AMYLASE GENE COPY NUMBER VARIATION

Background. The first reports of Copy Number Variations (CNVs) using Comparative Genome Hybridization on microarrays were published in 2004, based on BAC/PAC DNA (Nat Genet 36:949-51, 2004; Science 305:525-528, 2004). Soon after, oligo-microarrays replaced BAC/PAC arrays. In 2006, the Sanger Centre conducted a large-scale array study (Nature 444:444-454, 2006) that revealed significant CNV variation in the amylase gene (AMY1), which is expressed in the salivary glands and plays a role in starch digestion. This discovery drew attention, and in the following year they published a study titled “Diet and evolution of human amylase gene copy number variation” (Nat Genet 39:1256-1260, 2007). The study compared populations with high-starch diets to those with low-starch diets, and found that individuals from high-starch populations had significantly more AMY1 copies on average than those from low-starch populations. Their results suggest that diet-related selection pressures influenced AMY1 copy number variation. No variation was observed in chimpanzees.

Recently, Bolognini et al. (1, 2) revisited these findings by analyzing the domain (chr. 1p21.1) containing AMY1 (expressed in salivary glands), and AMY2A/AMY2B genes (expressed in pancreas) at the sequence level across various human populations, including 533 ancient DNA samples, three Neanderthals and one Denisovan. By examining the linkage disequilibrium in these regions, they were able to distinguish different haplotypes, which allowed them to trace the evolutionary history of these genes. Their findings suggest that the advent of agriculture, around 12,000 years ago, with its starch-rich diet (primarily cereals), exerted selective pressure that favored the duplication of the AMY genes. Interestingly, no such duplications were observed in non-human primates or other animals, except for a few “commensal” species such as dogs, pigs, rats, and mice.

The Bolognini et al. paper was published in Nature, on October 17, 2024 (online on September 4). The next day, on October 18, a paper on the same subject was published by Yılmaz et al. in Science (3,4). The main difference is that Yılmaz et al. found duplications of AMY1 in three of the six Neanderthal genomes and in one Denisovan genome. They concluded that the gene duplication occurred before modern humans diverged from Neanderthals and Denisovans, approximately 800,000 years ago.

Another explanation for these findings in Neanderthals and Denisovans could be **introgression**—the transfer of genetic material through interbreeding. Non-African genomes contain several segments of DNA inherited from these ancient cousins, and the AMY1 gene could be part of these **reciprocal exchanges**.

Both papers, however, agree on the crucial role of agriculture in driving the more recent duplication of AMY genes in humans.

Incidentally: it’s worth noting that the vitamin D-poor cereals-based diet played a crucial role in promoting lighter skin pigmentation.

1. https://www.nature.com/articles/s41586-024-07911-1
2. https://www.nature.com/articles/s41576-024-00782-2
3. https://www.science.org/doi/10.1126/science.adn0609

4. https://www.science.org/content/article/how-humans-evolved-starch-digesting-superpower-long-farming