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MICA immune complex formed with $\alpha 3$ domain-specific antibody activates NK function in Fc-dependent manner



Changchun Du

Genentech, USA

One of the mechanisms that tumors evade immune surveillance is the shedding of major histocompatibility complex (MHC) class I chain-related sequence A (MICA) and MICB from the tumor cell surface. MICA/B are ligands for the activating receptor NKG2D on NK and CD8⁺ T cells. MICA/B shedding reduces cell surface MICA/B and impairs NKG2D recognition. Shed MICA/B can also mask NKG2D receptor compromising the immune surveillance activity of NK cells. The study shows that soluble MICA (sMICA) suppressed human NK cell cytolytic activity *in vitro*. The NK suppression was not due to the downregulation of cell surface NKG2D. In the presence of MICA $\alpha 3$ domain-specific antibody, sMICA-mediated suppression was completely blocked and NK cell cytolytic activity was restored. In contrast, restoration effect was not observed when Fc effectorless mutant antibody was employed. Furthermore, MICA immune complex pre-formed with $\alpha 3$ domain-specific antibody (with wild type Fc) induced significant IFN- γ secretion by NK cells in the absence of tumor cells whereas MICA immune complex pre-formed Fc effectorless antibody failed to induce IFN- γ secretion. Results demonstrate that MICA $\alpha 3$ domain-specific antibody can overcome sMICA-mediated suppression of NK cytolytic activity. Furthermore, data suggest that the MICA immune complex formed with $\alpha 3$ -specific antibody can activate NKG2D receptor and restore NK cell function in Fc-dependent manner. The clinical utility of $\alpha 3$ domain-specific MICA/B antibody may hold great promise for immunotherapy of tumors those express and shed MICA/B.

Biography

Changchun Du has completed MD from YanBian University Medical School in China. Following the three years Resident training in the area of Infectious Diseases at Beihua University Medical School, he went to USA and he has been doing Research in Biotechnology since 1996. He is expertise in Hematology/Oncology and Cancer Immunology; he has been employed as Senior Scientific Researcher at Genentech for the past 14 years and published 16 papers in highly cited journals.

cdu@gene.com

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