Tumor suppressor genes speed up and slow down aging in engineered mouse

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Mayo Clinic researchers have developed an animal model that can test the function of two prominent tumor suppressor genes, p16 and p19, in the aging process. Scientists knew that both these genes were expressed at increased levels as humans and mice age, but their role in the aging process was not clear. Findings by the Mayo team show that p16 provides gas to accelerate cellular aging, while p19 stops that process.

The findings, to be published May 30 in the online issue of *Nature Cell Biology*, could help explain the development of some characteristics associated with aging, such as loss of muscle mass and strength or cataracts, and how they might be retarded.

"Scientists interested in aging have developed mice that lack p16 or p19, but these mice were not suitable for studies on aging because they all die of cancer before they even begin to age," says the study's first author, Darren Baker, a laboratory technician at Mayo Clinic and a doctoral candidate. "By crossing these mice with a mouse strain that ages five times faster than normal due to a mutation in the BubR1 gene, we were able to bypass this problem."

While other genes are involved in aging, the researchers firmly established that when too much p16 is produced, tissues start to age. Instead of driving aging, the p19 gene was found to counteract the effects of p16. This was completely unexpected, says Jan van Deursen, Ph.D., a molecular biologist at Mayo Clinic, because tissue culture experiments had predicted that p19 expression promotes aging.

Another important finding of the study is that initiation and progression of aging is caused, at least in part, by the accumulation of senescent or aging cells in tissues and organs. These senescent cells have an abnormal gene expression profile and secrete proteins that damage the surrounding cells, affecting tissue and organ function and aspects of aging.

Source: Mayo Clinic