening strategic partnerships and catalysing action at the intersection of health and social care. In the area of eldercare, the Foundation's work has grown to encompass a number of initiatives to alleviate the care burden and maximise the period of healthy living. These include mobilising community resources to fight frailty and dementia. Gym Tonic, a strength training programme which is safe and simple to use for seniors, is available at 29 locations islandwide and has more than 3,600 active seniors. The tech-enabled programme harnesses data analytics and customises training of seniors with machine learning. IngoT Person-Centred Care is a cloud-based care management system designed to empower senior care professionals to 'know' their clients better and improve productivity. It is deployed in 12 nursing homes and close to 50 day and home care sites.

For more information, visit <https://www.lienfoundation.org/>

Annex A - Clinical Research Studies undertaken by CHL

1. ABIOS (Ageing Biomarker Study in Singaporeans)

Project ABIOS (Ageing Biomarker study in Singaporeans): a joint collaboration between NUS Healthy Longevity TRP, NUHS Centre for Healthy Longevity, Alexandra Hospital, and Peking University. The Centre is able to measure one's facial biological age using biomarker analysis where one's tissues, organs and blood reflect one's "phenotypic age", more commonly known as biological age. One's biological age is dependent on various biomarkers that can change due to lifestyle and other health factors, making it easier to determine and track one's health through stress management, maintaining a healthy diet, etc.

This study aims to see if these age-related changes are expressed differently between young, middle-aged and elderly individuals who are physically active relative to those that are sedentary, or undergoing outpatient treatment for chronic disease.

The CHL is equipped with screening tools like the DNA methylation clock, facial ageing, inflammation and metabolism clocks. These capabilities are also supported by other screening platforms which measure arterial stiffness, skin autofluorescence (a non-invasive measure of damaged molecules in the skin), body composition (skeletal muscle, bone mass and fat mass) and anthropometry – height, body weight, waist-to-hip ratio, skeletal muscle, bone mass and fat mass, functional ability, lung function test, metabolic test and ECG. So far, respondents have been recruited over the past one year into various research studies. The Centre is still seeking more participants to help with investigating molecular and physiological markers of ageing and test novel interventions involving diet, exercise and nutraceuticals to enhance health span.

2. A community trial under Hacking Ageing initiatives funded by the Lien Foundation. Large-scale Community-based Observation and Intervention: To determine how Gym Tonic affects healthspan and biological age in elderly citizens. This project has two areas of focus: First, a retrospective study to analyze the existing database of up to 4,000 older participants (65 years old and above) that had undergone Gym Tonic since inception, to determine the extent of improvement in health outcomes. Second, a prospective cohort of 80 senior participants (65 years and above) over 9 months that will undergo the program. The primary outcomes will be the same as the retrospective study, with the addition of more comprehensive health and biomarker screening.

3. RESTORE (Rejuvenating Senescent Traits in Older Singaporeans through Regular Exercise)

Project RESTORE (Rejuvenating Senescent Traits in Older Singaporeans through Regular Exercise): a collaboration between NUS Healthy Longevity TRP, NUHS Centre for Healthy Longevity, Sport SG, Peking University and GERO LLC.

Age-related changes can be measured at the molecular and cellular levels. Through facial biological age and arterial stiffness and biological ageing signature, according to how many minutes of physical activity a person carries out per week.

This study aims to uncover how lifestyle, especially regular physical activity and healthy diet affect how one ages for a sustainable healthcare system. The Centre wants to discover how age-related health problems can be reduced when people practise healthier lifestyle choices before they reach old age. A person who is 70 years old and leading a healthy lifestyle may have the same biological age as a 45-year old person leading a poor lifestyle.

3. Project ABLE (Alpha-ketoglutarate supplementation lowers Biological agE in middle- aged adults (ABLE)): a joint collaboration between NUS Healthy Longevity TRP, NUHS Centre for Healthy Longevity, Alexandra Hospital.

Research participants will undergo a series of tests on special technology equipment and stations, including measuring facial ageing, completing questionnaires and functional tests (see Annex A). Besides onsite visits, participants will need to complete a three-day food diary (record all the food consumed in a normal week); carry/wear a physical activity device for a week; and submit bio specimens (blood, saliva, stool, buccal cheek cells). The participant will then receive test results relevant to cardiovascular, metabolic and bone health.

4. Alpha-ketoglutarate supplementation lowers Biological agE in middle-aged adults (ABLE)

Alpha-ketoglutarate (AKG), a nutritional supplement, has been shown to increase healthspan and lifespan in many pre-clinical models. The ABLE study will recruit middle-aged participants and investigate whether 6 months of daily AKG supplementation slows biological age, compared with a placebo control.

5. Personalizing Exercise for Enhancing Healthspan: Using Artificial Intelligence for N-of-1 exercise prescription (N-of-1)

The N-of-1 study aims to prescribe the optimal exercise intensity for young and middle-aged adults. Participants will perform bouts of aerobic exercise at different intensities (Low, Moderate, High). Physiological and biochemical biomarkers will be measured before and after each exercise. Artificial intelligence will be utilized to prescribe the optimal exercise intensity for each individual subject.

Anyone who is keen to participate in the above various studies can contact healthy_longevity@nus.edu.sg for more information.