

CLAIMS

What is claimed is:

1. A fusion protein comprising:
(a) an IgG4 antibody comprising: (i) a first polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 6 or 7; (ii) a second polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 12 or 13; and (iii) a third polypeptide comprising the amino acid sequence of SEQ ID NO: 146 but with a mutation at position 108 thereof; and
(b) a fourth polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 14;
wherein one or more polypeptides of the fusion protein are connected by a linker.
2. The fusion protein of claim 1, wherein the linker comprises the amino acid sequence of any one of SEQ ID NOs: 17–34.
3. The fusion protein of claim 1, wherein the third polypeptide comprises an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 14 only by conservative amino acid substitutions.
4. The fusion protein of claim 1, wherein the mutation is a S108P mutation.
5. The fusion protein of claim 1, wherein the linker connects the first polypeptide to the fourth polypeptide.
6. The fusion protein of claim 1, wherein the first polypeptide comprises an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 6 or 7 only by conservative amino acid substitutions.

7. The fusion protein of claim 1, wherein the second polypeptide comprises an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 12 or 13 only by conservative amino acid substitutions.
8. A pharmaceutical composition comprising:
the fusion protein of claim 1; and
a pharmaceutically acceptable excipient.
9. The fusion protein of claim 1, comprising: a polypeptide having at least 95% sequence identity with SEQ ID NO: 296 and a polypeptide having at least 95% sequence identity with SEQ ID NO: 295.
10. The fusion protein of claim 1, comprising: a polypeptide having at least 95% sequence identity with SEQ ID NO: 15 and a polypeptide having at least 95% sequence identity with SEQ ID NO: 294.
11. The fusion protein of claim 1, comprising: the amino acid sequence of SEQ ID NO: 15; and the amino acid sequence of SEQ ID NO: 294.
12. The fusion protein of claim 1, comprising: the amino acid sequence of SEQ ID NO: 296; and the amino acid sequence of SEQ ID NO: 295.
13. The fusion protein of claim 1, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 6 or 7.
14. The fusion protein of claim 1, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 12 or 13.
15. The fusion protein of claim 1, wherein the fourth polypeptide comprises the amino acid sequence of SEQ ID NO: 14.