

EXPERIMENTAL RHEUMATOLOGY

High cholesterol levels and osteoarthritis: the role of PCSK9 cholesterol homeostasis and the promotion of synovial inflammation.

Clinical relevance

Osteoarthritis (OA) is the most common disabling disease worldwide, characterized by joint pain and immobility. OA affects the whole joint, including articular cartilage, synovium, subchondral bone and ligaments. Synovial inflammation is present in approximately 50% of OA patients and aggravates cartilage degradation and ectopic bone formation in the joint. Currently, no curative treatment options are available. Patients receive symptomatic treatment and eventually joint replacement.

Background

One important risk factor for OA is metabolic syndrome (MetS), characterized by abdominal obesity, elevated blood glucose levels, high blood pressure, increased low density lipoprotein (LDL) and decreased high density lipoprotein (HDL) levels, particles responsible for the transport of cholesterol. One important factor in MetS is hypercholesterolemia. High systemic cholesterol levels are associated with the development and progression of OA. PCSK9 elevates cholesterol levels by binding to the LDL receptor, leading to its internalization and subsequent degradation. Anti-PCSK9 drugs have proven to be very successful in lowering of cholesterol levels and protects against other metabolic syndrome-associated diseases, such as atherosclerosis. Besides regulation of cholesterol levels, it has been implicated that PCSK9 enhances inflammation.

Goals

We aim to gain insight in the role of PCSK9 in (diet-induced) OA pathology. We will investigate the relation between PCSK9 stimulation and the production inflammatory mediators. Additionally, we will analyze if PCSK9 itself or these inflammatory mediators mediate (ox)LDL uptake and if PCSK9 correlates with presence of different inflammatory cell types involved in OA, such as monocytes and macrophages.

We offer

An internship position in a laboratory that is internationally renowned for its research combining diagnostics and therapeutic strategy in OA. You will participate in an interesting project where you will use different techniques, such as cell culture, RNA isolation, qPCR and FACS. Additionally, you will be given the opportunity to improve your scientific thinking, presentation skills and academic writing.

Contact

Department: Experimental Rheumatology

Supervisor: Yvonne van Gemert

Email address: Yvonne.vangemert@radboudumc.nl

Contact person: Peter van Lent

Telephone number: 024-3610512

Email address: Peter.vanlent@radboudumc.nl

Website: www.experimentalrheumatology.nl



Radboudumc
university medical center