Scientists discover switching off inflammatory protein leads to longer, healthier lifespans in mice

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Scientists at the Medical Research Council Laboratory of Medical Science and Imperial College London have discovered that 'switching off' a protein called IL-11 can significantly increase the healthy lifespan of mice by almost 25%.

The scientists, working with colleagues at Duke-NUS Medical School in
Singapore, tested the effects of IL-11 by creating mice that had the gene producing IL-11 (interleukin 11) deleted. This extended the lives of the mice by over 20% on average.

They also treated 75-week-old mice—equivalent to the age of about 55 years in humans—with an injection of an anti-IL-11 antibody, a drug which stops the effects of the IL-11 in the body.

The results, published in *Nature*, were dramatic, with mice given the anti-IL-11 drug from 75 weeks of age until death having their median lifespan extended by 22.4% in males and 25% in females. The mice lived for an average of 155 weeks, compared with 120 weeks in untreated mice.

The treatment largely reduced deaths from cancer in the animals, as well as reducing the many diseases caused by fibrosis, chronic inflammation and poor metabolism, which are hallmarks of aging. There were very few side effects observed.

Professor Stuart Cook, who was co-corresponding author, from the Medical Research Council Laboratory of Medical Science (MRC LMS), Imperial College London and Duke-NUS Medical School in Singapore, said, "These findings are very exciting. The treated mice had fewer cancers, and were free from the usual signs of aging and frailty, but we also saw reduced muscle wasting and improvement in muscle strength. In other words, the old mice receiving anti-IL11 were healthier."

"Previously proposed life-extending drugs and treatments have either had poor side-effect profiles, or don't work in both sexes, or could extend life, but not healthy life, however this does not appear to be the case for IL-11."

"While these findings are only in mice, it raises the tantalizing possibility
that the drugs could have a similar effect in elderly humans. Anti-IL-11 treatments are currently in human clinical trials for other conditions, potentially providing exciting opportunities to study its effects in aging humans in the future."

The researchers have been investigating IL-11 for many years and in 2018 they were the first to show that IL-11 is a pro-fibrotic and pro-inflammatory protein, overturning years of incorrect characterization as anti-fibrotic and anti-inflammatory.

Assistant Professor Anissa Widjaja, who was co-corresponding author, from Duke-NUS Medical School, Singapore, 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!"

"We found these rising levels contribute to negative effects in the body, such as inflammation and preventing organs from healing and regenerating after injury. Although our work was done in mice, we hope that these findings will be highly relevant to human health, given that we have seen similar effects in studies of human cells and tissues.

"This research is an important step toward better understanding aging and we have demonstrated, in mice, a therapy that could potentially extend healthy aging, by reducing frailty and the physiological manifestations of aging."

Previously, scientists have posited that IL-11 is an evolutionary hangover in humans, as while it is vital for limb regeneration in some animal species, it is thought to be largely redundant in humans.

However, after about the age of 55 in humans, more IL-11 is produced
and past research has linked this to chronic inflammation, fibrosis in organs, disorders of metabolism, muscle wasting (sarcopenia), frailty, and cardiac fibrosis. These conditions are many of the signs we associate with aging.

When two or more such conditions occur in an individual, it is known as multimorbidity, which encompasses a range of conditions including lung disease, cardiovascular disease, diabetes, vision and hearing decline and a host of other conditions.

Professor Cook said, "The IL-11 gene activity increases in all tissues in the mouse with age. When it gets turned on it causes multimorbidity, which is diseases of aging and loss of function across the whole body, ranging from eyesight to hearing, from muscle to hair, and from the pump function of the heart to the kidneys."

Multimorbidity and frailty are acknowledged to be among the biggest global health care challenges of the 21st century, according to many leading health bodies, including the NHS, and WHO.

Currently, no treatment for multimorbidity is available, other than to try to treat the separate multiple underlying causes individually.

The scientists caution that the results in this study were in mice and the safety and effectiveness of these treatments in humans needs further establishing in clinical trials before people consider using anti-IL-11 drugs for this purpose.

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