DESCRIPTION

METHOD FOR ALTERING PLASMA RETENTION AND IMMUNOGENICITY OF ANTIGEN-BINDING MOLECULES ~~IN BLOOD PLASMA AND METHOD FOR MODIFYING IMMUNOGENICITY~~

Technical Field

The present invention relates to methods for improving pharmacokinetics of an antigen-binding molecule in animals administered with the molecule and methods for reducing immune response to an antigen-binding molecule, by modifying the Fc region of the antigen-binding molecule which has an antigen-binding domain whose antigen-binding activity varies depending on ion concentration and an Fc region that has FcRn-binding activity in a neutral pH range. The present invention also relates to antigen-binding molecules that exhibit improved pharmacokinetics or reduced immune response in animals administered with the molecules. Furthermore, the present invention relates to methods for producing the antigen-binding molecules and to pharmaceutical compositions comprising as an active ingredient such an antigen-binding molecule.

Background Art

Antibodies are drawing attention as pharmaceuticals as they are highly stable in plasma and have few side effects. At present, a number of IgG-type antibody pharmaceuticals are available on the market and many antibody pharmaceuticals are currently under development (Non-patent Documents 1 and 2). Meanwhile, various technologies applicable to second-generation antibody pharmaceuticals have been reported, including those that enhance effector function, antigen-binding ability, pharmacokinetics, and stability, and those that reduce the risk of immunogenicity (Non-patent Document 3). In general, the requisite dose of an antibody pharmaceutical is very high. This, in turn, has led to problems, such as high production cost, as well as the difficulty in producing subcutaneous formulations. In theory, the dose of an antibody pharmaceutical may be reduced by improving antibody pharmacokinetics or improving the affinity between antibodies and antigens.

The literature has reported methods for improving antibody pharmacokinetics using artificial substitution of amino acids in constant regions (Non-patent Documents 4 and 5). Similarly, affinity maturation has been reported as a technology for enhancing antigen-binding ability or antigen-neutralizing activity (Non-patent Document 6). This technology enables enhancement of antigen-binding activity by introduction of amino acid mutations into the CDR region of a variable region or such. The enhancement of antigen-binding ability enables improvement of *in vitro* biological activity or reduction of dosage, and further enables