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Review

Modulation of cartilage's response to injury: Can chondrocyte apoptosis be reversed?☆

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ABSTRACT

Osteoarthritis is characterized by a chronic, progressive and irreversible degradation of the articular cartilage associated with joint inflammation and a reparative bone response. More than 100 million people are affected by this condition worldwide with significant health and welfare costs. Our available treatment options in osteoarthritis are extremely limited. Chondral or osteochondral grafts have shown some promising results but joint replacement surgery is by far the most common therapeutic approach. The difficulty lies on the limited regeneration capacity of the articular cartilage, poor blood supply and the paucity of resident progenitor stem cells. In addition, our poor understanding of the molecular signalling pathways involved in the senescence and apoptosis of chondrocytes is a major factor restricting further progress in the area. This review focuses on molecules and approaches that can be implemented to delay or even rescue chondrocyte apoptosis. Ways of modulating the physiologic response to trauma preventing chondrocyte death are proposed. The use of several cytokines, growth factors and advances made in altering several of the degenerative genetic pathways involved in chondrocyte apoptosis and degradation are also presented. The suggested approaches can help clinicians to improve cartilage tissue regeneration.

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Introduction

Osteoarthritis (OA) is characterized by a chronic, progressive and irreversible degradation of the articular cartilage associated with joint inflammation and a reparative bone response [1]. It is the most common cause of disability globally with more than 100 million people affected by this condition [2,3]. It is estimated that the annual cost of OA in the USA exceeds $89 billion [4,5].

Post-traumatic OA is a major clinical problem with significant health and welfare costs. It mostly affects young and active individuals. Our current conservative therapies are mostly palliative and limited to significant adaptation of life-style. As the disease progresses, surgical treatment is indicated but is limited to either joint fusion or joint replacement surgery [1,2,6–9]. Alternative treatments include bone marrow stimulation techniques, osteochondral grafts and autologous chondrocyte implantation. The results of these techniques have been variable [9,10,8,11,12]. The main obstacle in revolutionizing the treatment of post-traumatic OA is the complex and unmapped cascade of events, which are triggered at a cellular level and eventually lead to the articular damage.

Mechanism of post-traumatic osteoarthritis

The articular cartilage is subjected to the initial biomechanical insult, which results in an immediate wounding, necrosis and apoptosis of articular chondrocytes [13]. Thereafter and depending on the extent of the injury, a number of mechanisms can result in an hostile environment for chondrocytes thus promoting their apoptosis, compromising further the integrity of the articular cartilage [Fig. 1]. It should be noted that these changes occur in the chondrocytes and extacellular matrix of articular cartilage within weeks after an injury and continue till detectable radiological findings occur [14].

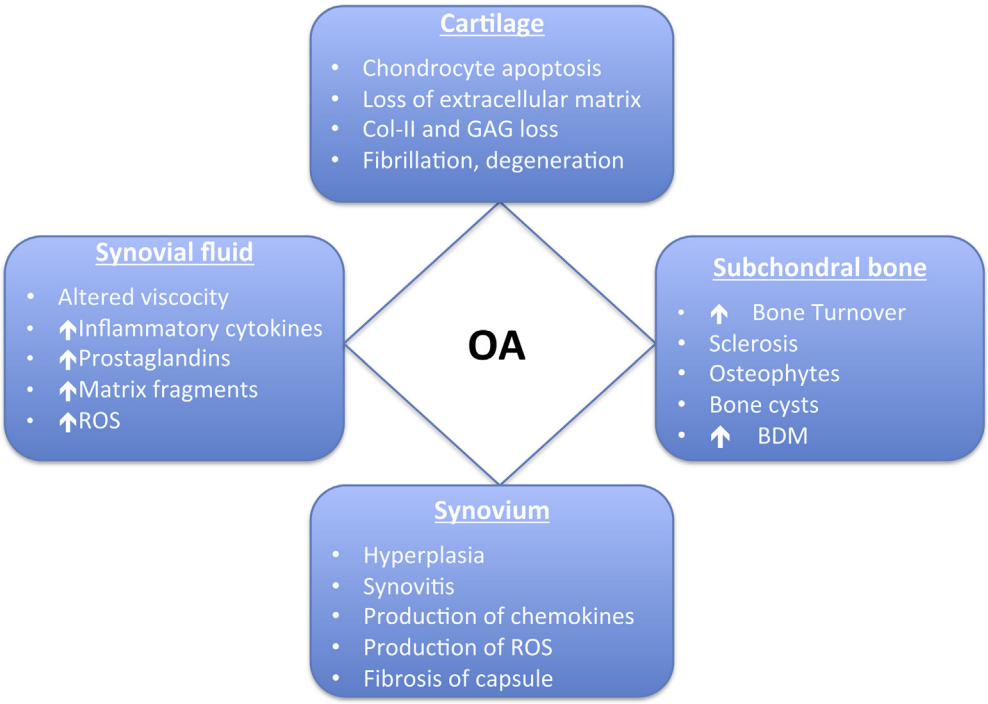

Fig. 1. Pathophysiological changes in post-traumatic OA.