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Plug-n-play in Staph adaptation

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Cathy Holding
Email: cathyholding@aol.com

By comparing *Staphylococcus aureus* strains, British researchers this week highlighted the important role played by easily exchanged, mobile genetic elements in the organism's global success and in the havoc they sometimes wreak in hospitals.

Matthew Holden, at the Wellcome Trust Sanger Institute in Cambridge, and colleagues compared two pathogenic *S. aureus* strains: a recent hospital-acquired representative of the epidemic methicillin-resistant *S. aureus* EMRSA-16 clone (MRSA252), and an isolate of an invasive community-acquired methicillin-susceptible *S. aureus* clone (MSSA476). The authors sequenced the isolates and compared them with published *S. aureus* genome sequences.

A pool of virulence and antibiotic resistance genes in the form of large mobile "accessory elements" is available for transfer between strains, Holden and colleagues report in the Proceedings of the National Academy of Sciences USA Early Online Edition (*Proc Natl Acad Sci USA* 2004, **101**:9786-9791).

No single strain has all these elements, but the ease of exchange is probably why the organism is so globally successful, according to Mark Enright, a coauthor from the University of Bath. "We found a good deal of similarity between the strains, and a surprisingly high level of variation," he said. "There were quite a lot of genes which were present in one strain but not in another, and a lot of these were of unknown function."

"If you look at the actual sequences they are generally the same: there's a skeleton, if you like, where all *Staph aureuses* are the same, and then there are regions that pop in and out," commented Matthew Avison from Bristol University, who was not involved in the study. "The challenge for the future is to understand which of these 'plug-and-play' items are actually important for specific characteristics of *Staph aureus*."

Avison said that while the resistance and virulence cassettes were well known, there were other subtler things that needed investigation, "like why some *Staph aureus* are good at causing epidemics, why some hang around in hospitals and become endemic strains. What makes one turn into the other? These things are also likely to be part mutation, part insertion."

In another article in the journal, Ben S. Cooper and colleagues write that the development of endemic populations and the occurrence of sudden outbreaks at previously MRSA-free hospitals are more likely to be due to changes in the community reservoir.

Cooper, from London's Royal Free and University College Medical School, said that although the proportion of people in the community carrying MRSA is very low - about 1% - "that reservoir is really extremely important in explaining what is going on in the longer term."

The authors used a mathematical model to show that changes in the community reservoir cause previously in-control hospitals to suddenly become overwhelmed with *S. aureus*infection. "Nationally, you do have this strong spatial effect - that the hospitals that have the big problems with MRSA are geographically clustered," Cooper told us. "That's gradually going to spread to the neighboring hospitals via the community reservoir and by direct transfer between hospitals."

Community-type isolates are becoming more common in hospitals, according to Avison. "Bizarrely, what you get is a series of isolates that are less and less resistant to other antibiotics," he said. One explanation was that certain antibiotics were not being used in hospitals because of the belief that they were ineffective, thus lifting the selection pressure for antibiotic resistance. The mobile resistance elements must exact a price on the organism, which was only acceptable in the "do-or-die" situation of an antibiotic, he said.

Meanwhile, Enright pointed out that in UK hospitals at the moment, "some level of resistance to vancomycin exists in every kind of MRSA."

But the majority of strains have arisen from mutations that have not spread from - and are unlikely to spread to - anywhere else, according to Neil Woodford, head of the Resistance Mechanisms Monitoring Unit at the Health Protection Agency in London.

"In terms of transferable vancomycin resistance, there are only three Staph isolates in the world that are known to have acquired resistance from another bug... vancomycin-resistant *Enterococcus*. And that's something that really needs to be put into perspective," said Woodford.

References

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