GENOME WATCH

Genomes on ice

Julian Parkhill

This month's Genome Watch discusses the analysis of a *Helicobacter pylori* genome from the preserved Copper-Age mummy known as the Iceman and how ancient genomes shed light on the history of bacterial pathogens.

Helicobacter pylori has long been the poster-child of bacterial phylogeography. As *H. pylori* is predominantly transmitted vertically within families and maintained long-term within populations, the ancestry of the bacterium reflects the ancestry and demography of its human host. However, *H. pylori* is one of the most recombinogenic bacteria known, meaning that reconstructing its ancestry is not simple. Nonetheless, some very elegant studies have shown that the genetic relationships of *H. pylori* can be reconstructed and that these relationships recapitulate the early migrations of humans out of Africa, followed by subsequent population movements related to events such as colonial expansion and the slave trade[1].

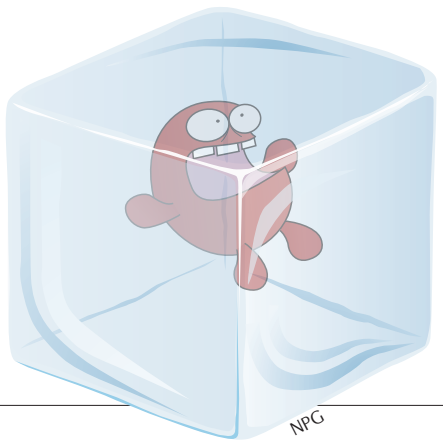
Although these studies enabled the mapping and dating of *H. pylori* expansions out of Africa by correlation with the archaeological dates of human migrations, one mystery remained: *H. pylori* infecting modern Europeans and their diaspora seemed to be a hybrid of older bacterial populations from Asia and Africa, although it was unclear when this hybridization had occurred, with estimates between 10,000–50,000 years ago. Now, analysis of a *H. pylori* genome from the 'Iceman' provides new insight into this problem.

The Iceman is a remarkable mummy of a man from southern Europe who died at high altitude in the Alps, and whose remains were preserved in the ice for 5,300 years, until their discovery in 1991. A recent paper described the sequencing of *H. pylori* from the stomach and gastrointestinal tract of the mummy[2] and showed that the Iceman was colonized by a single *H. pylori* strain. Notably, this strain was from the older population related to the Asian clade, rather than the Africa–Asia admixed population found in modern Europeans. Therefore, assuming that the strain isolated from the Iceman is representative of the European population at that time, these findings set an earliest possible date for hybridization between the Asian population and the African population, which is much more recent than previously hypothesized.

The analysis of bacterial DNA from ancient remains has a habit of overturning previous assumptions. For example, microbiologists believed that *Yersinia pestis*, the causative agent of modern plague, was also the cause of ancient plagues such as the Black Death (in the 14th–17th centuries) and the Justinian plague (in the 6th–8th centuries). However, historians challenged these ideas, arguing that many aspects of ancient plagues did not fit the epidemiology of *Y. pestis* and that other agents, such as haemorrhagic viruses, must have been the cause of those ancient plagues. The recovery of ancient bacterial genomes from skeletons associated with the Black Death, and more recently the Justinian plague[3], has shown that *Y. pestis* was indeed the cause of those plagues. Furthermore, these studies demonstrated that *Y. pestis* repeatedly emerged from China.

In an interesting parallel to the phylogeography studies of *H. pylori*, a genomic study of a large global collection of *Mycobacterium tuberculosis* elucidated the emergence and spread of tuberculosis. This study showed that the population structure of the pathogen could be overlaid on the population structure of its human host and that the phylogenetic structure created by the expansion of modern humans out of Africa mirrored the structure of the phylogeny of *M. tuberculosis*. These data led to the hypothesis that, as with *H. pylori*, *M. tuberculosis* had accompanied its host on its journey of colonization across the world, starting approximately 70,000 years ago[4]. However, more recent analysis of the genome sequences of *M. tuberculosis* from 1,000-year-old human remains in Peru provided a calibration point deep in the *M. tuberculosis* phylogenetic tree. Based on this new tree, the last common ancestor of the entire *M. tuberculosis* complex was dated to less than 6,000 years ago, suggesting that although this pathogen may well have come out of Africa, it is unlikely to have done so with the early radiations of modern humans[5].

Collectively, these studies demonstrate that as our expertise at recovering and analysing ancient DNA grows, our ability to date bacterial ancestry accurately will also grow, which will further our understanding of the emergence and spread of bacterial pathogens.



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Competing interests statement
The author declares no competing interests.