GENOME WATCH

Attack of the clones

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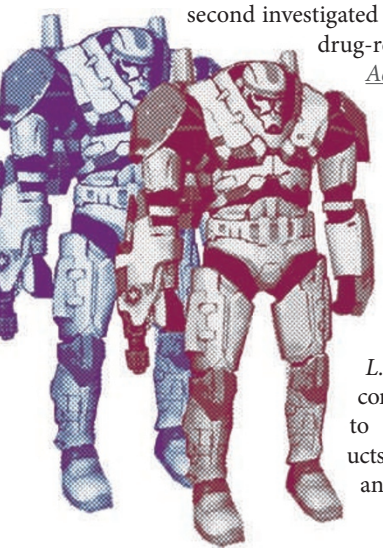
This month's Genome Watch discusses two recent examples of the use of next-generation sequencing techniques in public health settings.

Next-generation sequencing has hugely improved the speed with which we can generate whole-genome sequences. The first bacterial genome sequence, that of *Haemophilus influenzae*, was published in 1995 and took 1 year to complete, whereas draft bacterial genomes can now be produced in a matter of days. One application for the speedy generation of whole-genome sequences is in tracing the epidemiology of infectious diseases. The clonal expansion of a strain can confound analysis of its transmission, as isolates can seem to be identical by traditional typing methods such as pulsed-field gel electrophoresis (PFGE), multi-locus sequence typing (MLST) or variable-number tandem repeat (VNTR) analysis.

Two recent studies used high-throughput next-generation sequencing to explore the dynamics of infectious-disease outbreaks. The first analysed a national outbreak as it happened — a food-borne *Listeria monocytogenes* epidemic in Canada[1]— and the second investigated a spate of multi-drug-resistant (MDR) *Acinetobacter baumannii* infections in a single hospital in the United Kingdom[2].



In 2008, a nationwide epidemic of listeriosis in Canada was caused by *L. monocytogenes*-contaminated 'ready to eat' meat products[1]. Clinical isolates and samples taken from the food-processing facility involved were all identified as *L. monocytogenes* serotype 1/2a, which is frequently found in food-processing environments but is less often associated with epidemic listeriosis. The samples all had one of two very similar PFGE profiles, so a clinical isolate from each group was selected for 454 sequencing to examine the diversity within the outbreak and to discover the cause of this variation. A new plasmid, pLM5578, was identified and the isolates were shown to differ by 28 single-nucleotide polymorphisms (SNPs). The PFGE distinction between the isolates was shown to be caused by a prophage insertion of 33 kb. The plasmid was sporadically present in samples and included two regions containing cadmium resistance genes, which have been associated with resistance to the sanitizers that are used in food-processing facilities.

The first genome sequences in this study were available for analysis within 3 days. This rapid production of sequence data while the outbreak was ongoing allowed the researchers to screen for the plasmid, prophage and SNPs in other isolates, resulting in the identification of the three distinct but closely related strains that were involved in the outbreak.

Injured military personnel returning from Iraq and Afghanistan are frequently colonized with MDR *A. baumannii*, a nosocomial pathogen that usually causes ventilator-associated pneumonia and septicaemia on critical-care wards. It survives on medical equipment, fabrics and furniture and can colonize health care workers or patients without detection in routine clinical samples[3].

Selly Oak Hospital in Birmingham, UK, treats civilians and repatriated military casualties side by side. In 2008, MDR *A. baumannii* was isolated from four military and two civilian patients, all but one of whom had been treated in the intensive therapy unit (ITU)[2]. The six samples had PFGE and VNTR results matching *A. baumannii* European clone 1, as well as identical antibiotic resistance profiles. Lewis *et al.* sequenced the whole genome of each isolate on the 454 platform, and three well-validated SNPs were identified.

Various hypotheses had been proposed to explain the chain of bacterial transmission, and the genome data led the authors to support one particular scenario: the MDR *A. baumannii* wound infection of one military patient was transmitted to the civilian patient in the adjacent bed. As the civilian infection was not detected until several weeks after the military patient left, the bacteria may have colonized this patient at undetectable levels at an early stage; alternatively, the patient may have been colonized from the hospital environment.

Whole-genome sequencing using next-generation technologies has the potential to produce epidemiologically relevant data very quickly. This could be used to inform infection control by tracking transmission routes in a clonal outbreak or to identify virulence genes in an epidemic that is still unfolding. We expect that it will become increasingly popular as a tool in public health scenarios.

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1. Gilmour, M. W. *et al*. High-throughput genome sequencing of two *Listeria monocytogenes* clinical isolates during a large foodborne outbreak. *BMC Genomics* **11**, 120 (2010).
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Competing interests statement
The author declares no competing financial interests.

DATABASES
Entrez Genome Project: http://www.ncbi.nlm.nih.gov/genomeprj
Acinetobacter baumannii | *Haemophilus influenzae* | *Listeria monocytogenes*

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