Review

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Regenerative Medicine

Protein-based materials in load-bearing tissue-engineering applications

Proteins such as collagen and elastin are robust molecules that constitute nanocomponents in the hierarchically organized ultrastructures of bone and tendon as well as in some of the soft tissues that have load-bearing functions. In the present paper, the macromolecular structure and function of the proteins are reviewed and the potential of mammalian and non-mammalian proteins in the engineering of load-bearing tissue substitutes are discussed. Chimeric proteins have become an important structural biomaterial source and their potential in tissue engineering is highlighted. Processing of proteins challenge investigators and in this review rapid prototyping and microfabrication are proposed as methods for obtaining precisely defined custom-built tissue engineered structures with intrinsic microarchitecture.

Keywords: biomaterial • load bearing • protein • regeneration • scaffold • tissue engineering

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The need for organs and tissues is ever increasing due to the aging of the population, diseases, accidents and the limited availability of donors. Tissue engineering and regenerative medicine seek to construct substitutes to revitalize compromised tissues and improve organ functionality. The tissue-engineering idea is based on harnessing *in vitro* cell methods and bioactive agents with the goal of replacing or supporting the function of defective or injured body parts [1]. Polymeric scaffolds carry great importance in tissue engineering as they protect the cells against dynamic forces exerted by the body and provide appropriate surfaces for cell adhesion, proliferation and guide tissue formation with their inherent biochemical and topographical cues. In the biological tissues, cells reside on and interact with the extracellular matrix (ECM), which is composed of glycosaminoglycans and a fibrillar network of collagen and elastin (Figure 1A & B).

In order for the substitute materials to perform under predominantly load-bearing conditions they should match the compressive and tensile mechanical strength, and the elasticity of the target tissues. Another important criterion of a tissue-engineered construct must be the resistance to fatigue or to cyclic stresses caused naturally by pulsatile pressure in blood vessels, tensile stresses on tendon and compressive loads on bone tissues. The degradation profile should also comply with the healing timeline of the tissue to maintain mechanical stability of the wound site. Proteolytic enzymes in body fluids and hydrolytic cleavage lead to degradation of protein scaffolds *in vivo*. For example, scaffolds for bone tissue engineering are expected to disappear typically after 12–18 months without any immunological reactions [2]. For structural integrity and to extend the degradation time, the protein scaffold should be stabilized with physical or chemical crosslinking. The crosslink is expected to prolong the degradation time of protein scaffolds depending on the type of crosslinker and dosage. For example, medical collagen scaffolds implanted into rats were reported to be completely degraded in 8 weeks when chemically crosslinked, while enzymatically crosslinked scaffolds showed only a little degradation after

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