

NOVEL STRATEGIES FOR ENHANCING TISSUE INTEGRATION IN CARTILAGE REPAIR

L.C.Davies, B. Caterson and V.C. Duance

*Connective Tissue Biology Laboratories, School of Biosciences, Cardiff University,
Museum Ave, Cardiff. CF10 3US*

INTRODUCTION: Articular cartilage is unable to initiate a spontaneous repair response when injured due to its avascular and aneural properties. Within adult cartilage, chondrocytes are entrapped within an extensive extracellular matrix and are unable to migrate to sites of injury to regulate tissue repair. Injury to this tissue therefore inevitably leads to degeneration of the cartilage and the development of diseases such as osteoarthritis.

The surgical technique of autologous chondrocyte transplantation (ACT) was developed for the treatment of full thickness cartilage defects¹. Implantation of chondrocytes into the defect site repairs the injury with a mixture of fibrocartilaginous and hyaline-like tissue that poorly integrates with the existing cartilage and frequently degenerates with time. In this current study we have developed an in vitro model to investigate methods for enhancing this integration and the development of a more biomechanically stable repair tissue.

METHODS: Bovine articular cartilage explants from the *metacarpalphalangeal* joint were experimentally injured using a stainless steel trephine and cultured for a period of 28 days. Autologous chondrocytes in an agarose suspension were injected into the interface region at the injury site. Culture media was collected and analysed for proteoglycan and collagen content using the DMMB and hydroxyproline assays respectively. Matrix metalloproteinase (MMP) expression was also analysed using zymography and an adapted collagen fibril assay.

RESULTS: Morphological analyses indicate attempts at repair and integration within both

control and experimental treatment groups although the presence of autologous chondrocytes appeared to amplify this repair response. Considerable differences in proteoglycan release between injured explants and the intact control group were seen over the 28 day culture period although these differences were not statistically significant. Collagen release into the media was only seen at day 28 within the experimental culture group. Western Blotting will ascertain the nature of this collagen and whether it is present in media as a consequence of degradation or synthesis will be investigated using radiolabelling techniques. An up-regulation of MMPs 2 and 9 was seen within the experimental cultures compared to the controls using zymography and preliminary data also suggests up-regulation of collagenases in the experimental group.

DISCUSSION & CONCLUSIONS: As seen with clinical ACT treatment the presence of autologous chondrocytes appears to enhance repair and integration attempts however morphologically this repair tissue appears to be fibrocartilaginous. This in vitro model will enable the temporal and spatial expression of the chondrocytes to be monitored during the "repair process". Establishment of this in vitro model will allow investigation into the effects of different growth factors on enhancing this repair and integration process.

REFERENCES: ¹ Brittberg, M., A. Lindahl, et al. (1994) *N Engl J Med* **331**(14): 889-95.