IJAE
Vol. 118, n. 2 (Supplement): 180, 2013
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Reduced NK cell activity and abnormal expression of CCR7 and CXCR1 by NK cells analysis in patients with DOCK8 deficiency

G. Tabellini, S. Caracciolo, O. Patrizi, M. Benassi, S. Negri, M. Giacomelli, V. Lougaris, A. Plebani, R. Badolato and S. Parolini

University of Brescia, Brescia, Italy

DOCK8-deficiency is an autosomal recessive primary immunodeficiency that is characterized by multiple abnormalities of the immune system, including a defect of NK cell cytotoxicity which could not be restored after IL2 stimulation. Nevertheless, unanswered questions remain regarding how the absence of DOCK8 leads to predisposition for malignancy, viral, fungal, and bacterial infections.

To address these questions we have analyzed NK cell phenotype and functions in patients with DOCK8 deficiency. We observed that NK cells derived from five DOCK8-deficient patients displayed dramatically reduced cytotoxicity which was partially restored after IL-2 stimulation.

Analysis of activating and inhibitory NK receptors, including KIRs molecules, chemokine receptors and activation markers on gated CD56+cells by cytofluorimetric analysis showed a substantial defect of CCR7 expression by CD56bright NK cells. Noteworthy, we have also detected the expression of NKG2C and of the chemokine receptor CXCR1 on CD56dull NK cells in DOCK8-deficient cells.

Because CCR7 expression by NK cells can be induced after cell culture with IL18 we stimulated NK cells from DOCK-8 deficient patients with IL18. Despite unstimulated CD56bright NK cells from DOCK8 patients showed reduced CCR7 expression, we could not detect any increase of CCR7 on CD56 dull and bright NK cells of DOCK8-deficient patients, whereas CCR7 expression on NK cells derived from healthy donors significantly increased from 5% to 17%. Taken together our results suggest that NK cells of DOCK-8 deficient patients show reduced cytotoxicity and abnormal expression of the chemokine receptors CXCR1 and CCR7 suggesting an abnormal recruitment of these cells to secondary lymphoid organs.

Key words

Primary immunodeficiencies; NK cells; chemokine receptors.