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Application of Biomimetic Scaffolds for Tissue Engineering

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Tissue engineering is crucially important to help restore or enhance tissue and organ functions by employing a combination of cells, biological scaffolds and growth factors. A proper microenvironment is critical to guiding cells to assemble *de novo* functional tissues following their *in vivo* developmental processes. A biomimetic scaffold is key to construction of such a microenvironment, which should not only provide the temporary support for cells, but also elucidate proper cell-matrix interactions.

The biological functions are one essential design feature for biomimetic scaffolds in tissue engineering applications. Different bioactive materials including a large number of polymers and ceramics have now been widely used as tissue engineering scaffolds. Recently, hydrogels, composed of hydrophilic polymers that form three-dimensional (3D) networks, are particularly of interest as biomimetic scaffolds because of their good permeability of oxygen and nutrients as well as versatile bioactivities. The biological functions of hydrogels can be largely modulated based upon their diverse compositions. For example, hydrogels from natural extracellular matrix (ECM) components, such as collagen, fibrin and hyaluronic acid, can stimulate specific cell-matrix interactions at certain aspects. Hydrogels from synthetic polymers can be incorporated with natural ECM proteins or polysaccharides giving rise to the corresponding cell-matrix interactions. Small-size peptides can also be incorporated into hydrogel networks to elicit essential cell functions instead of proteins and polysaccharides. For instance, RGDS, derived from fibronectin, has been used to promote integrin-mediated adhesion for a multitude of cells [1]. Matrix metalloproteinase (MMP)-sensitive peptides, i.e. GGGPQGIWGQGK derived from collagen motifs, can be cleaved with MMPs secreted by cells for scaffold degradation [2].

The structural and mechanical properties are another key design feature for biomimetic scaffolds, considering they are extremely important to sustain appropriate functions of native tissues and organs. For example, heart valve leaflets with laminated structures show obviously different mechanical behaviors along the circumferential and radial directions (anisotropy), which allows them to withstand high mechanical stress along the circumferential direction and large strain along the radial direction [3]. Additionally, the anisotropic property of the scaffold is likely important to convey proper mechano-transduction signals to resident cells during tissue remodeling. Thus, it is critical to recapitulating such structural and mechanical properties of scaffolds for tissue engineering applications. Different methods have been developed to fabricate various structures mimicking those from ECMs in native tissues or organs. For example, electrospinning has been used to produce a myriad of nano- to micro-scale fiber structures, i.e. like collagen fibers in tissues [4]. Decellularization of tissues and organs has been widely performed to preserve their 3D structures as well as essential ECMs, while eliminating cellular components and blood [5]. 3D printing can now directly fabricate a scaffold with precisely spatial control of structures at micro-scale based on the reconstruction from micro-CT images of a tissue, even a whole organ, or based on a specific computer-aided design [6].

Altogether, biomimetic scaffolds with proper structural and mechanical properties and essential biological functions, are critical for tissue engineering. With the significant progress in the scaffold design in recent years, we expect more advanced tissue engineered products with versatile functions to be developed in the near future.

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