CHAPTER 17

Fc Receptor Targeting in the Treatment of Allergy, Autoimmune Diseases and Cancer

Akira Nakamura, Tomohiro Kubo and Toshiyuki Takai

Abstract

Fc receptors (FcRs) play an important role in the maintenance of an adequate activation threshold of various cells in antibody-mediated immune responses. Analyses of murine models show that the inhibitory FcR, FcyRIIB plays a pivotal role in the suppression of antibody-mediated allergy and autoimmunity. On the other hand, the activating-type FcRs are essential for the development of these diseases, suggesting that regulation of inhibitory or activating FcR is an ideal target for a therapeutic agent. Recent experimental or clinical studies also indicate that FcRs function as key receptors in the treatment with monoclonal antibodies (mAbs) therapy. This review summarizes FcR functions and highlights possible FcR-targeting therapies including mAb therapies for allergy, autoimmune diseases and cancer.

Introduction

FcRs are widely expressed on hemopoietic cells and distinguished by their structure, function, distribution and ligands, such as IgG, IgM, IgE and IgA. FcRs have homologous extracellular immunoglobulin domains, however, there are functionally two kinds of FcRs, the activation type and the inhibitory type FcRs. Recent analysis using FcRs-deficient mice have revealed that immune responses by antibodies depend upon regulation of activating and inhibitory FcR. Deletion of activating FcRs does not elicit antibody-mediated responses, whereas deletion of inhibitory FcRs causes excessive antibody responses, resulting in the development of allergic or autoimmune disorders.

Immunotherapy using mAbs is a new strategy against allergy, autoimmune diseases and cancer. Genetic engineering enabled the development of humanized antibodies, leading to rapid progress of mAb therapy. In particular, activating FcRs play a pivotal role in the effects of mAb therapy. In addition to mAbs therapy, recent studies reveal that an inhibitory FcR, FcyRIIB, contributes to the effect of intravenous immunoglobulin (IVIg) therapy. This review summarizes the immunological functions of FcRs and focuses on FcR-targeting therapy.

*Corresponding Author: Akira Nakamura—Department of Experimental Immunology and CREST program of Japan Science and Technology Agency, Institute of Development, Aging and Cancer, Tohoku University, Seiryo 4-1, Sendai 980-8575, Japan. Email: aki@idac.tohoku.ac.jp

Figure 1. Schematic structure of human and murine Fc receptors. Structures of human and murine Fc receptors with their subunits, FcRγ- and FcRβ-chain, are shown. Abbreviations: DC, dendritic cell; FcRn, neonatal Fc receptor; GPI, glycosylphosphatidylinositol; Ig, immunoglobulin; ITA, immunoreceptor tyrosine-based activation motif; ITIM, immunoreceptor tyrosine-base inhibitory motif; LC, Langerhans cell; NK, natural killer; poly-lgR, polymeric immunoglobulin receptor.