Rapid Fabrication Tissue Engineering by Plastic Compression

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INTRODUCTION:

Development of 3D connective tissues *in vitro* is heavily dependent upon remodelling of the matrix, in particular collagen by resident cells. This process is often difficult to control, slow and costly. This is the main question inherent in 3D tissue bioreactor operations, namely to get cells to 'fabricate' collagen matrices rapidly without the constraints of cell perfusion, spatial control and matrix density. We have tackled this by attempting to pre-fabricate the collagen template without relying on any cell activity at all. We have developed a process of 3D collagen tissue prefabrication by plastic compression (PC) of hyper hydrated native collagen gels[1].

METHODS:

Acellular and cell-seeded, hydrated type I collagen gels were made, as previously described[2], and routinely compacted by a combination of compression and blotting. The rate of compaction was controlled by the force applied and the extent of fluid removal to a porous 'sink'. Cellular collagen gels were made, using dermal fibroblasts and horse bone marrow stromal cells. These constructs were compressed using standardised protocol and rolled to form tight spiral rods. These were then cultured with or without tension in a bioreactor, for periods of up to 30 days.

RESULTS:

Highly structured and mechanically strong collagen constructs were made by using plastic compression. This fabrication process was cell independent. Where cellular constructs were fabricated, these retained good cell viability after undergoing plastic compression, with cells surviving 30 days in culture.

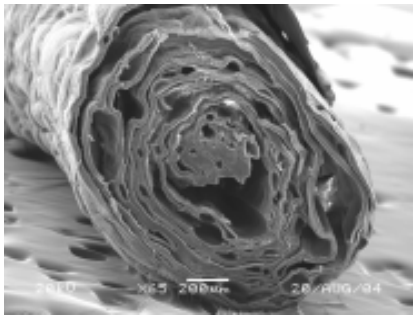

Figure 1. Shows rolling of the collagen sheet to give many adjacent spiral layers This is an SEM across the end of the construct (bar = 200 μm)

DISCUSSION & CONCLUSIONS:

The PC fabrication process will rapidly and efficiently make tissue-like matrices for cell culture. During the plastic compression process, a dense, strong matrix is formed, without the need for any cell activity. These plastic compressed constructs retain many features crucial for tissue-engineering purposes: high-density matrix protein, in this case collagen, biomimetic structure and functional mechanical strength with good cell viability.

REFERENCES:

1. Brown, R.A. Wiseman, M. Chuo, C.B. Cheema, U.Nazhat, S.N. 'Ultra rapid engineering of biomimetic materials and tissues.' (under review)

2. Prajapati RT, Chavally-Mis B, Herbage D, Eastwood M, Brown RA. 2000. 'Mechanical loading regulates protease production by fibroblasts in three-dimensional collagen substrates.' *Wound Repair Regen.* 8(3): 226-37

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