

Publication

Patent

Assessing Data Sets. PCT/AU01/00527

Journal Articles

Huygens, F., Stephens, A.J., Nimmo, G. and Giffard, P.M. 2004. *mecA* locus diversity in MRSA isolates in Brisbane, Australia, and the development of a novel diagnostic test for the Western Samoan Phage Pattern clone. *J. Clin Microbiol.* **42**:1947-1955

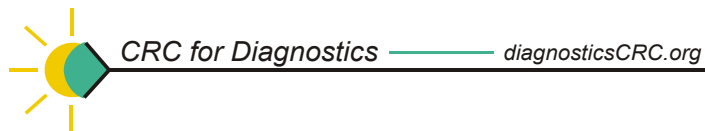
Robertson, G.A., Thiruvenkataswamy, V., Shilling, H., Price, E.P., Huygens, F., Henskens, F.A. and Giffard, P.M. 2004. Identification and interrogation of highly informative single nucleotide polymorphism sets defined by bacterial multilocus sequence typing databases. *J. Med. Microbiol.* **53**:35-45.

Howard, C., van Daal, A., Kelly, G., Schooneveldt, J., Nimmo, G. and Giffard, P.M. 2002. Identification and mini-sequencing based discrimination of SHV β -lactamases in nosocomial infection associated *Klebsiella pneumoniae* in Brisbane, Australia. *Antimicrob. Agents Chemother.* **46**:659-664

Huygens, F., Schooneveldt, J., Nimmo, G., Munckhof, W and Giffard, P.M. 2002. Genotyping of methicillin resistant *Staphylococcus aureus* by assaying for the presence of variable elements associated with *mecA*. *J. Clin. Microbiol.* **40**:3093-4097.

Information

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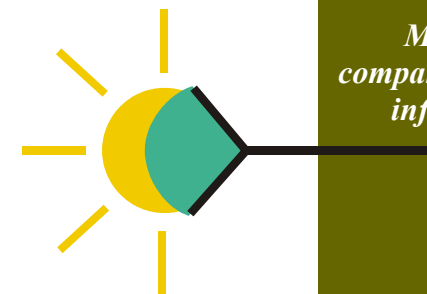
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Bacterial identification and genotyping

*Mining of
comparative genetic
information*



The CRC for Diagnostics

An Australian Co-operative Research Centre,
with world class researchers and end users
in a strong alliance of research & commercialisation expertise.

Minimum SNPs

Inspiration

Understanding the population structures and patterns of dissemination of infectious agents provides essential ammunition to those entrusted with infectious disease diagnosis, public health assurance, infection control & biodefense.

Comparative microbial genomics has revolutionized understanding of microbial population biology, evolution and molecular biology. We have exploited this to develop microbial genotyping approaches that are based upon the efficient use of genetic polymorphisms defined by the rapidly expanding databases of comparative microbial genomic data.

Central to our approach is the computerised analyses of comparative genetic data to identify minimal sets of polymorphisms for predefined levels of genotyping resolution.

Investigation

Software engineering

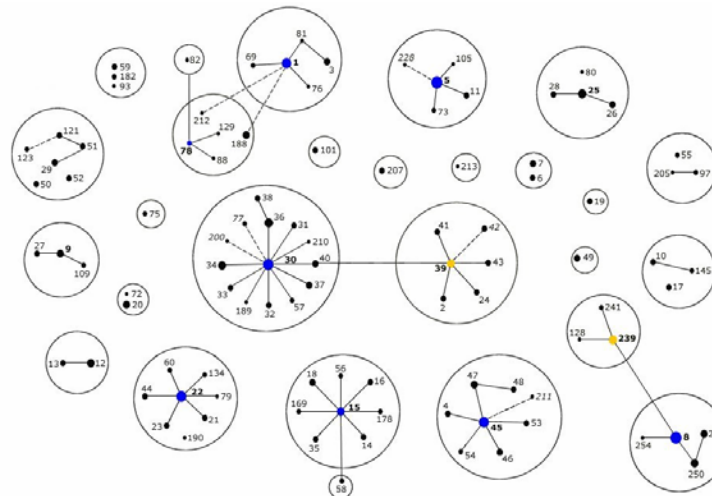
The software package “Minimum SNPs” was developed in a collaboration between the *CRC for Diagnostics* and the *Discipline of Computer Science and Software Engineering* at the University of Newcastle, Australia. This program takes comparative gene sequence data as input and provides as output sets of single nucleotide polymorphisms (SNPs) with a known level of discriminatory power.

Data mining

Sets of SNPs with high discriminatory power have been identified in a wide range of pathogenic bacteria. In all cases, a useful level of discrimination was achieved with just seven SNPs.

Reduction to practice

Procedures for interrogating SNP sets have been developed for *Neisseria meningitidis* (the meningococcus) and *Staphylococcus aureus* (the golden staph). These methods use the real-time PCR platform. Real-time PCR instruments are generic and cost effective, and the genotyping procedure is completed in a single step.



Population structure of *S. aureus*, with SNP genotypes circled

Validation

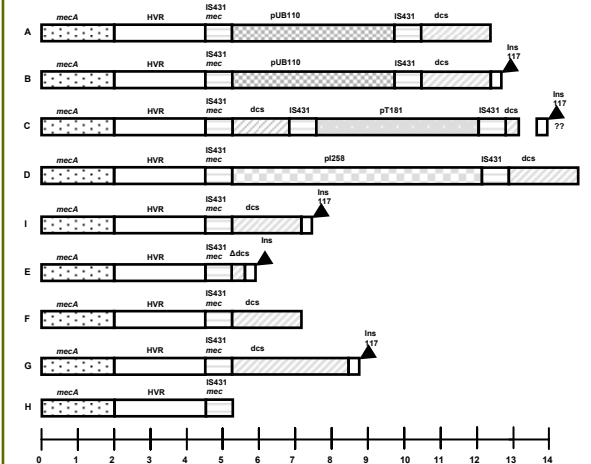
The resolving power of the *S. aureus* seven member SNP set has been tested extensively with various collections of isolates. The genotypes defined by the SNPs are almost entirely congruent with the natural groups within the species. Therefore, just seven SNPs can reveal the clonal complex of an isolate.



Award-winning students Erin Price and Alex Stephens

Application

SNP sets identified to date indicate the provenance of the relatively stable genome “backbones”. However, nearly all pathogenic bacteria carry suites of mobile genes that vary between strains and confer virulence and resistance properties. Our SNP-based genotyping can easily be combined with simultaneous assays for the presence of clinically-relevant mobile genes using Real Time PCR. This could lead to e.g. point-of-care procedures that very rapidly and cheaply provide both epidemiological fingerprints and a direct indication of virulence and resistance phenotypes.



Resistance gene variants in the *mecA* region of *S. aureus*