

The pathogenesis of *Staphylococcus epidermidis* biofilm-associated infections: the host and the pathogen perspective

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Staphylococcus epidermidis is a commensal bacterium that inhabits healthy human skin and mucosae. However, due to its capacity to attach to medical devices and form biofilms, *S. epidermidis* has emerged as one of the most common causes of healthcare-associated infections. Although biofilm formation on medical devices is classically associated with the development of chronic infections, the release of cells from the biofilm has been linked with the onset of acute infections, with bacteraemia as one of its major associated clinical manifestations. Despite the clinical relevance of biofilm disassembly, the interaction between biofilm-released cells and the host remains unclear. Hence, to better comprehend the pathogenesis of *S. epidermidis* biofilm-related infections, the interplay between *S. epidermidis* biofilm-released cells and the host immune system was investigated. The host immune response to the presence of biofilm-released cells was evaluated by analyzing the transcriptome of mouse splenocytes after 2 hours of the injection of the bacterium into the bloodstream. Data mining revealed that biofilm-released cells were particularly effective at activating inflammatory and antigen presenting cells and inducing cellular apoptosis. Moreover, these cells induced higher production of pro-inflammatory cytokines than biofilm or planktonic cells [1]. These results not only helped explaining the relapsing character of biofilm-originated infections but also raised important concerns regarding the use of compounds that cause biofilm disassembly as treatment strategy since biofilm-released cells can heighten the inflammatory response of the host, consequently augmenting disease severity. Finally, the response of biofilm-released cells to the presence of host factors was evaluated by analysing the transcriptome of the bacterium upon 2 hours of interaction with human blood. Data analysis showed that during interaction with human blood there was a dramatic alteration in the transcriptome of the bacterium, particularly in the transcription of genes encoding proteins involved in iron utilization, amino acids biosynthesis and biotin metabolism [2]. Iron and biotin are essential for prokaryotic central pathways being particularly important during infection constituting, therefore, potential targets for future studies aiming to develop strategies for the treatment of *S. epidermidis* biofilm-originated infections.

References

- [1] França, A, Pérez-Cabezas, B, Correia, A, Pier, GB, Cerca, N, Vilanova, M *Staphylococcus epidermidis* biofilm-released cells induce a prompt and more marked *in vivo* Inflammatory-type response than planktonic or biofilm cells. *Frontiers in Microbiology*, 7, 1530, 2016.
- [2] França, A, Pier, GB, Vilanova, M, Cerca, N. Transcriptomic analysis of *Staphylococcus epidermidis* biofilm-released cells upon interaction with human blood circulating immune cells and soluble factors. *Frontiers in Microbiology* 7, 1143, 2016.