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Biomimetic Hydrogels as Scaffolds for Tissue Engineering

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Hydrogels have been widely used as tissue engineering scaffolds due to their good biocompatibility, soft tissue-like properties, and highly water-swollen networks that allow permeability for oxygen, nutrients and water-soluble metabolites [1-3]. They can be fabricated from natural biopolymers, synthetic polymers or their hybrids. Biopolymer-derived hydrogels, such as collagen, fibrin and matrigel, usually have concerns in weak mechanical strength, potential immunogenic reactions and animal virus contamination [2]. To overcome these drawbacks, synthetic hydrogels have emerged as important alternatives because they have a well-defined structure, controlled chemical composition and tunable mechanical property. However, most synthetic materials are bio-inert [4]. To address this issue, more research has been focused on the design of biomimetic hydrogels, which aims to mimic the physicochemical and biological properties of natural materials for tissue engineering [4-6].

A desirable scaffold for tissue engineering should have the potential to provide an Extracellular Matrix (ECM)-mimetic microenvironment (Figure 1), in order to specially interact with the surrounding cells or tissues, and guide new tissue formation. The tissue of the human body contains significant extracellular space, into which tissue cells are embedded. Tissue dynamics, such as its formation, function and regeneration after damage, is the result of an intricate temporal and spatial coordination of numerous cellular events mediated by cell/ECM interactions [7]. The natural ECM is a complex porous and fibrillar structure filled with ECM molecules, including proteins, glycosaminoglycans and proteoglycans, and can provide an ideal microenvironment to support cell growth and tissue remodeling [8]. Cell and matrix biologists have long realized that the natural ECM is an attractive model for designing tissue engineering scaffolds [9,10].

The principle for designing biomimetic hydrogels is to mimic the natural extracellular microenvironment to facilitate the interactions between hydrogels and surrounding cells through molecular recognition, and further enhance specific cellular response and tissue regeneration [4,9]. The mimicry can be chemical or physical.

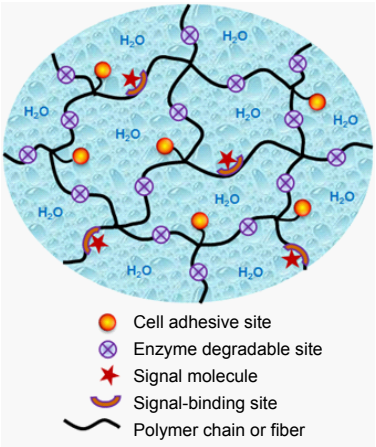

Figure 1: Schematic diagram of biomimetic hydrogel scaffolds with bioactive properties for cell adhesion, enzyme-sensitive degradation and specific binding of signal molecules.

Physical mimicry tries to mimic the porous and fibrillar structure and mechanical property of the ECM, which is essential for cell shape, migration and morphogenesis. Chemical mimicry intends to incorporate bioactive molecules into hydrogels, which is crucial for protein binding and downstream signal pathway. Natural biopolymers, such as proteins, enzymes and polysaccharides are attractive models for the design of biomimetic hydrogels with desired structures, mechanical properties and biological cues. To mimic the porous and fibrillar structure of the ECM, fibrous hydrogel scaffolds have been developed by electrospinning [11] and peptide self-assembly [12]. To incorporate ECM-like bioactivities, a variety of bioactive molecules (e.g. peptides, heparin and growth factors) derived from ECM components have been incorporated into synthetic hydrogels with ECM-mimetic biological properties, such as cell adhesion [13], proteolytic degradation [14] and growth factor-binding [15] (Figure 1). In addition, biomimetic hydrogels are also versatile for microfabrication to fabricate cell-encapsulated biochips and tissue chips [16,17].

In summary, biomimetic engineering of synthetic hydrogels is an attractive strategy to develop scaffolds for tissue engineering, which provides fundamental knowledge to understand cell/scaffold interactions, cellular response and tissue formation. The physicochemical and bioactive properties of biomimetic hydrogels can be fine-tuned through variations in the scaffold morphology, crosslinking density, molecular organization and biomolecule incorporation. However, current biomimetic hydrogel scaffolds are still lack of the hierarchical structure and multiple biofunctions of the ECM. An important future work is to mimic the structure, morphology and bioactivity of the ECM as closely as possible, in order to design synthetic hydrogels with an ideal biomimetic microenvironment to support cell growth and tissue regeneration.

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