GENOME WATCH

Keeping an eye on *P. aeruginosa*

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This month's Genome Watch looks at how whole-genome sequencing (WGS) can be used to track the source of *Pseudomonas aeruginosa* infection and to investigate the transition and adaptation of this opportunistic pathogen from the environment to the human host.

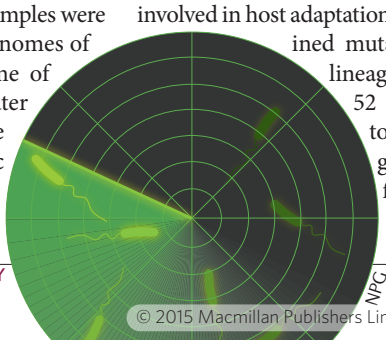
Pseudomonas aeruginosa is a Gram-negative bacterium that is widely present in soil and aquatic environments. However, it is also an opportunistic human pathogen, causing respiratory infections in patients with impaired immunity — including patients with cystic fibrosis[1] — and it is a major cause of hospital-acquired infections[2]. Two recent studies used whole-genome sequencing (WGS) to determine the source of this pathogen in an at-risk group of burn victims in a hospital setting[2] and to understand the genetic adaptations of genotypically different strains to the human airway[1].

Hydrotherapy is a common part of treatment for burn victims, involving either showering or bathing to aid wound cleansing, but it has been suggested that patients may acquire *P. aeruginosa* infections after exposure to contaminated water sources. However, current molecular typing techniques used to investigate the source of *P. aeruginosa* outbreaks in hospitals have limitations. Quick *et al.*[2] investigated whether WGS can be used to determine the source of infection in a cohort of burn victims at a recently opened burns centre in the United Kingdom. The authors collected samples from patients and hydrotherapy water outlets, and they found that half of these samples were positive for *P. aeruginosa*. The genomes of 141 isolates and the metagenome of a biofilm recovered from water fittings were sequenced using the Illumina Miseq and the Pacific Biosciences RS II platform, and the authors identified eight distinct clades, the most prevalent being clade E, which has been reported to be associated with water. The genotypes recovered from three patients were identical to isolates from the water supplies in their rooms and, furthermore, phylogenetic reconstruction showed clear clustering of genotypes and plasmids corresponding to room or water outlets. These findings suggest that a WGS approach is suitable to track the transmission of *P. aeruginosa* from the water supply system in a hospital to a patient.

In a second study, Marvig *et al.*[1] collected 474 isolates from the sputum of 34 newly infected children and young individuals with cystic fibrosis attending a clinical centre in Denmark to monitor long-term *P. aeruginosa* colonization. The isolates were sequenced on the Illumina HiSeq 2000 platform and grouped by identifying single nucleotide polymorphisms (SNPs). Isolates with <6,000 SNPs between them were designated clonal complexes. A total of 53 distinct clone types were identified, 43 of which were only observed in individual patients. This is in agreement with the notion that children with cystic fibrosis acquire unique *P. aeruginosa* strains from diverse environmental sources, leading to the presence of diverse genotypes within a cohort[3]. In a few cases, the isolates from different individuals were closely related, separated by <30 SNPs, which is indicative of patient-to-patient transmission or acquisition from a common source. In these cases, there were temporal overlaps in the patients' hospital attendance.

To investigate the evolution of genes involved in host adaptation, the authors examined mutation events in 36 lineages and identified 52 genes (referred to as pathoadaptive genes) that were frequently mutated. In addition, six lineages seemed to be hypermutators, having mutations in the DNA mismatch repair genes, and therefore accumulated greater genetic diversity during colonization. Ten of the identified pathoadaptive genes were associated with antibiotic resistance and eight with the regulation of biofilm formation, whereas the role of other candidate genes in pathogenesis was less apparent. The finding that there are similar mutations in genotypically different strains suggests that adaptation to the human host involves the evolution of particular traits, such as through the most frequently mutated gene *mexZ*, which is associated with resistance to one of the first-line antibiotics used in the clinic. Isolates from three patients from the burns centre also rapidly developed antibiotic resistance in response to treatment owing to the accumulation of mutations in known resistance genes; however, those genotypes did not persist in the ward environment[2].

In summary, these two studies show that WGS is a useful tool to trace the specific source of infection and to characterize the genes involved in adaptive evolution of *P. aeruginosa*, or other opportunistic pathogens, which may help control future outbreaks and guide treatment strategies.



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Competing interests statement
The author declares no competing financial interests.