ON THE PATHOGENESIS OF INFECTIONS ASSOCIATED WITH PERCUTANEOUS OSSEOINTEGRATED ORTHOPAEDIC IMPLANTS

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IV. Zaborowska M*, Taulé Flores C*, Vazirisani F, Thomsen P, Trobos M. Role of extracellular vesicles from Staphylococcus epidermidis on antibiotic tolerance, planktonic growth, and biofilm formation under antimicrobial selective pressure. In manuscript.
* Equal contribution.
On the pathogenesis of infections associated with percutaneous osseointegrated orthopaedic implants

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Abstract

Orthopaedic implants enable the restitution of locomotor function and improve the quality of life of many people. However, biomaterial-associated infection may occur due to the propensity of microorganisms to adhere and colonize implant surfaces. The objective was to gain knowledge on the pathogenesis of infections associated with percutaneous osseointegrated implants for lower limb amputation prostheses. The aims were to design in vitro methods for the evaluation of antimicrobial surface properties, evaluate a novel method for biofilm-susceptibility testing and characterising virulence factors in bacterial isolates from patients with implant-associated osteomyelitis, and to investigate extracellular vesicle (EV)-host cell and EV-bacterial cell interactions.

Results demonstrated that several methods, tailored to the specific surface modification and antimicrobial mode of action, should be applied to provide complementary information when evaluating the prophylactic and treatment effects of antimicrobial surfaces on planktonic and biofilm bacteria. The majority of clinical isolates of Staphylococcus spp. and Enterococcus spp. causing osteomyelitis were biofilm producers that required higher antimicrobial concentrations compared with non-producers. The biofilm susceptibility testing method may be useful to guide antimicrobial treatment decisions in orthopaedic implant-associated infection. All staphylococcal strains were able to produce EVs in vitro. A significantly higher level of cytotoxicity was induced in THP-1 monocytes by EVs compared with unstimulated controls. THP-1 cells internalised EVs and secreted proinflammatory cytokines to a greater degree than controls. Sub-inhibitory concentrations of gentamycin increased secretion of EVs and their protein content in S. epidermidis. EVs may play a role as survival factors by modulating cell growth and adherence to surfaces.

In conclusion, isolates from implant-associated infection reveal multiple virulence traits relevant for understanding and treating these infections. This thesis proposes EVs as a novel pathogenic mechanism of biomaterial-associated infection, requiring further research focus.

Keywords: osseointegration, amputation prosthesis, implant-associated infection, biofilm, staphylococci, extracellular vesicles, host defence, cytokines, cell death