EVOLUTION AND AGING

Evolution never had to solve aging, because it never saw it. That is the central idea of a new review in Nature Reviews Genetics by Dönertaş and Partridge (1), and it is another example of the trade-offs that run through biology.

Natural selection acts with full force until the onset of reproduction, and then weakens progressively during adulthood. What happens in late life falls into a "selection shadow", where harmful effects are poorly purged. Two classical mechanisms follow. Mutations that act only late in life can accumulate because selection cannot remove them. And alleles that are beneficial early in life, for instance for fertility, are favoured even when they cost us later. Repair itself has a cost: resources directed to reproduction are diverted from somatic maintenance, a special case of the same trade-off known as the disposable soma. In humans, genetic variants that increase reproduction tend to be associated with shorter survival, and most complex diseases with a significant genetic correlation show a positive association with fertility.

The review shows how this picture is supported by comparative genomics. The pathways whose late-life activity drives aging (nutrient sensing, DNA repair, protein quality control, inflammation) are strongly conserved across species, and the genes associated with longevity in humans (the GenAge set) show higher amino acid sequence identity with their mouse counterparts than length-matched control genes. Their conservation does not mean that they guarantee a long life: they are regulatory nodes that coordinate growth, reproduction and stress responses, functions too important in youth to tolerate change. This is what we would expect if evolution kept reusing the same ancient pathways for growth and reproduction, which then keep running in old age, at a cost, because selection cannot fine-tune them for late life.

In humans, longevity is highly polygenic, with hundreds of variants of tiny effect, and age-related diseases share a common genetic architecture, especially when their onset is at a similar age. Cellular senescence is a clear example of the trade-off: it protects us from tumours in youth, but later promotes inflammation and cancer.

Aging, in the end, is the price of a body optimised for youth.

1. https://www.nature.com/articles/s41576-026-00959-x