

Duke-NUS team finds protein that plays key role in ageing

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Mankind has been looking for the elixir of youth since time immemorial, and a recent discovery by Duke-NUS Medical School researchers of a key protein responsible for ageing may hold the key to this millennia-long pursuit.

In a world first, scientists confirmed that interleukin-11 – or IL-11 – promotes fat accumulation in the liver and abdomen, and reduces muscle and strength – two hallmarks of human ageing.

Their study, published on July 17 in leading scientific journal *Nature*, demonstrated in a pre-clinical model that a therapy countering the effects of IL-11 not only slowed ageing but also increased lifespan in mice.

It was by pure chance that IL-11's link to ageing was discovered, said first and co-corresponding author Anissa Widjaja from Duke-NUS' cardiovascular and metabolic disorders programme in a media briefing on July 17.

In 2017, the team was studying



Assistant Professor Anissa Widjaja says it was by pure chance that interleukin-11's link to ageing was discovered. A study by the Duke-NUS Medical School team showed in a pre-clinical model that a therapy countering the effects of the protein not only slowed ageing but also increased lifespan in mice. ST PHOTO: GAVIN FOO

the protein's role in causing excessive scarring in the heart and kidney when tissue samples sent over by a collaborator piqued Assistant Professor Widjaja's interest.

"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," she said.

Prof Widjaja explained that as humans become older, cells in the body accumulate damage.

IL-11 acts like an alarm system that perceives the body's damaged cells as a kind of infection, triggering an immune system response, resulting in inflammation in old age.

"It's like pouring petrol on a fire, and ageing will be accelerated with

IL-11 in all the body's organs," said Prof Widjaja.

In 2020, the research team conducted a 25-week experiment with mice. They injected an anti-IL-11 drug into 75-week-old mice – as an equivalent to 55-year-old humans. They then looked at what happened to the mice at 100 weeks of age, when they were as old as 70-year-old humans.

The team found that their metabolism 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.

Improved muscle function and an increased lifespan by up to 25 per cent were also observed.

"IL-11 is like a master switch for ageing. Anti-IL-11 therapy blocks the switch from being turned on, which means pathways to ageing are inhibited," said Prof Widjaja.

She added that the anti-IL-11 drug has a good safety profile and no observed toxicity in pre-clinical trials.

However, it will be some time before anti-IL-11 drugs can be commercialised, as they have to clear clinical trials for safety and efficacy first.

The team is currently looking for partners and funding to conduct phase one clinical trials, to assess a new drug's safety and side effects.

Dr Stuart Cook, senior author of the study and Tanoto Foundation Professor of Cardiovascular Medicine at the SingHealth Duke-NUS Academic Medical Centre, 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 ageing 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 ageing societies like Singapore's, this discovery could be transformative, enabling older adults to prolong healthy ageing, and reducing frailty and risk of falls while improving cardiometabolic health."

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