EXPERIMENTAL RHEUMATOLOGY

Osteoarthritis as a metabolic disease: How does oxidized LDL promote inflammation in osteoarthritis?

Clinical relevance

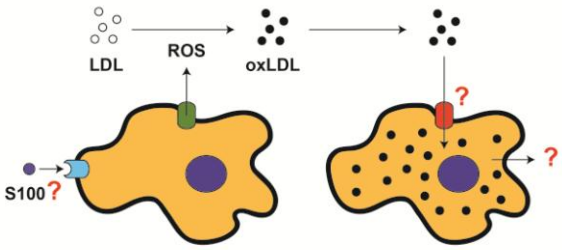
Osteoarthritis (OA) is a degenerative disease comprising the main reason of handicap in the Western world; the majority of people over 65 years of age show clinical symptoms of OA. The main characteristics of OA are breakdown of the articular cartilage, osteophyte formation (bony projections along the articular bone), and inflammation of the synovium (the tissue that lines the joint cavity). Synovial inflammation is present in more than 50% of OA patients and contributes to pathophysiology and clinical symptoms. Currently, no effective treatment for OA is available; severely affected joints eventually require joint replacement surgery. This urges for more research into the mechanism behind synovial inflammation in OA and how to possibly interfere in this process.

Background

Important risk factors for OA are age and obesity. It has long been thought that these risk factors induce OA via 'wear-and-tear', a biomechanical process in which cartilage degrades due to prolonged overloading. However, it has become clear that metabolic processes also play an important role in the development of OA. The theories describing OA as a metabolic disease are based on a strong link with metabolic syndrome. This western disease is a result from an unhealthy lifestyle and is characterized by high systemic cholesterol levels. Low-density lipoprotein (LDL), a particle responsible for cholesterol transport, is thought to be the decisive factor in making metabolic syndrome a risk factor for OA. High systemic levels of LDL result in increased joint damage in experimental mouse models of OA. In the inflamed synovium, which is characterized by high levels of radical oxygen species (ROS), LDL can be converted to oxidized LDL (oxLDL). Previous mouse studies performed in our lab have shown that oxLDL specifically, and not LDL, worsen synovial inflammation in experimental OA.

Goal

Our aim is to investigate the ability of OA associated inflammatory factors (S100, IL-1β) to induce ROS formation and oxLDL uptake by synovial cells. In addition, we'll investigate which receptors mediate oxLDL uptake and how the subsequent cellular response may contribute to synovial inflammation.



We offer

An internship in which you'll be involved in a running PhD-project in a lab which is internationally renowned for its research in osteoarthritis and synovial inflammation and S100 in particular. You'll gain practical experience in various biomedical techniques, most importantly being cell culture, RNA isolation, quantitative PCR, intracellular lipid staining and ROS analysis. In addition, you'll gain experience with analysis and interpretation of data and academic writing. We offer daily supervision by a PhD-student and you'll be involved in regular group meetings in which obtained results will be presented and discussed.

Contact

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