

MAN DOES NOT LIVE BY GENETICS ALONE

Nem só de genética vive o homem

Aging is one of the most complex issues in life sciences. The human aging process can be understood as a gradual deterioration of body functions that becomes recognizable at the end of the reproductive period. Studies on the dynamics of mortality were pioneers in providing a basis for the genetic contribution to human aging. The genetic component of human longevity has been analyzed for decades by comparing age at death for monozygotic and dizygotic twins, which has allowed to estimate in 25% the variation in longevity due to heritable factors, with an indication that this component is higher at advanced ages and more important in men than in women.^{1,2} Prior to these findings, Jarvik et al.³ had demonstrated that monozygotic twins aged 60 years and older showed a smaller difference in terms of variation in total length of life than dizygotic twins.

By understanding that the aging of multicellular organisms is a universal phenomenon and that the cellular level is the most fundamental level, from which one can attempt to control important age-related changes, biomedical research has consistently investigated the role of cycles of cell differentiation, growth and metabolic functioning in order to understand the triggers of senescence. Multicellular organisms are known to age concomitantly with a decline in specialized cell functions, as well as in the capacity for division and differentiation.⁴

However, many factors contribute to longevity, and the results to date of genetic studies examining this phenotype have been inconclusive regarding the real weight of this variable. To illustrate this scenario, a recent meta-analysis aimed at single nucleotide polymorphisms (SNP), which are the most common form of genetic variation among individuals, associated variations in 5 known genes (*ACE*, *APOE*, *FOXO3A*, *KLOTHO*, and *IL6*) with exceptional longevity, each of them in at least 3 independent studies. It is noteworthy that the individual effect size of each of these genes was quite modest (or even negligible), allowing to suggest that, only when multiple (hundreds or thousands) allelic variations are inherited simultaneously, there is a measurable contribution of genetics to longevity, which is consistent with the results for other polygenic and multifactorial traits.⁵

In contrast to the weight of genetics, a historical study investigated whether family socioeconomic status in childhood would be a predictor of mortality based on thousands of birth and death records of individuals from the Paris region born in 1914–1916.⁶ The records included information on parental occupation, legitimacy status, life events (*e.g.*, marriage, divorce), and precise date of death. The analysis revealed that, in both sexes, survival to age 31 years was markedly determined by legitimacy (higher survival for legitimate children) and paternal occupation (higher survival for those born to an upper-class or middle-class father). The difference in life expectancy between upper-class and workers' daughters was 4.4 years (95% confidence interval [95%CI], 1.2–7.6). Therefore, paternal occupation and legitimacy status were stronger predictors of offspring longevity than a possible genetic contribution in this historical cohort born during World War I and contemporary to World War II.

Considering that Brazil currently has statistics on mortality from external causes (including violence) compatible to those of countries involved in war, it can be assumed that family social conditions play a much more decisive role in the longevity of Brazilians than any genetic load inherited under these conditions. In this context, national public agendas (mainly for education, social security, and science and technology) have the challenge of prioritizing actions and research that have the potential to change the socioeconomic structure of the country without jeopardizing the educational and scientific investigations with the potential for translational application.

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