Scientists identify interleukin-11 as key driver of aging

July 17 2024

Asst Prof Anissa Widjaja viewing experimental data as part of her study on IL11. Credit: Duke-NUS Medical School, Norfaezah Binte Abdullah

An aging population will bring colossal health, social, and economic challenges over the coming decades. As people live longer, staving off

the physical decline and frailty that come with age has become a holy grail, with effective interventions projected to unlock significant societal and economic benefits. Estimates suggest that a slowdown in aging that increases life expectancy by one year alone is worth US$38 trillion.

In a discovery published in *Nature*, a team of scientists from Duke-NUS Medical School in Singapore may have found a key to slow aging.

The team demonstrated in preclinical models that the protein interleukin-11 (IL-11) actively promotes aging and that giving an anti-IL-11 therapy not only counteracts the deleterious effects of aging but also increases lifespan. Their discovery has the potential to play a significant role in countries' efforts to help their population live more years in good health.

IL-11 leads to fat accumulation and muscle mass loss, two key hallmarks of aging

In preclinical studies, the team found that with age, organs expressed increasing levels of the IL-11 protein, which, in turn, promoted fat accumulation in the liver and abdomen, and reduced muscle mass and strength—two conditions that are hallmarks of human aging.

According to the team, these results are the first in the world to demonstrate that IL-11 is a principal factor in aging.

First and co-corresponding author Assistant Professor Anissa Widjaja from Duke-NUS' Cardiovascular and Metabolic Disorders Program, said,

"This project started back in 2017 when a collaborator of ours sent us some tissue samples for another project. Out of curiosity, I ran some

experiments to check for IL-11 levels. From the readings, we could clearly see that the levels of IL-11 increased with age and that's when we got really excited."

Anti-IL-11 therapy counteracts effects of aging

After establishing IL-11's role in aging, the team demonstrated that by applying anti-IL-11 therapy in the same preclinical model, metabolism was improved, shifting from generating white fat to beneficial brown fat. Brown fat breaks down blood sugar and fat molecules to help maintain body temperature and burn calories.

The researchers also observed improved muscle function and overall better health in their study, as well as an increased lifespan by up to 25 percent in both sexes.

Unlike other drugs known to inhibit specific pathways involved in aging, such as metformin and rapamycin, anti-IL-11 therapy blocks multiple major signaling mechanisms that become dysfunctional with age, offering protection against multimorbidity from cardiometabolic diseases, age-related loss of muscle mass and strength as well as frailty.

In addition to these externally observable changes, anti-IL-11 therapy also reduced the rate of telomere shortening and preserved mitochondria's health and ability to generate energy.

Senior author Tanoto Foundation Professor of Cardiovascular Medicine at the SingHealth Duke-NUS Academic Medical Center Stuart Cook, who is also with Duke-NUS' Cardiovascular and Metabolic Disorders Program, said, "Our aim is that one day, anti-IL-11 therapy will be used as widely as possible, so that people the world over can lead healthier lives for longer. However, this is not easy, as approval pathways for drugs to treat aging are not well-defined, and raising funds to do clinical

trials in this area is very challenging."

Assessing the potential of the research, Professor Thomas Coffman, Dean of Duke-NUS, said, "Despite average life expectancy increasing markedly over recent decades, there's a notable disparity between years lived and years of healthy living, free of disease. For rapidly aging societies like Singapore's, this discovery could be transformative, enabling older adults to prolong healthy aging, reducing frailty and risk of falls while improving cardiometabolic health."

The team's previous research on IL-11's role in the heart and kidney (published in *Nature* in 2017), liver (published in *Gastroenterology* in 2019) and lung (published in *Science Translational Medicine* in 2019) led to the development of an experimental anti-IL-11 therapy.

In this latest work, the Duke-NUS team collaborated with scientists from the National Heart Center Singapore; the MRC Laboratory of Medical Sciences in the UK; the Max Delbruck Center for Molecular Medicine in Germany; and the University of Melbourne in Australia.

More information: Stuart Cook, Inhibition of IL-11 signalling extends mammalian healthspan and lifespan, *Nature* (2024). DOI: 10.1038/s41586-024-07701-9.
www.nature.com/articles/s41586-024-07701-9

Provided by Duke-NUS Medical School