

Fire came with costs

More details for science writers

Dr Jac Aarts, molecular biologist and lead author: 'The capacity to neutralise the adverse health effects of toxic substances is an important asset which increases 'Darwinian' fitness, especially through dietary flexibility, but also by improved resistance to environmental poisons. The latter has been particularly important for the human lineage during the tens, or perhaps hundreds of thousands of years in which it enjoyed the benefits of fire use. Cooking made it possible to utilize a wider range of food resources more effectively by improving the digestibility and detoxification of diet-borne toxic compounds. Its broad range of benefits is widely recognized in palaeoanthropology, but it is rarely acknowledged that fire can also provoke negative health effects including cancers and reduced reproductive success. This suggests that fire use might have resulted in genetic selection of new, derived genotypes conferring increased resistance to toxic fire-related compounds.' Co-author, Dr Wil Roebroeks, an archaeologist at Leiden University, who studies the deep prehistory of fire usage, says that it was crucial to tap into the knowledge of toxicologists and geneticists to test the hypothesis that '...during human evolution, selection pressure towards increased resistance against fire-related toxicants was generated once humans started to use fire on a routine basis. This hypothesis implied that these protective variants were the new beneficial mutants, derived alleles as compared to those found in the great apes considered as the closest control in evolutionary terms not exposed to smoke on a regular basis, and hence expected to carry a less efficient ancestral variant. Once present, these new beneficial variants will be under positive selection resulting in adaptation towards improved defence against smoke-related toxic compounds.'

Lessons from tobacco smoking

In this study, the team explored the available genomic information for evidence of such genetic adaptations. They profited from numerous epidemiological and biochemical studies of toxic compounds from tobacco smoke or heated food items, which made it possible to identify *the genes involved in their detoxification* and to categorize the allelic variants observed into *low- and high-risk variants*, the former conferring increased protection from adverse reproduction effects as compared with the latter. For the majority of gene polymorphisms (29 out of 35) affecting sensitivity to the adverse effects of genotoxic combustion and food heating products the team observed that Neanderthal and/or Denisovan hominins carried the protective (low-risk) allele. However, in 26 out of 29 cases the low-risk gene variant in ancient hominins appeared to be the ancestral allele, also found in the chimpanzee and/or gorilla. This obviously contradicted their hypothesis that the low-risk alleles were the newly derived (i.e. recent) alleles. Instead, the study shows that high-risk detoxification gene alleles became more numerous in modern humans, an increase which may have already started in early Upper Palaeolithic hunter-gatherers, suggesting that it preceded the major behavioural and dietary changes of the Neolithic.

Hitchhiking on old primate adaptations

Dr Aarts: 'That the protective variants are ancestral means that no adaptation of these genes could be demonstrated and does not allow us to conclude to what extent genetic selection pressure plays a role in the high prevalence of low-risk alleles in ancient hominins. Hominins have undergone major changes in diet and habitat since the human and chimpanzee lineages split, minimally 7-8 million years ago. The fact that, nevertheless, the majority of the gene loci studied here did not diversify by genetic drift since the gorilla and (chimpanzee – hominin) lineages diverged is consistent with the sustained functional importance of these protective gene variants, and it is possible that genetic selection plays a role in their maintenance.' Dr Roebroeks, co-author and archaeologist: 'Apparently, extant human smoke detoxification capacity is to a large degree hitchhiking on detoxification capacities developed a very long time ago in our deep primate past which had nothing to do with fire.' Aarts: 'This ancestral primate capacity is possibly directed towards the detoxification of plant polyphenols and controlling potentially hazardous indolocarbazole compounds originating from the diet of these early primates and UV-mediated oxidation of tryptophan in the skin.'

Testable hypothesis

Hominins must have undergone major dietary changes adapting to different habitats in the millions of years of ecological niche change since our last common ancestor with chimpanzees. It is surprising that, apparently, these changes did not lead to major changes in the genes under consideration here, an inference that can be tested more robustly when more high-coverage Pleistocene hominin genomes become available.

Why do modern humans exhibit a more 'relaxed' detoxification capacity?

Since the use of fire must have become common practice at some point during the evolution of modern humans, the unexpected recent relaxation in the defence against toxic smoke components may suggest that the genetic variants studied were less important than expected. However, in view of the epidemiology of tobacco smoking, a more likely explanation is that, compared with earlier hominins and great apes, the total toxic burden decreased recently, in spite of the additional challenge provided by the exposure to smoke. It is tempting to speculate that this could be due to the increased detoxification of foods by cooking, and/or the decreased exposure to UV-induced compounds that needed to be controlled due to cultural adaptations, such as clothing and housing.

Ah(a) moment

A paper that came out recently (in *Molecular Biology and Evolution*) suggested that a mutation in the Ah (aryl hydrocarbon) receptor may have made modern humans *better* at dealing with toxins from smoke. The Leiden/Wageningen team also identified that very same mutation, but hesitated to attach great significance to it. Dr Aarts: 'Complementary to that study of one fixed adaptation in one important regulator gene, we show a clearly opposite trend in a wide set of 35 other gene loci comprising 2 additional regulator and 16 other detoxification (effector) genes. Both regulator and effector genes ultimately determine the efficiency of detoxification in a very complex interaction, and it will be intriguing to study which were the driving forces behind these apparently opposite adaptations.'

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Fire Usage and Ancient Hominin Detoxification Genes: Protective Ancestral Variants Dominate While Additional Derived-Risk Variants Appear in Modern Humans

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