

14 **DIFFERENTIAL EXPRESSION OF DKK1 IN SYNOVIAL FIBROBLASTS FROM PATIENTS WITH RESOLVING AND EARLY RHEUMATOID ARTHRITIS**

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Background Dickkopf related protein 1 (DKK1) is an inhibitor of the Wnt signalling pathway involved in osteoblast growth and differentiation and cell adhesion and invasion in health and disease. In cancer, increased plasma levels of DKK1 have been associated with the osteolytic lesion of multiple myeloma and with tumour invasion and progression in solid tumours. In rheumatoid arthritis (RA) increased DKK1 plasma levels have been shown to correlate with inflammation and bone erosions. Our aim was to study expression of DKK1 in synovial fibroblasts from patients from three different clinical outcome groups: early RA, established RA and resolving arthritis.

Materials and methods Synovial tissue was obtained from ultrasound guided biopsies done at the time of first presentation to clinic. Resolving (n=8) and early RA (n=12) patients presented with arthritis of less than 3/12 duration and were followed up for 18/12 at which point a diagnostic category was assigned (resolving vs early RA). Established RA (n=9) was defined as RA of >3/12 duration. Synovial fibroblasts from tissue were cultured and mRNA quantified using real-time PCR. Values were expressed as 2^{-dCt} relative to glyceraldehyde 3-phosphate dehydrogenase.

Results DKK1 expression was higher in synovial fibroblasts from patients with early RA than in those from patients with resolving arthritis (0.024 vs 0.009, $p < 0.005$). There was no differential expression of DKK1 in the early RA and established RA groups.

Conclusion The question of why arthritis resolves in some patients but persists as RA in others is still not resolved. Mechanisms allowing perpetuation of inflammation and joint damage must be in place to allow this. DKK1 is an inhibitor of the Wnt signalling pathway that has been shown to promote cell invasion and imbalance of osteoblast/osteoclast function in a way that favours bone destruction in cancer. In RA it has been proposed as a biomarker of disease activity and bone erosions. RA synovial fibroblasts have an invasive phenotype and attach to and degrade cartilage causing permanent damage in disease. Our data suggests that DKK1 may be involved in mediation of these actions.