Intracellular Mechanisms Involved in the Osteogenic Potential of Titanium with Nanotopography

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Nanostructured titanium (Ti) surfaces produced by different treatments and exhibiting distinct patterns of topography may modulate osteoblast responses from cell attachment to extracellular matrix mineralization. A controlled chemical oxidation of Ti surfaces using a mixture of H_2SO_4/H_2O_2 creates a well-characterized nanotopography in terms of physical structure and surface chemistry. Compared with an untreated Ti surface, this nanotopography exhibits a three-fold increase in the surface roughness due to the presence of nanopits, an increase in the TiO_2 layer thickness, and low rates of contaminants. Studies from our research group revealed that the Ti with nanotopography enhances the osteoblast differentiation of cells grown under both osteogenic and non-osteogenic conditions. Considering the relevance of this finding, we are now investigating the intracellular mechanisms involved in the osteogenic potential of this surface. Our results have shown that the Ti with nanotopography induces osteoblast differentiation by at least two major pathways: (1) increasing the expression of $\alpha 1\beta 1$ integrin and modulating integrin signaling pathway and (2) up-regulating the BMP signaling pathway by a combination of increasing endogenous production of bone morphogenetic protein 2 (BMP-2) and down-regulating the expression of microRNA-4448, -4708 and -4773, which inhibit SMAD1 and SMAD4, both transducers of BMP-2 osteogenic signal.

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