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Spatial Layering of Cells in A Novel Poly(lactic acid-co-caprolactone)-Collagen Hybrid Construct

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INTRODUCTION: Advantages of synthetic polymers as a scaffolding material include the ability to produce them on a large scale and the ability to tailor their physical and mechanical properties to exact specification. A continuing difficulty is the uncertainty of cell seeding, largely due to a non-ideal surface chemistry. Natural biopolymers on the other hand, provide a substrate for cell-adhesion, are highly organized, and have the ability to induce tissue growth. A main disadvantage, however, is that they are less readily available and their mechanical and physical properties are difficult to control. The concept of combining these two biomaterials and their advantages is attractive. In this study we have fabricated a hybrid construct consisting of a synthetic polymer mesh coated with hyperhydrated collagen gels, which were plastic compressed.

METHODS: Hydrated collagen gels were plastic compressed onto a mesh of poly(lactic acid-co-caprolactone) (PLACL), resulting in two spaces and two surfaces for cell seeding. As the collagen and cell concentration depend on the amount of fluid leaving the collagen gels, the influence of varying load and the time of the plastic compression process was studied. The hybrid constructs were embedded and/or surface layered with human dermal fibroblasts (final concentration $2x10^6$ cells/ml) to mimic an (1) interstitial, an (2) epithelial and a (3) composite tissue, which were cultured for seven days under static conditions. Cell viability, directly after the plastic compression process and over the cultivation period, was qualitatively assessed with AlamarBlue. Quantitative analysis was performed at the end of the cultivation period to evaluate the short-term biocompatibility of the polymer collagen blend using fluorescence staining and confocal microscopy.

RESULTS: We found that the duration rather than the weight of the load in the plastic compression process determines the final collagen and cell density. No significant cell death was observed after the plastic compression of the interstitial equivalents, confirming previous reports of good cell viability retention [1]. The interstitial, epithelial and composite tissue equivalents showed no macroscopic signs of contraction and good cell proliferation with a two to three fold increase in cell number over 7 days. Quantitative analysis showed a homogenous cell distribution and good biocompatibility.

DISCUSSION & CONCLUSIONS: The aim of this study was to test “in vitro” a novel design of 3D tissue engineered construct capable of spatially layering different cell phenotypes using a hybrid PLACL -collagen construct to enhance or promote tissue repair processes “in vivo”. Plastic compression of hydrated collagen gels onto the surface of the polymer mesh allows for seeding of up to four cell layers to histologically mimic stratified tissues. The slow degrading biocompatible PLACL backbone provides for the mechanical support of the hybrid construct. The plastic compression process allows for cell independent compaction of the matrix to mimic “in vivo” cell and collagen densities, which has implications for implant integration, angiogenesis and other cell responses. The PLACL-Collagen hybrid construct has potential applications in bladder wall, blood vessels and skin, which are currently being explored.

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