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*DYNAMIC CHONDRON FUNCTION*

*IN*

*ARTICULAR CARTILAGE*

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A thesis submitted in partial fulfilment of the  
requirements for the degree of Doctorate of Philosophy,  
The University of Auckland, 2003

## 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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# TABLE OF CONTENTS

	<b>Page</b>
ABSTRACT	II
ACKNOWLEDGEMENTS	III
TABLE OF CONTENTS	IV
LIST OF TABLES	IX
LIST OF FIGURES	X
LIST OF VIDEO CLIPS (viewed from CD)	XII
<b>CHAPTER 1: INTRODUCTION</b>	<b>1</b>
1.1 Articular Cartilage Morphology	2
1.1.1 Zonal Organisation	4
1.1.1.1 Zone 1 – Superficial or Tangential Layer	6
1.1.1.2 Zone 2 – Middle, Transitional or Intermediate Layer	6
1.1.1.3 Zone 3 – Deep or Radial Layer	7
1.1.1.4 Tidemark	8
1.1.1.5 Zone 4 – Calcified Cartilage Layer	8
1.1.1.6 Chondroosseous Junction	9
1.1.2 Chondron Organisation	9
1.1.2.1 The Chondron	9
1.1.2.2 The Chondrocyte	11
1.1.2.3 The Pericellular Microenvironment	11
1.1.2.3.1 The Pericellular Matrix	12
1.1.2.3.2 The Pericellular Capsule	12
1.1.3 Matrix Organisation – Matrices External to the Chondron	14
1.1.3.1 Territorial Matrix	14
1.1.3.2 Interterritorial Matrix	15
1.2 Articular Cartilage Composition	15
1.2.1 Collagens	17
1.2.1.1 Fibril-Forming Collagens	20
1.2.1.2 Fibril-Associated Collagen With Interrupted Triple Helices	21

1.2.1.3	Short Chain Collagens	22
1.2.2	Glycosaminoglycans	23
1.2.3	Hyaluronan	24
1.2.4	Proteoglycans	24
1.2.4.1	Aggregating Proteoglycans	24
1.2.4.2	Non-Aggregating Proteoglycans and Others	27
1.2.4.3	Cell Surface Proteoglycans	31
1.2.5	Glycoproteins	31
1.2.6	Water	34
1.3	Material and Functional Properties of Articular Cartilage	35
1.3.1	Structural and Physicochemical Interaction of Cartilage Components	35
1.3.2	Biomechanical Behaviour of Articular Cartilage	42
1.3.3	Material Properties of the Chondron	44

## **RESEARCH THESIS HYPOTHESIS AND OBJECTIVES** 47

## **CHAPTER 2: MATERIALS & METHODS** 48

2.1	Materials	48
2.2	Methods	49
2.2.1	Tissue Sample Selection	49
2.2.2	Isolated Chondron and Chondrocyte Preparation	50
2.2.2.1	Mechanical Extraction of Chondrons (MC) – Serial Homogenisation	50
2.2.2.2	Enzymatic Extraction of Chondrons (EC) – Enzymatic Digestion	52
2.2.2.3	Enzymatic Extraction of Chondrocytes (IC) – Enzymatic Digestion	53
2.2.3	Agarose Gel and Alginate Preparations	54
2.2.3.1	Agarose Gel Preparation	54
2.2.3.2	Alginate Bead Preparation	55
2.2.4	Intact Tissue Preparation	55
2.2.4.1	Procedure	55

2.2.4.2	Isolation and Preparation of Vibratome Slices	55
2.2.5	Osmotics	56
2.2.6	Tissue Viability	56
2.3	Computer-Enhanced Video Microscopy Imaging System	61
2.3.1	Introduction	61
2.3.2	CEVM Components	62
2.4	Statistical Analyses	64
 <b>CHAPTER 3: CHARACTERISATION OF THE ENVIRONMENTAL PERFUSION CHAMBER</b>		
		66
3.1	Introduction	66
3.2	Design Parameters	68
3.3	The Chamber	69
3.4	Temperature Regulation	72
3.5	Perfusion Characteristics	76
3.6	Application of the Chamber	78
3.7	Summary and Conclusions	78
 <b>CHAPTER 4: DYNAMIC CHONDROCYTE BEHAVIOUR IN THE ENVIRONMENTAL PERFUSION CHAMBER</b>		
		80
4.1	Introduction	80
4.2	Materials and Methods	81
4.2.1	Materials	81
4.2.2	Tissue Sample Collection	82
4.2.3	Perfusion Chamber and Imaging System	83
4.2.4	Perfusion Media and Protocols	83
4.2.5	Analyses	83
4.3	Results	84
4.3.1	Intact Vibratome Sections – Deep Layer Cells <i>In situ</i>	84
4.3.2	Enzymatically Isolated Chondron	87
4.3.3	Enzymatically Isolated Chondrocyte	89
4.4	Discussion	94

4.4.1	Activity of Nucleus and Golgi Apparatus	94
4.4.2	Activity of Golgi Vesicles	99
4.4.3	Activity of Lipid Droplets	101
4.4.4	Activity of the Pericellular Matrix	102
4.5	Conclusion	103
 <b>CHAPTER 5: CHONDROCYTE VOLUME REGULATION IN INTACT EXPLANTS</b>		 105
5.1	Introduction	105
5.2	Materials and Methods	112
5.2.1	Materials	112
5.2.2	Isolation and Preparation of Tissue	112
5.2.2.1	Tissue Sample Collection	112
5.2.2.2	Preparation of Vibratome Slices	112
5.2.3	Environmental Perfusion Chamber and Imaging System	113
5.2.4	Osmotic Perfusion Protocols	113
5.2.4.1	Preparation of Media	113
5.2.4.2	Perfusion Protocols and Imaging	113
5.2.5	Analyses	114
5.2.5.1	Cell Viability	114
5.2.5.2	Area Analyses	115
5.2.5.3	Statistical Analyses	116
5.3	Results	116
5.3.1	Cell Morphology and Tissue Viability	116
5.3.2	Cross-Sectional Area and Calculated Mean Volume Analyses Under Isotonic Conditions	120
5.3.3	Dynamic Changes in Cell Size in Response to Altered Osmolality	122
5.3.3.1	Cross-Sectional Area Analyses Under Hypertonic Conditions	123
5.3.3.2	Cross-Sectional Area Analyses Under Hypotonic Conditions	124
5.4	Discussion	125
5.4.1	Cell Volume and Zonal Variation	126
5.4.2	Response to Osmotic Challenge	129



<b>CHAPTER 6: ISOLATED CELL PREPARATION – VOLUME REGULATION</b>	138
6.1 Introduction	138
6.2 Materials and Methods	146
6.2.1 Materials	146
6.2.2 Isolation and Preparation of Chondrons and Chondrocytes	146
6.2.2.1 Tissue Preparation	146
6.2.2.2 Mechanically Isolated Chondrons (MC)	146
6.2.2.3 Enzymatically Isolated Chondrons (EC)	147
6.2.2.4 Isolated Chondrocytes (IC)	147
6.2.2.5 Preparation of Agarose Gel Constructs	147
6.2.2.6 Immunohistochemistry	148
6.3 Environmental Perfusion Chamber and Imaging System	148
6.4 Osmotic Perfusion Protocols	149
6.4.1 Preparation of Media	149
6.4.2 Perfusion Protocol	149
6.5 Analyses	150
6.5.1 Cell Viability	150
6.5.2 Area Analyses	150
6.5.3 Statistical Analyses	150
6.6 Results	151
6.6.1 Structure and Composition	151
6.6.2 Cross-Sectional Area Analyses Under Isotonic Conditions	153
6.6.3 Chondrocyte Response to Osmotic Challenge	156
6.6.4 Cross-Sectional Area Analyses Under Hypertonic Conditions	158
6.6.5 Cross-Sectional Area Analyses Under Hypotonic Conditions	160
6.7 Discussion	160
<b>CHAPTER 7: GENERAL CONCLUSION</b>	170
<b>REFERENCES</b>	180
<b>APPENDICES</b>	i

## LIST OF TABLES

	<b>Page</b>	
Table 1	Zonal variation of articular cartilage	5
Table 2	Composition of articular cartilage	16
Table 3	Genetically distinct collagen types	18
Supplementary Table	Ionic and osmotic environment of articular chondrocytes	38
Table 4	Summary and comparison of cell isolation procedures	50
Table 5	Review of studies of articular cartilage – intact tissue volume regulation	110
Table 6	The mean values for the cross-sectional area of the chondrocyte, the pericellular microenvironment and chondron	120
Table 7	Cross-sectional area and volume calculations of chondrocytes from the superficial and deep layers, under isotonic conditions	121
Table 8	Relative mean change in cell volume of superficial and deep layer cells in response to osmotic challenge	123
Table 9	Comparison of reported cell volumes from the literature	127
Table 10	Cell volume variation with cartilage zones	128
Table 11	Comparison of response to osmotic challenge from the literature	131
Table 12	Review of studies of articular cartilage – isolated cell preparation volume regulation	143
Table 13	The mean values for the cross-sectional area of the chondrocyte, the pericellular microenvironment and chondron	154
Table 14	Relative mean change in cross-sectional area of chondrocytes and chondrons for all three preparations in response to osmotic challenge	158

## LIST OF FIGURES

		Page
Figure 1	Zonal organisation of articular cartilage	4
Figure 2	Schematic drawing of chondron and horizontal view of circumferential organisation of a chondron and its external matrices	10
Figure 3	Diagrammatic representation of interaction between type VI and pericellular capsule collagens and the chondrocyte membrane	22
Figure 4	The structure and organisation of aggrecan	26
Figure 5	Overview of the proteoglycans present in cartilage	29
Figure 6	Schematic representation of aggrecan aggregates in solution	35
Figure 7	Dense collagen network interacting with the macromolecular aggregates of aggrecan	39
Supplementary Figure	Schematic diagram illustrating the membrane transport processes identified in chondrocytes.	42
Figure 8	Constant stress applied to articular cartilage	43
Figure 9	Diagrammatic representation of a chondron at rest and under compression	45
Figure 10	Cell viability – vibratome sections labelled with LIVE/DEAD assay	59
Figure 11	Cell viability – isolated cells labelled with ethidium homodimer-1	60
Figure 12	Schematic diagram of CEVM system	63
Figure 13	The CEVM system	65
Figure 14	Environmental perfusion chamber – exploded view	70
Figure 15	Chamber and 'stage blanket' heating on microscope	74
Figure 16	Temperature regulation profile – setting for 34 °C	75
Figure 17	Equipment, chamber perfusion and perfusion profile	77
Figure 18	Dynamic behaviour - <i>in situ</i> - deep layer chondron	86

Figure 19	Dynamic behaviour – enzymatically isolated chondron	88
Figure 20	Enzymatically isolated chondrocyte cultured in agarose	89
Figure 21	Dynamic behaviour – enzymatically isolated chondrocyte A	92
Figure 22	Dynamic behaviour – enzymatically isolated chondrocyte B	93
Figure 23	Schematic representation of proteoglycan and hyaluronan synthesis	100
Figure 24	Vibratome sections of superficial and deep layer cells stained with ALIVE/DEAD viability assay	118
Figure 25	Digital DIC micrograph of vibratome sections from the superficial and deep layer	119
Figure 26	Graph showing mean cross-sectional areas of the chondrocyte, pericellular microenvironment and chondron at day 1 under isotonic conditions for both superficial and deep layer cells	121
Figure 27	Boxplot of mean chondrocyte volumes of superficial and deep layer cells	122
Figure 28	Digital DIC micrographs of vibratome sections showing the response of superficial and deep layer cells to osmotic challenge at day 1	124
Figure 29	Graph of relative percentage change in cross-sectional area of the chondrocyte and chondron under osmotic challenge	125
Figure 30	Graph comparing relative percentage change in cell volume in response to osmotic challenge to results from previous studies	130
Figure 31	Digital DIC micrographs of three cell preparations	151
Figure 32	Single optical sections showing distribution of type VI collagen and keratan sulphate	152
Figure 33	Mean cross-sectional areas of the chondrocyte, pericellular microenvironment and chondron under isotonic conditions	155
Figure 34	Digital DIC micrographs showing the effect of osmotic challenge at day 1, in the three different cell preparations	157
Figure 35	Relative percentage changes in cross-sectional areas of the chondrocyte and chondron in response to osmotic challenge	159

## LIST OF VIDEO CLIPS (viewed from CD)

	<b>Video</b>
<b>Chapter 3</b> <i>Perfusion characteristics</i>	V1
<b>Chapter 4</b> <i>Dynamic behaviour</i>	
Intact tissue - Deep layer chondron	V2
Enzymatically isolated chondron	V3
Enzymatically isolated chondrocyte - Cell A	V4
Enzymatically isolated chondrocyte - Cell B	V5
<b>Chapter 5</b> <i>Volume regulation - Intact tissue</i>	
Superficial layer chondron	V6
Deep layer chondrons A – sectioned parallel to articular surface	V7
Deep layer chondrons B – sectioned perpendicular to articular surface	V8
<b>Chapter 6</b> <i>Volume regulation – Isolated tissue</i>	
Mechanical chondron – Cell A	V9
Mechanical chondron – Cell B	V10
Enzymatically isolated chondron – Alginate	V11
Enzymatically isolated chondrons – Cell A & B	V12
Enzymatically isolated chondrocyte – Cell A	V13
Enzymatically isolated chondrocyte – Cell B	V14