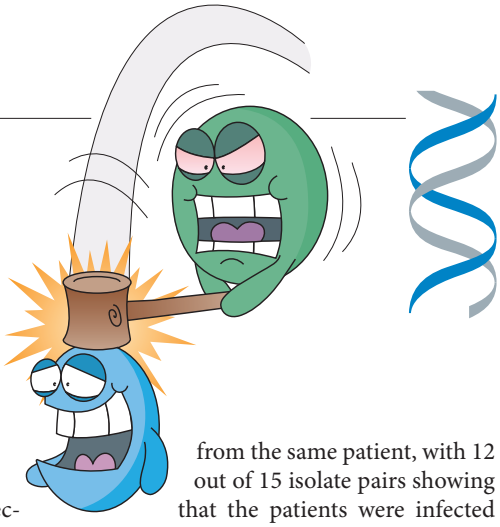
GENOME WATCH

Klebsiella pneumoniae: when a colonizer turns bad



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This month's Genome Watch highlights how whole-genome sequencing (WGS) and epidemiological studies can be combined to explore the link between colonization and infection by *Klebsiella pneumoniae* in patients who are hospitalized.

Klebsiella pneumoniae is one of the most common causes of hospital-acquired infections worldwide and, owing to the high prevalence of antibiotic-resistant strains, it has become a serious public health concern. In most cases, this opportunistic pathogen colonizes the gut, throat or nasal passages without causing disease, but in some cases it can cause lung, skin, urinary tract and bloodstream infections. Recently, two studies investigated whether *K. pneumoniae* infections are caused by carriage strains from the same patient.

In the first study, Martin *et al.*[1] screened patients who were admitted to intensive care unit (ICU) and oncology wards at the University of Michigan Hospital in the United States[1]. Patients were screened for gastrointestinal colonization with *K. pneumoniae* on arrival and were then monitored over a 3-month period for possible respiratory, urinary tract or bloodstream infections. Carriage and disease strains of *K. pneumoniae* were directly compared to determine whether the colonizing strain had caused the infection by sequencing the capsule export gene (*wzi*). Matching *wzi* pairs were subsequently analysed by WGS and core genome multilocus sequence typing (cgMLST), which compares the sequences of more than 600 chromosomal genes.

Of the 1,765 patients, 406 were colonized with *K. pneumoniae* on admission to the hospital. Of these 406 patients, 21 (5.2%) developed an infection with *K. pneumoniae*, whereas only 18 (1.3%) patients who were not colonized developed an infection. Analysing carriage and disease isolates from the same patient revealed that for 13 out of the 16 patients the infection was caused by their colonizing strain. Sequencing the *wzi* gene from a selection of carriage strains showed 43 different *wzi* genotypes in 40 patients, which suggests that colonizing *K. pneumoniae* isolates are very phylogenetically diverse.

In the second study, Gorrie *et al.*[2] used genomics to analyse colonization and infection with *K. pneumoniae* in 498 patients who were admitted to an ICU in Melbourne, Australia. *K. pneumoniae* carriage rates were 19% for patients who had recent healthcare contact and 6% for patients who were admitted directly from the community. During the study, 49 patients became infected with *K. pneumoniae*, which represents 16% and 3% of the colonized and non-colonized groups, respectively. Rather than using WGS for confirmation of potential matching isolates, the authors sequenced and analysed the genomes of all of the carriage and disease *K. pneumoniae* strains that were isolated from patients who had been admitted to the ICU. They defined *K. pneumoniae* lineages using the RAMI algorithm[3] (a tool that identifies and characterizes phylogenetic clusters in microbial communities), and they also counted single-nucleotide differences between sequences to determine the relatedness of isolates in the same lineage.

The *K. pneumoniae* isolates in this study were unexpectedly patient-specific, with only 19% of lineages identified in more than one patient and 49% of infections caused by a lineage that was unique to that patient. Five likely transmission chains were identified in the ICU, which accounted for 12% of infections. Similar to the first study, the authors found that disease *K. pneumoniae* isolates were very likely to match the carriage isolate from the same patient, with 12 out of 15 isolate pairs showing that the patients were infected by the same strain that they carried.

Together, these studies present robust genomic evidence that the gastrointestinal microbiota is a substantial source of hospital-acquired *K. pneumoniae* infections, with ~80% of infections in patients who were colonized caused by their own carriage strain. Genome sequencing has enabled researchers to explore the link between colonization and infection at very high resolution, and to confirm this epidemiological link in patient groups in two different continents. Importantly, knowing that many infections are self-acquired from a patient's own gastrointestinal microbiota, rather than being hospital-acquired, provides new options for treatment. Screening for colonization on admission to hospital, as well as the characterization of carriage *K. pneumoniae* isolates in patients that are at risk, could help to guide treatment decisions and inform infection control programmes. In addition, there is potential for developing new therapeutic interventions to protect patients from infections that are caused by the *K. pneumoniae* isolate that they carry.

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1. Martin, R. M. *et al.* Molecular epidemiology of colonizing and infecting isolates of *Klebsiella pneumoniae*. *mSphere* **1**, e00261-16 (2016).
2. Gorrie, C. L. *et al.* Gastrointestinal carriage is a major reservoir of *Klebsiella pneumoniae* infection in intensive care patients. *Clin. Infect. Dis.* http://dx.doi.org/10.1093/cid/cix270 (2017).
3. Pommier, T. *et al.* RAMI: a tool for identification and characterization of phylogenetic clusters in microbial communities. *Bioinformatics* **25**, 736–742 (2009).

Competing interests statement
The author declares no competing interests.