



The Science of Ageing

HEALTHY LONGEVITY

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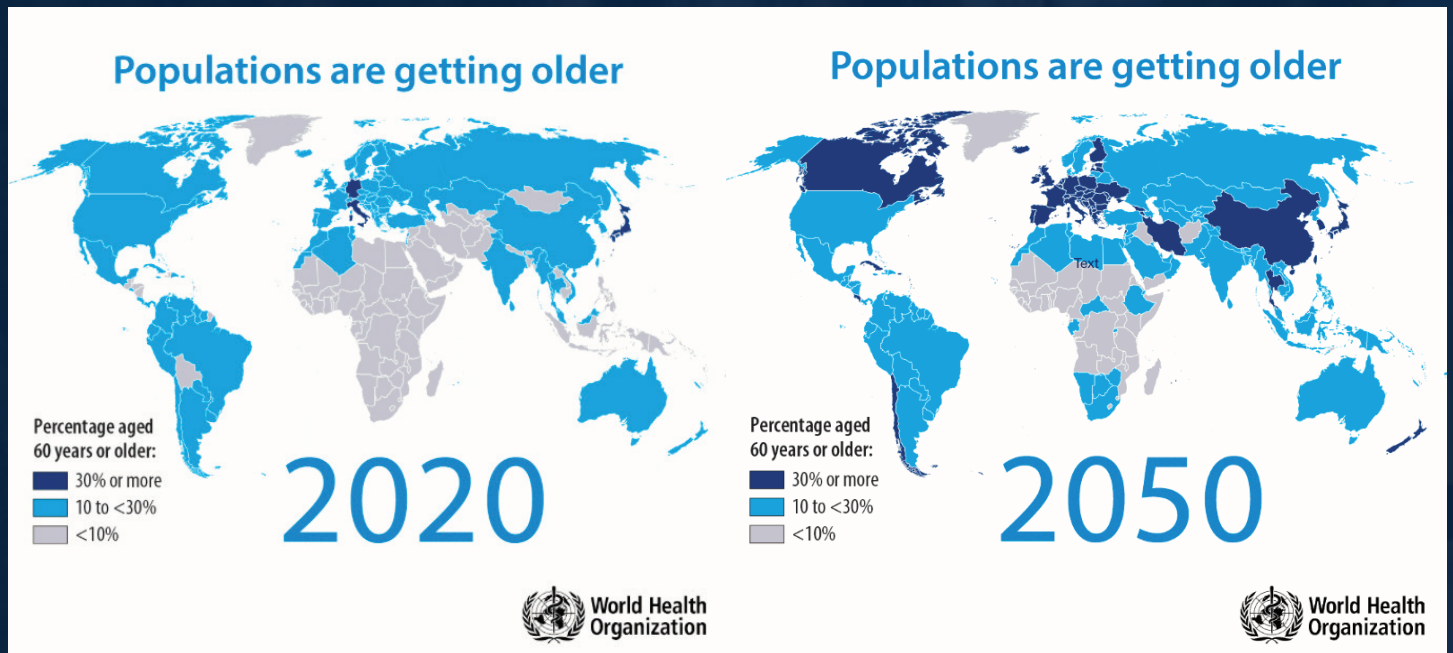
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# Introduction



## Why is it important?

Singapore, like many other countries, is experiencing mounting, ageing-related health problems that are taking a toll on the society and its resources. Tackling these problems requires in-depth basic research that could feed the healthcare industry and clinics with innovative leads and ideas that could be strategically exploited to sustain economic productivity and enable active, functional and dignified ageing amongst our senior citizens. The Department of Biochemistry at the NUS Yong Loo Lin School of Medicine has a wide-ranging expertise to tackle the basic science of ageing, as well as bringing discoveries from bench to bedside. The collaborators and their research teams are establishing research platforms to allow innovative interrogation of the underlying mechanisms of ageing and ageing-associated disorders. With these new breakthroughs in research technology, there is hope to translate these important advances into tangible societal benefits in the near future.

## What does it mean to delay ageing?

Ageing is the greatest risk factor that gives rise to chronic illnesses like cancer, Alzheimer's Disease, and cardiovascular diseases. It can be said that ageing can be seen as the actual root cause of those diseases, making the elderly population more susceptible as they advance in years. When experts talk about delaying the ageing process, it has less to do with the concept of immortality but more to do with delaying the onset of those age-related diseases, allowing for more healthy years. Keeping people healthier for longer is what "Healthy Longevity" encompasses. With this in mind, ageing research proposes a new biomedical paradigm for the 21st century. Instead of the current "sick-care approach", that tries to cure each disease individually once it has happened and is in progress, ageing interventions are the repertoire of the "healthcare approach" paradigm that aims to keep people healthy and prevent the chronic age-related diseases in the first place. Additionally, infectious diseases like COVID-19 affect the aged more than the young. Hence, keeping people younger through anti-ageing interventions can help prevent unnecessary fatalities in global pandemics.

# 「Ageing Centres Worldwide」



16

Oceania

65

Europe

10

Asia

92

North America

# The Webinar



## Agenda:

In this Healthy Longevity series, we envision a gamut of disciplines from academic research to industrial markets, in addressing critical healthcare concerns in societies. These strategies broadly include, but are not limited to:

1. Surpassing treatment of individual diseases to healthspan and lifespan extension
2. Veering the focus of managing isolated diseases to preventing multiple diseases

Ageing is the primary driver of chronic diseases in elderly individuals. Poor ageing is characterised by reduced or impaired functioning of multiple organ systems, including the cardiorespiratory, metabolic, immune and musculoskeletal systems. The current model of clinical medicine is reactive and disease-centric, focusing on secondary and tertiary treatment of age-related diseases. With the burgeoning ageing populations across the world, including Singapore, this prevailing approach may not be the most efficient method of alleviating the current burdens of healthcare systems, that is increasing healthcare costs and the finite healthcare resources that is available for public use.

## The Webinar:

The NUS Yong Loo Lin School of Medicine and Professor Brian Kennedy are proud to be hosting the Healthy Longevity monthly webinars from November 2020 to March 2021.

## Healthy Longevity Community:

This virtual series brings together highly-esteemed and prominent speakers from a wide range of fields associated with ageing. They are notable experts from large and small biotech industries to academic institutions. These experts aim to provide revolutionary insights on the growing and evolving science of ageing. Participants will be informed of the prospects of combatting and preventing the debilitating ageing process through multi-disciplinary and integrated approaches aimed at extending both health span and lifespan.

# The Webinar



## THE HOST

### PROF. BRIAN KENNEDY

Distinguished Professor, Department of Biochemistry and Physiology, Yong Loo Lin School of Medicine, NUS, Singapore.

Director of National University Health System (NUHS) Centre for Healthy Ageing, Singapore.

Professor, Buck Institute for Research on Ageing, Novato, CA, USA.

Adjunct Professor, Leonard Davis School of Gerontology, USC, Los Angeles, CA, USA.

Affiliate Faculty, Department of Biochemistry, University of Washington, Seattle, WA USA.

## NOVEMBER SPEAKERS



### Dr. Matt Kaeberlein

Dr. Matt Kaeberlein is Professor of Laboratory Medicine and Pathology at the University of Washington.

**Topic:** Targeting biological ageing: A new paradigm for 21st century medicine.



### Paul Irving

Paul Irving is chairman of the Milken Institute Centre for the Future of Ageing. **Topic:** The Impacts of Population Ageing.



### Dr. Aubrey de Grey

Dr. Aubrey de Grey is the Chief Science Officer of SENS Research Foundation. **Topic:** Can damage repair give us indefinite youth?



PROFESSOR BRIAN KENNEDY

## About Professor Brian Kennedy

As a reputable researcher in the area of ageing biology, Professor Brian Kennedy has been recognised for his research in finding translational solutions to delay, detect, prevent and treat diseases associated with ageing. He is a Distinguished Professor in Biochemistry and Physiology at the NUS Yong Loo Lin School of Medicine. Director of the Centre for Healthy Longevity at the National University Health System. From 2010 to 2016, he was President and CEO of the Buck Institute for Research on Ageing. Prof Kennedy currently remains a Professor in the Institute, where his lab addresses the biology of ageing. During his tenure at the Buck Institute, seven start-up companies were created in the Biotechnology space.

## Professional Experience

Prof Kennedy is also actively involved in the setting up of a number of biotechnology companies, having served in many different roles, as Founder, a member of the various Executive Boards and Scientific Advisory Boards, a consultant and a scientist conducting sponsored research for companies like Centaura, Unity Biopharma and Milltrust International.

He is an inventor with several patents under his belt, which have been licensed to Biotech companies. According to Ageing Analytics Agency, Dr. Kennedy is listed as the 'Top 24 Entrepreneurs' among 'Top-100 Longevity Leaders' with cross sector industry involvement of entrepreneurs and research academia.

# Kennedy Lab

In the Kennedy lab, research work is focused on understanding the biology of ageing and translating research discoveries into new ways of delaying, detecting, preventing and treating human ageing and associated diseases.

## Current Research Projects

Over the years, several small molecules, such as *Rapamycin*, *Alpha-Ketoglutarate* and *Metformin*, have become prominent in the field of ageing research. These molecules have been proven to extend the healthy lifespan across different species of model organisms, such as a single-cell life like the Baker's yeast or complex organisms like the fruit fly *Drosophila melanogaster*, to mammals like mice and dogs. Existing across all animal lifeforms since the beginning of time, the primary role of these evolutionary-conserved molecules is to act on pathways and biological mechanisms. Since the same biological mechanisms are found in humans, there is hope that interventions can be done to these biological mechanisms, with the aim of delaying ageing and enhancing healthy longevity.

Prof Kennedy's research plays a crucial role in this area. Currently, a large part of his research uses the latest molecular, biological techniques and advanced Artificial Intelligence methodologies to screen novel molecules that affects healthy longevity.

Prof Kennedy's research extends to proving that these novel molecules is effective in humans. The Alpha-Ketoglutarate molecule has been approved to be used in clinical trials in Singapore, bringing anti-ageing interventions one step closer to reality. Also, this research seeks to bring clarity to the kinds of effects surfaces in the ageing process, as a result from lifestyle interventions, such as physical exercise.

In addition, the lab also aims at deciphering the effect of lifestyle interventions such as physical exercise on the ageing process and therefore running clinical trials with elderly people. Many of those small molecular compounds that slow the ageing process occur naturally in small doses. Below a list of some of the most common ones that have undergone research and are candidates for clinical trials.

## Small Molecules:

### Rapamycin

This small molecule is named after its place of discovery, Rapa Nui or the Easter Islands. It has emerged as one of the most promising candidates that slows ageing. It is typically known to suppress immune responses during organ transplants, but it also extends one's healthy lifespan, making it one of the most promising candidates to be used to slow down the biological effects of ageing.

### Alpha Ketoglutarate (AKG)

Naturally present in animals and humans, Alpha-Ketoglutarate, or AKG, is a small metabolite, that generates and creates energy for the body, and synthesises new proteins in muscles. This metabolite is often included in supplements for bodybuilders. However, the AKG metabolite has also shown to extend one's healthy lifespan. Given its high safety assurance track record, AKG is currently used in healthy longevity clinical trials.

### Spermidine

This is another compound of the polyamine family that is present in the body. It derives its name from "sperm" as it was originally isolated from semen. Spermidine levels decrease with age, but studies have shown that supplementing the spermidine compound is beneficial to delaying various age-related symptoms.

### Metformin

Metformin is an FDA-approved drug, which has been used in medication for diabetic patients for the past 60 years. As various studies have shown that it delays ageing in animals, it is now being included in healthy longevity clinical trials and studies for humans. One of the studies, known as "Targeting Ageing with Metformin", is an ongoing study which assesses the effects of metformin on ageing in a cohort of 3000 individuals.





## PROFESSOR MATT KAEBERLEIN

### About Prof Matt Kaeberlein

Prof. Matt Kaeberlein is a Professor of Laboratory Medicine and Pathology at the University of Washington (UW) School of Medicine, with adjunct appointments in the University of Washington's Department of Genome Sciences and Department of Oral Health Sciences. Prof. Kaeberlein's research interests are focused on biological mechanisms of ageing in order to facilitate translational interventions that lengthens one's healthspan and boosts quality of life. As an author of more than 200 scientific papers, his work has been recognised by several prestigious awards including Young Investigator awards from the Ellison Medical Foundation and the Alzheimer's Association, the Vincent Cristofalo Rising Start in Ageing Research Award, the Murdock Trust Award, and the NIA Nathan W. Shock Award.

Prof. Kaeberlein has been awarded Fellow status with the American Association for the Advancement of Science (AAAS), the American Ageing Association (AGE), and the Gerontological Society of America (GSA). Prof. Kaeberlein is currently the CEO and Chair of the American Ageing Association. He also served on the Board of Directors for the Federation of American Societies for Experimental Biology (FASEB) and AGE, and on the Council for GSA.

Prof. Kaeberlein is the founding Director of the University of Washington (UW) Healthy Ageing and Longevity Research Institute, the Director of the NIH Nathan Shock Centre of Excellence at University of Washington, Director of the T32 Biological Mechanisms of Healthy Ageing Training Programme, and founder and co-Director of the Dog Ageing Project.

# Kaeberlein Lab

## Matt's Research

We have seen that *Rapamycin* treatment is effective against severe mitochondrial disease when administered very early to very sickly mice (similar to kids with Leigh Syndrome). This treatment has also proven to rejuvenate several functional measures of ageing and increases lifespan quite dramatically when given transiently late in life.



Prof Matt Kaeberlein's interest in ageing stemmed from his experience in the Biology PHD programme at the Massachusetts Institute of Technology (MIT) as a first-year graduate student. During his first semester, Prof Kaeberlein heard a talk by Dr Lenny Guarente about how his lab was studying ageing at the cellular level using yeast. It was intriguing that a complex subject such as ageing could be distilled using the tools of biochemistry, genetics and molecular biology. Fascinated, Prof Kaeberlein eventually joined Dr Guarente's lab to pursue ageing as his PHD thesis research topic. While ageing research has evolved since his graduate days, Prof Kaeberlein continues to be intrigued by the complexity of biological ageing and its fundamental mechanisms by which ageing changes the physiological state and drives decline in function and disease.

In this paper of using Rapamycin to rejuvenate oral health in ageing mice, it was established that an ageing mouse serves as a suitable model for periodontal disease, an underappreciated ageing disease that affects up to 2/3 of the elderly and is associated with increased mortality and risk of contracting age-related diseases like diabetes, heart diseases and dementia. It was discovered that ageing mice typically develops three primary clinical features of periodontal disease – gingival inflammation, loss of periodontal bone, and dysregulation of the oral microbiome. After observing middle-aged candidates receiving eight weeks of Rapamycin treatment, it has been proven to be sufficient to reverse the progression of these phenotypes. It suggests that short-term Rapamycin treatment may be clinically useful for treating periodontal diseases in humans.



TAKE CARE OF PERSONAL HEALTH. FOCUSING NOW ON DISEASE PREVENTION AND WELLNESS WILL INCREASE MILLENNIALS' ODDS OF ENJOYING A LONG HEALTH SPAN TO MATCH A LONGER LIFE.

“

Paul Irving

PAUL IRVING

## About Paul Irving

Paul Irving is chairman of the Milken Institute Center for the Future of Ageing, chairman of Encore.org, and distinguished scholar-in-residence at the University of Southern California Davis School Of Gerontology. Previously, he served as the Milken Institute's president, an advanced leadership fellow at Harvard University, and chairman and CEO of Manatt, Phelps & Phillips, LLP, a national law and consulting firm.

Mr. Irving holds various portfolios, from serving on the National Advisory Council of the Stanford University Distinguished Careers Institute to serving on various Ageing Research Committees, such as the Global Coalition on Ageing Advisory Council and the Purposeful Ageing Los Angeles Steering Committee. As a member of the National Academy of Medicine Commission for Healthy Longevity, he previously served on the Bipartisan Policy Center Senior Health and Housing Task Force and as a participant in the 2015 White House Conference on Ageing.

As an author and editor of “The Upside of Aging: How Long Life Is Changing the World of Health, Work, Innovation, Policy, and Purpose”, and a contributing writer for Forbes and Harvard Business Review, Mr Irving regularly speaks and writes about investment and innovation in the longevity economy, the changing culture of ageing in America and the world, and helping older adults find productivity and purpose.



Dr. AUBREY de GREY

## About Dr Aubrey de Grey

Based in Mountain View, California, United States of America, Dr Aubrey de Grey is a biomedical gerontologist and Chief Science Officer of SENS Research Foundation, and a California-based biomedical research charity that performs and funds laboratory research dedicated to combating the ageing process. In addition, he is Editor-in-Chief of Rejuvenation Research, the world's highest-impact peer-reviewed journal focused on ageing interventions. He received his Ph.D. in biology from the University of Cambridge. Dr de Grey is a Fellow of both the Gerontological Society of America and the American Ageing Association, and sits on the editorial and scientific advisory boards of numerous journals and organisations. His research interests encompass the characterisation of all the types of self-inflicted cellular and molecular damage that constitute mammalian ageing and the design of interventions to repair and obviate that damage. Apart from his research work, Dr de Grey is a highly sought-after public speaker at scientific conferences, Universities and companies, specialising in areas ranging from pharmaceuticals to life insurance.

## Glossary:

**Metabolism:** The network of processes that keeps an organism alive day to day.

**Age-related damage:** Changes to an organism's microscopic structure that accumulate as side-effects of metabolism

**Age-related pathologies:** Decline in mental and physical functions arising from the accumulation of damage beyond tolerable levels.

**Ageing:** The combination of the accumulation of age-related damage and the progression of age-related pathologies.

**Maintenance:** Medical elimination of damage

**Biological age:** The amount of damage in the body.

**Rejuvenation:** Medical reversion of an organism to a younger biological age.

**Longevity:** A statistically likely side-effect of the absence of age-related pathology.

**Immortality:** A religious concept not studied by biologists.

**Cell senescence:** An aberrant, irreversible and toxic state into which cells occasionally fall.

**Telomere:** Specific DNA-protein structures found on both ends of a chromosome that protects the genome from degradation, unnecessary cell recombination and fusion.

# Targeting Biological Ageing

## Webinar Insights:



### Prof. Matt Kaeberlein

Professor of Laboratory Medicine and Pathology at the University of Washington provided some insights from the webinar:

“

*It's not only about life expectancy. Those added years which are predicted to be spent in relatively good health because we've had this simultaneous effect on multiple diseases of ageing at the same time. The concept called the longevity dividend is introduced, which is the idea that you actually get more from target-ing ageing directly than targeting individual diseases. The goal isn't so much to extend lifespan, but it's to maximise the period of life that is spent in good health by pushing those diseases of ageing back as far as possible into the later years of life to extend this period of life that's free from diseases.*

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# The Impacts of Population Ageing

## Webinar Insights:



### Paul Irving

Paul Irving is chairman of the Milken Institute Center for the Future of Ageing. He share his insights from the webinar:

“

*The geroscience has increased lifespan, and frankly, increased healthspan. But if you think about it, you know, you go back 150 years or so, we have basically doubled average lifespans across. I think, in many ways, that is the most miraculous thing that science has given us throughout history. So here we've achieved all these things as a result of advancements in sanitation and safety and obviously, medical science in many, many ways. So we have all this extra time that people like you have given us, and we really have no idea what to do with it.*

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# Can Damage Repair Give Us Indefinite Youth?

## Webinar Insights:



### Dr. Aubrey de Grey

As Chief Science Officer of SENS Research Foundation, Dr. Aubrey de Grey shares his insights from the webinar:

“

*Geriatric medicine is certain to become progressively less effective as the person gets older. It's never going to work. So you might think, well hang on, why are people still trying to do this? Why is that still the main para-digm in keeping people healthy late in life? Is the answer that there's no alternative? Well, I'm about to say no, that's not the answer. The answer, I believe, is simply because people are not thinking correctly about it. This is the way that we should and actually be thinking about the answer to this ques-tion, how can people be saved?*

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# December Speakers



## Prof. Valter Longo

Prof Valter Longo is the Edna M. Jones Professor of Gerontology and Biological Sciences and Director of the Longevity Institute at the University of Southern California Leonard Davis School of Gerontology, Los Angeles, one of the leading centre for research on ageing and age-related diseases. Prof Longo is also the Director of the Longevity and Cancer Programme at the IFOM Institute of Molecular Oncology in Milan, Italy.



## Prof. Alexey Moskalev

Prof. Alexey Moskalev holds a Doctor of Biology. He is a Corresponding Member of Russian Academy of Sciences, the Head of the Laboratory of Geroprotective and Radioprotective Technologies in the Institute of Biology of Komi Scientific Centre of the Ural Branch of the Russian Academy of Sciences. He is the author of more than 100 publications in the area of ageing genetics and longevity and radiation genetics. Alexey participated in the work of identifying mechanisms of exceptional longevity of *Myotis brandtii* bats and grey whale mammalian species.



## Prof. Beatrix Vereijken

Beatrix Vereijken is Professor in Medicine / Human Movement Science at the Department of Neuromedicine and Movement Science at the Norwegian University of Science and Technology in Trondheim. She has a MSc in Experimental Psychology and a PhD in Human Movement Science, both from the Netherlands. Her research interests revolves around changes in motor control as one advances in age and experience, issues of stability and complexity, and healthy active ageing.