The transcriptome of *S. epidermidis* biofilm-released cells when exposed to whole human blood or its cellular and soluble factors

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Staphylococcus epidermidis biofilms present on medical devices are frequently associated with the development of chronic infections. However, it has been recently shown that the cells released from these biofilms are involved in the manifestations of acute infections, with bacteremia being one of these. Nevertheless, despite the impact of these infections on patients' quality of life, nothing is known regarding the role of biofilm-released cells (Brc) in the pathophysiology of *S. epidermidis* biofilm-related infections. Here, we developed an *in vitro* model to obtain and subsequently characterize *S. epidermidis* Brc. Key parameters such as (i) quantification of biofilm biomass and concentration of Brc; (ii) kinetics of Brc; and (iii) Brc antimicrobial tolerance were addressed. Brc transcriptome was then sequenced upon interaction with (i) whole human blood; (ii) human plasma; (iii) polymorphonuclear cells (PMN) or (iv) mononuclear cells (MN) suspended in donors' plasma. Using the transcriptome of Brc exposed to plasma as control, we observed that when in the presence of whole human blood Brc uniquely expressed 174 genes, 52 when incubated with PMN and 65 only when interacting with MN. Gene ontology analysis was performed and significant enrichment was only found in the presence of whole blood and within the downregulated genes. Interestingly, when analyzing, gene-by-gene, the lists of genes differentially expressed under all the conditions tested, we have observed that the great majority of the genes with higher alterations (both up- and down-regulations) encode hypothetical proteins. Henceforth, in order to fully understand the changes made by *S. epidermidis* Brc when interacting with human blood and its particular cellular components, the function of these hypothetical proteins need to be uncovered.