

Researchers identify genetic signatures of exceptional longevity in re-published study

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While environment and family history are factors in healthy aging, genetic variants play a critical and complex role in conferring exceptional longevity, according to researchers from the Boston University Schools of Public Health and Medicine, Boston Medical Center, IRCCS Multimedica in Milan, Italy, and Yale University.

Published in [PLoS ONE](#), after peer review, the research findings are the corrected version of work originally published in Science in July 2010. The revised publication includes additional authors who independently assessed and helped to produce a valid genotype data set, for which the same analysis as in the original paper was performed. It also contains an additional replication data set of subjects with an average age of 107.

[Centenarians](#) are a model of healthy aging, as the onset of disability in these individuals is generally delayed until they are well into their mid-90s. Because exceptional longevity can run strongly in families, and numerous animal studies have suggested a strong [genetic influence](#) on [life span](#), the researchers set out to determine which genetic variants play roles in human survival beyond 100 years of age. They used a well-established Bayesian [statistical method](#) for determining which single [nucleotide polymorphisms](#) (SNPs, or genetic variants) could, as a group, be used to categorize subjects as centenarians versus controls, based solely upon the [genetic information](#). The predictive sensitivity of the model they developed, which contains 281 SNPs, increased with the age of the subject, supporting the hypothesis that genes play an increasingly strong role in survival in centenarians. The model was able to predict

exceptional longevity with 60 to 85 percent accuracy, depending on the average age of the replication sample that was used. The older the sample, the stronger the sensitivity. Many of the 130 known genes associated with the SNPs in the [prediction model](#) have been shown by other gerontologists to play roles in age-related diseases and aging, said the study's lead researchers, Paola Sebastiani, PhD, professor of biostatistics at the BU School of Public Health, and Thomas Perls, MD, MPH, associate professor of medicine at the BU School of Medicine.

"This is a useful step towards meaningful predictive medicine and personal genomics," said Dr. Perls, a geriatrician at Boston Medical Center. "When people can do this kind of analysis on whole genome sequences for traits that have important genetic components, the predictive value should be even better."

The new study differs from the earlier study, voluntarily retracted by the authors, in several ways: A select group of faulty SNPs was eliminated from this study ;an additional sample of extremely old study subjects was added; and researchers from Yale University were called in to independently validate the data and methodology. The corrected study, as did the original, found that subjects who shared the same profile of variations for genetic markers in the model appeared to share similar levels of risk for various traits or diseases associated with exceptional longevity -- most notably, in their ages of survival. "Further study of these genetic characteristics may yield a better understanding of the genetic and biological bases of delaying or escaping age-related diseases and achieving longer survival," Dr. Perls said. "The novel approach to genetic data that is described here is likely applicable to other complex inherited traits, and we look forward to other research groups applying these methods to their data."

More information: The full study is available here:
[dx.plos.org/10.1371/journal.pone.0029848](https://doi.org/10.1371/journal.pone.0029848)

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