Autoimmune priming, tissue attack and chronic inflammation – the three stages of rheumatoid arthritis

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[Abstract]
Here, I will discuss rheumatoid arthritis (RA) as a prototype for chronic autoimmune disease to propose that the pathogenesis of autoimmune diseases could be divided into three discrete stages. First, yet unknown environmental challenges seem to activate innate immunity thereby providing an adjuvant signal for the induction of adaptive immune responses that lead to the production of autoantibodies and determine the subsequent disease development. Second, a joint-specific inflammatory reaction occurs. This inflammatory reaction might be clinically diagnosed as the earliest signs of the disease. Third, inflammation is converted to a chronic process leading to tissue destruction and remodeling. I will discuss the stages involved in RA pathogenesis and the experimental approaches, mainly involving animal models that can be used to investigate each disease stage. In particular I will focus on the tissue attack and how this could be prevented. Although the focus is on RA, it is likely that a similar stepwise development of disease also occurs in other chronic autoimmune settings such as multiple sclerosis (MS), type 1 diabetes (T1D) and systemic lupus erythematosus (SLE).