

Claims

We claim:

1. A recombinant protein comprising:
 - a unit of an antigen;
 - a unit of a Fc fusion comprising a CH2 domain and a CH3 domain of an IgG;
 - a unit of a variable heavy chain (VH) domain of the IgG;
 - a unit of a CH1 domain of the IgG; and
 - a unit of a light chain variable (VL) domain of the IgG,wherein:
 - the unit of the antigen is not an epitope of the IgG;
 - the unit of the antigen is linked to the unit of the VH domain of the IgG at the N-terminus or to the CH3 domain of IgG at the C-terminus;
 - the unit of the CH1 domain of IgG is linked to the CH2 domain of the IgG; and
 - the unit of the VL domain of the IgG is fused to the unit of the VH domain of the IgG and to the CH1 domain of the IgG.
2. The recombinant protein of claim 1, wherein the IgG is 6D8 antibody.
3. The recombinant protein of claim 2, wherein the Fc fusion comprises the substitution mutations E345R, E430G, and S440Y.
4. A recombinant protein comprising:
 - a unit of an antigen;
 - a unit of a Fc fusion comprising a CH2 domain and a CH3 domain of an IgG;
 - a unit of a variable heavy chain (VH) domain of the IgG;
 - a unit of a CH1 domain of the IgG;
 - a unit of a light chain variable (VL) domain of the IgG; and
 - a unit of a light chain constant (CL) domain of the IgG,wherein:
 - the IgG is 6D8 antibody;
 - the Fc fusion comprises the substitution mutations E345R, E430G, and S440Y;
 - the unit of the antigen is not an epitope of the IgG;
 - the unit of the CH1 domain of IgG is linked to the CH2 domain of the IgG;

the unit of the VL domain of the IgG is linked to the unit of the CL domain of the IgG;

the unit of the CL domain of the IgG is linked to the CH1 domain of the IgG;
and

the unit of the antigen is linked to the CH3 domain of the IgG.

5. The recombinant protein of any one of claims 1-4, further comprising a unit of an epitope tag, wherein the epitope tag is an epitope of the IgG.

6. The recombinant protein of claim 5, wherein the epitope tag comprises the sequence YKLDIS (SEQ ID NO. 1) and the unit of the epitope tag is linked to the unit of antigen.

7. The recombinant protein of claim 6, wherein the epitope tag comprises the sequence VYKLDISEA (SEQ ID NO. 2).

8. The recombinant protein of claim 6, wherein the epitope tag consists of the sequence YKLDIS (SEQ ID NO. 1).

9. The recombinant protein of claim of 2, comprising:
two units of the antigen;
two units of the Fc fusion;
two units of the CH1 domain of the IgG;
two units of the VH domain of the IgG; and
two units of light chain variable (VL) domain of the IgG,
wherein a disulfide bond formed at the linkage of the CH2 domain and the CH1 domain of the IgG links the two units of the Fc fusion.

10. The recombinant protein of claim 9, wherein each unit of the VL domain of the IgG is linked to a unit of VH domain of the IgG and the CH1 domain of the IgG.

11. The recombinant protein of claim 10, wherein the recombinant protein does not comprise any light chain constant (CL) domain of the IgG.

12. The recombinant protein of any one of claims 9-11, further comprising two units of an epitope tag, wherein:

each unit of the epitope tag comprises the sequence YKLDIS (SEQ ID NO. 1),
the two units of the epitope tag are linked to the two units of the Fc fusion at the C-terminus of the CH3 domain of the IgG, and
the two units of the antigen are linked to the two units of the VH domain of the IgG.

13. The recombinant protein of any one of claims 9-11, further comprising two units of an epitope tag, wherein:

each unit of the epitope tag comprises the sequence YKLDIS (SEQ ID NO. 1),
the two units of the epitope tag are linked to the two units of the antigen, and
the two units of the antigen are linked to the two units of Fc fusion at the C-terminus of the CH3 domain of the IgG.

14. The recombinant protein of claim 12 or 13, wherein the epitope tag comprises the sequence VYKLDISEA (SEQ ID NO. 2).

15. The recombinant protein of claim 12 or 13, wherein the epitope tag consists of the sequence YKLDIS (SEQ ID NO. 1).

16. A recombinant protein comprising:

two units of an antigen;
two units of a Fc fusion;
two units of a VH domain of the IgG; and
two unit of a CH1 domain of the IgG,
wherein:

the antigen is not an epitope of the IgG;
the two unit of the antigen are linked to the two units of the VH domain of the IgG at the N-terminus; and
the two units of the CH1 domain of IgG are linked to the two units of the Fc fusion at the CH2 domain of the IgG.

17. The recombinant protein of claim 16, wherein the recombinant protein does not comprise a light chain constant (CL) domain of the IgG and does not comprise a light chain variable (VL) domain of the IgG.
18. The recombinant protein of any one of claims 1-17, wherein the antigen comprises K301-T406 of Accession No. AMC13911.1.
19. The recombinant protein of any one of claims 1-17, wherein the antigen comprises at least one sequence selected from the group consisting of SEQ ID NOs. 34-72.
20. The recombinant protein of claim 19, wherein the antigen comprises at least three sequences, at least six sequences, or at least nine sequences selected from the group consisting of SEQ ID NOs. 34-72.
21. The recombinant protein of any one of claims 1-20, wherein the recombinant protein is produced in a transgenic plant.
22. The recombinant protein of claim 21, wherein the transgenic plant is silenced for xylosyltransferase and fucosyltransferase.
23. An immunologic composition comprising:
at least one recombinant protein of any one of claims 1-22, or
at least one recombinant protein of any one of claims 1 and 3-22, wherein the antibody is the 6D8 antibody.
24. A method of producing the recombinant protein of any one of claims 1-22, the method comprising:
introducing into a first agrobacterium a binary vector selected from the group consisting of: pBYR11eM-h6D8ZE3, pBYR11eMa-BAZE3-Hgp371, pBYR11eMa-BAZE3-H, pBYKEMd-HZE3, pBYKEMd-ZE3H, pBYKEMd-ZE3Hx, pBYKEMd-HVLZe, pBYKEMd2-HVL-Hx, pBYKEMd2-HVLZnt, pBYKEMd2-ZHVLnt, pBYKEMd2-ZHVLLe, pBYKEMd2-ZHVLhx, pBYKEAM-N12MHd, pBYKEAM-NPHd, pBYKEAM-NSHd, pBYKEAM-NTHd, pBYKEHM-CPHd, pBYKEHM-CSHd, and pBYKEHM-CTHd;
infiltrating a plant part with the first agrobacterium containing the binary vector to produce a transformed plant part; and

extracting crude protein from the transformed plant part; and
purifying the extracted crude protein.

25. The method of claim 24, wherein the binary vector introduced into agrobacteria is selected from the group consisting of: pBYR11eM-h6D8ZE3, pBYR11eMa-BAZE3-Hgp371, pBYR11eMa-BAZE3-H, and pBYKEMd-HZE3, the method further comprises:

introducing pBYKEMd-6D8K into a second agrobacterium; and

infiltrating the plant part with the second agrobacterium containing pBYKEMd-6D8K to produce a transformed plant part,

wherein the plant part is co-infiltrated with the second agrobacterium containing pBYKEMd-6D8K and the first agrobacterium containing the binary vector.

26. Use of at least one recombinant protein selected from the recombinant protein of any one of claims 1-22 or the immunologic composition of claim 23 in the manufacture of a medicament for inducing an immune response in a subject against an antigen, wherein the recombinant protein or the immunologic composition is to be administered to the subject.

27. The use of claim 26, wherein the antigen is from Zika virus, and wherein a recombinant protein of any one of claims 18, 21, and 22 or the immunologic composition of claim 23 is to be administered to the subject.

28. The use of claim 27, wherein the antigen is from norovirus, and wherein a recombinant protein of any one of claims 19-22 or the immunologic composition of claim 23 is to be administered to the subject.

29. At least one recombinant protein selected from the recombinant protein of any one of claims 1-22 or the immunologic composition of claim 23 for use in therapy.