Oriented lamellar silk fibrous scaffolds to drive cartilage matrix orientation: Towards annulus fibrosus tissue engineering


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Available online 27 May 2012

Keywords:
Biomimetic material
Intervertebral disc tissue engineering
Silk
Extracellular matrix
Fibrous scaffold


1. Introduction

The cellular alignment and architectural organization of the fibrous extracellular matrix (ECM) of a tissue play fundamental roles in its biomechanical properties. The multilamellar, fiber-reinforced composite structure of the intervertebral disc (IVD) provides shock-absorbing capabilities to the spinal column and imparts flexibility between adjacent vertebrae. The annulus fibrosus (AF) part of the IVD consists of 15–25 concentric layers; each layer is reinforced by collagen fibers aligned at an approximately 30° angle with respect to the transverse plane of the disc, but in alternate directions in successive layers [1]. This cross-aligned, fiber-reinforced organization is critical for proper biomechanical functioning of the AF. It allows the conversion of compressive force to lateral force to withstand extrinsic tensile stresses (circumferential, longitudinal and torsional), and ultimately makes the spine flexible enough to bend and twist in all directions.

Orientation is evident even from the early stages of disc development. In the embryonic stage, longitudinally aligned collagen fibers radiate into the cartilaginous layer of the primordial vertebral body (the predecessor of Sharpey's fibers), along which AF progenitor cells and the other deposited ECM components become precisely oriented [2,3]. Age-dependent dehydration of the nucleus pulposus (NP) and crack development in the AF layers [4], probably caused by a number of factors such as metabolic changes, genetic predisposition and biomechanical issues [5], lead to degeneration of the disc. A reduction in the diameter and increased fibrillation of collagen fibers [6], the disorientation of fiber alignment and a decline in ECM turnover are hallmarks of IVD degeneration.

Replacement of degenerated disc by a tissue engineered substitute could offer major advantages over arthroplasty or the implantation of a prosthetic disc, in terms of the initial matching of biomechanical properties and adaptive remodeling over the long term. Recently, several attempts have been made to engineer AF tissues using scaffolds with a variety of chemical compositions and architectures [5,7–12]. However, none of these studies could successfully simulate the precise anatomical orientation of collagen fibers in lamellar multilayered AF tissue. As a result, the mechanical properties of most of these engineered tissues were several orders of magnitude below the stiffness of IVD, especially under tension and compression, and would therefore be expected to provide insufficient mechanical support after implantation at the intervertebral joint site.