Smoker-survivor genes may have long ancestral history of fighting toxins

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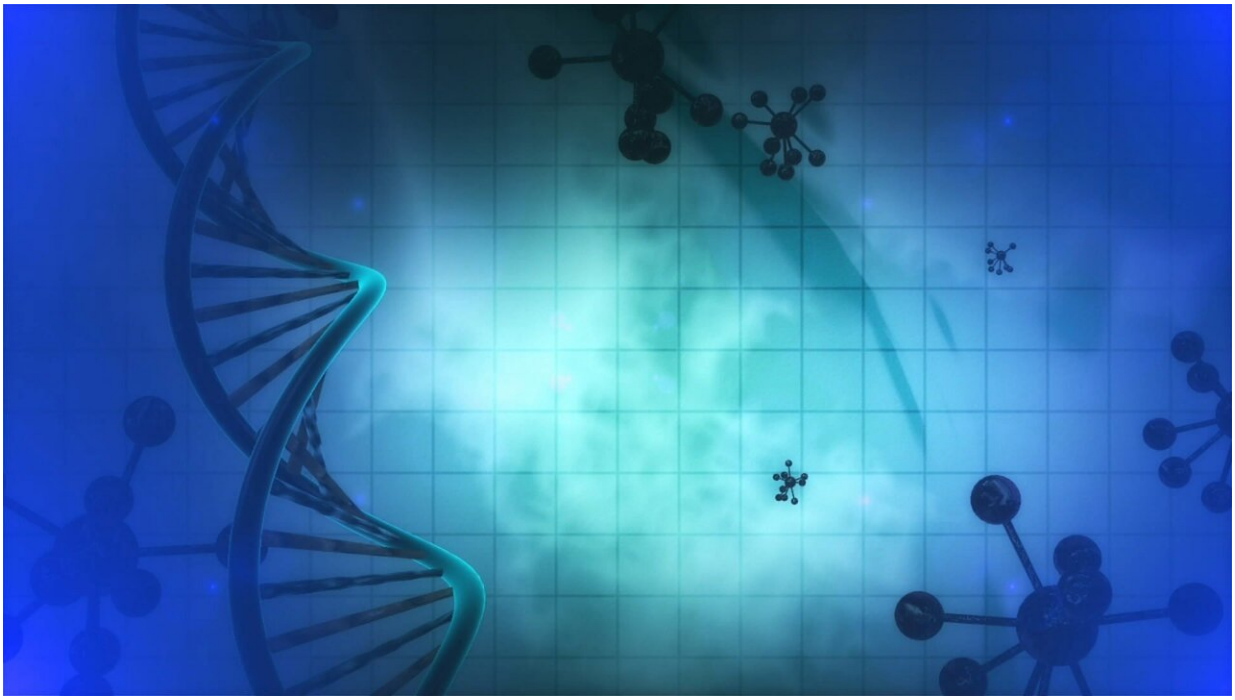

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Longevity genes that helped humans survive ancient airborne toxins may be the same genes that make humans resilient to pollution from fossil fuels and cigarette smoke today, according to a study published in the December 2019 issue of The *Quarterly Review of Biology*. In "The Exposome in Human Evolution: From Dust to Diesel," Ben Trumble (Arizona State University) and Caleb Finch (University of Southern

California) examine the myriad toxins that humans have encountered through our evolutionary history and the immunity-related genes that have countered their harmful effects. "We hypothesize that adaptation to ancient pathogens and airborne toxins may, in some cases, be protecting us today from novel airborne pollutants such as cigarettes and diesel smoke," Trumble and Finch write. "Further inquiry into these unexplored domains of genetic processes may inform the future of human health and longevity during global warming."

Trumble and Finch's paper is a detailed examination of the human exposome—the interactions between human genes and the various environmental hazards we encountered through our evolutionary history. Each new environmental hazard posed a unique threat to humans and was addressed with various genes related to immunity. The authors focused in particular on genes of host defense and brain development during the evolution of the long human lifespan.

As human ancestors diverged from great apes, they encountered an array of new environmental hazards. First, as sub-Saharan Africa shifted from forest to savanna, humans breathed mineral dust and fecal aerosols from roaming herd animals and ingested pathogens from rotting meat. With the discovery of fire, humans were exposed to toxins from smoke and the charred meat that they cooked. Later, as hunting and gathering gave way to an agricultural life, humans were exposed to new toxins from domesticated animals and limited sanitation in dense living quarters. Although an understanding of infectious disease and hygiene emerged, the industrial revolution ushered in the modern-day hazards airborne pollutants and cigarettes.

Trumble and Finch found that some genes appear to have provided benefits through long stretches of evolutionary time and in very different environments. The gene AHR appears to have made archaic humans more resistant to toxins in domestic cooking fires than their Neandertal

counterparts. "AHR is important in detoxifying response to modern domestic smoke, including responses to cigarette smoke," they write. "We hypothesize that genetic adaptations to ancient airborne toxins may play important roles in ameliorating the effects of exposures today, including the survival of some elderly lifetime cigarette smokers."

Many other genes grew to lose their benefits over time, or, in the case of ApoE, became dependent on the environment in determining which version is the most beneficial. The ancestral version of ApoE was highly beneficial for survival in environments with high levels of infection. However, it also negatively impacts artery and brain aging, and is associated with shorter life spans. A newer version of the gene appears to have more beneficial effects, including lower cholesterol in meat-eating populations. The fact that the ancestral version of ApoE is still prevalent in the population is an important example of the human environment changing faster than our gene pools can keep up, Trumble and Finch write. It may regain its adaptive value, however, as global warming promotes the recurrence of global infections through the expansion of insect populations, such as malaria-carrying mosquitoes.

Understanding the extent of these historical gene-environment interactions is key to meeting future global health challenges. "Understanding the full breadth and history of the human exposome will inform the future of human health and longevity during the emerging ecological shifts from dust to diesel and beyond."

More information: Benjamin C. Trumble et al, The Exposome in Human Evolution: From Dust to Diesel, *The Quarterly Review of Biology* (2019). DOI: 10.1086/706768

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