Versatile Scaffolds of Nanowires on Ti for Smart Bone Implants and Stents

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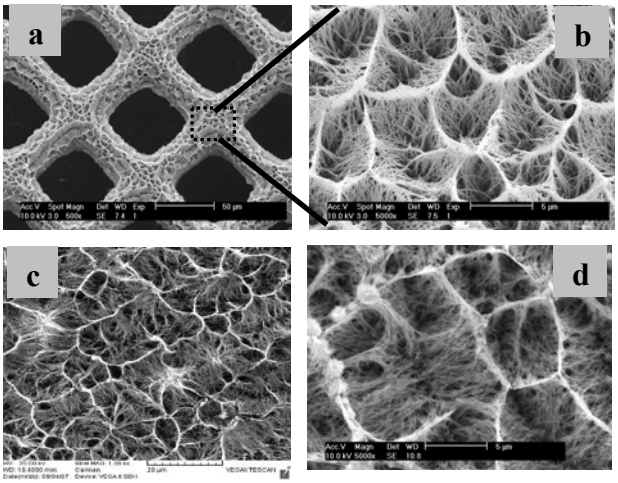
MOTIVATIONS: Typical natural extracellular matrixes for bone-replacement would be too fragile to support weight. Smooth hydroxyapatite coatings on implantable Ti lack macropores for accommodating tissue integration. Polymer coating for enhancing the tissue adhesion/intervention is vulnerable to biodegradation thus functional for short time, which is also a long unmet challenge of biodegradation for drug-eluting stent (DES). In USA, the DES targets the #1 cause of death, while the bone-implant deals with the #1 cause of disability. To tackle these problems, we here report a tailored metal-corrosion route to large-scale solution engineering of scaffolds of titanate nanowires on implantable Ti at low temperature for potential applications in smart bone implants and DES.

METHODS: (I).Ti plate substrates were placed in a Teflon-lined vessel with 10 mL of 1.0 mol/L NaOH solution, which was then hydrothermally heated at 160−250 °C for 2−10 hours. The Ti substrates, being covered by the titanate nanowires scaffolds, were collected, rinsed with deionized water, and dried in air. **(II).** The scaffolds on titanium were sterilized in 70% ethanol, rinsed in sterile 0.9% saline, and put on cell-culture plates on which. mesenchymal stem cells (MSC) (transduced with GFP in DMEM-LG of 10% FBS) were introduced for adhesion for 24 hours. Another media, containing 10mM sodium β-glycerophosphate, 100 nM dexamethasone, and 50 nM ascorbate (Sigma, St. Louis, MO), was used to promote the osteoblast differentiation. For *in vivo* testing, the scaffold-coated Ti meshes were implanted into SCID mice after the adherence of cells, and removed after 4 weeks of the implantation. **(III).** The *in vivo* samples were examined under a low-vacuum SEM operation mode (Philips SEM XL30). X-Ray radiographs were taken with the AXR Minishot 100 beryllium source (Associated X-Ray Imaging Corp., Haverhill, MA) with a 20-second exposure at 42 kV. All the studies and procedures were approved by the Institutional IRB and the Animal Care and Use Committee.

RESULTS: The nanowires were formed to root firmly inside Ti substrate and simultaneously self-assemble on the top into the scaffolds so as to form robust coating of scaffolds on Ti. Thus-coated Ti implants have good cellular compatibility and mechanical toughness. On that basis, the nanowire-scaffolds have been made to possess open-pores 2−10 microns large for promoting mesenchymal stem cells' adhesion/proliferation, and loading/releasing drugs. Then, coating hydroxyapatite on the scaffolding nanowires turns the biocompatible scaffolds to be bioactive for shortening the healing time. For developing new DES, the scaffolds pores have been shaped to have small opening (<50 nm in diameter) and large volume for potentially loading more drug and then releasing it over a longer time. Such multifunctional bioscaffolds could be effectively sterilized in ethanol, autoclave heating, and UV irradiation with no damage to the scaffold structure, showing new potentials in developing smart surgical tools such as smart catheters. Further, the versatile nanowire-scaffolds can survive from hundreds of mechanical bends, with no debris being found under the optical and scanning electron microscopes, suggesting the Ti coated with such nanowire-scaffods could be applicable to the development of new DES without the biodegradation problems thus the high fatal rate.



SEM images of nanowire scaffolds on Ti meshes (a-b), scaffold-coated Ti after 600 mechanical bends (c), and the scaffolds coated with HAP (d).

CONCLUSIONS: This work demonstrates an industry-viable method for large-scale productions of future bone implants and DES both of which possessing additional programmable drug elution functions, which has been widely highlighted in public media such as AAAS, ACS, MRS, MaterialsToday, BONEZone, etc.

ONGOING/NEAR-FUTURE WORK: Introducing proteins (e.g. growth hormone) and stem cells (e.g. MSC) onto the scaffolds may empower us to precisely regulate proliferations of MSC so as to enhance our understanding of roles of the proteins/MSC in the healing process. Further, integrating biosensing mechanisms onto the DES or bone implant could make such DES and bone implants to be even smarter, enabling us to identify/monitor/control biochemical and physiological key steps in the bone-healing or anti-restenosis processes.

REFERENCES:

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