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Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP)

CONIUGARE RICERCA E PRATICA CLINICA IN IMMUNO-ALLERGOLOGIA

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TITOLO: p85a is an intrinsic regulator of human Natural Killer cell effector functions

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TESTO:

PIK3R1 encodes for p85a, one of the catalytic subunits involved in the PI3K cascade. Available data from animal models regarding the role of p85a in NK cell maturation and function are contrasting. Recently, a dominant activating mutation in p85a was identified in 12 patients affected with a rare form of primary immunodeficiency. We decided to evaluate the role of the dominant p85a activating mutation in human NK cell maturation and function. We show that p85a plays an essential role in human NK cell effector functions: while individuals with dominant activating p85a mutations show normal NK maturation, their functional capacities are impaired. Mutant human NK cells fail to degranulate upon IL-2 stimulation against the K562 target line and fail to produce IFN-gamma upon IL-12 and IL-18 stimulation. Interestingly, although mutant human IL-2 activated NK cells maintain their cytotoxic capacity in redirected killing experiments, they fail to do so against autologous and heterologous EBV infected B cells. These data suggest that p85a plays an essential intrinsic role for human NK cell effector functions such as cytotoxicity, IFN-gamma production and autologous and heterologous EBV-infected B cell recognition. These findings may be of important significance for better understanding and managing different clinical conditions, such as primary immunodeficiencies and lymphoid malignancies.

Abstract per il Congresso

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