Nanotechnology in Orthopaedics

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Nanotechnology provides a multitude of novel tools for applications in orthopaedics, including the meniscus, osteochondral defects, osseointegration of materials, vertebral disk regeneration and repair, and targeted drug delivery.

Meniscus

The high incidence of meniscal injuries, coupled with the structure's limited healing capacity, has created a demand for the use of tissue-engineered biomaterials in meniscal repair and replacement. Baker et al[1] showed that aligned nanofibrous scaffolds formed by electrospinning contain the microstructural features and nanolength scales of native extracellular matrix components and provide a substrate conducive to mesenchymal stem cell (MSC) expression of fibrous chondrogenic markers. Nonetheless, these constructs ultimately failed to achieve mechanical equivalence with fibrochondrocyte controls. However, when a similar MSC-laden scaffold based on poly(ε-caprolactone) was coupled with cyclic, physiologic tensile loading,[2] increased fibrocartilage gene expression, collagen deposition, and tensile modulus resulted. Nanotechnology for meniscal repair is still in its infancy, but the initial data appear promising.

Osteochondral Defects

Injuries to articular cartilage remain one of the most challenging issues in orthopaedics. Current treatments that focus on recruitment of MSCs generally result in mechanically inferior fibrocartilagenous tissue.[3] Tissue-engineering strategies to develop scaffolds for osteochondral repair procedures are quite desirable, but to date they have not seen widespread clinical success.[4] Design of a multiphase material that incorporates the different biochemical and biomechanical properties of articular cartilage and subchondral bone, and that also can address the independent requirements for cartilage and bone regeneration in an osteochondral defect, is a major challenge.

Tampieri et al[5] used biomimetic nanotechnology to develop a multiphase gradient scaffold with the biologic and functional properties of both bone and cartilage. An integrated composite was created with a bone-like layer of scaffold, a tidemark region with less mineralization, and a cartilaginous layer; the composite was shown to differentially support cartilage and bone generation in vivo. Promising data from the initial studies of this construct, commercialized as Fin-Ceramica Faenza SpA (Faenza, Italy), led to a recent clinical pilot study for osteochondral defect repair in 28 patients.[6] Statistically significant improvement in clinical scores was obtained with a 24-month follow-up, with 70% of patients showing complete filling of the osteochondral defect and complete integration of the graft on MRI.

Bone

Poor osseointegration can be a major contributor to implant loosening and subsequent failure. Modification of implant surfaces using nanotechnology has great potential for extending the life of the implant. Many nanofiber scaffolds made for tissue engineering have shown increased MSC osteogenic differentiation,[7,8] as well as increased osteoblast attachment and proliferation onto nanostructured surfaces, including ceramics and metals.[9,10] However, there have been few studies that tested the mechanical strength of the bone-implant interface of nanostructures with increased osseointegration. Bjursten et al[11] investigated the influence of nanotopographic surface modification by comparing the bonding strength of two titanium implant surfaces, nanosurfaced titanium dioxide (TiO_2) nanotubes and a roughened TiO_2 grit-blasted surface, in rabbit tibias. The nanostructured titanium showed a ninefold improvement in pull-out strength and greater bone-implant contact and bone formation.

Nanocomposites that mimic bone in structure and composition have also been under active investigation. Recently, Zhang and colleagues[12,13] developed injectable nanostructured three-dimensional hydrogel scaffolds that showed enhanced osteoblast adhesion and displayed suitable mechanical properties to fill and repair bone defects. Scaffolds with mechanical properties in the range of human cancellous bone have been developed, but fabricating scaffolds with mechanical performance close to compact bone remains a challenge.[14]

Vertebral Disk

Nanotechnology has also been investigated for annulus fibrosus (AF) engineering. Nerurkar and colleagues[15,16] created electrospun scaffolds as a template for new AF tissue formation; however, the tensile moduli of these constructs reached only one third to one half that of a native lamella. Subsequently, a bilamellar construct with opposing collagen orientations of ±30° was created that showed a circumferential tensile modulus that closely replicated that of native AF.[17] These advances in nanostructured scaffolds for vertebral disk engineering also appear promising.

Targeted Drug Therapy

Nanotechnology is being used in the field of targeted drug therapy for long-term inhibition of bacterial growth. Although earlier studies successfully incorporated large molecules, such as growth factors, into nanostructured materials,[18] more recent studies have created nanofibrous scaffolds that incorporate smaller molecules, such as doxycycline[19] and silver particles.[20] These can be released in a controlled fashion with long-term duration.[19] Recently, Li et al[21] developed implant nanocoatings that contain proteins monocyte chemotactic protein-1 and interleukin-12, which prevent infection by enhancement of the recruitment and activation of macrophages. These applications have great potential for use in treatment of dental, periodontal, and bone infections.

Within the field of orthopaedics, further investigations into the long-term viability and toxicity of nanomaterials, in addition to direct comparisons of nanostructured materials and traditional materials, will enable a more definitive answer to the promise of this technology.

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