VASCULAR TRANSMIGRATION OF SYNOVIAL FIBROBLASTS FROM PATIENTS WITH RHEUMATOID ARTHRITIS IS INFLUENCED BY EXTRACELLULAR RNA/DNA AND THE TYPE OF ENDOTHELIAL CELLS

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Background Cartilage destruction in joints of patients with rheumatoid arthritis (RA) is driven by synovial fibroblasts (SF). We demonstrated that RASF migrate to distant cartilage within the blood stream in the SCID-mouse model. Previous work showed that extracellular RNA is required for endothelial permeability and lymphocyte transmigration. Influence on RASF transmigration and invasion by intravenous injection of extracellular RNA/DNA and use of different endothelial cells (EC) was analysed.

Material and methods To determine the adherence of RASF and OASF to EC we used a cell-to-cell binding assays. The RASF transmigration was examined using two-chamber-assays with different EC (HUVEC, HUAEC and primary venous EC). Cartilage was coimplanted with RASF subcutaneously at the ipsilateral side (I) and without RASF at the contralateral side (C) of a SCID mouse. The animals were divided into three groups: Group (1) received 42μg DNase/kg; group (2) received 42 μg RNase/kg; group (3) received saline solution injected intravenous prior to the surgery and every other day. After 45 days the implants were removed and RASF invasion was analysed.

Results The adherence of RASF to EC monolayers was medium-dependent and increased in comparison to OASF. RASF are able to pass all EC monolayers. In vivo, a significant reduction of cartilage invasion at the ipsilateral side was detectable after treatment with RNase and DNase ((I) control: 2.3±0.7, RNase: 1.2±0.6, p=0.048; DNase: 0.8±0.3, p=0.007). In contrast, contralateral cartilage invasion was not affected ((C) control, 1.3±0.7 vs RNase: 1.2±1.2, p=0.74; DNase: 1.1±0.6, p=0.73). RNase or DNase injection did not inhibit RASF invasion and migration (RNase (I) vs (C): p=0.77; DNase (I) vs (C): p=0.35).

Conclusion The potential of RASF to attach to and to pass EC monolayers at the arterial and especially the venous side underline the ability for vascular transmigration. The ipsilateral RASF invasion is reduced by intravenous injection of RNase and DNase but the invasion at the contralateral side is unaffected. That showed that the migration of RASF is not inhibited, but the effect of RNase and DNase is higher on non-migrating RASF in contrast to migrating RASF.