DYNAMIC CHONDRON FUNCTION

IN

ARTICULAR CARTILAGE

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ABSTRACT

This study examined the behaviour of articular cartilage chondrocytes and the role of the pericellular microenvironment in modifying cellular behaviour during dynamic loading events. While the structural composition and metabolic function of the chondron have been examined previously, little is known about its physiology. Consequently, it was hypothesised that 'the chondrocyte behaves dynamically within the chondron microenvironment, and that the microenvironment plays a critical role in minimising the volume regulatory activity required to maintain the health of the chondrocyte throughout the physicochemical changes associated with the loading cycle.'

Four research objectives addressed the hypothesis. The first was to develop an environmental perfusion chamber and experimental protocols for dynamic imaging of articular chondrocytes *in vitro* and *ex vivo* using time-lapse video microscopy. The system developed, which was composed of a chamber and unique complimentary heating system, enabled temperature control, media perfusion and variable delivery of environmental factors, over long imaging periods without fluctuations in focus or loss of cell viability.

Secondly was to examine short and long term behaviour of chondrocytes cultured in agarose gel, alginate beads and vibratome prepared explants. The results showed dynamic activity of cytoplasmic organelles, constant changes in position of the chondrocyte within the microenvironment and cellular secretory events that influenced its organisation. Unique information regarding these biological responses will be vital for future research.

Thirdly was to examine the role of the microenvironment and its territorial and interterritorial matrices in volume regulation of intact tissue. The microenvironment occupies a critical position between the bulk of the cartilage matrix involved in load bearing deformation and physical changes and the chondrocyte, which attempts to minimise its volume regulatory response while maintaining active metabolic management of the matrices.

Fourthly was to examine the role of the microenvironment in volume regulation isolated chondrocytes. Its robust structure appears responsible for physical and chemical protection of the chondrocyte. This study provided the first evidence that the microenvironment can influence the volume regulatory response of the chondrocyte. The composition and integrity of the microenvironment influence the ability of the chondrocyte to respond to osmotic challenge and the intact microenvironment functions efficiently *in vivo* to minimize the exposure of the chondrocyte to dynamic osmotic challenges that could compromise function.

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