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Computational methods reveal how hospital-acquired bacteria spread

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Scientists at the Academy of Finland's Centre of Excellence in Computational Inference Research have developed novel computational methods that have yielded essential knowledge of how hospital-acquired bacteria spread and develop. These new methods, based on randomised algorithms, make it possible to analyse extensive genomic data significantly faster and more efficiently than previously. By applying these results, it is possible to better follow hospital-acquired infections in the future, or even fight them in real time.

The new methods are used to develop models of the evolution of bacteria and viruses. "Essential for the evolution of the bacteria that cause hospital-acquired infections is the horizontal gene transfer. It means that several different cell processes transfer genes between the lineages of the same and different species so that the bacterium becomes resistant to antibiotics and the virulence factor rapidly spreads in the population," explains group leader, Professor Jukka Corander. Corander's group is part of the Centre of Excellence in Computational Inference Research.

This so-called recombination of bacteria makes it much more complicated to carry out evolution analyses. To facilitate such analyses, Corander's group in cooperation with researchers from Harvard University and the Wellcome Trust Sanger Institute has developed a number of methods based on smart randomised algorithms. These methods facilitate efficient and reliable analyses of extensive genomic data. With the current, most commonly used computational methods this

work would take several months or even several years.

Two of the group's methods have recently been applied by an international study. This study demonstrated that more than half of the genetic variation of the MRSA bacteria (i.e. methicillin-resistant strains of Staphylococcus aureus) is caused by horizontal genomic transfer. This shows that the evolutionary analyses of the strains of bacteria are necessary when investigating the spread of bacteria in a host population. This horizontal variation significantly distorts the results received from normal evolutionary analyses.

"On the basis of the results from these analyses, i.e. the evolutionary variation, we're able to estimate when a certain strain of the MRSA bacterium has entered a country and started to spread to hospitals. This is the first time we have been able to prove that the interplay between the horizontal genomic variation and the mutational genomic variation may vary significantly across geographical locations and even between individual hospitals," Corander says. According to Corander, these insights open up new opportunities for in-depth studies on the spread and variation of MRSA and related causalities.

In another recently published study, Corander's group investigated the origin and evolution of the *Enterococcus faecium* bacterium that has adapted to survive in hospital environments. By using its analysis methods, the group found out that the forms of the bacteria originate from several independent sources, which is contrary to previous knowledge. In the nuclear genome of hospital strains of *E. faecium*, fewer signs of horizontal transfer were found than expected. This discovery led to a hypothesis that strains of bacteria that have adapted to survive in hospital environments may become either genetically or ecologically more isolated after horizontal transfer.

MRSA is a globally spread bacterium that is especially troublesome in

hospitals. It is resistant to most antibiotics and annually causes the death of tens of thousands of people in the US, for instance. According to cautious estimates, the annual costs incurred by MRSA infections amount to several billion US dollars. In recent years, the *E. faecium* bacterium has become one of the major causes of hospital-acquired infections and its antibiotic-resistant strains have caused severe hospital epidemics worldwide.

More information: Santiago Castillo-Ramirez, Jukka Corander, Pekka Marttinen, Mona Aldeljawi, William P Hanage, Henrik Westh, Kit Boye, Zeynep Gulay, Stephen D Bentley, Julian Parkhill, Matthew T Holden and Edward J Feil (2012) Phylogeographic variation in recombination rates within a global clone of Methicillin-Resistant Staphylococcus aureus (MRSA) Genome Biology, 13:R126 doi:10.1186/gb-2012-13-12-r126. genomebiology.com/2012/13/12/R126/abstract

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