CLAIMS

1. An antibody or an antigen-binding fragment thereof, preferably specifically binding to human IL-12/IL-23 p40, wherein 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 or SEQ ID NO: 24; and

(2) an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in any one of SEQ ID NO: 6, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID N: 15, SEQ ID NO: 17 and SEQ ID NO: 25;

preferably,

the HCDR1 comprises or consists of a sequence set forth in SEQ ID NO: 3 or 26, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence,

the HCDR2 comprises or consists of a sequence set forth in SEQ ID NO: 4, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, and

the HCDR3 comprises or consists of a sequence set forth in SEQ ID NO: 5, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; and

the antibody further comprises:

an LCDR1, comprising or consisting of a sequence set forth in SEQ ID NO: 8, 19, 20 or 27, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence,

an LCDR2, comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 9, 21 or 28, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, and

an LCDR3, comprising or consisting of a sequence set forth in SEQ ID NO: 10, 22 or 23, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody comprises framework regions (FRs) in the heavy chain variable 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, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 29, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 29; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 30, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 30, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the 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, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 31, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the 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, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 32, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the 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: 33 or 41, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 33 or 41, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid

mutations (preferably substitutions, insertions or deletions) compared to the sequence set forth in SEQ ID NO: 33 or 41; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 34, 42, 45 or 47, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 34, 42, 45 or 47, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 34, 42, 45 or 47; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 35, 43, 46 or 48, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 35, 43, 46 or 48, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 35, 43, 46 or 48; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 36 or 44, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 36 or 44, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 36 or 44.

3. The antibody or the antigen-binding fragment thereof according to claim 1 or 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 or 24,

a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 1 or 24, or

an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence set forth in SEQ ID NO: 1 or 24; and

a light chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25,

a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25, or

an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25.

4. The antibody or the antigen-binding fragment thereof according to any one of claims 1-3, 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; preferably, the heavy chain constant region is an Ig gamma-1 chain C region (more preferably an Ig gamma-1 chain C region of GenBank ACCESSION No. P01857); the light chain constant region is an Ig kappa chain C region (more preferably an Ig kappa chain C region of GenBank ACCESSION No. P01834).

5. The antibody or the antigen-binding fragment thereof according to any one of claims 1-4, wherein the antibody comprises or consists of a heavy chain set forth in SEQ ID NO: 19 and a light chain set forth in SEQ ID NO: 20.

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1-5, wherein the antigen-binding fragment is selected from the group consisting of: Fab, Fab', $F(ab')_2$, Fd, Fv, dAb, Fab/c, complementarity determining region (CDR) fragment, single chain antibody (e.g., scFv), bivalent antibody and domain antibody.

7. The antibody or the antigen-binding fragment thereof according to any one of claims 1-6, wherein the antibody is a humanized antibody, a chimeric antibody or a multispecific antibody (e.g., a bispecific antibody).

8. 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 about 10^{-5} M, e.g., less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or 10^{-10} M or less.

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 an EC_{50} of less than about 100 nM, e.g., less than about 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.

10. An isolated polypeptide, selected from the group consisting of:

(1) an isolated polypeptide comprising sequences set forth in SEQ ID NOs: 3, 4 and 5 or SEQ ID NOs: 26, 4 and 5, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising sequences set forth in SEQ ID NO: 8, 19 or 20, SEQ ID NO: 9 or 21, SEQ ID NO: 10, 22 or 23 or SEQ ID NOs: 27, 28 and 22;

(2) an isolated polypeptide comprising sequences set forth in SEQ ID NO: 8, 19 or 20, SEQ ID NO: 9 or 21, SEQ ID NO: 10, 22 or 23, or SEQ ID NOs: 27, 28 and 22, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising sequences set forth in SEQ ID NOs: 3, 4 and 5;

(3) an isolated polypeptide comprising a sequence set forth in SEQ ID NO: 1 or 24, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising a sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; and

(4) an isolated polypeptide comprising a sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising a sequence set

forth in SEQ ID NO: 1 or 24, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

11. An isolated polynucleotide encoding a polypeptide, selected from the group consisting of:

(1) an isolated polynucleotide encoding a polypeptide comprising sequences set forth in SEQ ID NOs: 3, 4 and 5, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising sequences set forth in SEQ ID NO: 8, 19 or 20, SEQ ID NO: 9 or 21, SEQ ID NO: 10, 22 or 23 or SEQ ID NOs: 27, 28 and 22;

(2) an isolated polynucleotide encoding a polypeptide comprising sequences set forth in SEQ ID NO: 8, 19 or 20, SEQ ID NO: 9 or 21, SEQ ID NO: 10, 22 or 23, or SEQ ID NOs: 27, 28 and 22, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising sequences set forth in SEQ ID NOs: 3, 4 and 5;

(3) an isolated polynucleotide encoding a polypeptide comprising a sequence set forth in SEQ ID NO: 1 or 24, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising a sequence set

forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; and

(4) an isolated polynucleotide encoding a polypeptide comprising a sequence set forth in SEQ ID NO: 6, 11, 13, 15, 17 or 25, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide specifically binds to human IL-12/IL-23 p40 protein domain as part of an anti-human IL-12/IL-23 p40 protein domain antibody, the antibody further comprising a sequence set forth in SEQ ID NO: 1 or 24, a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

12. The polynucleotide encoding a polypeptide according to claim 11, wherein

the polynucleotide comprises or consists of a nucleotide sequence set forth in SEQ ID NO: 2 or 37, or a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence; or

the polynucleotide comprises or consists of a nucleotide sequence set forth in SEQ ID NO: 7, 12, 14, 16, 18 or 38, or a sequence having at least 80%, 81%, 82%,

83%, 84%, 85%, 86%, 87%, 88%, 89% or 90%, preferably at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the sequence.

13. A vector, comprising the polynucleotide according to any one of claims 11-12.

14. A host cell, comprising the polynucleotide according to any one of claims 11-12 or the vector according to claim 13.

15. A method for preparing the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, comprising: culturing the host cell according to claim 14 in a suitable condition, and isolating the antibody or the antigen-binding fragment thereof from the cell cultures.

16. An antibody conjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9 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; preferably, the conjugated moiety is 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 1-9.

18. A multispecific antibody, preferably a bispecific antibody, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-9.

19. A kit, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 16, the fusion protein according to claim 17, or the multispecific antibody according to claim 18, wherein preferably, the kit further comprises a second antibody specifically identifying the antibody or the antigen-binding fragment thereof; optionally, the second

antibody further comprises a detectable label, such as a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol.

20. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 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.

21. A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 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.

22. The pharmaceutical composition according to claim 21, wherein the pharmaceutical composition is in a form suitable for administration by subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

23. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 21 in preparing:

a medicament for blocking the binding of human IL-12/IL-23 p40 protein domain to human IL-12Rβ1 or human IL-23R,

a medicament for blocking the activity of human IL-12/IL-23 p40 protein domain or down-regulating the level thereof, or

a medicament for blocking cellular response mediated by the binding of human IL-12Rβ1 or human IL-23R to p40 protein domain, wherein

preferably, a ligand of the human IL-12/IL-23 p40 protein domain is human IL-12Rβ1 or human IL-23R.

24. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 21 in preparing a medicament for treating autoimmune diseases (e.g., plaque psoriasis or systemic lupus erythematosus) or ulcerative colitis (e.g., refractory or recurrent).

25. An *in vitro* method, comprising administering a cell comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 21, or administering to a subject in need an effective amount of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the antibody conjugate according to claim 16, the fusion protein according to claim 17, the multispecific antibody according to claim 18 or the pharmaceutical composition according to claim 21, wherein the method is selected from the group consisting of:

a method for blocking the binding of human IL-12/IL-23 p40 protein domain to ligand IL-12Rβ1 or IL-23R,

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

a method for blocking cellular response mediated by the binding of human IL-12Rβ1 or human IL-23R to p40 protein domain, wherein

preferably, a ligand of the IL-12/IL-23 p40 is IL-12Rβ1 or IL-23R.