Role of polymorphic Fc gamma receptor IIIa and EGFR expression level in cetuximab mediated, NK cell dependent in vitro cytotoxicity of head and neck squamous cell carcinoma cells

Andrés López-Albaitero · Steve C. Lee · Sarah Morgan ·
Jennifer R. Grandis · William E. Gooding ·
Soldano Ferrone · Robert L. Ferris

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Unfortunately a typo error has occurred in line 27 of the original abstract. The final text should read “VF and FF” instead of “VF and VV”.

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A. López-Albaitero · S. C. Lee · S. Morgan ·
J. R. Grandis · R. L. Ferris
Department of Otolaryngology,
University of Pittsburgh, Pittsburgh, PA, USA

J. R. Grandis
Department of Pharmacology,
University of Pittsburgh, Pittsburgh, PA, USA

W. E. Gooding
Biostatistics Facility,
University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA

S. Ferrone
Department of Surgery,
University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA

S. Ferrone · R. L. Ferris
Department of Immunology,
University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA

S. Ferrone · R. L. Ferris
Cancer Immunology, Immunotherapy and Immunoprevention
Program, University of Pittsburgh Cancer Institute,
Pittsburgh, PA, USA

R. L. Ferris (✉)
The Hillman Cancer Center Research Pavilion,
5117 Centre Avenue, Room 2.26b, Pittsburgh, PA 15213, USA
e-mail: ferrisrl@upmc.edu

The correct text is given below:

Abstract

Immunotherapy with the EGFR-specific mAb cetuximab is clinically effective in 10–20% of patients with squamous cell carcinoma of the head and neck (SCCHN). Little information is available about the mechanism(s) underlying patients' differential clinical response to cetuximab-based immunotherapy, although this information may contribute to optimizing the design of cetuximab-based immunotherapy. Our understanding of these mechanisms would benefit from the characterization of the variables which influence the extent of cell dependent-lysis of SCCHN cells incubated with cetuximab in vitro. Therefore, in this study we have investigated the role of FcγR IIIa-158 genotype expressed by effector NK cells, cetuximab concentration, and EGFR expression level by SCCHN cells in the extent of their in vitro lysis and in the degree of NK cell activation. PBMC or purified CD56⁺ NK cells genotyped at IIIa codon 158 and SCCHN cell lines expressing different levels of EGFR have been used as effectors and targets, respectively, in antibody dependent cellular cytotoxicity (ADCC) assays. Furthermore, supernatants from ADCC assays were analyzed for cytokine and chemokine levels using multiplexed ELISA. We found that the extent of lysis of SCCHN cells was influenced by the EGFR expression level, cetuximab concentration, and FcγR polymorphism. Effector cells expressing the FcγR IIIa-158 VV allele were significantly ($P < 0.0001$) more effective than those expressing FcγR IIIa VF and FF alleles in mediating lysis of SCCHN cells expressed higher levels of the activation markers CD69 and CD107a, and secreted significantly ($P < 0.05$) larger

amounts of inflammatory cytokines and chemokines. IL-2 or IL-15 treatment increased cetuximab-mediated ADCC by poor binding Fc γ R IIIa 158 FF expressing NK cells. The importance of the Fc γ R IIIa-158 polymorphism in cytotoxicity of SCCHN cells by NK cells supports a potential role for immune activation and may explain patient variability

of cetuximab mediated clinical responses. Cellular and secreted immune profiles and Fc γ R genotypes from patients' lymphocytes may provide clinically useful biomarkers of immune activation in cetuximab treated patients.