

A general mechanism for anti-tumor therapy based on Fc receptor engagement

Jeffrey V. Ravetch

The Rockefeller University, New York, NY, USA

Abstract

The impressive success of IgG based anti-tumor therapeutics has focused attention on the mechanism of antibody mediated cytotoxicity and the role of cellular effector responses triggered by Fc receptor ligation. A large body of pre-clinical animal data supports an unequivocal role for ADCC as a central mechanism for anti-tumor therapeutics augmented by contributions from immune complex mediated dendritic cell maturation initiated by FcR signaling. Supportive data has been accumulated in patient populations demonstrating a strong correlation between clinical response and alleles of activating FcRs. These results point to the importance of engineering the Fc domain to optimize activation FcR engagement in preference over inhibitory signaling. Such optimization can be achieved by amino acid and glycan modifications to the IgG Fc. Novel animal models have been developed for the *in vivo* evaluation of modified IgGs that will enable improved therapeutics based on rational engineering of the Fc domain.