Stevens Institute of Technology

Nanotechnology Graduate Program

Bridging the gap between *in vitro* and *in vivo* evaluation of biomaterials-associated infections

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Biomaterial-associated infections (BAI) are the major cause of implant failure and can develop many years after implantation. BAI can develop from peri-operative microbial contamination of implant surfaces during implantation, immediately post-surgery during hospitalization, or by late hematogenous spreading from infections elsewhere in the body. The microorganisms involved in BAI are resistant to antibiotics due to their biofilm mode of growth. In most cases researchers have predicted the outcome of the race for the surface by in vitro evaluation of biomaterials or functional coatings either for their ability to resist bacterial adhesion and biofilm formation or for their ability to support mammalian cell adhesion and proliferation. However, the effects of bacteria including the influence of their activity and toxins on mammalian cell adhesion and proliferation remained unknown. This could completely change the fate of a biomaterial implant according to the concept of the "race for the biomaterial surface." We have developed a method to bridge the gap between in vitro and in vivo evaluation of biomaterials-associated infections. The competition of bacteria and mammalian cells on different biomaterials with and without various brush coatings have been studied in a parallel plate flow system. In a peri-operative model we demonstrated that the outcome of the competition between Staphylococcus epidermidis and U2OS cells appeared to be dependent on the number of bacteria present prior to U2OS cell seeding. It is known that bacterial virulence is a contributing factor in pathogenesis of BAI. U2OS cells are able to adhere, spread and grow in the presence of adhering S. epidermidis but not in the presence of the more virulent Staphylococcus aureus or Pseudomonas aeruginosa, which cause death of the adhering U2OS cells. In a post-operative model we have observed that a critical coverage by host cells is needed to effectively protect a biomaterial implant against S. epidermidis. The potential of bifunctional coatings to reduce the risk of infection in the applications requiring tissue integration is demonstrated with a bioactive PEG (RGD-PEG) coating. In vivo more cells types are playing a role in BAI, therefore we have introduced immune cells (macrophages) in our system during the competition between bacteria and mammalian cells. Results showed that despite the presence of macrophages, mammalian cells lost the race for the surface in the presence of the highly virulent S. aureus. The effect of brush-coatings in vivo in a murine model showed that brush-coatings can help to lower the BAI during revision surgery.

Professor Henny C. van der Mei is a Professor in Microbiology at the University Medical Center Groningen (UMCG) and University of Groningen, The Netherlands. Her research interests center on biomaterials-associated infections, bacterial adhesion mechanisms, surface modification of biomaterials, and atomic force microscopy. She has authored or co-authored 395 journal publications and 36 book chapters. She has supervised 45 theses on subjects varying from mouthrinses, contact lenses, biofilm formation on hip prostheses, to polymer brushes and mechanisms of microbial adhesion.

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