GENOME WATCH

# Genomic polish for shoe-leather epidemiology

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This month's Genome Watch highlights the advantages of using whole-genome sequencing for infectious-disease surveillance and infection control.

Whole-genome sequencing has the potential to transform clinical microbiology and is emerging as a useful tool for the detection of infectious agents and for monitoring disease trends and outbreaks. Among the most prominent nosocomial pathogens are *Klebsiella pneumoniae* and methicillin-resistant *Staphylococcus aureus* (MRSA). In the United States, approximately 70% of *K. pneumoniae* strains that harbour the plasmid-encoded *K. pneumoniae* carbapenemase (*KPC*) gene belong to sequence type 258 (ST258), and in the United Kingdom, the predominant MRSA clone is ST22 UK EMRSA-15. Both of these multidrug-resistant bacteria are associated with infection outbreaks, but standard genotyping techniques (such as multilocus sequence typing) do not provide sufficient resolution to definitively assign particular strains to an outbreak, much less to specifically infer transmission routes between individuals. However, two recent studies combined whole-genome sequencing and shoe-leather epidemiology to overcome these limitations.

Snitkin *et al.*[1] retrospectively sequenced *KPC*-encoding *K. pneumoniae* strains from 18 patients involved in a suspected hospital outbreak in the USA. All of the strains were closely related, with a total of 41 SNPs across their genomes, suggesting that they were likely to be part of an outbreak. The authors sequenced seven strains isolated from the index patient during her 1-month stay at the hospital, revealing that three distinct strains were present at different anatomical sites. By integrating the genomic data with detailed epidemiological information, the authors found that these distinct strains were involved in three independent transmission events from the index patient to other patients.

In the second study[2], Harris *et al.* investigated a suspected MRSA outbreak in a special-care baby unit in the United Kingdom. The strains involved were initially identified by an unusual antibiotic resistance pattern. Whole-genome sequencing revealed that 14 of the strains differed by only 20 SNPs, which allowed the authors to assign them to an outbreak cluster. By integrating detailed epidemiological and genomic data, the analysis revealed that the outbreak involved a further ten patients and had spread from the special-care baby unit to the maternity ward and the wider community.

Sixty-four days after the last MRSA-positive patient had left the special-care baby unit, another patient carrying the outbreak strain was identified. Subsequent screening of the staff identified an individual colonized with the outbreak strain. Importantly, sequencing of 20 colonies from this staff member revealed a mixture of variants of the outbreak strain, some that were closely related to those from the first period of the outbreak, and others that were more closely related to variants from the second period of the outbreak. This was considered to be consistent with carriage of the outbreak strain across the 64-day gap and transmission by this staff member to the last patient in the outbreak.

Three key points are evident from these studies. First, although whole-genome sequencing provides accurate resolution of strains involved in an outbreak, shoe-leather epidemiology (an investigation of the people and places where the disease outbreak actually occurs) is crucial for understanding transmission routes among individuals. Infection control practitioners and epidemiologists can then intervene to prevent further spread, as in the case of the MRSA outbreak, when the staff member was identified and subsequently decolonized.

Second, with the increasing availability and reducing costs of sequencing, a greater sampling depth will be possible. Sequencing of multiple colonies from multiple time points from multiple patients will provide novel insights into the dynamics of colonization, transmission and disease.

Finally, the ability to accurately identify transmission routes raises ethical issues. Many hospitals now report rates of infections with multidrug-resistant bacteria, and our knowledge of how these organisms are acquired and transmitted is becoming more detailed. Should patients be able to access not only hospital infection rates but also information pertaining to exactly how these infections are acquired? Guidelines exist for health care staff with blood-borne viral infections, but we will also need to carefully consider how to manage information about health care staff who might be carriers of multidrug-resistant bacteria.


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2. Harris, S. R. *et al.* Whole-genome sequencing for analysis of an outbreak of meticillin-resistant *Staphylococcus aureus*: a descriptive study. *Lancet Infect. Dis.* 13 Nov 2012 (doi:10.1016/S1473-3099(12)70268-2)

**Competing interests statement**
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