EDITORIAL

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EDITORIAL

Scaffold technologies for controlling cell behavior in tissue engineering

Guest Editors

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Scientists in the field of tissue engineering are now applying the principles of cell biology, material science and biomedical engineering to create biological substitutes that will restore and maintain normal function in diseased and injured tissues/organs [1–3]. Tissue-engineered scaffolds should (i) facilitate the localization and delivery of tissue-specific cells to precise sites in the body, (ii) maintain a three-dimensional architecture that permits the formation of new tissues, and (iii) guide the development of new tissues with appropriate function. Moreover, it has been demonstrated that tissue morphogenesis is heavily influenced by the interactions between cells and the extracellular matrix (ECM) during normal tissue development. While simple polymeric scaffolds that have been used in the past provide architectural support for neo-tissue development, they do not adequately mimic the complex interactions between tissue-specific cells and the tissue-specific ECMs that promote functional tissue regeneration. Thus, future advances in tissue engineering will depend on the development of novel scaffolding systems that actively modulate cell behaviors for functional tissue regeneration. In this regard, the present special issue describes the current status of scaffold technologies in tissue engineering and regenerative medicine applications.

This special issue includes a range of review and original articles related to various scaffolding technologies in tissue engineering. Oh and Lee review hydrophilization of synthetic biodegradable polymeric scaffolds for improving cell/tissue compatibility [4]. This technique has been considered as a simple and effective approach to achieve desirable *in vitro* cell culture and *in vivo* tissue regeneration within the synthetic polymeric scaffolds. Today, electrospinning has been widely used as a fabrication method to generate nanofibers with a diameter range of several micrometers to 100 nm or less for various tissue applications. Although many other scaffold fabrication technologies are used in tissue engineering applications, few provide scaffolds with the critical similarities to natural ECM, which electrospinning of nanofibers can provide. Electrospinning has become a popular alternative fabrication method during the previous two decades, as it can be applied to many disciplines and is a relatively simple and inexpensive scaffold fabrication process. Shin and colleagues review the current approaches to the development of electrospun nanofibers as a scaffold for tissue engineering application [5]. These electrospun scaffolds can also be functionalized by adding biochemical and mechanical cues to enhance cellular interactions for tissue engineering applications. Levorson *et al* describe their work with fabrication and characterization of multi-scale electrospun scaffolds for cartilage regeneration [6]. These scaffolds were able to maintain scaffold cellularity in serum-free conditions as well as aid the deposition of glycosaminoglycans. Xu *et al* present a novel controllable dual protein delivery system through electrospun fibrous scaffolds with different hydrophilicities [7].

Hydrogels can be used in injectable approaches to cell therapy and tissue engineering, which offers several advantages. This approach can replace multiple surgeries with minimally invasive injection procedures. However, the hydrogel-based biomaterials used in these studies have been limited by low-dimensional stability and limited nutrient and oxygen supply. To overcome these problems, Lee and colleagues developed injectable alginate particle-embedded fibrin hydrogels for soft tissue reconstruction [8]. They demonstrate that fibrin may enhance cell proliferation and accelerate the formation of ECM proteins in the alginate–fibrin system, while the alginate particles could contribute to volume retention. This injectable hybrid system composed of degradable and non-degradable hydrogels may be a preferred approach to repair soft tissue defects.

In the absence of methods for *de novo* construction of a true ECM mimic from purified components, such as collagen and elastin, decellularized tissue matrices are currently

considered an ideal scaffolding system due to their structural and mechanical similarity to native tissues and because they contain tissue-specific ECM proteins which remain after decellularization. Yoo and colleagues review decellularization techniques and possible methods for using these decellularized matrices for whole organ engineering [9]. Kim *et al* developed a composite scaffold which is composed of collagen matrix derived from decellularized porcine bladder submucosal matrix and synthetic poly(lactide-*co*-glycolide) polymer [10]. This composite scaffold provides a microenvironment that can facilitate osteogenic differentiation of amniotic fluid-derived stem cells. Also, Choi *et al* investigated the interactions between the ECM environment and human corneal endothelial cells to improve cell proliferation and function [11].

Lastly, biomedical imaging supports the development of enabling technologies including real-time, non-invasive tools for assessing the function of engineered tissues and real-time assays that monitor the interaction of cells and their environment at the molecular and organelle level. For instance, implanted scaffolds eventually degrade and are replaced by cells generating an essentially normal tissue over time. Thus, the rate of scaffold degradation and ECM production by cells must be equivalent for successful outcomes. In order to avoid these pitfalls, non-invasive optical imaging is currently being investigated for real-time monitoring of *in situ* degradation of implanted scaffolds, as well as that of cellular behaviors, using a combination of nanoparticles and tissue-engineered scaffolds. Owens *et al* developed highly charged cyanine fluorophores for trafficking scaffold degradation [12], and they continually developed near-infrared lipophilic fluorophores for tracing tissue growth [13]. These approaches will play a key role in monitoring the fate of implanted scaffolds and cells in the body, which will be helpful in translating tissue engineering strategies to the clinic.

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