

The 8th of June 2016 Maria Lennerås defended her thesis entitled "A methodological platform to study molecular biocompatibility of biomaterials, Experimental and clinical studies". The main aim of this project was to advance the scientific understanding of the mechanisms of osseointegration and tissue regeneration at biomaterials. The project aimed to develop a methodological platform for determination of cellular and molecular biocompatibility of biomaterials *in vivo*. In this project, a combination of highly sensitive molecular techniques such as qPCR in combination with other techniques, like biomechanics and histology, were used to investigate the mechanisms of osseointegration.

In the clinical situation, there is a need for highly sensitive molecular tools to evaluate the process of biomaterial integration as well as to study the pathological conditions associated with biomaterials. The technique qPCR was used in a clinical study with retrieved prosthetic material due to post-integration complication (e.g. mechanical failure or infection) and the genetic analyses are coupled to radiological findings and bacterial presence.

The *in vivo* studies with retrieved titanium implants of machined or oxidized surface revealed at the early time points after implantation that the oxidized implants were associated with significantly higher gene expression of integrins whereas the machined surface showed significantly higher expression of inflammatory markers like TNF- α and IL-1 β . An interesting observation was the firm anchorage of the mesenchymal-like cells on the oxidized implants by extending their processes onto the volcano-shaped pores as revealed by SEM. Furthermore, in comparison to machined implants, higher removal torque values were recorded for the oxidized implants at all time periods. This was in conjunction with more bone in direct contact with the implant for the oxidized implants compared to machined. 3 days after implantation, the oxidized implants showed a significantly upregulated expression of both RANK and RANKL, as well as OPG, compared with the machined implants.

The clinical paper with retrieved prosthetic material revealed a relatively higher gene expression of the pro-inflammatory marker TNF- α in association with positive cultures of *S. aureus* (irrespective of sampling site). Importantly, a correlation was also found between fixture loosening and a lower expression of IL-10 and osteocalcin.

The knowledge gained from the present studies is vital and crucial in order to understand the mechanisms behind osseointegration and the role of material surface properties. The main advances in this project were the optimizations of new analytical tools for studying cellular phenotypes as well as levels of secreted proteins and biomolecules. In addition, the molecular techniques used in the present project can provide new tools for screening, diagnosis and monitoring of implants in clinical care.