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Abstract (oral session)

The genomic and genetic determinants of biofilm formation in Staphylococcus aureus EMRSA-15

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Objectives: EMRSA-15 (CC22 SCCmecIV) is currently the major cause of nosocomial methicillin-resistant Staphylococcus aureus (MRSA) infections in European hospitals. We have previously shown a reference EMRSA-15 strain from the European collection HARMONY (H-EMRSA-15) to be a prolific biofilm former on static and dynamic flow assays. Here we analyzed the genome and transcriptome of H-EMRSA-15 to study the underlying basis of biofilm formation. Methods: Genomic DNA extracted from H-EMRSA-15 was NcoI-restricted, optically mapped (Opgen, Gaithersburg, USA), and compared to an in silico map of the recently sequenced UK-EMRSA-15 (NC_017763). The entire genome of H-EMRSA-15 was sequenced (Illumina HiSeq2000), assembled and also mapped to UK-EMRSA-15 (CLC Genomics v5.1, CLC Bio, Denmark) to screen for polymorphisms, and insertions/ deletions. RNA extracted (ExpressArt RNAready Kit, Amptec GmBH) from H-EMRSA-15, grown as planktonic cultures and as dynamic flow biofilms for 72 hours, was hybridised to S. aureus Genechip arrays (Affymetrix). Results: The H-EMRSA-15 genome was larger (2861287 bp) than UK-EMRSA-15 (2832299 bp) and harboured a 14218 bp island that was homologous to SaPIbov5, a pathogenicity island of bovine origin. The H-EMRSA-15 genome also showed 19 indels, 137 single and 3 multiple nucleotide variants, which mapped to genes involved in aminoacid metabolism; carbohydrate transport and metabolism; cell wall/membrane/envelope biogenesis; and nucleotide transport and metabolism. One of the SNP-containing genes encodes a hypothetical protein possessing GGDEF and DHH domains (SAEMRSA15_00140), which might modulate cellular c-di-GMP levels resulting in changes in exopolysaccharide production and biofilm formation. Transcriptomics data revealed 272 biofilm-induced genes (5-fold or higher increase in expression). 56 of these genes were with known functions encoding DNA repair, recombination, transcription, translation, transport as well as known determinants of biofilm formation (agrC and sarA), whereas 216 biofilm-induced genes were found to encode proteins with mostly unknown functions (Figure), but also those including phage and prophage related proteins, such as transposase, pathogenicity island protein, phage terminase, phage antirepressor, prophage L54a. Conclusions: This study reveals distinct genomic features of Harmony-EMRSA-15 and highlights the potentially essential role of the 'mobilome' in biofilm formation in this highly successful clone.

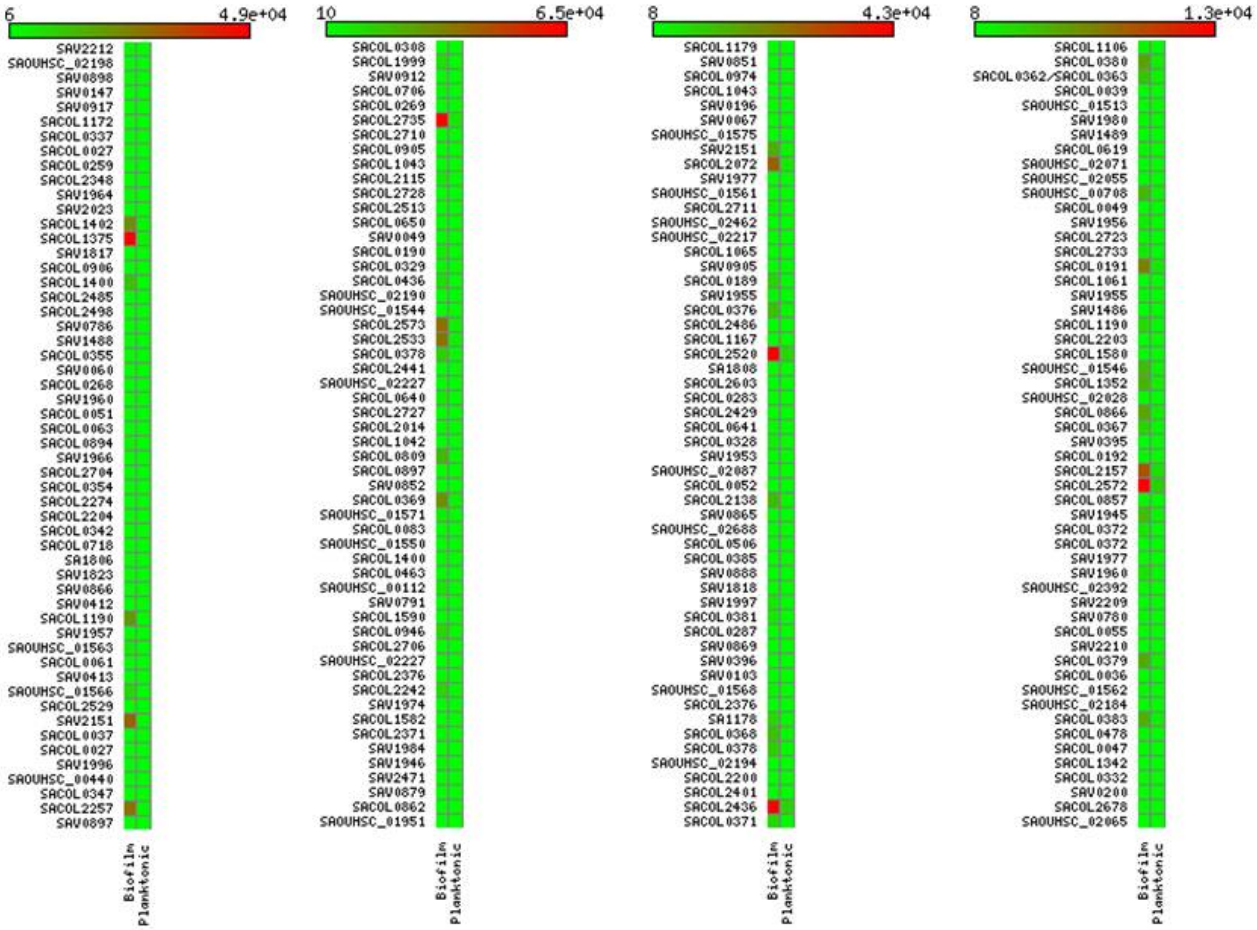

Figure: Heatmap of 216 differentially expressed genes in biofilm compared to planktonic cells of *S. aureus* Harmony-EMRSA-15