

Claims

1. An antibody which binds to human DR5 and comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH and VL regions comprise VHCDR1, VHCDR2, and VHCDR3 domains comprising the amino acid sequences set forth in SEQ ID NOs: 1, 8, and 3, respectively, and VLCDR1, VLCDR2 and VLCDR3 domains comprising the amino acid sequences set forth in SEQ ID NO: 5, the sequence FAS, and SEQ ID NO: 6, respectively, and

a Fc region of a human immunoglobulin IgG, wherein in the Fc region, the amino acid at the position corresponding to E430 in human IgG1 is mutated to G, wherein the numbering is according to the EU Index.

2. The antibody of claim 1, wherein the antibody is an IgG1, IgG2, IgG3, IgG4, IgE, IgD or IgM isotype.

3. The antibody of claim 1, wherein the antibody is humanized or chimeric.

4. A composition comprising at least one antibody according to claim 1 and a carrier.

5. A nucleic acid construct comprising a nucleic acid encoding the heavy and light chain variable regions of the antibody according to claim 1.

6. An expression vector comprising one or more nucleic acid constructs according to claim 5.

7. A host cell comprising the expression vector of claim 6.

8. A kit comprising the antibody of claim 1, and instructions for use.

9. The composition of claim 4, which comprises

(a) a first antibody that binds to human DR5 and comprises VH and VL regions, wherein the VH region comprises VHCDR1, VHCDR2, and VHCDR3 domains comprising the amino acid sequences set forth in SEQ ID NOs: 1, 8, and 3, respectively, and the VL region comprises VLCDR1, VLCDR2, and VLCDR3

domains comprising the amino acid sequences set forth in SEQ ID NO: 5, the sequence FAS, and SEQ ID NO: 6, respectively, and

(b) a second antibody that binds to human DR5 and comprises VH and VL regions, wherein the VH region comprises VHCDR1, VHCDR2, and VHCDR3 domains comprising the amino acid sequences set forth in SEQ ID NOs: 10, 2, and 11, respectively, and the VL region comprises VLCDR1, VLCDR2, and VLCDR3 domains comprising the amino acid sequences set forth in SEQ ID NO: 13, the sequence RTS, and SEQ ID NO: 14, respectively,

wherein both the first antibody and second antibody comprise a Fc region of a human immunoglobulin IgG, and wherein in the Fc region of both the first antibody and second antibody, the amino acid at the position corresponding to E430 in human IgG1 is mutated to G.

10. The antibody of claim 1, wherein the antibody comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 9 and 7, respectively.

11. The antibody of claim 1, wherein the antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 38 and 39, respectively.

12. A composition comprising the antibody of claim **11** and a carrier.

13. The composition of claim **12**, further comprising an antibody which comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.

14. The composition of claim **9**, wherein the second antibody comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 12 and 15, respectively.

15. The composition of claim **9**, wherein the second antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.

16. The composition of claim **9**, wherein the first antibody comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 9 and 7, respectively.

17. The composition of claim **16**, wherein the second antibody comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 12 and 15, respectively.

18. The composition of claim **16**, wherein the second antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.

19. The composition of claim **9**, wherein the first antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 38 and 39, respectively.

20. The composition of claim **19**, wherein the second antibody comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 12 and 15, respectively.

21. A composition comprising:

- (a) a first antibody that binds to human DR5 and comprises a heavy chain variable (VH) region and a light chain variable (VL) region, wherein the VH region comprises VHCDR1, VHCDR2, and VHCDR3 domains comprising the amino acid sequences set forth in SEQ ID NOs: 1, 8, and 3, respectively, and the VL region comprises VLCDR1, VLCDR2, and VLCDR3 domains comprising the amino acid sequences set forth in SEQ ID NO: 5, the sequence FAS, and SEQ ID NO: 6, respectively, and
- (b) a second antibody that binds to human DR5 and comprises VH and VL regions, wherein the VH region comprises VHCDR1, VHCDR2, and VHCDR3 domains comprising the amino acid sequences set forth in SEQ ID NOs: 10, 2, and 11, respectively, and the VL region comprises VLCDR1, VLCDR2, and VLCDR3 domains comprising the amino acid sequences set forth in SEQ ID NO: 13, the sequence RTS, and SEQ ID NO: 14, respectively,

wherein both the first antibody and second antibody comprise a Fc region of a human immunoglobulin IgG, and wherein in the Fc region of both the first antibody and second antibody, the amino acid at the position corresponding to E430 in human IgG1 is mutated to G.

22. A composition comprising:

- (a) a first antibody that binds to human DR5 and comprises a heavy chain variable (VH) region and a light chain variable (VL) region comprising the amino acid sequences set forth in SEQ ID NOs: 9 and 7, respectively, and
- (b) a second antibody that binds to human DR5 and comprises a VH region and a VL region comprising the amino acid sequences set forth in SEQ ID NOs: 12 and 15, respectively,

wherein both the first antibody and second antibody comprise a Fc region of a human immunoglobulin IgG, and wherein in the Fc region of both the first antibody and second antibody, the amino acid at the position corresponding to E430 in human IgG1 is mutated to G.

23. A composition comprising:

- (a) a first antibody that binds to human DR5 and comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 38 and 39, respectively, and
- (b) a second antibody that binds to human DR5 and comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.