

Claims

1. An isolated antibody or antigen binding portion thereof that specifically binds to human CD40 comprising:

the CDRs of antibody 12D6-24 wherein CDRH 1, CDRH2 and CDRH3 comprise residues 31-35, 50-66 and 99-108, respectively, of SEQ ID NO: 12 and CDRL1, CDRL2 and CDRL3 comprise residues 24-39, 55-61 and 94-102, respectively, of SEQ ID NO: 9, wherein the antibody further comprises an Fc region modified to enhance specificity of binding to Fc.gamma.RIIb, wherein the Fc region comprises a sequence selected from the group consisting of SE (SEQ ID NO: 66), SELF (SEQ ID NO: 67), P238D (SEQ ID NO: 68), V4 (SEQ ID NO: 69), V4 D270E (SEQ ID NO: 70), V7 (SEQ ID NO: 71), V8 (SEQ ID NO: 72), V9 (SEQ ID NO: 73), V9 D270E (SEQ ID NO: 74), V11 (SEQ ID NO: 75), and V12 (SEQ ID NO: 76).

2. The antibody of claim 1 comprising: the heavy and light chain variable regions of antibody 12D6-24 comprising residues 1-119 and 1-112 of SEQ ID NO: 12 and SEQ ID NO: 9, respectively.

3. The antibody of Claim 1 exhibiting an A/I ratio of less than 5.
4. The antibody of Claim 3 exhibiting an A/I ratio of less than 1.

5. The antibody of Claim 1 comprising heavy and light chain sequences selected from the groups consisting of:

- a) the heavy and light chains of antibody 12D6-24-P238D comprising the sequences of SEQ ID NO:13 and SEQ ID NO:9, respectively;
- b) the heavy and light chains of antibody 12D6-24-SE comprising the sequences of SEQ ID NO:14 and SEQ ID NO:9, respectively;
- c) the heavy and light chains of antibody 12D6-24-SELF comprising the sequences of SEQ ID NO:15 and SEQ ID NO:9, respectively;
- d) the heavy and light chains of antibody 12D6-24-V4 comprising the sequences of SEQ ID NO:16 and SEQ ID NO:9, respectively;
- e) the heavy and light chains of antibody 12D6-24-V4 D270E comprising the sequences of SEQ ID NO:17 and SEQ ID NO:9, respectively;
- f) the heavy and light chains of antibody 12D6-24-V8 comprising the sequences of SEQ ID NO:18 and SEQ ID NO:9, respectively;
- g) the heavy and light chains of antibody 12D6-24-V9 comprising the sequences of SEQ ID NO:19 and SEQ ID NO:9, respectively;
- h) the heavy and light chains of antibody 12D6-24-V9 D270E comprising the sequences of SEQ ID NO:20 and SEQ ID NO:9, respectively;
- i) the heavy and light chains of antibody 12D6-24-V11 comprising the sequences of SEQ ID NO:21 and SEQ ID NO:9, respectively; and
- j) the heavy and light chains of antibody 12D6-24-V12 comprising the sequences of SEQ ID NO:22 and SEQ ID NO:9, respectively.

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6. A pharmaceutical composition comprising:
- a) the antibody, or antigen binding portion thereof, of claim 1; and
 - b) a carrier.

7. The antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 for use in therapy.
8. The antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 for use as a medicament.
9. The antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 for use in the treatment of cancer, wherein a T-cell mediated immune response against the cancer is to be stimulated.
10. The antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 for use in the treatment of chronic viral infection, wherein a T-cell mediated immune response against the viral infection is to be stimulated.
11. The antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 for use according to claim 9, wherein the cancer is selected from the group consisting of: bladder cancer, breast cancer, uterine/cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, sarcoma, and virus-related cancer.
12. Use of the antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 in the manufacture of a medicament for the treatment of cancer, wherein a T-cell mediated immune response against the cancer is to be stimulated.

13. Use of the antibody, or antigen binding portion thereof, of claim 1, the antibody of any one of claims 2 to 5 or the composition of claim 6 in the manufacture of a medicament for the treatment of chronic viral infection, wherein a T-cell mediated immune response against the viral infection is to be stimulated.

14. The use according to claim 12, wherein the cancer is selected from the group consisting of: bladder cancer, breast cancer, uterine/cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, sarcoma, and virus-related cancer.