

Aging Reversed in Mice, Say Scientists

Study Suggests Scientists Reversed Age-Related Diseases in Mice. By LARA SALAHI Nov. 29, 2010

Scientists have turned back the clock in mice they engineered to age faster than normal, an advance they suggest is the first time aging in mice has been reversed.

Researchers at Harvard-affiliated medical centers genetically manipulated mice to age faster, and then used gene therapy to lengthen telomeres -- compounds found at the ends of strands of DNA -- which reversed age-related problems such as decreased brain function and infertility.

"We at best expected it to be a slowing of the process or perhaps an arresting of the process. We did not anticipate that it would be so dramatic a reversal in all of the problems that the animal was experiencing," said Dr. Ronald DiPinho, professor of medicine at Harvard University Medical School and co-author of the paper published Sunday in the journal *Nature*. "We were so struck by the findings that we rushed to get the study published."

A human cell holds 23 pairs of chromosomes, each containing protective caps at each end called telomeres. Enzymes called telomerases protect the telomeres and reduce DNA damage thought to contribute to tissue aging. But as we age, our cells produce less telomerase; telomeres are cut shorter and eventually fail to protect DNA from damage.

Researchers boosted telomerase in the mice cells -- which hold 20 pairs of chromosomes -- to prevent telomeres from getting shorter. They found restoring the enzyme not only stopped aging but revived failing organs and even restored dark fur to mice who had turned grey. DePinho said the mice that were equivalent to ages 80 to 90 in human years returned to the equivalent of middle age.

"This [research] indicates there's a point of return for these tissues," said DePinho. "The fact that you can bring a tissue to the brink and then bring it back this dramatically is remarkable."

Previous studies suggest that even in humans, shorter telomeres may be associated with age-related diseases such as heart disease and Alzheimer's disease.

In fact, the brains of the age-modified mice were 75 percent of the size of a normal brain, much as happens in a patient with Alzheimer's disease. But when researchers reactivated the telomerase, the brains returned to a normal size, according to the study.

The aging process is complex and telomeres are just one element that contributes to its course. But DePinho said this is one step in learning more about not only the slowing of aging, but also the reversal.

"Telomere dynamics in mice has taught us the role of telomeres in [diseases like] cancer and helped us better understand how to take advantage of these situations," said DePinho.

Still, DePinho said the research is an early look down the pipeline for subsequent studies. Researchers plan to study the potential benefits in normal aging in mice before understanding whether the process might work in humans.

"We want to understand what contribution this makes to the aging process in conjunction with other factors that are responsible for the aging process," said DePinho. "We need to do a more careful analysis of these tissues and their cells to ascertain whether or not we could further regulate the process."