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ePoster Session
Microbial pathogenesis reloaded

Comparative population genomics and the emergence of opportunistic pathogenicity in the nosocomial bacterial pathogen Staphylococcus epidermidis

Leonardos Mageiros*[1], Guillaume Meric[2], Thomas Wilkinson[3], Samuel Sheppard[3]

[1]*Swansea University, College of Medicine, Medical Microbiology and Infectious Diseases, Swansea, United Kingdom*

[2]*Swansea University Medical School, Institute of Life Science 1, Medical Microbiology and Infectious Disease, Swansea, United Kingdom*

[3]*Swansea University, College of Medicine, Medical Microbiology and Infectious Disease, Swansea, United Kingdom*

Background: Many important human pathogens can arise from a background commensal bacterial population. *Staphylococcus epidermidis* is a clinically important pathogen, ubiquitous on the skin of healthy individuals and causing frequent nosocomial disease, including severe infection of indwelling devices. Effective treatment is difficult, as infections can be caused by antibiotic-resistant isolates. Evidence from *in vitro* assays have demonstrated that pathogenic strains display phenotypic differences, such as enhanced biofilm formation, compared to carriage strains. This suggests that there may be a sub-set of strains in the commensal skin environment that have a greater propensity to cause disease.

Material/methods: We present a comparative analysis on 415 whole-genome sequences from genetically diverse *S. epidermidis* from clinical infections as well as asymptomatic isolates. Whole-genome alignments were obtained using a gene-by-gene approach and robust phylogenetic trees were constructed. Groups of genetically related isolates where identified to create a suitable dataset to be analysed using a recently-developed pangenome-wide association study (pan-GWAS) pipeline. Candidate genes associated with pathogenicity where associated with various complex phenotypes tested *in vitro.*

Results: Statistically significant disease associated genetic variation was identified, clustering in multiple genomic hot spots. Genes statistically associated with pathogenicity included biofilm formation, cell wall and fibronectin adhesion, cell toxicity and methicillin resistance. Commensal and pathogenic Isolates were phenotypically tested in toxicity, biofilm, adhesion and immune response assays in bacteraemia and skin cell infection models. Clusters of genes, with disease associated elements, were correlated with results from *in vitro* assays to investigate functional variation associated with enhanced propensity to cause disease.

Conclusions: In this study, we present a novel approach to identify genetic elements associated with opportunistic pathogenicity. The detection of candidate genes and alleles correlated with specific virulence factors in *S. epidermidis* enhances understanding of the evolutionary mechanisms

underlying the emergence of an important opportunistic pathogen and provides targets for diagnostic tests aim at reducing nosocomial infection.