Poster # 65

Function of *Staphylococcus aureus* biofilm - studied *in vitro*, in guinea pigs and in a patient

Lone Heimann Larsen[1], Yijuan Xu[2,3], Henrik C. Schønheyder[1,4] and Trine Rolighed Thomsen[2,3]

1. Department of Clinical Microbiology, Aalborg University Hospital, Aalborg, Denmark
2. Biotech, Danish Technological Institute, Aarhus, Denmark
3. Department of Chemistry and Bioscience, Aalborg University
4. Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

8th ASM Conference on Biofilms
October 7 – 11, 2018
Washington, DC
AMERICAN SOCIETY FOR MICROBIOLOGY

Introduction

Staphylococcus aureus is a major human pathogen. It has the ability to adapt to a biofilm mode of growth in response to the host environment, and this is crucial for its leading role in device-related infections and chronic infections. However, little is known about stepwise changes in virulence expression and metabolism from inception of infection to establishment of chronic biofilm infections.

Aim

To identify and compare the *in vivo* transcriptional changes of a clinical *S. aureus* strain (SAU060112) during infection development *in vitro*, in a guinea pig biofilm model and in a patient with an infected prosthetic joint.

Methods

Isolate SAU060112

Synovial fluid from patient

Material aspirated from subcutaneous tissue cages

Total RNA extraction (PowerLyser® Ultraclean® Tissue & Cells RNA Isolations Kit)

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Removal of human RNA (MICROB*Enrich*™)

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→ Removal of bacterial rRNA (RiboZero rRNA Removal Kit (Bacteria))

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Sequencing library prep (Illumina® TruSeq® Stranded mRNA Library Prep)

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→ Sequencing on Illumina

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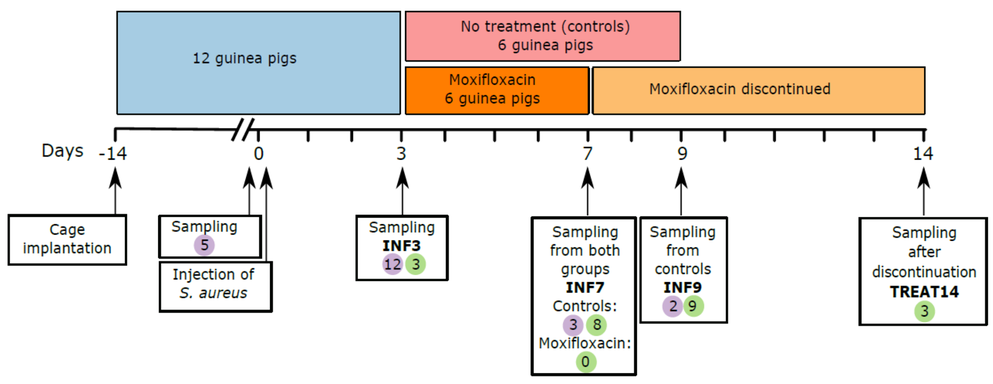
Bioinformatics analysis on CLC genomic workbench

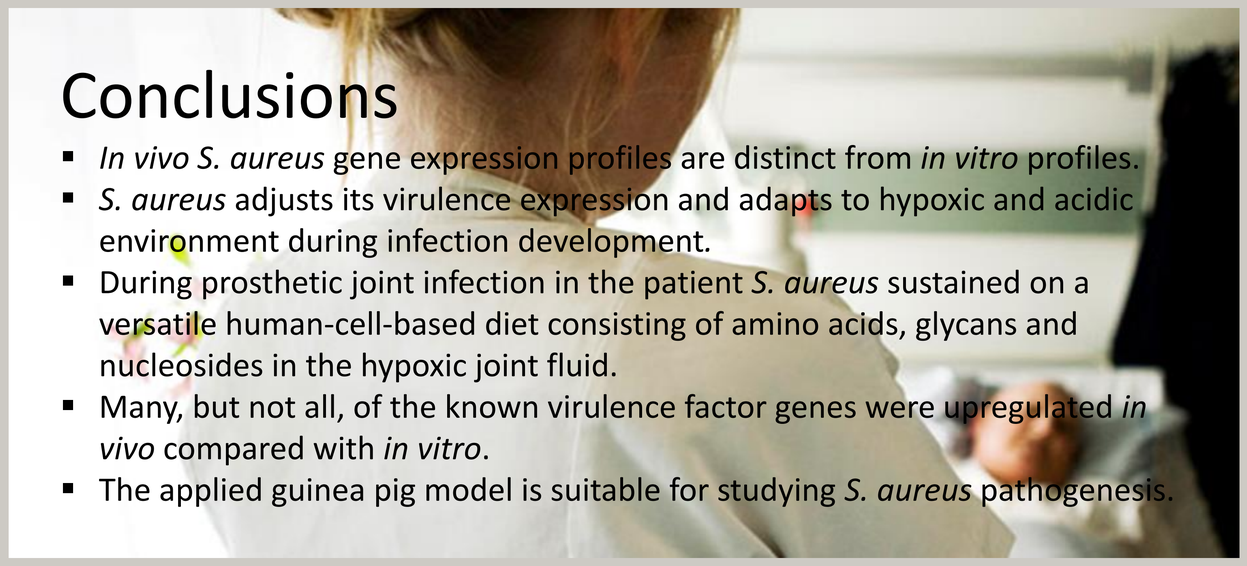
NMR measurement

A controlled study of infection development in guinea pig model:



Reference: Xu et al. (2016). *In vivo* gene expression in a *Staphylococcus aureus* prosthetic joint infection characterized by RNA sequencing and metabolomics: a pilot study. BMC Microbiology, 16(1), 80.

Conclusions



- *In vivo S. aureus* gene expression profiles are distinct from *in vitro* profiles.
- *S. aureus* adjusts its virulence expression and adapts to hypoxic and acidic environment during infection development.
- During prosthetic joint infection in the patient *S. aureus* sustained on a versatile human-cell-based diet consisting of amino acids, glycans and nucleosides in the hypoxic joint fluid.
- Many, but not all, of the known virulence factor genes were upregulated *in vivo* compared with *in vitro*.
- The applied guinea pig model is suitable for studying *S. aureus* pathogenesis.

Results

Principal component analysis showed

- *In vivo* gene expression profiles were distinctly different from *in vitro* cultures of *S. aureus.*
- The guinea pig data grouped together with a patient case of prosthetic joint infection.

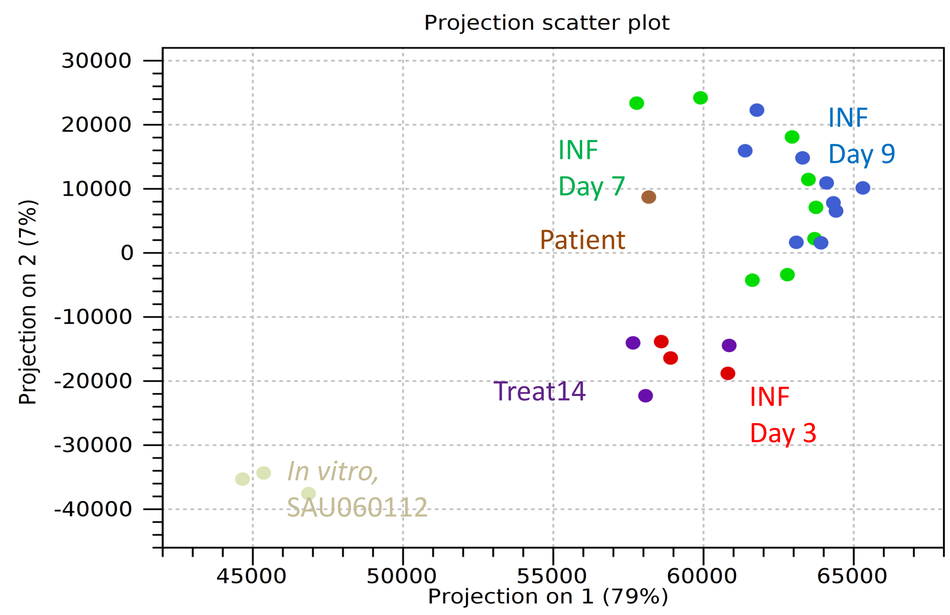


Figure 1 Principal component analysis of all transcriptome profiles

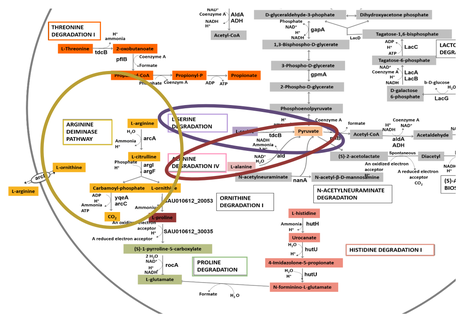


Figure 2 All enzymes in the pathway for amino acid degradation are highly expressed in the patient sample

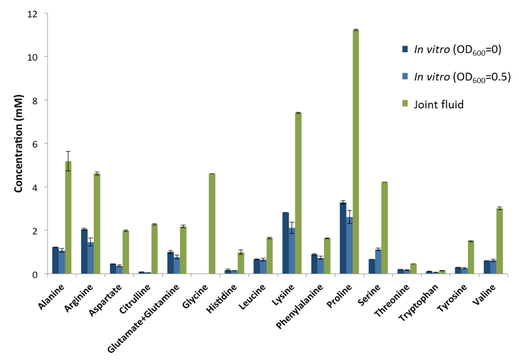


Figure 3 Free amino acids were abundant in the infected joint fluid from the patient

Differential gene expression in the guinea pig model showed

- Virulence genes: 16 were upregulated at infection day 3 compared to infection day 7 and 9.
- Metabolic pathways: the arginine deiminase pathway and the urea degradation pathway were upregulated at day 7 and 9 compared to day 3 and Treat14.
- This indicated decreased virulence expression and a response to the acidic environment during infection development.

Acknowledgement: This study was prepared within the framework of the 'Prosthetic-Related Infection and Pain' (PRIS) - Innovation project. http://www.joint-prosthesis-infection-pain.dk The study was supported by a grant for the PRIS Innovation Consortium from The Danish Council for Technology and Innovation (no. 09–052174). The research protocol was approved by the Danish Animal Ethics Council (2015-15-0201-00620).

Contact: Trine Rolighed Thomsen
trt@dti.dk
+45 72201828

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