

Chapter 7

Regeneration of Articular Cartilage: Opportunities, Challenges, and Perspectives

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ABSTRACT

This chapter reviews the structure and function of articular cartilage and the pathogenesis of Osteoarthritis (OA) before exploring the challenges associated with cartilage repair and regeneration. Surgical techniques for cartilage repair are critically reviewed and special emphasis is placed upon arthroscopic lavage and debridement, microfracture, bone marrow stimulation, and autologous osteochondral allografting. Biomimetic models of cartilage relevant to cartilage regeneration and tissue engineering research are reviewed along with microenvironmental approaches that preserve the chondrocyte phenotype using a combination of biomimetic 3-dimensional cell culture systems and growth factor supplementation. Future refinement of tissue-engineering approaches for cartilage repair will benefit significantly from advances in cell-based repair strategies. The author provides his own perspectives by highlighting and prioritizing areas for future investigation.

INTRODUCTION

Damage to articular cartilage is a relatively common type of joint injury in humans and animals. In humans the majority of cases involve damage to the knee joint. Symptoms of cartilage damage

include swelling, joint pain, and stiffness. It is difficult to quantify how common cartilage damage is because many people with mild cartilage damage do not seek medical advice and the injury may go untreated for many years, exacerbating the problem at a later date when treatment becomes

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necessary. However, cartilage damage is thought to be quite common in humans and animals. Cartilage damage due to trauma is particularly common in people under 35 years of age. Younger people are more physically active and their participation in high-impact athletic activities means that they are at a much greater risk of cartilage injury than older people. Cartilage damage associated with Osteoarthritis (OA) is often seen in adults over 50 years of age and is much more common in women than in men of the same age group. Defects in articular cartilage present the orthopedic surgeon with an extremely challenging clinical problem (Kalsen, Gikas, & Briggs, 2010). In situations where cartilage defects are very large corrective surgical options are limited and outcomes are uncertain. Unlike other tissues, mature articular cartilage does not possess its own blood supply. The poor vascularization results in cartilage tissue having a low normoxic value (Kay, Richardson, & Forsyth, 2011). When damage does occur, the lack of vasculature means that damaged cartilage will not heal as quickly as well vascularized tissues such as skin and muscle. Cartilage heavily relies on diffusion of oxygen and nutrients from subchondral bone and synovial fluid. When traumatic injury occurs the supply of oxygen and nutrients may be further impaired. The Extracellular Matrix (ECM) of cartilage tissue actually acts as a barrier to the recruitment of inflammatory cells and may impede the movement systemic factors. In addition, aging can significantly reduce the ability of cartilage to repair itself. All these factors conspire to make cartilage repair and regeneration a difficult challenge. The aim of this book chapter is to explore the major challenges in this area of regenerative medicine and highlight some opportunities for future developments in cartilage repair and regeneration. This chapter starts by discussing the structure and function of articular cartilage before reviewing the mechanisms involved in cartilage degeneration in OA. It then addresses the current opportunities and challenges associated with the regeneration and repair of articular cartilage

defects. Cell-based repair strategies including Autologous Chondrocyte Implantation (ACI) are reviewed and the potential of Mesenchymal Stem Cell (MSC) therapy are briefly discussed. Biomimetic models of cartilage relevant to cartilage regeneration and tissue engineering are reviewed in detail. The author also provides his own perspectives on this topic and highlights key areas for future investigation.

STRUCTURE AND FUNCTION OF ARTICULAR CARTILAGE

Articular cartilage (also known as hyaline cartilage) is a tough yet flexible and mechanically compliant connective tissue. It is a load-bearing tissue with unique biological and biomechanical characteristics (Figure 1).

Cartilage is found at the end of long bones in the articulating surfaces of joints. In normal synovial joints, cartilage is a smooth and translucent tissue that acts as a cushion to absorb shock and allows the bones to glide over each other with frictionless articulation. It is sub-classified into three different types: elastic cartilage, hyaline cartilage, and fibrocartilage. These types of cartilage differ in the relative amounts of three principal components, namely collagen fibers, ground substance (proteoglycans) and elastin fibers.

Anatomically, normal articular cartilage is composed of three main zones and the tidemark, which separate articular cartilage from subchondral bone (Figure 2). The zones of cartilage are based on the shape of the chondrocytes, the composition of the ECM and the orientation of the type II collagen with respect to the articulating surface and the subchondral bone. The superficial zone (tangential zone) makes up 10% of articular cartilage. This is the thinnest layer. Type II collagen fiber orientation is parallel to the articulating surface in the joint. This zone has flattened chondrocytes, condensed collagen fibers, and sparse

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