4 INVESTIGATING THE CELLULAR COMPOSITION OF LYMPH NODES IN PRECLINICAL AND EARLY INFLAMMATORY ARTHRITIS: A FEASIBILITY STUDY

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Background and objectives Rheumatoid arthritis (RA) is an immune-mediated inflammatory disease of unknown aetiology. To ultimately cure or prevent this chronic disease, it is critical to understand the earliest changes in the immune system that cause RA. Recent work has shown that systemic autoimmunity precedes inflammation in the synovium of RA patients. Animal models have suggested that changes in the lymph nodes may precede those in the synovial tissue. To provide insight into the immunological mechanisms involved in the pathogenesis of RA, the authors developed a method to obtain lymph node biopsies under local anaesthesia and investigated the lymph node cellular composition and distribution in individuals at risk of developing RA, early arthritis patients and healthy controls.

Materials and methods Six individuals without any evidence of arthritis upon physical examination who were positive for IgM rheumatoid factor and/or anticitrullinated protein antibodies were included. For comparison 12 early arthritis patients (1× systemic lupus erythematosus, 1× psoriatic arthritis, 1× gout, 5× undifferentiated arthritis and 4× RA; disease duration <1 year, disease-modifying antirheumatic drug naïve), and four autoantibody negative healthy controls without joint complaints were included in the study. All study subjects underwent ultrasound-guided inguinal lymph node biopsy. Different T lymphocyte subsets were analysed by multi-colour flow cytometry using labelled antibodies specific for CD3, CD4, CD8, CD45 and CD69.

Results The procedure was well tolerated; no complications occurred. Different T cell subsets could be distinguished and differences between autoantibody positive individuals at risk of developing RA, early arthritis patients and healthy controls could be observed. Interim analysis indicate an increase of activated CD69+ T cells in the early arthritis as well as in the at risk group compared to the control group. Interestingly, the CD4/CD8 distribution within the activated T cells was significantly changed in the early arthritis patients compared to healthy controls and the same trend was observed for the at risk group.

Conclusions Flow cytometry analysis of ultrasound-guided inguinal lymph node biopsies is a feasible method for investigating the cellular composition of lymph nodes in the earliest phases of inflammatory arthritis. These preliminary results suggest increased CD8+ T cell activation within lymph nodes of early arthritis patients as well as in autoantibody positive individuals at risk of developing RA. This method provides a unique tool to investigate the immunological changes in the lymph node compartment in the earliest phases of inflammatory arthritis. These data support the rationale for larger studies using more extensive panels of cellular markers.