EXPERIMENTAL RHEUMATOLOGY

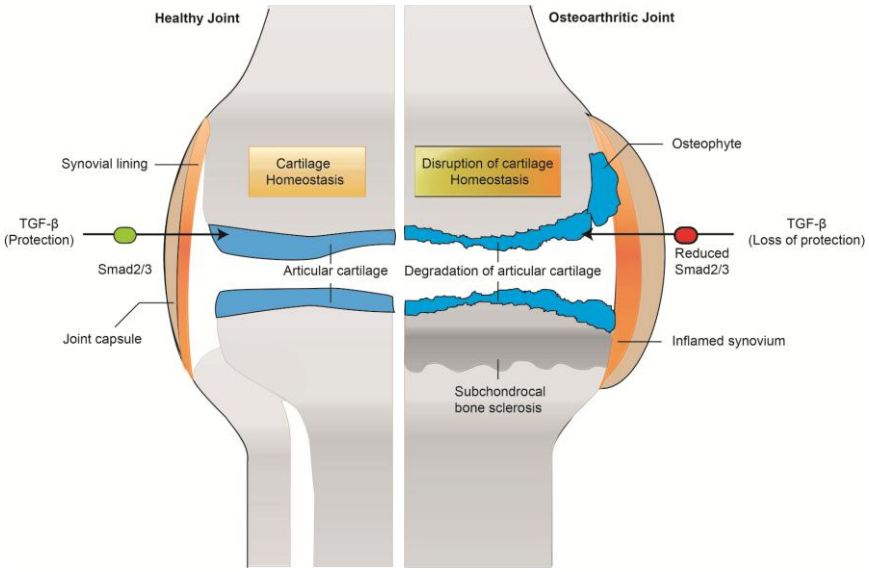
Regulation of IL-6 signaling by TGF-β in chondrocytes – studying age-related changes in articular cartilage

Clinical relevance

Osteoarthritis (OA) is the world's most common joint disease, and cartilage degradation is its main hallmark. Eventually, OA leads to pain and disability, greatly affecting quality of life of patients. Many risk factors for OA have been identified , such as obesity, female gender, but the main risk factor is ageing. To better comprehend why ageing is such an important risk factor, studies have focused on age-related changes in cartilage, as this is the main tissue affected during disease.

Background

Osteoarthritis (OA) is characterized by destruction of articular cartilage leading to loss of joint function and pain. This breakdown of cartilage tissue results from a shift in balance between extracellular matrix synthesis and its degradation. Transforming growth factor-β is a growth factor crucial for the maintaining the homeostatic balance of healthy articular cartilage. However, it is shown that TGF-β signaling is less effective upon ageing, possibly contributing to the development of OA. Next to the regulation of matrix synthesis, TGF-β can potently block the effect of pro-inflammatory cytokines such as IL-1β and TNF-α, present during osteoarthritis. However, the effects of TGF-β on the signaling pathway of the pro-inflammatory cytokine IL-6 in chondrocytes are unknown. In OA, IL-6 is abundantly present in serum and synovial fluid and is even considered predictive for disease progression. IL-6 is considered to be a catabolic mediator in cartilage, contributing to increased expression of catabolic mediators such as matrix metalloproteinases -3 and -13. Although it is evident that TGF-β and IL-6 play important roles in regulating chondrocyte behavior, a link between these two cytokines in the cartilage remains to be identified



Goals

Our aim is to investigate if TGF-β can modulate IL-6 signaling in articular chondrocytes. We will study effects of TGF-β on several components of the IL-6 signaling pathway, such as its mediator p-STAT3 and the IL-6 receptors (gp130 and IL6R). Furthermore, we will test if co-stimulation with TGF-β affects IL-6 induced gene expression in articular chondrocytes. To study if ageing, an important OA risk factor, changes TGF-β effects on the IL-6 signaling pathway we will perform these studies in cartilage obtained from individuals with a wide age range.

We offer

We are working in a state of the art laboratory that is internationally renowned for its osteoarthritis research, especially regarding TGF-β signaling. You will participate in a project that includes a broad spectrum of techniques including, amongst others, work with patient material, histology, immunohistochemistry, cell culture, Western Blot, and qPCR. You will be able to improve your laboratory skills, develop your scientific thinking and expand your knowledge on molecular processes and immunology.

Contact

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