



Antibody Fc: Chapter 12. Fc γ Receptor Polymorphisms and Susceptibility to Infection

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Fc γ receptors (Fc γ R) mediate many effector functions of antibody and are critical for defense against pathogens, including bacteria, viruses, and parasites. A number of single nucleotide polymorphisms have been identified in both activating and inhibitory Fc γ R genes that affect either the binding affinity for IgG or receptor function. Reviewing the available evidence from murine knockout mice, in vitro studies utilizing human cells, and genetic studies in humans, the current view on the role of Fc γ R polymorphisms in susceptibility to infection will be summarized here. Genetic studies have often yielded conflicting results, which may be due to small sample size or the inherent difficulties associated with genotyping the FCGR locus, or they may reflect differences in the functional importance of interactions between Fc γ R and its ligands (IgG versus CRP) in differing clinical manifestations of infectious disease. The engagement of the inhibitory Fc γ R limits the proinflammatory response initiated by Fc γ R ligation. FCGR polymorphisms that favor activating Fc γ R may result in excessive inflammation that is deleterious to the host, despite its efficacy in eliminating the pathogen. Overall, pathogen encounter is likely to be the main factor driving the retention of FCGR polymorphisms within the gene pool. Evidence suggests that potent infections, such as malaria, have exerted a significant evolutionary pressure on the maintenance and prevalence of Fc γ R polymorphisms in different populations.

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