Identification of T cells undergoing/escaping tolerance to self-type II collagen in an autoimmune animal model for rheumatoid arthritis

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Rheumatoid Arthritis (RA) is a chronic autoimmune disease affecting around 1% of the population worldwide. Inflammation mostly affects synovial joints and results in cartilage and bone destruction. The reason why people get arthritis is not known however it depends on environmental and genetic factors. Certain MHCII molecules are associated with the disease suggesting a mechanism with a T cell involvement. In order to study immunopathological mechanism of the disease and potential therapeutic compounds, animal models are widely used.

Collagen induced arthritis (CIA) is well established animal model in which susceptible strains are immunized with collagen II. In CIA, B cell and T cell involvement is observed and the model is associated with certain MHC II molecules, like in RA. However induction of CIA is mostly achieved by heterologous collagen II i.e non-mouse collagen II with an adjuvant. As a result, highly crossreactive B cell response is induced with between mouse and heterologous CII while T cells only recognize heterologous collagen II. The explanation is that the T cells are naturally tolerized against mouse-CII, but how this is accomplished and why some mice, despite T cell tolerance, still develop CIA is not elucidated yet. In this project, we tried to investigate how T cells acquire tolerance to self-collagen II, and once they are tolerized how they escape from the tolerance and start disease by using animal models for rheumatoid arthritis. For this purpose, we used different T cell receptor transgenic mice to check effect of post-translational modifications of collagen II molecule and to track T cells in physiological conditions in mice. Additionally, we investigated CIA susceptibility of humanized mouse models in which mice express human MHCII molecules.

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