



POSTER PRESENTATION

Open Access

Triggering of viral RNA sensors induces CD55 expression on synovial fibroblasts

Olga N Karpus^{1*}, Kirstin M Heutinck^{1,2}, Paul JM Wijnker¹, Paul Peter Tak³, Jorg Hamann¹

From 6th European Workshop on Immune-Mediated Inflammatory Diseases
Nice, France. 23-25 November 2011

Background

CD55 (decay-accelerating factor) is a complement-regulatory protein, which is highly expressed by fibroblast-like synoviocytes (FLS). CD55 is also a ligand for CD97, an adhesion-type G protein-coupled receptor abundantly present on leukocytes. We recently showed that lack of either CD55 or CD97 ameliorates disease in murine collagen-induced and K/BxN serum transfer models of arthritis (*Arthritis Rheum.* 2010 Apr;62(4):1036-42). Little is known regarding the regulation of CD55 expression in FLS. We therefore investigated the effect of Toll-like receptors ligation and pro-inflammatory cytokines on CD55 expression.

Materials and methods

Synovial fibroblasts, obtained from biopsy samples of arthritis patients, were cultured and stimulated with cytokines (TNF, IFN γ , IL-1 β , IL-6, IFN α) or TLR ligands (LTA, poly(I:C), LPS, imiquimod, CpG). Expression of CD55 was measured by flow cytometry using domain-specific monoclonal antibodies and recombinant CD97-loaded fluorescent beads. Chloroquine was used to inhibit TLR3 activity. Upregulation and functionality of dsRNA sensors in response to poly(I:C) or 5'-triphosphate RNA was analyzed by PCR. Apoptosis was measured by PI/annexinV staining and was blocked with the pan-caspase inhibitor Q-VD-OPH.

Results

Cultured synovial fibroblasts of patients with rheumatoid arthritis (RA), osteoarthritis, psoriatic arthritis, and spondylarthritis express equal amount of CD55. Stimulation of RA-FLS with IL-1 β ($p=0.02$) and poly(I:C) ($p=0.001$) induced a significant upregulation of CD55. Engagement of TLR3 by the dsRNA analog poly(I:C) was confirmed

using chloroquine, an inhibitor of endosomal acidification that impairs TLR3 signaling. Synovial fibroblasts also expressed the cytoplasmic dsRNA sensors melanoma differentiation-associated gene 5 (MDA5) and retinoic acid-inducible gene I (RIG-I). Stimulation of these receptors with either poly(I:C) or 5'-triphosphate RNA induced CD55 expression, but, in case of MDA5, also induced significant cell death ($p<0.001$) that was caspase-dependent. Upregulation of CD55 in response to dsRNA receptor activation increased the binding capacity of synovial fibroblasts for CD97-loaded beads.

Conclusions

We identify dsRNA as a potent inducer of CD55 upregulation on synovial fibroblasts. Our findings suggest that CD55 induction by viral dsRNA or dsRNA may facilitate the accumulation of CD97-expressing inflammatory immune cells in the synovial tissue.

Author details

¹Dept. of Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands. ²Renal Transplant Unit, Academic Medical Center, Amsterdam, The Netherlands. ³Division of Clinical Immunology and Rheumatology, Academic Medical Center, Amsterdam, The Netherlands.

Published: 23 November 2011

doi:10.1186/1479-5876-9-S2-P41

Cite this article as: Karpus et al.: Triggering of viral RNA sensors induces CD55 expression on synovial fibroblasts. *Journal of Translational Medicine* 2011 **9**(Suppl 2):P41.

¹Dept. of Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands

Full list of author information is available at the end of the article