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COMPARISON OF SYNOVIAL TISSUE CYTOKINE MRNA PROFILES IN VERY EARLY ARTHRITIS PATIENTS WITH DIVERGENT OUTCOMES

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10.1136/annrheumdis-2011-201231.10

Background and objectives In the earliest clinically apparent phases of arthritis, it is difficult to distinguish patients who will develop RA from those whose disease will resolve. The authors hypothesised that synovial tissue cytokine expression would differ between early patients with these distinct outcomes. As control groups the authors included patients with newly presenting established RA and individuals with no evidence of inflammatory arthritis.

Materials and methods Synovial tissue biopsies were obtained from 18 early synovitis patients who eventually developed RA (according to 1987 American College of Rheumatology (ACR) criteria within 18 month follow-up) and 13 early synovitis patients with self-limiting disease; all samples were collected within 12 weeks of the onset of any musculoskeletal symptom attributed to inflammatory arthritis. In addition, 12 patients with established RA (according to 1987 ACR criteria with a symptom duration of >3 months at sample collection), and 12 control subjects undergoing arthroscopy with no macroscopic or radiological evidence of inflammatory pathology were studied. No individuals were taking disease-modifying antirheumatic drug therapy at the time of sample collection. mRNA expression of 135 cytokines and related molecules (including interleukins, tumour necrosis factor

family members, chemokines, growth factors, interferons and adipokines) was determined by real-time PCR using microfluidic cards. The Kruskal-Wallis test and Dunn's post-test were used for comparison of four groups, and the Mann-Whitney test was used for paired analysis.

Results Of the 135 cytokines analysed, 20 genes were differentially expressed between the four groups (early resolving synovitis, early RA, established RA and controls), 16 genes were not detected and 99 genes did not show statistically significant differences between groups. Significant differences included higher levels of IFN β in established RA compared to early RA. Levels of IL-1 α , IL-2 and IL-21 were significantly higher in established RA than early resolving synovitis patients. Conversely, XCL1 and VEGF α were higher in early resolving synovitis patients than established RA. The levels of many cytokines and chemokines were elevated in the synovium of early and established arthritis patients compared to control subjects. 11 genes were significantly different between anticitrullinated protein antibodies (ACPA)-positive and ACPA-negative RA patients.

Conclusions The profile of cytokine mRNA expression in patients with synovitis is consistently different to that of uninflamed synovial tissue. Although significant differences exist between cytokine expression levels in different outcome groups and time points in RA disease, for the majority of cytokines studied, expression is similar between groups and may reflect the extent of inflammation rather than showing specificity for its outcome in early arthritis.