Published online 21 January 2010 | Nature | doi:10.1038/news.2010.25

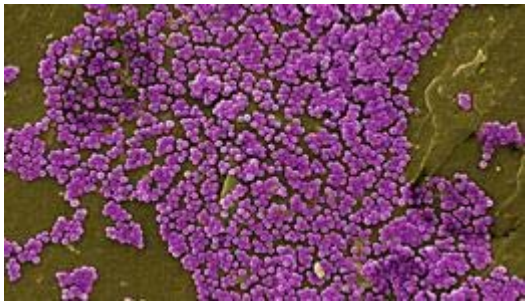
News

Superbug family tree sketched out

Next-generation genome sequencing enables detailed tracking of MRSA infections.

Lucas Laursen

Antibiotic-resistant bacteria have families, too, according to a study that uses the detailed genetic relationships of bacterial strains to map out how certain infections spread within hospitals and countries. The genomic-sequencing technology that made the study possible could one day enable hospital administrators to track infections back to the individuals and objects that transmit them, say the study authors.



The spread of MRSA has been mapped using genetic sequencing.

Janice Haney Carr/CDC

The team studied different samples of a strain of methicillin-resistant *Staphylococcus aureus* (MRSA) called sequence type 239 (ST239). The bacterium poses a huge health-care problem because it is easily transferred in hospitals and is resistant to multiple antibiotics, so MRSA infections in humans are difficult to treat and can be lethal.

ST239 was originally identified and characterized using a technique from the first generation of genomics technology, known as multilocus sequence typing (MLST), which measures mutations in a handful of core genes. Because these core genes are the least likely to mutate, the method yields family trees of bacterial relatedness with too few branches to study an infection's spread in much detail.

"According to MLST, all of these samples are identical," says co-first author Simon Harris of the Wellcome Trust Sanger Institute in Hinxton, near Cambridge, UK. But faster, next-generation sequencing technology now makes it possible to scan the entire genome of MRSA strains at low cost. The team used this genome-wide high-resolution method to select 4,310 variable sites in the genome, which enabled them to individually identify each of 63 samples of MRSA ST239.

"Genome-wide high-resolution sequencing is going to give us a way to use molecular genetics to track epidemiological spread, potentially at the level of a single transmission," says evolutionary biologist Carl Bergstrom of the University of Washington in Seattle, who was not involved in the study.

Diverse origins

The team computed the most likely family tree that would account for the genetic differences between the MRSA samples. The tree reflected the geographic origins of the samples, which ranged from Australia and Argentina to Turkey and Thailand. However, certain exceptions revealed transmission of MRSA between countries. Within the branch of the tree containing samples largely from Thailand were two samples from MRSA outbreaks in Denmark and the United Kingdom, suggesting that those

outbreaks occurred after a transmission event from Thailand, write the researchers in this week's *Science*[1].

There was also a strong connection between samples from Brazil and Portugal, which led the team to link a 1997 outbreak of MRSA in Portugal with a strain transmitted from Brazil. The earliest origin of this strain of MRSA, however, appears to have been in Europe, says Harris.

In addition, the study reveals that MRSA accumulates one single-nucleotide mutation about every 6 weeks. This is faster than previous estimates for similar bacteria, write the authors, but is in line with recent research suggesting that mutation rates depend on a number of factors, including bacterial population size. The team also found evidence of independent, parallel evolution in different branches of the MRSA strain as a response to antibacterial treatments in hospitals.

Screen dream

Knowing the detail of how such infections spread is crucial information for epidemiologists and public-health workers, says Bergstrom: "This possibility of getting the exact transmission sequence in an outbreak would be tremendously valuable." To prevent disease spread, clinicians can design hospital protocols differently if they know whether the strain is spread evenly throughout the human population, or if just a couple of individuals are super-transmitters. The information might also help them to prescribe antibiotics that would be effective against the specific strain found in the hospital — avoiding antibiotics with broader activity which may have allowed MRSA to develop resistance in the first place.

Study author Sharon Peacock, a microbiologist at the University of Cambridge, UK, explains that the team's ambitions are to adapt the technique so that people "with a relatively low level of training" can do pathogen genetic screening in clinics worldwide.

To try to prevent the spread of MRSA in the United Kingdom, hospitals there already have initiatives such as increased hand-washing and first-generation diagnostic screening that have cut the number of MRSA-related deaths, Peacock adds. But screening prices for the new technology, currently around £200 (US$320) per patient, should continue to drop, allowing such tests to be used in hospitals. "This gives you the potential to work out what interventions will most effectively break the transmission of any bacterial pathogen," Bergstrom says.

References

1. Harris, S. R. *et al. Science* **327,** 469-474 (2010).

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Nature ISSN 0028-0836 EISSN 1476-4687