Gene linked to youthful appearance may help solve ageing puzzle

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Credit: Vlad Vasnetsov from Pexels

How long you live depends in part on the genes you inherit. For example, those suffering from Werner's syndrome have inherited two defective copies of a gene coding for an enzyme that is involved in DNA

replication and repair.

A lack of this enzyme produces premature cell senescence – the build up of dysfunctional cells as we age which causes damage to tissue – and elevated levels of inflammatory proteins. The end result is the early development of many conditions seen in older people, such as cardiovascular disease, osteoporosis, grey hair, wrinkled skin and shrinkage of the thymus. Werner's syndrome is perhaps the nearest thing we will ever see to true accelerated ageing.

At the other end of the scale are individuals who carry rare variants of the Foxo3a gene who show high physical and cognitive function late in life, as well as lower incidences of some age-related diseases and better self-reported health. Those fortunate enough to carry two copies of one of these rare variants have roughly three times the average chance of living into their late nineties. In essence, Foxo3a and wrn variants determine the biological age of those who carry them.

Genes and perceived age

In contrast, a new study published in Current Biology reports the first genetic variants to influence how old those who carry them are perceived to be by others. Groups of four observers estimated the facial age and percentage of facial skin covered by wrinkles in more than 2,600 mainly white Dutch participants in their mid-60s (an average of about 1.3% of skin was wrinkly). Reassuringly, the real age of the subjects correlated strongly with how old the investigators thought they looked and, perhaps unsurprisingly, the more wrinkled the face the older the observers guessed the person was.

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A study entitled "scientists discover that wrinkled people look quite old" would hardly have made headlines. However, after investigating the genomes of the participants, the researchers discovered that changes in a gene known as MC1R were strongly associated with perceptions of facial age. People unfortunate enough to inherit two defective MC1R variants (including those which cause red hair and pale skin) were rated by the observers as being about two years older than people whose MC1R genes were working properly. Those who inherited one "good" variant and one "bad" one looked about a year older. So the gene could successfully explain why some guesses were off.

This is the latest discovery of a gene involved in ageing. For example, a study published earlier this year showed that the gene IRF4 is involved in the greying of hair by helping to regulate the production and storage of melanin. It is clear that some of these "ageing genes" have major effects on health while others' influence is a little more aesthetic – which makes them far from unimportant.

Evolutionary importance

So just what is MC1R doing? It could just be cosmetic, but this gene carries the information for a receptor which plays a key role in the synthesis of melanin (which blocks UV light) and prevents inflammation – a major driver of ageing. Defective forms of this can in fact predispose someone to skin cancer.

Why could this matter? Genes have to be passed from one generation to the next. Over a billion years ago there was selection for any genetic variation which allowed early organisms to reproduce more successfully than their competitors even if these genes led to decreased survival later on. This Faustian bargain, known as "antagonistic pleiotrophy", is all that ageing is.

However, in more evolved species, the situation is complicated by sex. Mates have to be selected, attracted and sometimes kept which results in competition both between members of the same sex and between sexes. This process influences ageing because, depending on the species, the process of either competing for a mate or being the object of competition can shorten lifespan. For example, female fruit flies that mate regularly have shortened lifespans due to the damaging effects of chemicals that male flies secrete to destroy the sperm of previous mates.

It is now recognised that humans also (albeit subconsciously) follow evolutionary drivers in mate selection and retention. Human males

typically desire youth in partners more strongly than females do (because female fertility declines much more sharply with age). Given this context, carrying a gene variant that accidentally makes you look even older than you really are (or worse which truthfully advertises your above average propensity to skin cancer) is hardly an advantage, especially if you are a woman.

On the plus side, across 37 different cultures one of the top three most strongly desired traits in a long term partner for both sexes is kindness. There are probably genes for that as well, but it is at least independent of wrinkles.

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