IDENTIFICATION AND ENGINEERING OF ANTIBODIES WITH VARIANT HEAVY CHAINS AND METHODS OF USING SAME

ABSTRACT

The present invention relates to molecules, particularly polypeptides, more particularly immunoglobulins (e.g., antibodies), comprising a variant heavy chain, which variant heavy chain comprises constant domains from more than one IgG isotype. The variant heavy chain of the invention may further comprise at least one amino acid modification relative to the parental heavy chain, such that the Fc region of said variant heavy chain binds an FcγR with an altered affinity relative to a comparable molecule comprising the wild-type heavy chain. The molecules of the invention are particularly useful in preventing, treating, or ameliorating one or more symptoms associated with a disease, disorder, or infection. The molecules of the invention are particularly useful for the treatment or prevention of a disease or disorder where an enhanced efficacy of effector cell function (e.g., ADCC) mediated by FcγR is desired, e.g., cancer, infectious disease, and in enhancing the therapeutic efficacy of therapeutic antibodies the effect of which is mediated by ADCC.

Figure No. 17A