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Longevity tied to genes that preserve tips of chromosomes

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A team led by researchers at Albert Einstein College of Medicine of Yeshiva University has found a clear link between living to 100 and inheriting a hyperactive version of an enzyme that rebuilds telomeres - the tip ends of chromosomes. The findings appear in the latest issue of the *Proceedings of the National Academy of Sciences*.

Telomeres play crucial roles in aging, cancer and other biological processes. Their importance was recognized last month, when three scientists were awarded the 2009 Nobel Prize in Physiology and Medicine for determining the structure of telomeres and discovering how they protect chromosomes from degrading.

Telomeres are relatively short sections of specialized DNA that sit at the ends of all chromosomes. One of the Nobel Prize winners, Elizabeth Blackburn, Ph.D., of the University of California at San Francisco, has compared telomeres to the plastic tips at the ends of shoelaces that prevent the laces from unraveling.

Each time a cell divides, its telomeres erode slightly and become progressively shorter with each cell division. Eventually, telomeres become so short that their host cells stop dividing and lapse into a condition called cell senescence. As a result, vital tissues and important organs begin to fail and the classical signs of aging ensue.

In investigating the role of telomeres in aging, the Einstein researchers studied Ashkenazi Jews because they are a homogeneous population that

was already well studied genetically. Three groups were enrolled: 86 very old - but generally healthy - people (average age 97); 175 of their offspring; and 93 controls (offspring of parents who had lived a normal lifespan).

"Telomeres are one piece of the puzzle that accounts for why some people can live so long," says Gil Atzmon, Ph.D., assistant professor of medicine and of genetics at Einstein, Genetic Core Leader for The LonGenity Project at Einstein's Institute for Aging Research, and a lead author of the paper.

"Our research was meant to answer two questions: Do people who live long lives tend to have long telomeres? And if so, could variations in their genes that code for telomerase account for their long telomeres?"

The answer to both questions was "yes."

"As we suspected, humans of exceptional longevity are better able to maintain the length of their telomeres," said Yousin Suh, Ph.D., associate professor of medicine and of genetics at Einstein and senior author of the paper. "And we found that they owe their longevity, at least in part, to advantageous variants of genes involved in telomere maintenance."

More specifically, the researchers found that participants who have lived to a very old age have inherited mutant genes that make their telomerase-making system extra active and able to maintain telomere length more effectively. For the most part, these people were spared age-related diseases such as cardiovascular disease and diabetes, which cause most deaths among elderly people.

"Our findings suggest that telomere length and variants of telomerase genes combine to help people live very long lives, perhaps by protecting

them from the diseases of old age," says Dr. Suh. "We're now trying to understand the mechanism by which these genetic variants of telomerase maintain telomere length in centenarians. Ultimately, it may be possible to develop drugs that mimic the telomerase that our centenarians have been blessed with."

More information: The study, "Genetic Variation in Human Telomerase is Associated with Telomere Length in Ashkenazi Centenarians," appears in the November 9 online issue of the *Proceedings of the National Academy of Sciences.*

Source: Albert Einstein College of Medicine (news : web)