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Influence of shear stress on Staphylococcus aureus adhesion to endothelial cells mediated by Fibronectin-binding protein A and Clumping factor A in an in vitro model of endovascular infections

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Introduction: Staphylococcus aureus (S. aureus) is a pathogen most frequently associated with endovascular infections such as infective endocarditis. In order to cause endovascular infections, S. aureus needs mechanisms to adhere to endothelial cells lining the vessel wall and subendothelial matrix. Various staphylococcal surface proteins have been described to mediate adhesion to host cells and to extracellular matrix proteins, e.g. fibronectin (Fn)-binding protein A (FnBPA) and clumping factor A (ClfA). However, most of these interactions are studied in static conditions, and may not be representative for endovascular infections in the human body, where S. aureus initial adhesion to the vessel wall occurs in flowing blood. Lactococcus lactis (L. lactis) are poorly pathogenic bacteria known to lack adhesion molecules for human matrix proteins. L. lactis expressing single staphylococcal surface proteins have been described before to study the contribution of single staphylococcal surface proteins in S. aureus infective endocarditis. In the present study we aimed to investigate how ClfA, FnBPA and FnBPA subdomains (A, A+16, ABC, CD) contribute to bacterial adhesion to endothelial cells and subendothelial matrix in flow conditions.
Methods: We investigated adhesion of L. lactis expressing ClfA, FnBPA or FnBPA subdomains to Fn, Fg, intact and damaged endothelial cells and fibrin under shear stress. Fluorescently labelled L. lactis were perfused over a surface coated with Fn, Fg endothelial cells or fibrin in a micro-parallel flow chamber.
Results: We observed that the adhesion to Fn involved the CD domain and the A+16 domain of FnBPA not only in static conditions, but also under shear stress. Adhesion to Fg was facilitated by ClfA and the A16+ domain. The adhesion to intact endothelial cells was mediated by Fn and when Fg was added to the bacterial perfusate, adhesion of ClfA and the A16+ domain increased.
Conclusion: Our data show that the adhesion of S. aureus to endothelial cells via FnBPA is primarily mediated by Fn under shear stress. Further studies will focus on concomitant infections with the specific L. lactis strains to allow to rank the importance of Fn and Fg mediated S. aureus adhesion in bacterial recruitment to the vessel wall.