Dendritic cells manipulating immune responses: Understanding the role of Flt3L and Flt3-dependent DCs in rheumatic diseases
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preface
Scope of the Thesis

Dendritic cells (DCs) are a heterogeneous population of cells that reside in a privileged position at the border between innate and adaptive immunity, orchestrating a large panel of physiological and pathological responses.

Chapter 1 provides an updated view on the role and importance of the different DC subsets for the initiation/maintenance or dampening of immune responses with special focus on autoimmune and inflammatory diseases.

In Chapter 2 we addressed the question: Is Fms-like tyrosine kinase 3 ligand (FLT3L)/FLT3 axis deregulated in rheumatoid arthritis (RA) patients? And if so, is this pathway modulated in response to effective therapy in RA?

After prednisolone treatment
In Chapter 3 we studied the role of Flt3L signaling in the pathogenesis of collagen-induced arthritis (CIA) using a mouse model with constitutive Flt3L gene ablation.

Immune response in WT mice – high T and B cell responses

Immune response in Flt3L−/− mice - reduced T and B cell responses
In Chapter 4 we focused at understanding the contribution of particular migratory dermal DC, subsets, more specifically the importance of CD103⁺ DCs, for the initiation of CIA.

In Chapter 5 we aimed to analyze the CD141⁺ DC subset (human homologue of mouse CD103⁺ DCs) and the nature of its in situ functional profile at the site of inflammation in human arthritis.
In Chapter 6 we focused in more detail on the modulation of CLEC9A, a c-type lectin receptor specifically expressed on CD141+ DCs and involved in crosspresentation of dead associated antigens to CD8+ T cells, after adalimumab therapy in PsA patients.

Chapter 7 was dedicated to understand the prospective role of Flt3L-driving bone damage in human and animal models of arthritis.
In Chapter 8 we integrated the knowledge obtained in the previous chapters from this thesis with the current view of how the immune process develops in arthritic diseases. Understanding how the immune process is initiated and regulated might provide new possibilities for effective therapeutic intervention.