

Researchers discover new genetic factors associated with successful aging in the Amish

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Avoiding disease, maintaining physical and cognitive function, and continuing social engagement in late life are considered to be key factors associated with what some gerontologists call "successful aging." While conducting studies of Amish families in Indiana and Ohio, a group of researchers led by William K. Scott, PhD, Professor of Human Genetics at the University of Miami Miller School of Medicine, began to notice that a significant number of people over age 80 in these communities demonstrated the three main factors associated with successful aging.

In the current study, Scott and his colleagues investigated the genetic differences between Amish individuals who had successfully aged compared with individuals from the general population to see what genetic factors are keeping them healthier and happier well into their later years.

A total of 263 volunteers, age 80 and older, were enrolled in a population-based door-to-door survey of Amish communities in Indiana and Ohio. The researchers studied this particular Amish population because they have fairly large families with well-documented genealogies. Furthermore, because they live relatively homogeneous lives, nongenetic factors such as environment and diet would have a smaller effect on successful aging, as compared to the general population. Study participants who scored in the top third of the sample for lower limb function, required little assistance with self-care tasks, had no symptoms of depression, and expressed a high level of life satisfaction were considered to be 'successfully aged' (73 participants in total). The



remaining 190 study participants were retained as controls.

Researchers have theorized for some time that mitochondria – the organelles that produce energy in human cells – may play a role in aging. There is evidence that people who age successfully have genetically different mitochondria when compared to the general population. Furthermore, mitochondrial lineages described by patterns of common genetic variants (or "haplogroups") have also been shown to be associated with increased longevity in different populations. To better understand these underlying genetic factors, Dr. Scott and his colleagues studied the influence of mitochondrial haplogroups on successful aging and sought to identify the common genetic variations in the mitochondrial genome that are potentially associated with successful aging in a sample of Amish individuals age 80 and older.

The common variations in the mitochondrial genome define distinct 'haplogroups that are found in specific geographic regions around the world. For this study, Scott's research team looked at the nine most common European haplogroups, since the Amish are descendants of individuals from Europe.

The current research results indicate that one fairly rare mitochondrial haplogroup found in only 2% of all Europeans – which is known as 'haplogroup X' – was found in 15% of the successfully aged Amish population (versus only 3% of the controls) and had a significant positive association with successful aging. On the other hand, the researchers also reported that another mitochondrial haplogroup called 'haplogroup J' which is typically found in about 10-25% of Southern Europeans, was found in only 5% of the Amish population and had a negative association with successful aging factors.

Thus, a significant positive association with successful aging was found with mitochondrial haplogroup X (which was more prevalent among the



successfully aged Amish population), while a negative association was found with haplogroup J (which is more prevalent in European populations than the Amish). All positively associated alleles were found together on haplogroup X, while all negatively associated alleles fell in haplogroup J. All positively associated alleles were found together on haplogroup X (1719A), while all negatively associated alleles fell in haplogroup J (rs2854122, rs3135030, and 10398G). These data represent a novel association of mitochondrial haplogroup X with successful aging that conflicts with previous positive associations of haplogroup J with longevity in other populations.

"In this study, we focused on looking for genes that may have an influence on keeping people healthy, rather than identifying genes associated with disease," said William Scott, PhD, the senior author of the research abstract presented at the ASHG 2010 Annual Meeting. "Our research results support the idea that mitochondria play an important role in aging, and our findings also suggest a specific subset of genetic variants that might influence successful aging in this group of people."

"In our future research, it is important that we attempt to broadly associate this mitochondrial variation to aging in this population, figure out what it does biologically, and then see if we can reproduce it in other samples," said Scott. "Furthermore, we will also need to look more closely at the mitochondrial genome for specific variants that influence aging."

Provided by American Society of Human Genetics

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