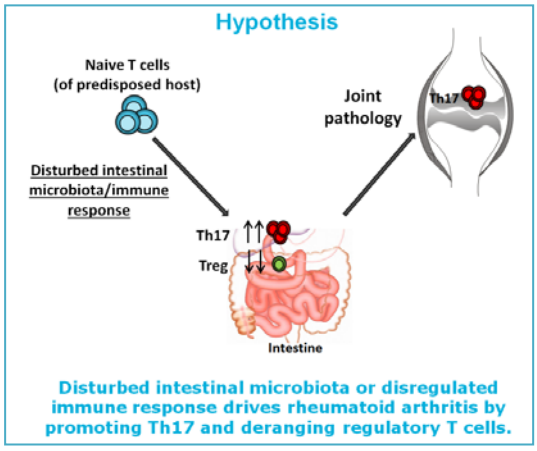
EXPERIMENTAL RHEUMATOLOGY

Title
The role of intestinal microbiota in driving T cell-mediated auto-immune arthritis in mice

Clinical Relevance
Rheumatoid Arthritis (RA) is one of the most common auto-immune diseases that affects up to 1% of the population worldwide. RA patients suffer from chronic inflammation of the joints, leading to progressive physical disability and pain. RA is generally considered a multifactorial disease in which both genetic and environmental factors play a role. A better understanding of the factors involved in RA development might lead to the discovery of new therapeutic targets or even preventive measures.

Background
Genetic predisposition to RA confers the presence of HLA-DRB1 allele and several polymorphisms mainly regulating activation of T lymphocytes. However, the presence of susceptibility factors are neither necessary nor sufficient to explain the disease development, underlining a critical role for environmental factors. Th17 cells are considered to be a major pathogenic mediator in RA. RA patients have a higher number of Th17 cells compared to healthy individuals.

The intestine is the main source of Th17 cells in the body and recent studies showed that intestinal bacteria are of great influence on the T cell balance. A recent study showed that RA patients have an altered intestinal bacterial composition compared to healthy controls. Several animal studies showed that germ-free (lacking all bacterial flora) mice have almost no Th17 cells, and are resistant to severe auto-immune arthritis. This is extremely relevant when put in the context of disturbed microbiota composition and increased Th17% in RA patients.



Disturbed intestinal microbiota or disregulated immune response drives rheumatoid arthritis by promoting Th17 and deranging regulatory T cells.

Goals
Within this project we aim to investigate which selective groups of intestinal microbiota are responsible for driving experimental auto-immune arthritis in mice. Furthermore, we will study the relationship between specific intestinal bacteria and the intestinal as well as joint-related T cell subsets with relevant function for the disease, including Th1, Th17 and regulatory T cells.

We Offer
You will participate in an interesting project that includes a broad spectrum of techniques including, amongst others, animal models of arthritis, isolation of lymphocytes from several organs, histology, cell culture, FACS, luminex and qPCR. In addition, you will be able to expand your knowledge on immunological processes involved in auto-immune arthritis.

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