

CLAIMS

1. A polypeptide having IgG cysteine protease activity and comprising or consisting of an amino acid sequence which is:
- 5 (i) SEQ ID NO: 1; or
- (ii) SEQ ID NO: 2; or
- (iii) a variant of SEQ ID NO: 1 or SEQ ID NO: 2, which has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid modification(s) relative to SEQ ID NO: 1 or SEQ ID NO: 2 respectively, provided that the sequence retains: (a) an asparagine (N) at the position which corresponds to
- 10 position 95 of SEQ ID NO: 5, (b) an aspartic acid (D) at the position which corresponds to position 99 of SEQ ID NO: 5 and (c) an asparagine (N) at the position which corresponds to position 226 of SEQ ID NO: 5, and provided that the polypeptide is at least as effective at cleaving human IgG as the polypeptide consisting of the amino acid sequence of SEQ ID NOs: 1 or 2 respectively, when measured in the same assay.
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2. The polypeptide according to claim 1, wherein at least one of the modifications in (iii) does not result in the same amino acid as is present in the corresponding position in the polypeptide sequence of SEQ ID NO: 3, preferably wherein all of the modifications in (iii) do not result in the same amino acid as is present in the corresponding position in the
- 20 polypeptide sequence of SEQ ID NO: 3.
3. A polypeptide according to claim 1 or 2, wherein the polypeptide further comprises an additional methionine at the N terminus and/or an additional histidine tag at the C terminus.
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4. A polypeptide according to any one of the preceding claims, wherein the polypeptide is more effective at cleaving human IgG than an IdeZ polypeptide and/or is at least as effective at cleaving human IgG as an IdeS polypeptide, when measured in the same assay.
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5. A polypeptide according to any one of the preceding claims, wherein the polypeptide is more effective at cleaving human IgG than an IdeS polypeptide when measured in the same assay, optionally wherein efficacy is measured *in vitro* in a blood or serum sample taken from a human subject.

6. A polypeptide according to claim 5, wherein the polypeptide is at least 1.2 fold, preferably 1.3 fold, most preferably 1.4 fold more effective at cleaving human IgG than an IdeS polypeptide when measured in the same assay.
- 5 7. A polypeptide according to any one of the preceding claims, wherein said polypeptide is less immunogenic than an IdeS polypeptide and/or is not more immunogenic than an IdeZ polypeptide, when measured in the same assay.
8. A polypeptide according to any one of the preceding claims, wherein the polypeptide
10 is less immunogenic than an IdeS polypeptide, preferably wherein the immunogenicity of the polypeptide is no more than 85% of the immunogenicity of an IdeS polypeptide when measured in the same assay.
9. A polynucleotide encoding a polypeptide according to any one of the preceding
15 claims.
10. An expression vector comprising the polynucleotide according to claim 9.
11. A host cell comprising the polynucleotide according to claim 9 or expression vector
20 according to claim 10, which is preferably a bacterial cell, most preferably a cell of *E. coli*.
12. A composition comprising a polypeptide according to any one of claims 1 to 8 and at least one pharmaceutically acceptable carrier or diluent.
- 25 13. A polypeptide according to any one of claims 1 to 8 for use in the treatment of the human or animal body.
14. A method for the prevention or treatment of a disease or condition in a subject, which method comprises administering to the subject a polypeptide according to any one of claims 1
30 to 8 or the composition of claim 12 to the subject in a prophylactically or therapeutically effective amount.

15. A method according to claim 14, wherein said disease or condition is a disease or condition mediated in whole or in part by pathogenic IgG antibodies, preferably wherein said disease or condition is listed in Table D.
- 5 16. An *ex vivo* method for the cleavage of IgG, the method comprising contacting a sample containing IgG with a polypeptide according to any one of claims 1 to 8 under conditions which permit IgG cysteine protease activity to occur.
17. A method according to claim 16 which is conducted to generate Fc, Fab and/or
10 F(ab')₂ fragments.
18. A method according to claim 15 or 16 wherein the sample is a blood sample taken from a subject suffering from a disease or condition as defined in claim 15.

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