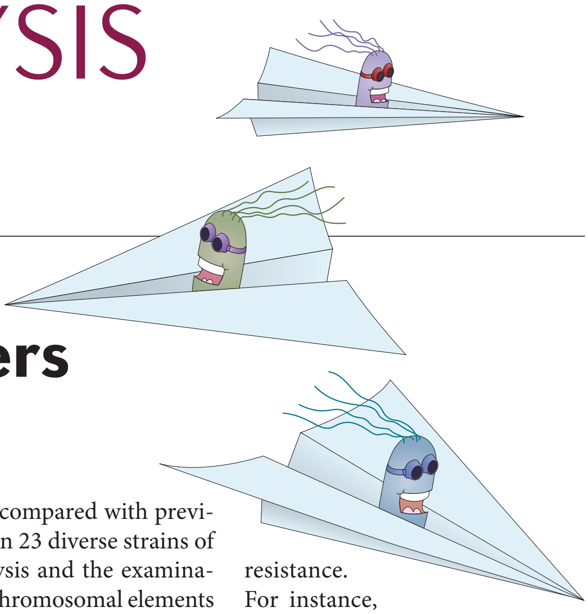
NEWS & ANALYSIS



GENOME WATCH

Bacterial frequent flyers

Ankur Mutreja

This month's Genome Watch describes how sequencing technology is providing insight into the geographical relationships and global travel of bacterial pathogens.

Phylogeography analyses the genomic relationships between strains of a particular bacterium and couples this with geographical information about the origins of the strains to infer how species move over time. This growing field is providing insights into how pathogenic bacteria travel across the globe from endemic areas to non-endemic areas, where outbreaks are becoming more common. With more air travel today than ever before, there is growing evidence that asymptomatic carriers can transport diseases under the radar of the health authorities[1]. Although measures to contain the introduction of new pathogens are rolled out quicker today than they have been in the past, they are no match for the ease with which a disease can spread in today's globalized world.

Tracing strains within a single bacterial outbreak is often impossible using traditional typing methods owing to the low underlying genetic diversity. However, the latest sequencing technologies can differentiate strains at high resolution using genome-wide SNP analysis, which can be carried out within a clinically relevant time frame.

The cholera outbreak that followed the 2010 Haitian earthquake seemed to be the result of an imported pathogen, as there had been no cholera in Haiti for the preceding 100 years. To investigate in more detail, researchers sequenced the genomes of two Haitian isolates of the causative pathogen, *Vibrio cholerae*, obtaining results in <24 hours using Pacific Biosciences third-generation single-molecule real-time DNA sequencing[2]. For comparison, three other isolates were sequenced, one from South America and two from South Asia. The sequence data for these five strains were then compared with previously published data on 23 diverse strains of *V. cholerae*. SNP analysis and the examination of hypervariable chromosomal elements supported a close relationship between the Haitian and South Asian isolates, whereas the South American strains were found to be distantly related[2].

Another group used Illumina Genome Analyzer IIx technology to sequence 24 Nepalese *V. cholerae* isolates[3], which they compared to three previously sequenced Haitian isolates and seven isolates from South Asia and South America. Phylogenetic analyses showed that all the Nepalese isolates cluster in a single clade that also contains isolates from Haiti and Bangladesh. Within this clade, the Nepalese strains are subdivided into four closely related subclades, one of which shows that the Haitian strains are closely related to a particular group of Nepalese strains, with only one or two non-synonymous SNPs separating them. When combined with antimicrobial-susceptibility tests and pulsed-field gel electrophoresis results, these data also support the South Asian origin of the Haitian cholera outbreak[3].

Using Illumina technology, researchers at the Sanger Institute added to this global data by sequencing 136 global *V. cholerae* isolates[4]. This work showed that strains which have travelled across the globe in the past 73 years (representing a seventh cholera pandemic) had a single source in an endemic area and travelled to non-endemic areas in independent but overlapping waves. The work also identified three cases for which the most probable explanation for the phylogenetic results observed is that travellers carried *V. cholerae* in their gut, suggesting that sporadic transmission of cholera is not uncommon.

As tourism has flourished, so has the global spread of pathogens and antibiotic resistance. For instance, a recent study used PCR typing and digestion by S1 nuclease to identify the presence of the antibiotic resistance gene bla_{NDM-1} in 147 *Escherichia coli* and *Klebsiella pneumoniae* isolates from India, Pakistan and the United Kingdom[5]. When they combined their data with the travel history of UK patients in the study, they found that all 37 UK isolates were from patients who had travelled to India or Pakistan within the past year or had links with these countries. Adding to the worrying picture, most of the isolates carried genes on easily transferable plasmids.

Phylogenomics is a powerful tool to understand the global epidemiology of pathogens. In order to draw robust conclusions, detailed metadata must be superimposed on phylogenetic information. In the future, genomic data might be used to provide evidence to scientists and policy makers, allowing better-informed public health decisions at local, national and international levels.

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Competing interests statement

The author declares no competing financial interests.