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***S. epidermidis* response to human blood and its cellular and soluble components**

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Staphylococcus epidermidis, a normal inhabitant of healthy human skin and mucosae, can cause persistent and relapsing infections due to its ability to adhere to medical devices and form biofilms. Hence, *S. epidermidis* is considered one of the most important medical device-associated nosocomial agents, being particularly associated with vascular catheters. Although the biofilms formed on these catheters are in constant contact with human blood, their mutual interaction is poorly understood. Here, we evaluated the expression of genes associated with biofilm formation (*icaA*, *aap*, *bhp*), immune evasion (*icaA*, *mprF*, *sepA*) and programmed cell death (*IrgB*), as well as biofilm structure and viability, upon bacterial interaction with human blood and its components. We observed that contact with human blood increased the transcription of *icaA* and *bhp* but decreased *aap*, *sepA* and *IrgB* gene expression, when compared with plasma. In contrast, no significant transcriptional alterations were detected upon contact with purified mononuclear cells, whereas purified polymorphonuclear cells lead to increased *bhp* and *mprF* gene expression. Furthermore, human blood reduced by 50% the number of viable cells within the biofilm and induced significant alterations in its structure, with the creation of a fibre-like matrix. In conclusion, our study reveals that *S. epidermidis* biofilms adapt to particular environmental stress by changing the expression of specific genes and by altering their structure. Despite these overall observations, significant variability was found between different blood donors, suggesting that particularities of the host immune system may strongly affect the outcome of *S. epidermidis* infections.