



Antibody Fc: Chapter 13. Role of IgG Fc Receptors in Monoclonal Antibody Therapy of Cancer

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Marije B. Overdijk, Sandra Verploegen, Wim K. Bleeker, Paul W.H.I. Parren Historically, lack of specificity for cancer cells has been a major problem in cancer treatment; however, the development of monoclonal antibodies (mAbs), which combine high specificity with multiple mechanisms of action (MoAs), started a revolution in anti-cancer treatment options which continues to date. As of January 2013, 15 major antibody products were being marketed for cancer treatment in various countries around the globe, 10 of which are unmodified mAbs, which generally have multiple potential MoAs and may act via direct, Fab-domain-related effects or indirect, Fc-domain-related effects. Fc-domain-related effects consist of immune-mediated effector functions, which include complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP). ADCC and ADCP depend on the engagement of Fcy-receptors (FcyR) on immune effector cells by Fcdomains clustered due to antibody-antigen binding. Similarly, CDC depends on the engagement of proteins of the complement system by clustered antibody Fc domains. In this chapter, preclinical and clinical studies with approved anti-cancer mAbs are reviewed, with an emphasis on the role of FcyR-mediated effector functions. The importance of therapeutic antibody–FcyR interactions for human treatment can be deduced from correlations of clinical responses with FcyR polymorphisms, results supported by a wealth of preclinical and in vitro studies.

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