

CLAIMS

1. An antibody or an antigen-binding fragment thereof specifically binding to human IL-12/IL-23 p40, wherein according to Kabat, IMGT, Chothia or AbM
5 numbering system, the antibody comprises:
- (1) an HCDR1, an HCDR2 and an HCDR3 contained in a heavy chain variable region set forth in SEQ ID NO: 1; and
 - (2) an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in SEQ ID NO: 6;
- 10 wherein the antigen-binding fragment is selected from the group consisting of: Fab, Fab', F(ab')₂, Fv, Fab/c, single chain antibody, and bivalent antibody.
2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein:
- 15 the HCDR1 comprises or consists of a sequence set forth in SEQ ID NO: 3, the HCDR2 comprises or consists of a sequence set forth in SEQ ID NO: 4, and the HCDR3 comprises or consists of a sequence set forth in SEQ ID NO: 5; and the antibody further comprises:
- 20 an LCDR1, comprising or consisting of a sequence set forth in SEQ ID NO: 8, an LCDR2, comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 9, and an LCDR3, comprising or consisting of a sequence set forth in SEQ ID NO: 10.
3. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody comprises framework regions (FRs) in the heavy chain variable
25 region and FRs in the light chain variable region, wherein
- (1) the FRs in the heavy chain variable region comprise FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 29; the FR-H2 comprises or consists of an
30 amino acid sequence set forth in SEQ ID NO: 30; the FR-H3 comprises or

- consists of an amino acid sequence set forth in SEQ ID NO: 31; the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 32;
- (2) the FRs in the light chain variable region comprise FR-L1, FR-L2, FR-L3 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 41; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 42; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 43; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 44.
4. The antibody or the antigen-binding fragment thereof according to claim 2, wherein the antibody comprises:
- (1) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 1,
a sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO: 1; and
a light chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 6, or
a sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO: 6.
5. The antibody or the antigen-binding fragment thereof according to any one of claims 1-4, wherein the antibody further comprises a heavy chain constant region and a light chain constant region, and the constant regions are derived from species other than murine, e.g., from a human antibody, preferably from a human IgG, more preferably from IgG1.
6. The antibody or the antigen-binding fragment thereof according to claim 5, wherein the heavy chain constant region is an Ig gamma-1 chain C region of GenBank ACCESSION No. P01857; the light chain constant region is an Ig kappa chain C region of GenBank ACCESSION No. P01834.

7. The antibody or the antigen-binding fragment thereof according to any one of claims 1-6, wherein the antibody comprises or consists of a heavy chain set forth in SEQ ID NO: 49 and a light chain set forth in SEQ ID NO: 50.
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8. The antibody or the antigen-binding fragment thereof according to any one of claims 1-7, wherein the antibody is scFv, a humanized antibody, a chimeric antibody or a multispecific antibody (e.g., a bispecific antibody).
- 10 9. The antibody or the antigen-binding fragment thereof according to any one of claims 1-7, wherein the antibody binds to human IL-12/IL-23 p40 protein domain with a K_D of less than 10^{-5} M, e.g., less than 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or 10^{-10} M or less.
- 15 10. The antibody or the antigen-binding fragment thereof according to any one of claims 1-7, wherein the antibody binds to human IL-12/IL-23 p40 protein domain with an EC_{50} of less than 100 nM, e.g., less than 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, 0.1 nM or less.
- 20 11. An isolated polynucleotide encoding the antibody or antigen-binding fragment according to any one of claims 1 to 10.
12. A vector, comprising the polynucleotide according to claim 11.
- 25 13. A host cell, comprising the polynucleotide according to claim 11 or the vector according to claim 12.
- 30 14. A method for preparing the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, comprising: culturing the host cell according to claim 13 in a suitable condition, and isolating the antibody or the antigen-binding fragment thereof from the cell cultures.

15. An antibody conjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-10 and a conjugated moiety coupled thereto, wherein the conjugated moiety is a purification tag (e.g., a His tag), a cytotoxic agent or a detectable label.
16. The antibody conjugate according to claim 15, wherein the conjugated moiety is a His tag, a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol.
17. A fusion protein, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-10.
18. A multispecific antibody, preferably a bispecific antibody, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-10.
19. A kit, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, the antibody conjugate according to claim 15 or 16, the fusion protein according to claim 17, or the multispecific antibody according to claim 18.
20. The kit according to claim 19, wherein the kit further comprises a second antibody specifically identifying the antibody or the antigen-binding fragment thereof.
21. The kit according to claim 20, wherein the second antibody further comprises a detectable label, such as a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol.
22. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, the antibody conjugate according to claim 15 or 16, the fusion

protein according to claim 17 or the multispecific antibody according to claim 18 in preparing a kit for detecting the presence or level of human IL-12/IL-23 p40 protein domain in a sample.

- 5 23. A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, the antibody conjugate according to claim 15 or 16, the fusion protein according to claim 17 or the multispecific antibody according to claim 18, and optionally, a pharmaceutically acceptable carrier and/or an excipient.

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24. The pharmaceutical composition according to claim 23, wherein the pharmaceutical composition is in a form suitable for administration by subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

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25. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, the antibody conjugate according to claim 15 or 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 23 or 24 in preparing a medicament for
20 treating autoimmune disease or ulcerative colitis.

26. Use according to claim 25, wherein the autoimmune disease is plaque psoriasis or systemic lupus erythematosus, or ulcerative colitis is refractory or recurrent.

- 25 27. An *in vitro* method, comprising administering a cell comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-10, the antibody conjugate according to claim 15 or 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 23 or 24, wherein the method is selected from the group consisting
30 of:

a method for blocking the binding of human IL-12/IL-23 p40 protein domain to ligand IL-12R β 1 or IL-23R,

a method for down-regulating the activity or the level of human IL-12/IL-23 p40 protein domain, and

- 5 a method for blocking cellular response mediated by the binding of human IL-12R β 1 or human IL-23R to p40 protein domain, wherein preferably, a ligand of the IL-12/IL-23 p40 is IL-12R β 1 or IL-23R.