GENOME WATCH

Back to the Future!

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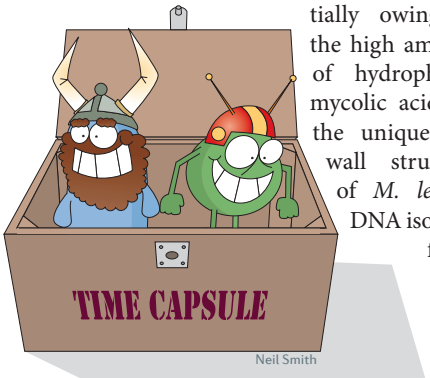
This month's Genome Watch highlights how the study of ancient DNA can increase our understanding of the evolution of pathogens.

Recent advances in the isolation and handling of DNA from ancient samples allow us to step back in time and observe diseases and their impact on shaping and changing human history. *In silico* reconstruction of ancestral states using modern strains and phylogenetic methods is one way to look back; the sequencing of ancient bacterial DNA obtained from human remains is another. Finding suitable samples that show low levels of contamination is a challenge, and not every bacterial disease will be amenable to study. However, the use of ancient bacterial DNA can provide new insights into the evolution of pathogens. Two recent publications using this approach were able to clarify some of the most fervidly discussed questions in palaeomicrobiology.

Mycobacterium spp. have a great impact on human health, as two major diseases, tuberculosis and leprosy, are caused by members of this genus. The first genomic information from medieval *Mycobacterium leprae* is now available[1]. In this study, the remains of humans infected with leprosy were identified in Sweden, Denmark and the United Kingdom based on skeletal deformations. The DNA seemed to be well preserved, potentially owing to the high amount of hydrophobic mycolic acids in the unique cell wall structure of *M. leprae*. DNA isolated from five bone and teeth samples of different individuals was sequenced and yielded deep enough coverage to provide assemblies of ~90% of each bacterial genome. Gene order within the compared genomes was highly conserved, and only a few mutations between the ancient strains and 11 modern strains were found. Five new pseudogenes of unknown function were detected in the modern isolates, but no novel pseudogenes were found in the ancient DNA. Together, these findings suggest that the decline in leprosy prevalence in sixteenth-century Europe was due to human factors such as improved social conditions, rather than reduced bacterial virulence. Leprosy is thought to have originated in Africa, from where it spread through the Middle East and into Europe[2]. Phylogenetic analysis of the ancient genomes showed that three of the ancient strains support this hypothesis, as these European isolates were similar to modern Middle-Eastern ones. The other two strains provided substantiating evidence for the subsequent introduction of leprosy from Europe into the Americas.



Yersinia pestis, the causative agent of plague, has been shown to be responsible for both the Black Death from the fourteenth to the seventeenth centuries and the modern pandemic in the nineteenth and twentieth centuries. *Y. pestis* has also been suggested to be the cause of the Justinianic Plague of the sixth to eighth centuries, a proposal that was the focus of a recent genome-based study[3]. Samples were obtained from the teeth of ostensible plague victims in an early-medieval cemetery in Bavaria, Germany; given the controversy over the origins of the pandemic, extreme care was taken during handling to prevent contamination. It was not necessary to sequence the whole genomes, as genotyping of five significant SNPs, which occur along specific branches of the *Y. pestis* phylogenetic tree, allows the correct placing of strains within the tree[4]. Genotyping the five SNPs determined that the ancient Bavarian strain falls into the oldest part of the tree and is distinct from any modern lineage. This provides compelling evidence that *Y. pestis* was indeed the cause of the Justinianic Plague. Age estimates for the phylogeny of *Y. pestis* have been calculated previously[5], and the age of the branch for the putative Justinianic plague strain compared well with radiocarbon dating of the human remains from the Bavarian cemetery. The placement of the ancient strain within a global *Y. pestis* context also suggested that, as with other plague waves, the Justinianic Plague most probably originated in Asia.

For Mark Twain[6], "no occurrence is sole and solitary, but merely a repetition of a thing which has happened before, and perhaps often." This might be true for the evolution of pathogens as well. By looking at the past and comparing ancient and present genomes, we can learn how their future might look. Watch out for the old things — they stick around!

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Competing interests statement
The authors declare no competing financial interests.