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Influence of extracellular rnas, released by rheumatoid arthritis synovial fibroblasts, on their adhesive and invasive properties

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Abstract

© 2016 by The American Association of Immunologists, Inc. Extracellular RNA (exRNA) has been characterized as a molecular alarm signal upon cellular stress or tissue injury and to exert biological functions as a proinflammatory, prothrombotic, and vessel permeability-regulating factor. In this study, we investigated the contribution of exRNA and its antagonist RNase1 in a chronic inflammatory joint disease, rheumatoid arthritis (RA). Upon immunohistochemical inspection of RA, osteoarthritis (OA), and psoriatic arthritis synovium, exRNA was detectable only in the RA synovial lining layer, whereas extracellular DNAs were detectable in various areas of synovial tissue. In vitro, exRNA (150-5000 nt) was released by RA synovial fibroblasts (RASf) under hypoxic conditions but not under normoxia or TNF- α treatment. RNase activity was increased in synovial fluid from RA and OA patients compared with psoriatic arthritis patients, whereas RNase activity of RASf and OASf cultures was not altered by hypoxia. Reduction of exRNA by RNase1 treatment decreased adhesion of RASf to cartilage, but it had no influence on their cell proliferation or adhesion to endothelial cells. In vivo, treatment with RNase1 reduced RASf invasion into coimplanted cartilage in the SCID mouse model of RA. We also analyzed the expression of neuropilins in synovial tissue and SF, as they may interact with vascular endothelial growth factor signaling and exRNA. The data support the concepts that the exRNA/RNase1 system participates in RA pathophysiology and that RASf are influenced by exRNA in a prodestructive manner. *The Journal of Immunology*, 2016, 197: 2589-2597.

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