Aims of the study

The pathogenesis of two important inflammatory rheumatic diseases, rheumatoid arthritis and ankylosing spondylitis, is not clear. In both diseases an immune response against an unknown autoantigen could play a crucial role. T cell responses to antigens derived from bacteria such as klebsiella or to autoantigens derived from the cartilage such as proteoglycan have been tested in AS, but no convincing evidence for their involvement has been obtained to date.

G1, gp39 and collagen II derived from proteoglycan aggrecan have been suggested as candidate autoantigen in AS over the last years. In this study, I applied the more sensitive and more specific technique of antigen-specific cytometry to investigate the T cell response to various cartilage-derived autoantigens. Taking IFNγ as primary outcome parameters I set out to quantify the antigen specific T cell response in peripheral blood (PB) and synovial fluid (SF) of patients with AS, RA and controls to answer the question whether T cells specific for the G1-domain of aggrecan and to single G1-derived peptides are detectable in AS-patients and controls, and compared this to the response after stimulation with GP39 and collagen II proteins.

AS is the final outcome in between 20-50% of HLA-B27 positive patients with reactive arthritis or inflammatory bowel disease. Therefore, the question has been raised whether the immunopathology in AS is caused by an antibacterial immune response. To search for possible bacterial antigen, I looked for T cell responses to Yersinia 19KD in AS patients by flow cytometry and compared this response with that in RA-patients and controls.

Based on high interspecies sequence homologies, inducible tissue expression and a strong immunogenicity, hsp have been repeatedly incriminated to be involved in various autoimmune diseases. To answer whether h-hsp60 is involved in the pathogenesis of AS, cytokine secretion triggered by h-hsp60 was also analysed at single cell level by flow cytometry in AS- and RA-patients as well as in controls.

To further analyse T cell response to G1-domain in AS patients, G1 specific T cell was separated by IFNγ secretion assay, its specificity was checked by restimulation with G1 protein.

Treatment of active AS with the monoclonal anti- TNFα antibody infliximab is clinically highly effective, the precise mechanism of action, however, is not known. Another aim of this study was to assess any change in the capacity of $CD4^+$ and $CD8^+$ T cells to produce cytokines during treatment. I conducted a double-blind, placebo-controlled, multicenter trial of infliximab in active AS. The antigen specific and non-specific cytokine production during treatment with infliximab was investigated in peripheral blood (PB) from 20 randomly selected patients (10 underwent infliximab treatment and 10 placebo as controls) to answer the question whether and how the cytokine pattern changed after treatment and whether this be related to the clinical effect.