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Differential responses of osteoblast lineage cells to nanotopographically-modified, microroughened titanium–aluminum–vanadium alloy surfaces

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ABSTRACT

Surface structural modifications at the micrometer and nanometer scales have driven improved success rates of dental and orthopaedic implants by mimicking the hierarchical structure of bone. However, how initial osteoblast-lineage cells populating an implant surface respond to different hierarchical surface topographical cues remains to be elucidated, with bone marrow mesenchymal stem cells (MSCs) or immature osteoblasts as possible initial colonizers. Here we show that in the absence of any exogenous soluble factors, osteoblastic maturation of primary human osteoblasts (HOBs) but not osteoblastic differentiation of MSCs is strongly influenced by nanostructures superimposed onto a microrough Ti6Al4V (TiAlV) alloy. The sensitivity of osteoblasts to both surface microroughness and nanostructures led to a synergistic effect on maturation and local factor production. Osteoblastic differentiation of MSCs was sensitive to TiAlV surface microroughness with respect to production of differentiation markers, but no further enhancement was found when cultured on micro/nanostructured surfaces. Superposition of nanostructures to microroughened surfaces affected final MSC numbers and enhanced production of vascular endothelial growth factor (VEGF) but the magnitude of the response was lower than for HOB cultures. Our results suggest that the differentiation state of osteoblast-lineage cells determines the recognition of surface nanostructures and subsequent cell response, which has implications for clinical evaluation of new implant surface nanomodifications.

1. Introduction

Bone and joint injuries are among the most reported health problems in the United States [1]. Although orthopaedic implants provide a good option for joint replacements, with success rates continually improving, they still have undesirable failure rates in patients who are compromised by disease or age (i.e., patients who are often the ones most in need) [2,3].

Surface topographical modifications at the micrometer and nanometer scales have driven improved success rates for dental implants by mimicking the hierarchical structure of bone associated with regular bone remodeling [4,5]. In this process, damaged bone is resorbed by osteoclasts, which produce resorption lacunae containing high microroughness generated after mineral dissolution under the ruffled border [6], as well as superimposed nanoscale features created by the collagen fibers exposed at the surface [7]. New bone formation by osteoblasts is coupled with these primed surfaces, possibly after recognition of structural and chemical cues [8,9]. Thus, surface topographical modifications have been exploited for implant design in order to achieve direct and intimate contact between the bone and the surface of the implant (osseointegration). Indeed, the beneficial effects of microroughness for bone formation have been well established in the literature [10], and the addition of nanostructures to the implant surface (to mimic more closely the natural structure of bone) has shown promising results *in vitro* [11], *in vivo* [12] and clinically [13,14], validating the biological relevance of nanotopography for bone formation.

Titanium (Ti) and its alloys are widely-used metals for dental and orthopaedic implant applications due to their favorable

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