

Improved Muscle Regeneration into a Joint Prosthesis with Mechano-Growth Factor Loaded within Mesoporous Silica Combined with Carbon Nanotubes on a Porous Titanium Alloy

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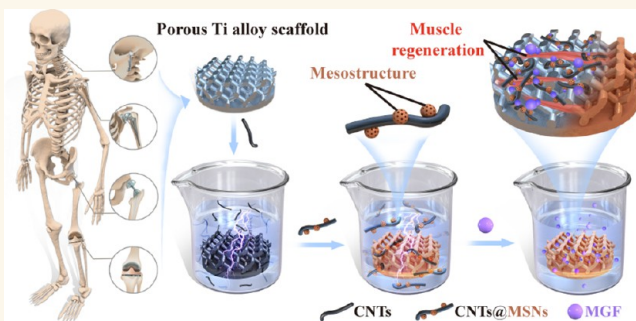
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ABSTRACT: Total joint replacement (TJR) is widely applied as a promising treatment for the reconstruction of serious joint diseases but is usually characterized by critical loss of skeletal muscle attachment to metal joint prostheses, resulting in fibrous scar tissue formation and subsequent motor dysfunction. Tissue engineering technology may provide a potential strategy for skeletal muscle regeneration into metal joint prostheses. Here, a porous titanium (Ti) alloy scaffold coated with carbon nanotubes (CNTs) and mesoporous silica nanoparticles (MSNs) through electrophoretic deposition (EPD) was designed as a mechano-growth factor (MGF) carrier. This two-layered coating exhibits a nanostructured topology, excellent MGF loading, and prolonged release performance *via* covalent bonding to improve myoblast adhesion, proliferation and myogenic differentiation in porous Ti alloy scaffolds without cytotoxicity. The Akt/mTOR signaling pathway plays a key role in this process. Furthermore, *in vivo* studies show that the scaffold promotes the growth of muscle, rather than fibrotic tissue, into the porous Ti alloy structure and improves muscle-derived mechanical properties, the migration of satellite cells, and possibly immunomodulation. In summary, this nanomaterial-coated scaffold provides a practical biomaterial platform to regenerate periprosthetic muscle tissue and restore comparable motor function to that of the natural joint.

KEYWORDS: total joint replacement, porous titanium alloy, tissue engineering, mesoporous silica nanoparticles, myogenic differentiation, muscle regeneration



Skeletal muscle, accounting for approximately 45% of human body weight, is responsible for maintaining motor function and has an intrinsic ability to regenerate after minor injuries and exercise with the help of satellite cells that reside on the surface of myofibers beneath the basal lamina.^{1,2} However, the regeneration of skeletal muscle is usually hindered after prosthesis reconstruction surgery. At present, total joint replacement (TJR) is usually required to treat severe damage to the anatomic construction or joint function due to end-stage joint diseases, including severe osteoarthritis, trauma, ankylosis, and autoimmune disease. TJR is usually characterized by a loss of skeletal muscle mass, resulting in a severe muscle function impairment and aesthetic defects.^{3,4} However, at present, surgeons usually only focus on

replacing bone with a prosthesis and do not attempt the reattachment or regeneration of periprosthetic muscle tissue. Hip abductor muscle deficiency results in an unstable hip joint and dislocation following total hip replacement.⁵ Similarly, total shoulder replacement may lead to a permanent loss of subscapularis function;⁶ patients often experience functional

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