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POSTER PRESENTATION Open Access

TNF and IL-6 differentially regulate the production of DKK-1, a master regulator of bone remodelling, by fibroblast-like synoviocytes

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Background

Different inflammatory joint diseases have distinct patterns of bone damage with pronounced erosions in rheumatoid arthritis (RA), a combination of bone destruction and formation in psoriatic arthritis (PsA), and new bone formation in spondyloarthritis (SpA). Although the underlying mechanisms remain elusive, blocking of DKK-1 reverses the bone-destructive pattern to a bone-forming pattern in experimental arthritis.

Aim

In order to delineate the role of DKK-1 in arthritis, we analyzed the regulation of DKK-1 expression in the inflamed peripheral joint of different types of inflammatory arthritis *ex-vivo* and in fibroblast-like synoviocyte (FLS) cultures *in vitro*.

Patients and methods

IL-6, DKK-1, TNF, and IL-1 beta levels in synovial fluid (SF) and synovial FLS lines were determined by ELISA. DKK-1 serum levels were assessed before and after IL-6R blockade in RA patients.

Results

SF DKK-1 levels were similar between 4 disease groups with a striking variability within each cohort. As DKK-1 production is strongly upregulated by TNF, we explored this inter-individual variability by correlating DKK-1 levels with pro-inflammatory cytokines levels. TNF and IL-1 beta levels were significantly higher in RA than SpA SF and did not correlate with DKK-1. In contrast, there was a striking inverse correlation between DKK-1 and IL-6 in both RA and SpA. Consistent with these data, in vitro DKK-1 production by FLS was strongly induced by TNF but clearly suppressed by IL-6 in dose-dependent manner. Preliminary data suggest that this regulation of DKK-1 by IL-6 is also relevant in vivo as treatment with the anti-IL-6 R antibody, tocilizumab, induced a transient upregulation of DKK-1 serum levels in RA patients.

Conclusions

DKK-1 is abundantly expressed in the inflamed joint of both destructive and remodelling forms of arthritis. However, DKK-1 production by FLS is differentially regulated by TNF and IL-6. The relative balance between these factors in the arthritic joints may determine the pattern of inflammation-induced tissue remodelling.

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