

# An age-old puzzle solved: Who will live to be 100

Genetic test identifies potential centenarians with 77-per-cent accuracy, researchers say



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Medical Reporter — U.S. scientists say they have discovered the genetic signature of an exceptionally long life, and with nothing more than a DNA sample they can predict – with 77 per cent accuracy – those biologically built to live beyond a century.

They also predict that such a test, based on a set of 150 genetic markers, will be available to the curious by summer's end.

“It’s really quite revolutionary,” said Thomas Perls, associate professor of medicine at Boston University and senior author of a research paper published online Thursday by the journal *Science*. “With the accuracy we’ve demonstrated, companies are going to pick this up. We’ll see it on the market in a month.”

The study, which involved more than 1,000 subjects in the New England Centenarian Study and more than 1,200 controls, found that people who live into their hundreds are genetically special.

Lifestyle choices seem to play the lead role in determining who will make it to age 85. But living beyond that age, a trait that runs in families, seems to depend largely on genes, and researchers worry the news will make some people reckless with their health.

“What do you do when you’re told you absolutely don’t have the [genetic] signature for exceptional longevity or you [do] have it? ... Do you go and do a lot of risk-taking behaviours and say, ‘Well, I’m hanging it up,’ or does it give you impetus to take all the more better care of yourself?” said Dr. Perls, director of the New England study. “What are people going to do with this, what health or financial decisions might they make?”

Dr. Perls said that given the complications of interpreting the data, it’s premature for a test that predicts longevity to hit the mass market, and he notes that the study’s authors have no financial interest in such a test. But the Boston team does plan to launch a website as early as next week where people who happen to have their genetic data can input it and learn, for free, about their longevity

profile.

“We want the opportunity to give people reasonable advice about what to do with the information,” said Dr. Perls, “and [to] counter any unreasonable claims [from private companies] of how the data can be interpreted.”

For one thing, the data is based solely on Caucasians, and Dr. Perls suspects different ethnic groups will have different genetic markers for longevity.

As well, the researchers note that some of the centenarians studied carried none or very few of the genetic markers. In these cases, they say, other unknown genetic traits and environmental factors likely account for longevity.

The study suggests that many more of us than generally thought – an estimated 15 per cent – have the genetic potential to live a very long life. But things like accidents, wars and bad habits combine to keep the numbers of centenarians extremely low. Only one in 6,000 people reaches 100 in industrialized countries. Only one in seven million survive beyond 110, achieving so-called “super-centenarian” status.

But the work also has troubling implications, as it casts doubt on the validity of many genetic tests now widely used to gauge people’s risk of developing everything from cancer to cardiovascular disease.

Researchers have long assumed that centenarians must carry fewer disease-related genes than most people, since heart attacks, strokes and dementia hit them very late in life or not at all. But the Boston team found centenarians have as many disease-related genes as other people, suggesting that the genetic traits involved in extreme longevity also protect them against illness.

If this is correct, researchers say judging a person’s risk for any disease cannot be properly done without knowing what other protective markers they may or may not have. “These tests could be highly inaccurate,” Dr. Perls said.

As baby boomers grey, the hunt for genes linked to healthy aging has become a high priority. Many researchers have focused on a few candidates that look promising in studies of long-living fruit flies and worms.

But the Boston team took a different route. Lead author Paola Sebastiani, professor of biostatistics at the university’s school of public health, scanned the entire genome for a type of mutation known as an SNP, a single nucleotide polymorphism, akin to a one-chemical change in the code of DNA.

The human genome has about 300,000 SNPs. Dr. Sebastiani designed a program to rank those most likely to play a role in determining lifespan, which produced a list of 2,500. Over two years she and

her team pared that down to 150 by testing which SNPs are most likely to identify a centenarian.

They found that regardless of any other factor, the presence or absence of these markers allowed them to distinguish centenarians from controls 77 per cent of the time. Most centenarians fell into 19 different clusters based on the combinations of markers they carry, and researchers found each cluster has its own aging profile. They also found the markers seem to have a dosing effect – the more of them a person has, the longer they live, and they can stay healthy well into their hundreds.

The markers involve some 70 genes; one of them may protect against Alzheimer's disease. But the function of most of the genes is a mystery, and researchers hope future studies will help all people delay the degeneration of aging.

Angela Brooks-Wilson, a geneticist who leads a “super-seniors” study at the BC Cancer Agency in Vancouver, called the Boston study “an important contribution to the field.”

“Its real value is not in individuals being able to predict their lifespan,” she said, “but in the genes it identifies, and figuring out their functions so that it will allow us to maximize healthy lifespan for the general population.”

Aside from their genes, nothing in particular about the centenarians in the New England study predicted the long life ahead of them. Some have lived disease-free for 100 years. But some have survived cancer. Most drink in moderation. Several have smoked – most in the distant past, but others more recently – and very few are vegetarians.

Study participant Onie Ponder of Ocala, Fla., is not surprised by the role of genes – “My grandmother lived to 93,” she said. “We thought that was old.”

But Mrs. Ponder is now 111, the oldest person in the state, the 10th oldest in the United States and 26th oldest in the world. Speaking sprightly on the phone from her assisted-living centre, she said, “When I was growing up I never thought I would be this old.”

The mother of two sons and grandmother to 16 doesn't believe diet played a major role – “I eat whatever I want. Lately, it's been Rice Krispies for dinner because I want to lighten my diet.” Rather, Mrs. Ponder suspects her active youth helped bless her with a long, healthy life. “I walked everywhere. ... I had to; we didn't have any cars.”

Mrs. Ponder takes little medication, can still rise out of her own chair and walk to dinner, and since losing her sight at 100, orders historical audio books from the blind centre. She has listened to more than 200 of them.

Said her youngest son, 74-year-old Carswell Ponder: “I hope I have her genes.”



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