

NOVEL POLYMERS FOR STUDIES IN STEM CELL DIFFERENTIATION AND NUCLEUS PULPOSUS SUPPLEMENTATION

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Background: Degenerative disc disease has been implicated as a major component of spine pathology. Currently, the two major clinical procedures for treating disc degeneration are disc excision and spinal fusion. Although these procedures offer relatively good short-term clinical results in relief of pain, in many instances, these treatment modalities have been disappointing because of altered spinal mechanics leading to subsequent degeneration at adjacent disc levels.

Biological repair of the degenerate disc would be the ideal treatment and recent advances in tissue engineering offer the unique opportunity to engineer a replacement nucleus pulposus (NP) using polymer-cell constructs and growth factors.

Rational for using chitosan and mesenchymal stem cells: Chitosan has been chosen because it is injectable (very soluble at room temperature but gelling at 37°C), biocompatible and can retain more than 80% of the proteoglycan and collagen produced by entrapped cells (1,2). This is of particular importance because any scaffold designed for disc use must be able to retain proteoglycan if a functional tissue is to be achieved.

Furthermore, the scaffold will allow implantation without major surgical disruption of the annulus fibrosus (AF). We use human adult mesenchymal stem cells (MSCs) because the use of stem cells is essential for clinical application if an autologous source of cells is to be used.

Rational for using nitrogen rich plasma polymers: MSCs are pluripotent progenitor cells with the ability to generate cartilage, bone, muscle, tendon, ligament disc and fat. However, recent evidence indicates that a major drawback of current cartilage and

intervertebral disc tissue engineering is that human MSCs isolated from some arthritic patients (a clinically relevant source of stem cells) express type X collagen (a marker of chondrocyte hypertrophy associated with endochondral ossification) (3). Some studies have attempted to use growth factors to inhibit type X collagen expression, but none has addressed the possible effect of the chemical composition of the substratum on stem cell hypertrophy.

Here, we examine the growth and differentiation potential of human MSCs cultured on extremely N-rich plasma polymer layers, which we call "PPE:N" (N-doped plasma-polymerised ethylene, containing up to 36% [N]). We show that PPE:N almost completely suppresses the expression of type X collagen. In contrast, neither aggrecan nor type 1 collagen expression was significantly affected. These results indicate that PPE:N coatings may be suitable surfaces for inducing MSCs to a disc-like phenotype for tissue engineering of intervertebral discs, in which hypertrophy is suppressed.

REFERENCES:

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