Molecular and cellular interactions on noble metal nanopatterned surfaces

– applications towards bone, soft tissue and infection control

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i föreläsningssalen på våning 5, avdelningen för biomaterialvetenskap, Arvid Wallgrens backe 20, onsdagen den 28 maj 2014, kl 9.00
av

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Fakultetsopponent: Professor James D. Bryers, Department of Bioengineering, University of Washington, Seattle, USA

Avhandlingen baseras på följande delarbeten:

I. Suska F, Svensson S, Johansson A, Emanuelsson L, Karlholm H, Ohrlander M, Thomsen P. *In vivo* evaluation of noble metal coatings. Journal of Biomedical Materials Research. Part B, Applied Biomaterials 2010; 92(1): 86-94

II. Svensson S, Suska F, Emanuelsson L, Palmquist A, Norlindh B, Trobos M, Bäckros H, Persson L, Rydja G, Ohrlander M, Lyvén B, Lausmaa J, Thomsen P. Osseointegration of titanium with an antimicrobial nanostructured noble metal coating. Nanomedicine: Nanotechnology, Biology and Medicine 2013; 9(7): 1048-56

III. Svensson S, Forsberg M, Hulander M, Vazirisani F, Palmquist A, Lausmaa J, Thomsen P, Trobos M. Role of nanostructured gold surfaces on monocyte activation and *Staphylococcus epidermidis* biofilm formation. International Journal of Nanomedicine 2014; 9: 775-94

IV. Svensson S, Trobos M, Hoffman M, Norlindh B, Petronis S, Lausmaa J, Suska F, Thomsen P. A novel soft tissue model for biomaterial-associated infection and inflammation – bacteriological, morphological and molecular observations. In manuscript.

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ABSTRACT

Biomaterial-associated infection is recognised as one of the main risks for failure of medical devices. The presence of a foreign material in tissues has been suggested to compromise the ability of host cells to eradicate infection. In addition, a protective biofilm formed by bacteria limits the effectiveness of administered antibiotics, which underscores the importance of preventive measures. The use of implant surface modifications that resist bacteria is a promising approach to reduce the infection risk. A nanopatterned noble metal coating, applied on catheters, has shown up to 50% reduction of infections in the clinic. The aim of the present project was to investigate the material–tissue interactions of nanopatterned noble metal coatings, especially with respect to their role in inflammation and bioburden control. Several microscopy techniques, cellular and microbiological techniques, and molecular analyses have been used.

The results show that the processes of inflammation and fibrosis can be modulated depending on the combination of noble metals in the coating (silver, gold and palladium). Noble metal coated titanium implants displayed a comparable bone response to that of clinically used machined titanium and was shown to reduce *Staphylococcus aureus* adhesion *in vitro*. To separate the effects of noble metal chemistry from nanotexture, the specific effects of nanostructures on host defence cells (monocytes) and *Staphylococcus epidermidis* were evaluated using gold model surfaces with or without immobilised gold nanoparticles on the surface. The presence of nanostructures did not affect monocyte behaviour but reduced bacterial viability and biofilm formation on the surfaces, indicating a bactericidal effect induced by nanoscale surface features. An *in vivo* infection model to study early inflammatory events was developed. The presence of *S. epidermidis* induced significantly more inflammatory cell recruitment, cell activity and cell death. A trend towards a more intense inflammatory response and a reduced amount of viable bacteria was observed around the noble metal coated implants.

In conclusion, nanostructured noble metal coatings are biocompatible in soft tissue and bone, which render them a suitable option in many new application areas. The anti-infectious potential of the coatings may partly be related to physical interactions of bacteria with the surface nanostructures and partly related to an intensified inflammatory response due to the material surface chemistry.

Keywords: Nanotopography, noble metals, titanium, biocompatibility, osseointegration, inflammation, host defence, monocytes, infection control, antimicrobial, staphylococci

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