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Summary ~~of the Invention~~

[Problems to be Solved by the ~~Invention~~Present Disclosure]

The present ~~invention~~ disclosure was achieved in view of the above circumstances. An objective of the present ~~invention~~ disclosure is to provide polypeptides whose stability has been improved by modifying amino acids in the antibody Fc region.

In one aspect, there is provided a polypeptide comprising an antibody Fc region, wherein at least one amino acid has been modified in a loop region of the Fc region, and the polypeptide has improved stability as compared to that of a parent polypeptide.

In another aspect, there is provided a method for improving stability of a polypeptide comprising an antibody Fc region as compared to that of a parent polypeptide by introducing at least one amino acid modification to a loop region of the Fc region.

In another aspect, there is provided a method for producing a polypeptide comprising an antibody Fc region, which has at least one amino acid modification in a loop region of the Fc region, and has improved stability as compared to that of a parent polypeptide, wherein the method comprises the steps of: (a) introducing at least one amino acid modification to a polypeptide comprising an antibody Fc region at a loop region of the Fc region; (b) determining the stability of the polypeptide modified in step (a); and (c) selecting a polypeptide with improved stability as compared to that of the parent polypeptide.

In another aspect, there is provided a method for producing a polypeptide comprising an antibody Fc region, which has at least one amino acid modification in a loop region of the Fc region, and has improved stability as compared to that of a parent polypeptide, wherein the method comprises the steps of: (a) modifying a nucleic acid encoding the polypeptide so as to improve its stability as compared to that of the parent polypeptide; (b) introducing the modified nucleic acid into a host cell and culturing the cell to induce expression of the nucleic acid; and (c) collecting the polypeptide from the host cell culture.

In another aspect, there is provided a nucleic acid encoding a polypeptide comprising an antibody Fc region, which has at least one amino acid modification in a loop region of the Fc region, and has improved stability as compared to that of a parent polypeptide.

In another aspect, there is provided a vector comprising the nucleic acid as defined above.

In another aspect, there is provided a host cell transformed with the vector as defined above.

In another aspect, there is provided a pharmaceutical composition comprising the polypeptide as disclosed herein, or a polypeptide produced by the method as disclosed herein.

In another aspect, there is provided an agent for treating or preventing an immune-inflammatory disease or cancer, which comprises the pharmaceutical composition as defined above.

In another aspect, there is provided the use of the pharmaceutical composition as defined above in the preparation of an agent for treating or preventing an immune-inflammatory disease or cancer.

[Means for Solving the Problems]

The present inventors considered that, in the production of modified Fc regions, it would be desirable to enhance their function while maintaining antibody stability, or to recover stability that had been reduced due to functional enhancement.

The present inventors conducted dedicated studies, and as a result succeeded in obtaining polypeptides with an antibody Fc region which have been modified in at least one amino acid in a loop region of the Fc region and which thereby have improved stability as compared to that of a parent polypeptide.

Furthermore, by combining multiple amino acid modifications in the loop region, polypeptides with improved thermal stability and maintained or enhanced FcγR-binding activity, and polypeptides with improved thermal stability and decreased FcγR-binding activity, as compared to those of a parent polypeptide, were successfully obtained. Furthermore, polypeptides not only with improved thermal stability and adjusted FcγR-binding activity but also with decreased aggregate content were successfully obtained.

More specifically, the present ~~invention~~ disclosure relates to the following:

[1] a polypeptide comprising an antibody Fc region, wherein at least one amino acid has been modified in a loop region of the Fc region, and the polypeptide has improved stability as compared to that of a parent polypeptide;

[2] the polypeptide of [1], wherein the stability is assessed or determined using melting temperature (Tm) as an index;

Ewing's sarcoma, osteosarcoma, chondrosarcoma, leukemia, lymphoma, myeloma, or other solid organ tumors.

63. Use of the pharmaceutical composition of claim 59 in the preparation of an agent for treating or preventing an immune-inflammatory disease or cancer.