Characterization of the expression and function of CCR7 on fibroblast like synoviocytes

Brühl H.¹, Mack M.², Niedermeier M.³, Lochbaum D.¹, Schölmerich J.¹, Straub R.¹
(1) Klinik und Poliklinik für Innere Medizin 1, Regensburg, (2) Klinik und Poliklinik für Innere Medizin 2, Regensburg

Zielsetzung
The expression and the function of the chemokine receptor CCR7 was characterized on fibroblast like synoviocytes (FLS) of patients with rheumatoid arthritis (RA) and osteoarthritis (OA) and on dermal fibroblasts.

Methodik
Immunofluorescence was performed on synovial tissue from patients with RA and OA. Frozen tissue sections were double-labeled for CCR7 and CD3 (T cells) or CCR7 and prolyl-4 (fibroblasts). FLS were obtained after enzymatic digestion of synovial tissue of patients undergoing knee joint replacement surgery and taken into culture for chemokine receptor analysis by flow cytometry, PCR and functional tests. To study the response of FLS to CCR7 ligands and other chemokines, migration assays were performed in modified Boyden chambers. The secretion of VEGF, chemokines and cytokines after stimulation with CCR7 ligands was evaluated by ELISA and Luminex.

Ergebnisse
By immunofluorescence, PCR and FACS we show that CCR7 is expressed on FLS in the synovial tissue of patients with RA and OA. In contrast no relevant CCR7 expression was found on dermal fibroblasts. In functional tests we demonstrate that FLS migrate in response to CCR7 ligands. Stimulation of FLS with CCL19 results in an increased secretion of VEGF.

Schlussfolgerung
CCR7 is functionally expressed on FLS of patients with OA and RA. In addition to chemotaxis, FLS respond to CCR7 stimulation with an enhanced VEGF secretion. CCR7 ligands have previously been shown to be expressed in proximity to perivascular infiltrates in the inflamed synovial tissue of RA patients. By activating FLS though CCR7, CCL19 could contribute to enhanced angiogenesis.