IJAE
Vol. 120, n. 1 (Supplement): 44, 2015
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

B7-H6-mediated downregulation of NKp30 in NK cells contributes to ovarian carcinoma immune escape

Silvia Pesce[1], Giovanna Tabellini[2], Claudia Cantoni[3], Ornella Patrizi[2], Daniela Coltrini[2], Fabio Rampinelli[4], Jessica Matta[5], Eric Vivier[5], Alessandro Moretta[6], Silvia Parolini[2], Emanuela Marcenaro[6]

[1] Dipartimento di Medicina Sperimentale-Sezione di Istologia, Università degli Studi di Genova, Genova, Italy - [2] Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, Brescia, Italy - [3] Dipartimento di Medicina Sperimentale e Istituto Giannina Gaslini, Università degli Studi di Genova, Genova, Italy - [4] Dipartimento di Ostetricia e Ginecologia, Spedali Civili di Brescia, Brescia, Italy - [5] Centre d'Immunologie de Marseille-Luminy, INSERM U1104, CNRS UMR7280 and Hôpital de la Conception, Marseille, France - [6] Dipartimento di Medicina Sperimentale-Sezione di Istologia e Centro di Eccellenza per le Ricerche Biomediche, Università degli Studi di Genova, Genova, Italy

In this study the phenotype and function of tumor-associated NK cells from peritoneal fluids of a selected cohort of patients with seropapillary ovarian carcinoma were analyzed. In >50% of these patients the expression of the activating receptor NKp30 (1) in tumor-associated NK cells was substantially reduced as compared to autologous peripheral blood NK cells. The impaired expression of this receptor was associated with the presence of one of its cellular ligands (B7-H6) (2), which was detectable as a surface/cytosolic molecule in tumor cells and as a soluble molecule in the peritoneal fluid. NK cells from patients expressing this NKp30low phenotype displayed an impaired IFNγ production and cytolytic function when tested against target cells expressing surface B7-H6. Our data also suggest that in these patients the defective expression and function of NKp30 may be induced by the chronic engagement of this receptor by soluble B7-H6 or by tumor cells expressing this ligand. The impairment of NK cell functions described herein could represent a novel mechanism by which the tumor microenvironment may contribute to the escape from immune surveillance.

This work was supported by grants awarded by Associazione Italiana Ricerca per la Ricerca sul Cancro (AIRC)-Special Project 5x1000 no. 9962 and IG 2014 Id. 15704 (Alessandro Moretta); PRIN 2010 (Alessandro Moretta); Progetto di Ricerca Fondazione Carige 2013 (Emanuela Marcenaro); Progetto di Ricerca di Ateneo 2014 (Emanuela Marcenaro). Eric Vivier laboratory is supported by the European Research Council (THINK Advanced Grant), by Equipe Labellisée La Ligue and by institutional grants from INSERM, CNRS, and Aix-Marseille University to CIML.

References:

[1] Pende D, Parolini S, Pessino A, Sivori S, Augugliaro R, Morelli L, et al. Identification and molecular characterization of NKp30, a novel triggering receptor involved in natural cytotoxicity mediated by human natural killer cells. J Exp Med 1999; 190:1505-16.

[2] Brandt CS, Baratin M, Yi EC, Kennedy J, Gao Z, Fox B, et al. The B7 family member B7-H6 is a tumor cell ligand for the activating natural killer cell receptor NKp30 in humans. J Exp Med 2009; 206:1495-503.

Keywords

B7-H6; NKp30; Ovarian Carcinoma; NK cells; Mechanism of Escape.