6 SLE IMMUNE COMPLEXES UPREGULATE THE EXPRESSION OF SLAMF7 (CD319) ON PLASMACYTOID DENDRITIC CELLS

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10.1136/annrheumdis-2011-201230.6

Background and objectives Patients with SLE have an activated type I interferon (IFN)-system due to an ongoing IFNα production by plasmacytoid dendritic cells (pDCs) stimulated by nucleic acid-containing immune complexes (ICs). The IFNα production is promoted by NK cells via MIP-1β, and LFA-1-mediated cell-cell contact. Because genome-wide linkage studies in SLE have shown a strong association with the 1q23-region, which harbors the genes for the signaling lymphocyte activation molecules (SLAMs), the authors investigated whether any of the SLAM family members were involved in the pDC-NK cell cross-talk.

Materials and methods PBMCs and purified pDCs or NK cells from healthy donors were stimulated with medium or IC consisting of purified SLE-IgG and U1snRNP particles (SLE-IC). The mRNA-expression of the SLAM genes was determined in cell cultures of pDCs or NK cells. Surface expression of SLAMF1-7 on pDCs and NK cells in PBMC cultures were assessed by flow cytometry. Intracellular staining of IFNα was correlated to SLAM expression. The expression of SLAMF7 on pDCs and NK cells was compared between healthy donors and patients with SLE (n=9).

Results The most prominent change in SLAM mRNA-expression following SLE-IC-stimulation was seen for *SLAMF7* on NK cells (2.1-fold increase). In PBMCs stimulated with SLE-IC, the median fluorescence intensity (MFI) for SLAMF7 increased on pDCs and $CD56^{dim}$ NK cells (2.7- and 2.0-fold, respectively). In purified SLE-IC-stimulated pDC- or NK cell-cultures, SLAMF7-expression was only increased on $CD56^{dim}$ NK cells. Co-cultivation of pDCs and NK cells restored the up-regulation of SLAMF7 on pDCs. SLAMF7-expression was significantly higher on IFNα producing pDCs compared to IFNα negative pDCs (p=0.048; 5255±1302 vs 3046±1519 (MFI±SD)). The frequency of $SLAMF7^{+}$ $CD56^{bright}$ NK cells were higher in patients with SLE compared to controls (p=0.0497; 18.3%±9.8% vs 10.0%±6.4% (mean±SD)). No difference in SLAMF7-expression between patients and controls was detected on pDCs or $CD56^{dim}$ NK cells.

Conclusions The authors have shown that the co-stimulatory molecule SLAMF7 is induced on pDCs and $CD56^{dim}$ NK cells by SLE-IC and that the upregulation on pDCs is dependent on NK cells. The IFNα producing pDCs were characterised by a higher expression of SLAMF7 and an increased frequency of $SLAMF7^{+}$ $CD56^{bright}$ NK cells were seen in patients with SLE. The functional consequence of the increased SLAMF7 expression for pDC-NK cell cross-talk is currently being investigated. Because SLAMF7 increases NK cell cytotoxicity and B cell proliferation, the observed SLE-IC-mediated upregulation of SLAMF7 may be of importance in the autoimmune disease process.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2011-201230.6 on 22 February 2012. Downloaded from http://ard.bmj.com/ on April 23, 2024 by guest. Protected by copyright.