

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising an engineered immunoglobulin A subclass 2 (IgA2) antibody or a functional fragment thereof and a pharmaceutically acceptable carrier, diluent or excipient, wherein the engineered IgA2 antibody or a functional fragment thereof comprises an antibody antigen binding domain; and a constant domain, wherein the constant domain comprises an IgA2 heavy chain constant region, wherein the IgA2 heavy chain constant region comprises an IgA2 CH1 region, an IgA2 CH2 region, and an IgA2 CH3 region, wherein the IgA2 CH3 region comprises:
 - a. an amino acid substitution at N135, and
 - b. a deletion of C147 and Y148,
 each relative to a wildtype (WT) IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
2. The pharmaceutical composition of claim 1, wherein the IgA2 CH1 region comprises an amino acid substitution at P124, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
3. The pharmaceutical composition of claim 2, wherein the amino acid substitution at P124 is P124R, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
4. The pharmaceutical composition of claim 1, wherein the IgA2 CH1 region comprises an amino acid substitution at N45.2, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
5. The pharmaceutical composition of claim 4, wherein the amino acid substitution at N45.2 is N45.2G or N45.2A, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
6. The pharmaceutical composition of claim 1, wherein the amino acid substitution at N135 is N135Q, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.

7. The pharmaceutical composition of claim 1, wherein the IgA2 heavy chain constant region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 18-21.
- 5 8. The pharmaceutical composition of claim 1, wherein the IgA2 CH2 region comprises an Asn to Gly, an Asn to Gln, or an Asn to Thr amino acid substitution corresponding to amino acid residue 23 of SEQ ID NO: 110.
- 10 9. The pharmaceutical composition of claim 1, wherein the IgA2 CH2 region comprises at least one amino acid substitution of a residue corresponding to any one of amino acid residues 97, 98, and 99 of SEQ ID NO: 110.
- 15 10. The pharmaceutical composition of claim 1, wherein the IgA2 CH2 region comprises at least one amino acid substitution of a residue corresponding to amino acid residue 24 or 25 of SEQ ID NO: 110.
- 20 11. A pharmaceutical composition comprising an engineered immunoglobulin A subclass 2 (IgA2) antibody or a functional fragment thereof and a pharmaceutically acceptable carrier, diluent or excipient, wherein the engineered IgA2 antibody or functional fragment thereof comprises an antibody antigen binding domain; and a constant domain, wherein the constant domain comprises an IgA2 heavy chain constant region, wherein the IgA2 heavy chain constant region comprises an IgA2 CH1 region, an IgA2 CH2 region, and an IgA2 CH3 region, wherein
- 25 a. the IgA2 CH1 region comprises an amino acid substitution of N45.2, and
- b. the IgA2 CH3 region comprises a deletion of residues P131 to Y148,
- each relative to a wildtype (WT) IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
- 30 12. The pharmaceutical composition of claim 11, wherein the IgA2 CH1 region comprises an amino acid substitution at P124, relative to a wildtype (WT) IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.
13. The pharmaceutical composition of claim 12, wherein the amino acid substitution at P124 is P124R, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.

14. The pharmaceutical composition of claim 11, wherein the IgA2 CH2 region comprises an Asn to Gly, an Asn to Gln, or an Asn to Thr amino acid substitution corresponding to amino acid residue 23 of SEQ ID NO: 110.

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15. The pharmaceutical composition of claim 11, wherein the IgA2 CH2 region comprises at least one amino acid substitution of a residue corresponding to any one of amino acid residues 97, 98, and 99 of SEQ ID NO: 110.

10 16. The pharmaceutical composition of claim 11, wherein the IgA2 CH2 region comprises at least one amino acid substitution of a residue corresponding to amino acid residue 24 or 25 of SEQ ID NO: 110.

15 17. The pharmaceutical composition of claim 11, wherein the amino acid substitution of N45.2 in the IgA2 CH1 region is N45.2G or N45.2A, relative to the WT IgA heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 1, numbering according to IMGT scheme.

18. Use of the composition of claim 1 in the manufacture of a medicament for inducing antibody-dependent cell-mediated cytotoxicity (ADCC) in a subject.

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19. Use of the composition of claim 11 in the manufacture of a medicament for inducing antibody-dependent cell-mediated cytotoxicity (ADCC) in a subject.