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

Niklas Hagberg,^{1,*} Jakob Theorell,^{2,*} Gunnar V Alm,³ Maija-Leena Eloranta,¹ Yenan Bryceson,² Lars Rönnblom¹ ¹Department of Medical Sciences, Uppsala University, Uppsala, Sweden; ²Center for Infectious Medicine, Department of Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden; ³Department of Biomedical Sciences and Veterinary Public Health, Swedish University of Agricultural Sciences, Uppsala, Sweden

*Both authors contributed equally.

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Background and objectives Patients with SLE have an activated type I interferon (IFN)-system due to an ongoing IFN α production by plasmacytoid dendritic cells (pDCs) stimulated by nucleic acid-containing immune complexes (ICs). The IFN α production is promoted by NK cells via MIP-1 β , 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 IFN α 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 IFN α producing pDCs compared to IFN α negative pDCs (p=0.048; 5255 $\pm$ 1302 vs 3046 $\pm$ 1519 (MFI $\pm$ SD)). The frequency of SLAMF7⁺ CD56^{bright} NK cells were higher in patients with SLE compared to controls (p=0.0497; 18.3% $\pm$ 9.8% vs 10.0% $\pm$ 6.4% (mean $\pm$ 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 IFN α 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.