Single gene change increases mouse lifespan by 20 percent

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By lowering the expression of a single gene, researchers at the National Institutes of Health have extended the average lifespan of a group of mice by about 20 percent—the equivalent of raising the average human lifespan by 16 years, from 79 to 95. The research team targeted a gene called mTOR, which is involved in metabolism and energy balance, and may be connected with the increased lifespan associated with caloric restriction.

A detailed study of these mice revealed that gene-influenced lifespan extension did not affect every tissue and organ the same way. For example, the mice retained better memory and balance as they aged, but their bones deteriorated more quickly than normal.

This study appears in the Aug. 29 edition of *Cell Reports*.

"While the high extension in lifespan is noteworthy, this study reinforces an important facet of aging; it is not uniform," said lead researcher Toren Finkel, M.D., Ph.D., at NIH's National Heart, Lung, and Blood Institute (NHLBI). "Rather, similar to circadian rhythms, an animal might have several organ-specific aging clocks that generally work together to govern the aging of the whole organism."

Finkel, who heads the NHLBI's Laboratory of Molecular Biology in the Division of Intramural Research, noted that these results may help guide therapies for aging-related diseases that target specific organs, like Alzheimer's. However, further studies in these mice as well as human cells are needed to identify exactly how aging in these different tissues is connected at the molecular level.

The researchers engineered mice that produce about 25 percent of the normal amount of the mTOR protein, or about the minimum needed for survival. The engineered mTOR mice were a bit smaller than average, but they otherwise appeared normal.

The median lifespan for the mTOR mice was 28.0 months for males and 31.5 months for females, compared to 22.9 months and 26.5 months for normal males and females, respectively. The mTOR mice also had a longer maximal lifespan; seven of the eight longest-lived mice in this study were mTOR mice. This lifespan increase is one of the largest observed in mice so far.

While the genetically modified mTOR mice aged better overall, they showed only selective improvement in specific organs. They generally outperformed normal mice of equivalent age in maze and balance tests, indicating better retention of memory and coordination. Older mTOR mice also retained more muscle strength and posture. However, mTOR mice had a greater loss in bone volume as they aged, and they were more susceptible to infections at old age, suggesting a loss of immune function.

In addition to the NHLBI, this study was carried out by intramural researchers at the NIH's National Cancer Institute; National Institute of Diabetes and Digestive and Kidney Diseases; and National Institute on Aging.

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