

## Genetic Finding May Provide a Test for Longevity

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The New York Times

01.07.2010

If you were going to live to be 100, would you want to know it?

When it becomes affordable to have one's genome sequenced, perhaps in a few years, a longevity test, though not a foolproof one, may be feasible, if a new claim holds up. Scientists studying the genomes of centenarians in New England say they have identified a set of genetic variants that predicts extreme longevity with 77 percent accuracy.

The centenarians had just as many disease-associated variants as shorter-lived mortals, so their special inheritance must be genes that protect against disease, said the authors of the study, a team led by Paola Sebastiani and Thomas T. Perls of Boston University. Their report appears in Thursday's issue of Science.

The finding, if confirmed, would complicate proposals for predicting someone's liability to disease based on disease-causing variants in the person's genome, since much would depend on whether or not an individual possessed protective genes as well.

"I think it's a quite striking finding," said Nir Barzilai, an expert on longevity at the Albert Einstein College of Medicine. It shows that only a limited number of favorable genes are required to attain great age, he said. Identifying these genes would provide protection against all the diseases of old age, a more powerful strategy than tackling each disease one by one.

"I feel there's an elephant in the room and no one realizes it's really important — this is the next step to make us all healthy," Dr.

Barzilai said.

The Boston University team found the genetic variants with a statistical technique called a genome-wide association study. This is the technique that researchers had hoped would lay bare the genetic roots of common diseases like Alzheimer's or cancer, but it has largely failed to do so, raising the question of how the Boston University team was more successful while using a smaller sample size than usual. The team analyzed the genomes of 1,055 centenarians.

Dr. Sebastiani said the reason for their success was that living past 100 was such an extreme form of longevity that any genes involved would give very powerful signals of their presence, offsetting the reduced statistical power of the small sample.

She found that 150 genetic variants were associated with extreme longevity. She then looked at a different sample of centenarians from those involved in her study and found that more than three-quarters possessed many of the 150 genetic variants she had already identified. The other centenarians had few or none of the protective variants, which means there are many more yet to find, Dr. Sebastiani said.

But Kari Stefansson, a geneticist who has looked for determinants of longevity among the Icelandic population, said of the current study that he was "amazed at how many loci of genome-wide significance have been found in a modest sample size."

Dr. Stefansson said he had been able to accumulate a larger collection of centenarians, despite Iceland's small population, because his company, Decode Genetics, has analyzed most of the genomes of living Icelanders and in addition can compute the genomes of Icelanders who lived long ago from the genomes of their descendants. None of the Boston University team's 150

genetic variants is present among Icelandic centenarians, he said.

Dr. Perls said at a press conference Wednesday that there were about 80,000 centenarians alive at any one time in the United States. Some 15 percent of his control group, and presumably of the population at large, have the potential to live to be 100, according to the test based on the 150 variants. But they fail to attain that age because of accidents or unhealthy living, he said.