



# Antibody Fc: Chapter 17. Fc Protein Engineering

*Roy Jefferis*

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Diversity of antigen-binding specificity may be considered the hallmark of antibodies; however, the human IgG-Fc region also exhibits binding specificity for multiple ligands. Evolution of the IgG-Fc has resulted in the generation of interaction sites for endogenous (self) ligands that recruit and activate mechanisms facilitating the removal and destruction of antibody–pathogen immune complexes. However, pathogens (bacteria and virus) have co-evolved to elaborate IgG-Fc binding proteins that seek to subvert these protective mechanisms. The four human IgG subclasses exhibit differential binding specificity for these ligands, and the choice of IgG subclass for an antibody therapeutic allows selection for a ligand binding profile appropriate for the intended use. The profile of IgG-Fc ligand binding specificities is being extended through the generation and selection among multiple IgG-Fc mutant proteins. Of particular interest has been the development of mutant aglycosylated antibodies that retain or acquire ligand binding activities. This extends possible production vehicles to include prokaryotic systems, although an increased potential for inducing anti-drug antibodies may be a limiting factor.

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