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Stem Cell Fate Decision Depending on TiO2 Nanotubular Geometry

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Abstract : In clinical application of TiO2 implants on tooth and hip replacement, migration, adhesion and differentiation of neighboring mesenchymal stem cells onto implant surfaces are critical steps for successful bone regeneration. In a recent decade, accumulated attention has been paid on nanoscale electrochemical surface modifications on TiO2 layer for improving bone-TiO2 surface integration. We generated, on titanium surfaces, self-assembled layers of vertically oriented TiO2 nanotubes with defined diameters between 15 and 100 nm and here we show that mesenchymal stem cells finely sense TiO2 nanotubular geometry and quickly decide their cell fate either to differentiation into osteoblasts or to programmed cell death (apoptosis) on TiO2 nanotube layers. These cell fate decisions are critically dependent on nanotube size differences (15-100nm in diameters) of TiO2 nanotubes sensing by integrin clustering. We further demonstrate that nanoscale topography-sensing is feasible not only in mesenchymal stem cells but rather seems as generalized nanoscale microenvironment-cell interaction mechanism in several cell types composing bone tissue network including osteoblasts, osteoclast, endothelial cells and hematopoietic stem cells. Additionally we discuss the synergistic effect of simultaneous stimulation by nanotube-bound growth factor and nanoscale topographic cues on enhanced bone regeneration.

Keywords : TiO2 nanotube, stem cell fate decision, nano-scale microenvironment, bone regeneration
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