

EXPERIMENTAL RHEUMATOLOGY

Title

Can we inhibit the alarmins S100A8/A9 and thereby dampen the immune response in osteoarthritis?

Clinical Relevance

Osteoarthritis (OA) is a joint disease that affects millions of people worldwide. Patients suffer from swollen joints, stiffness and pain. The disease is characterized by breakdown of the cartilage and inflammation in a lot of patients. Current treatment consists of pain medication, corticosteroids to reduce the inflammation and eventually joint replacement surgery.

Background

Inflammation in OA is mainly exerted by innate immune cells, like monocytes, macrophages and neutrophils. One of the factors produced in high amounts by monocytes and neutrophils is the S100A8/A9 protein complex, which is a damage-associated molecular pattern (DAMP). S100A8/A9 can signal via toll-like receptor 4 (TLR4) and has a pro-inflammatory response, thereby leading to more activation of monocytes and neutrophils and more inflammation. Its levels are elevated in OA and predictive for the development of the disease. Induction of OA in knee joints of S100A8/A9 deficient mice significantly suppressed development of synovial inflammation and joint destruction.

Goals

In this project, we are developing inhibitors for S100A8/A9 to be able to specifically dampen the immune response that occurs in OA. A high-throughput screening has been performed before, and 40 potential compounds were selected for further investigation. Here we try to characterize the effects of the compounds found and we are making derivatives to find molecules that inhibit the S100A8/A9 with high potency.

We Offer

This project is a very interdisciplinary project, which contains both organic chemistry (performed at the department of Biomolecular Chemistry, FNWI) and biology (performed at the department of Experimental Rheumatology, RIMLS). Depending on your background and interests, it would be possible to define a more chemistry- or biology-oriented project. It is also possible to combine both fields in one internship. Techniques that can be involved are synthetic chemistry, cell culture, FACS, qPCR, and cell viability assays. You will be able to improve your laboratory skills and develop your scientific thinking.

Contact

Department:	Experimental Rheumatology
Daily supervisor:	Yvonne Bartels
Email address:	Yvonne.bartels@radboudumc.nl
Principal Investigator:	Peter van Lent
Email address:	Peter.vanLent@radboudumc.nl
Website:	www.experimentalrheumatology.nl

