

CLAIMS

1. An immunoglobulin G (hereinafter described as IgG) antibody which binds to death receptor 3 (DR3) and antagonizes TL1A induced DR3 activation, wherein the antibody has a decreased or no agonistic activity against DR3 through their binding, and wherein the antibody comprises amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:16 to18, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22 to24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:16, 17, 80, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22-24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:16, 17, 80, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22, 81, 24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs: 16, 17, 80, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22, 82, 24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:16-18, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22, 81, 24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs: 16-18, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22, 82, 24, respectively; amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:16, 17, 80, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:22, 83, 24, respectively; or amino acid sequences of CDR1 to CDR3 of VH of SEQ ID NOs:28 to 30, respectively, and amino acid sequences of CDR1 to CDR3 of VL of SEQ ID NOs:34 to 36, respectively.

2. The antibody according to claim 1, which binds to an epitope included in a cysteine-rich domain (hereinafter described as CRD) of DR3.

3. The antibody according to claim 1, which binds to an epitope comprising at least one amino acid residue presented in CRD1 or CRD4 of DR3.

4. The antibody according to claim 1, wherein the antibody is selected from the group consisting of:

(i) an IgG2 antibody;

- (ii) an IgG2 antibody variant comprising a hinge domain from IgG2 and a domain exchange in at least one of CH1, CH2, and CH3; and
 - (iii) an IgG2 antibody variant comprising CH1 from IgG4, a hinge domain from IgG2, CH2 from IgG4, and CH3 from IgG4,
- wherein an amino acid residue at EU numbering position 409 in the CH3 domain is Lys.

5. The antibody according to claim 1, which neutralizes and/or antagonizes an activity of DR3 induced through TL1A ligand binding.

6. The antibody according to any one of claims 1 to 5, wherein the agonistic activity is at least one selected from the phosphorylation of p65 subunit of NF-kappa B, cytokine release from DR3 expressed cells, the proliferation of DR3 expressed cells, the apoptosis of DR3 expressed cells.

7. The antibody according to any one of claims 1 to 6, which is at least one antibody selected from (i) to (iii) as described in the following;

- (i) an antibody which competitively binds to DR3 with the anti-DR3 monoclonal antibody 142A2 or 142S38B,
- (ii) an antibody which binds to an epitope included in the epitope recognized by the anti-DR3 monoclonal antibody 142A2 or 142S38B, and
- (iii) an antibody which binds to same epitope recognized by the anti-DR3 monoclonal antibody 142A2 or 142S38B,

wherein antibody 142S38B comprises the VH region having the amino acid sequence of SEQ ID NO: 27 and the VL region having the amino acid sequence of SEQ ID NO: 33, and wherein antibody 142A2 comprises the VH region having the amino acid sequence of SEQ ID NO: 15 and the VL region having the amino acid sequence of SEQ ID NO: 21.

8. The antibody according to claim 1, which comprises an amino acid sequence of VH of SEQ ID NO:15 and an amino acid sequence of VL of SEQ ID NO:21, an amino acid sequence of VH of SEQ ID NO:76 and an amino acid sequence of VL of SEQ ID NO:21, an amino acid sequence of VH of SEQ ID NO:15 and an amino acid sequence of VL of SEQ ID NO:77, an amino acid sequence of VH of SEQ ID NO:15 and an amino acid sequence of VL of SEQ ID NO:78, an amino acid sequence of VH of SEQ ID NO:15 and an amino acid

sequence of VL of SEQ ID NO:79, an amino acid sequence of VH of SEQ ID NO:76 and an amino acid sequence of VL of SEQ ID NO:79, or an amino acid sequence of VH of SEQ ID NO:27 and an amino acid sequence of VL of SEQ ID NO:33.