Chemokine ENA-78/CXCL5 is Produced by OA Synovial Fibroblasts in Response to a Matrix Damage Stimulus and is Found in Synovial Fluid Collected from Patients After ACL Injury
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Cartilage degradation, the major hallmark of osteoarthritis (OA), is primarily due to the overproduction of secreted matrix metalloproteinases (MMP)s by chondrocytes; however, synoviocytes also contribute to this activity by releasing OA mediators that exacerbate joint destruction. The crosstalk between synovial cells and chondrocytes could be crucial, due to further secretion of key cytokines and chemokines that intensify catabolic signaling and activity in both cell populations. Indeed, synovial fibroblasts have been hypothesized to express cytokines and MMPs in response to matrix protein fragments found in the cartilage and synovium of human OA joints. After treating human osteoarthritic synovial fibroblasts and articular chondrocytes with a fragment of the matrix protein fibronectin (FN-f) found in OA joints, we compared production of MMP-1, MMP-13, and IL-6 from both cell types using immunoblots. Furthermore, we used protein arrays to measure 80 different cytokines/chemokines to map synovial fibroblast's secretome following FN-f induction. Many cytokines/chemokines were shown to be oversecreted following FN-f treatment, including MCP-1, RANTES, MIP-1 beta, and ENA-78 (CXCL5). We focused specifically on the chemokine ENA-78 (CXCL-5), which had not been previously studied in OA and used an ENA-78 ELISA to quantitate production by synovial fibroblasts and articular chondrocytes. We also examined ENA-78 in synovial fluid from patients who had torn their anterior cruciate ligament (ACL) and noted concentrations varying from less than 10 pg/mL to 1.4 ng/mL. These results significantly correlated with an MRI measure of decreased cartilage proteoglycan density measurements and more severe patient reported Knee Injury and Osteoarthritis Outcome Scores (KOOS) scores. These studies will define a new pathway in OA that could serve as a target for disease modification.