Biomimetic Nanostructured Surfaces for Enhanced Osseointegration

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Introduction: Placement of prosthetic skeletal implants has improved the quality of life for millions of people in the world. It is estimated that over 500,000 total joint replacements, primarily hips and knees, and between 100,000 and 300,000 dental implants are used each year in the United States alone [1]. The success of these implants depends on acquiring and retaining stable fixation of the device at the bony site. A goal of current orthopedic biomaterials research is to design implants that induce controlled, guided, and rapid healing [2, 3]. In order to achieve this, the bone cells should be able to adhere on the surface, differentiate and deposit bone matrix. The cellular response of adhesive cells can be regulated by modifying the surface chemistry or the topography at nanoscale of the substrate. It is well known that by providing the surface nanoarchitecture comparable to that of bone nanostructure improved matrix deposition. Also, it is well known that modification of substrates with proteins and peptides influences cell adhesion as well as differentiation. Thus, in this work we have used nanotubular titania surfaces and have modified the surface with two peptides: -CGGNGEP**RGD**TYRAY- which is known to improve the bone cell adhesion and -RDLG**WQDWIIA**PEGYAAYYC- which is known to improve bone cell differentiation. We hypothesize that increasing cell adhesion and spreading will promote differentiation of MSCs into osteoblast-like cells under osteogenic conditions.

Methods: Titania nanotubular surfaces were fabricated using an anodization process [4, 5]. Figure 1 shows the SEM image of fabricated titania nanotubular surface. These surfaces were modified with the cell adhesion and differentiation peptides using covalent coupling technique. The surfaces were characterized using X-ray photoelectron spectroscopy to access the amount of peptides present on the surfaces. Marrow stromal cells were seeded on modified and unmodified nanotubular surfaces and their adhesion, proliferation and viability were evaluated after 7 days of culture. The differentiation was accessed by measuring the alkaline phosphatase activity and in vitro matrix deposition on the surfaces for upto 4 weeks of culture.

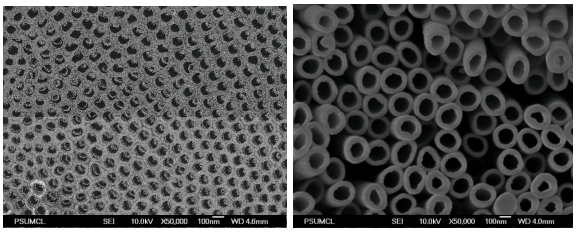

Figure 1. SEM image of titania nanotubular surface

Results/Discussion: Nanostructured surfaces have known to improve bone cell adhesion and differentiation. In this study, we have shown that altering the surface properites at a topographical as well as biomolecular level, the performance of bone cells can be significantly enhanced. **Figure 2(a)** and **(b)** shows fluorescence microscopy images of MSCs on modified and unmodified surfaces respectively stained with calcein. The images suggest that the cells are viable on these surfaces after 7 days of culture. Furthermore, closer inspection of cells on modified nanotubular surfaces reveals the formation of clusters, which is a normal phenotypic behavior of MSCs absent in unmodified surfaces.

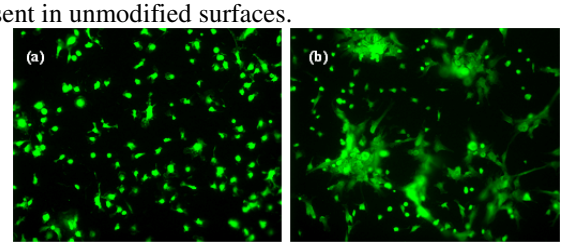

Figure 2. Fluorescence microscopy images of live marrow stromal cells (a) unmodified and (b) modified surfaces

Conclusions: The development of biomimetic nanostructured platforms based on novel metal-oxide films can provide insight into cell-material interactions for the development of improved implant surfaces. In this work, we demonstrated that nanotubular titania surfaces provide a favorable template for bone cell growth and differentiation.

References:

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