Genes identified that extend life

For as long as people have been around to contemplate their existence, there has likely been the natural existence of the philosophical question: 'How can I live longer?' This thought process was the foundation for the creation of the 'fountain of youth' mythos, the elaboration of thoughts about religion and an afterlife to extend one's life beyond its natural endpoint, and a thousands-of-years quest for medicine that can make us live longer.

At some level, everything in the universe has a lifespan: There is a lifecycle in the stars themselves, where they are born, mature, and then begin to run out of fuel and progress on to various end stages. The universe itself is estimated to be about 13.8 billion years old, and is expected to cease to exist in a couple of potential ways—either by contracting upon itself in a 'big crunch' or continuing to expand until a state of 'heat death.' Even the subatomic particles themselves (protons, neutrons, electrons, etc.) have known or suspected lifespans. So the notion of a progression of life along a timescale is a very common theme in the universe. But while particles, planets, and stars cannot contemplate their existence or survival, we can. And we often do.

The story of genes and genetic heritability is never open-and-shut, and remarks made about one's development in life, disease progression, or lifespan commonly include a statement like 'it's a combination of genes and lifestyle (or environment).' This is because there is a profound influence on our genes of the environment, our exposures, and the things that happen to us (or what we willingly participate in). So while genes aren't the *only* story, we can think of them like the ink used to write our lives' chapters – and what we do in our lives determines the length and quality of the stories. Genes aren't destiny, but they're a part of the underlying structure of the story. What if we found genes associated with a longer life? Can we get more ink to write longer life stories?

While it is true that certain genes influence longevity, and we can find that certain families have members who live longer on average than the rest of the population—it's again not destiny. There are factors which become significant within families such as hereditary diseases, as well as lifestyle and behavioral factors such as exercise, diet, alcohol consumption, and smoking. So the research started with the idea that there are more robust genes likely in the population which *tend* to lead to longer lives. Over the last few decades, the research had taken a different direction: It assumes that all creatures on Earth have genes associated with the aging process, that this information is part of any cell that has a nucleus and a finite age limit, and if we wind back the clock long enough in time, there should be common ancestry for when this longevity information was incorporated into the genome (called orthologous genes).

A lot of aging and longevity data have been gathered over the decades on the *C. elegans* nematode—it is among the most-characterized creatures in the world due to its incredibly small genome. And while that has made it easy to study, it was found that about 1% of its genes could be participative in its aging process and lifespan.

To extend the reach of the research into more and varied animals, scientists looked at the genes of the *C. elegans* worm, zebrafish, and mice—and especially for those genes which were orthologous (closely-

related to each other). After screening over 40,000 genes for their effect during different phases of the creatures' lives, the researchers looked at messenger RNA (mRNA) levels as a proxy for gene activity—genes transcribe mRNA, which is then used to code for the creation of proteins. So if there is a lot of mRNA for a specific gene, it is considered to be very active; very few copies of mRNA and it is considered to be low activity. A statistical analysis looking for principal components helped researchers to identify the genes which seemed to be proportional across the lifespans of the three different animals. And from this, about 30 genes seemed to have orthology and to therefore in this context be related to the aging process itself.

For example, one of the genes was the *bcat-1* gene, and when its effect was blocked, the lifespan of the *C. elegans* worm was extended by about 25 percent. On average, a five percent lifespan extension effect was observed by blocking 12 of the identified orthologous genes. Not only were increased lifespans observed (and seen to be extended), but other parameters of the worms' vitality were affected, such as accumulation of aging pigments of the skin, movement speed, and reproduction frequency. All of these measures were improved with the increased lifespan.

The extension of this research in humans seeks to measure relevant parameters of health and vitality such as blood sugar control and cholesterol levels; Measuring lifespans in humans for this research isn't practical, as it would require decades for adequate data to be amassed that may show a significant difference. But importantly, the goal for researchers isn't just to increase lifespan (because of the mental and physical decline associated with straight aging) – but instead to focus on the 'healthspan,' which is the extension of the healthy, functional phases of life. There are implications for the improvement of quality of life in senescent populations, major health care cost reductions, and other benefits.

The research is very nascent, but judging by the speed at which resveratrol supplements were touted and found on the market after they were associated with effects on antioxidation and sirtuin, it may not be more than 10-15 years before initial attempts are made to toggle these genes on the consumer level.

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