There is substantial evidence that IL-23 responsive cells are associated with autoimmune inflammatory diseases and cancer. In particular, an IL-23 specific inhibitor (i.e. an inhibitor that inhibits IL-23 but not IL-12) would be particularly useful as inhibiting IL-23 without affecting IL-12 is hypothesized to maximize therapeutic benefit while minimizing the risk of suppression of host defenses.

Antibodies that specifically bind to the p19 subunit of IL-23 are potentially useful inhibitors, see, for example, WO 2007/024846 and WO 2007/027714. A problem with the antibodies disclosed in WO 2007/024846, at least, is the potential for tissue cross-reactivity, in particular, the potential to bind retinal tissue, which is a safety concern. Furthermore, the antibodies disclosed in WO 2007/024846, at least, have sub-optimal physical-chemical properties, for example, extreme hydrophobicity leading to aggregation, that present a significant barrier to production of the antibodies on an industrial scale. Additionally, no antibody targeting the p19 subunit of IL-23 has been approved for therapeutic use.

Thus, there remains a need for IL-23 antibodies. In particular, there remains a need for IL-23 antibodies that bind with high affinity to the p19 subunit of IL-23, in particular, human IL-23, and do not bind to the p40 subunit of the related cytokine family member, IL-12. More particularly, there remains a need for IL-23 antibodies that bind with high affinity to the p19 subunit of IL-23 and do not observably exhibit tissue cross-reactivity, in particular, retinal tissue cross-reactivity. There is also a need for IL-23 antibodies that possess pharmaceutically acceptable physical-chemical properties that facilitate development, manufacturing or formulation.

Summary

In one aspect, there is provided an antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In another aspect, there is provided a DNA molecule comprising a polynucleotide sequence encoding a light chain polypeptide having the amino acid sequence SEQ ID NO: 10.

In another aspect, there is provided a DNA molecule comprising a polynucleotide sequence encoding a heavy chain polypeptide having the amino acid sequence SEQ ID NO: 9.

In another aspect, there is provided an isolated polynucleotide encoding an antibody as disclosed above.

In another aspect, there is provided a vector comprising a polynucleotide as disclosed above.

In another aspect, there is provided a recombinant host cell comprising the DNA molecule as disclosed above and the DNA molecule as disclosed above, which cell is capable of expressing an antibody comprising a heavy chain and a light chain, wherein the heavy chain comprises amino acid SEQ ID NO: 9 and the light chain comprises amino acid sequence SEQ ID NO: 10.

In another aspect, there is provided a recombinant host cell transformed with the polynucleotide as disclosed above, which cell is capable of expressing an antibody comprising a heavy chain and a light chain, wherein the amino acid sequence of the heavy chain is SEQ ID NO: 9 and the amino acid sequence of the light chain is SEQ ID NO: 10.

In another aspect, there is provided a process for producing an antibody that binds to the p19 subunit of human IL-23 comprising a heavy chain and a light chain, wherein the heavy chain comprises amino acid sequence SEQ ID NO: 9 and light chain comprises amino acid sequences SEQ ID NO: 10, said process comprising the steps of:

a) Cultivating a recombinant host cell as disclosed above under conditions such that said antibody is expressed; and

b) Recovering from said host cell the expressed antibody.

In another aspect, there is provided a process for producing an antibody that binds to the p19 subunit of human IL-23 comprising a heavy chain and a light chain, wherein the amino acid sequence of the heavy chain is SEQ ID NO: 9 and the amino acid sequence of the light chain is SEQ ID NO: 10, said process comprising the steps of:

a) cultivating a recombinant host cell comprising a first polynucleotide sequence encoding the polypeptide sequence given by SEQ ID NO: 9 and a second polynucleotide sequence encoding the polypeptide sequence given by SEQ ID NO: 10, under conditions such that said polypeptide sequences are expressed; and

b) recovering from said host cell an antibody comprising a heavy chain and a light chain, wherein the polypeptide sequence of said heavy chain is given by SEQ ID NO: 9 and the polypeptide sequence of said light chain is given by SEQ ID NO: 10.

In another aspect there is provided an antibody produced by the process as disclosed above.

In another aspect there is provided a pharmaceutical composition comprising an antibody as disclosed above and one or more pharmaceutically acceptable carriers, diluents or excipients.

In another aspect there is provided use of an antibody as disclosed above in the manufacture of a medicament for the treatment or prevention of an autoimmune or inflammatory condition, wherein the condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, psoriasis, inflammatory bowel diseases, ankylosing spondylitis, graft-versus-host disease, lupus and metabolic syndrome.

In another aspect there is provided use of an antibody as disclosed above in the manufacture of a medicament for treating or preventing cancer.

In another aspect there is provided an antibody as disclosed above for use in therapy.

In another aspect there is provided an antibody as disclosed above for use in the treatment of an autoimmune or inflammatory condition, wherein the condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, psoriasis, inflammatory bowel diseases, ankylosing spondylitis, graft-versus-host disease, lupus and metabolic syndrome.

In another aspect there is provided an antibody as disclosed above for use in the treatment of cancer.

Detailed Disclosure

The present invention provides an antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In an embodiment of the present invention, the antibody comprises a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the

heavy chain comprises a heavy chain variable region (HCVR), wherein the amino acid sequence of the LCVR is SEQ ID NO: 8 and the amino acid sequence of the HCVR is SEQ ID NO: 7.

CLAIMS:

1. An antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

2. An antibody according to claim 1, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the amino acid sequence of the LCVR is SEQ ID NO: 8 and the amino acid sequence of the HCVR is SEQ ID NO: 7.

3. An antibody according to claim 2, comprising two light chain variable regions (LCVRs) and two heavy chain variable regions (HCVRs), wherein the amino acid sequence of each LCVR is SEQ ID NO: 8 and the amino acid sequence of each HCVR is SEQ ID NO: 7.

4. An antibody according to claim 1 or 2, wherein the amino acid sequence of the light chain is SEQ ID NO: 10 and the amino acid sequence of the heavy chain is SEQ ID NO: 9.

5. An antibody according to claim 4, comprising two light chains and two heavy chains, wherein the amino acid sequence of each light chain is SEQ ID NO: 10 and the amino acid sequence of each heavy chain is SEQ ID NO: 9.

~~6. An antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions LCDR1, LCDR2,~~

~~and LCDR3, and the HCVR comprises complementarity determining regions HCDR1, HCDR2, and HCDR3, and wherein LCDR1 consists of amino acid sequence SEQ ID NO:4, LCDR2 consists of amino acid sequence SEQ ID NO:5, LCDR3 consists of amino acid sequence SEQ ID NO:6, HCDR1 consists of amino acid sequence SEQ ID NO:1, HCDR2 consists of amino acid sequence SEQ ID NO:2, and HCDR3 consists of amino acid sequence SEQ ID NO:3.~~

~~7. An antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR chain comprises amino acid sequence SEQ ID NO: 8 and the HCVR chain comprises amino acid sequence SEQ ID NO: 7.~~

~~8. An antibody that binds to the p19 subunit of human IL-23 comprising a light chain and a heavy chain, wherein the light chain comprises amino acid sequence SEQ ID NO: 10 and the heavy chain comprises amino acid sequence SEQ ID NO: 9.~~

~~9~~6. A DNA molecule comprising a polynucleotide sequence encoding a light chain polypeptide having the amino acid sequence SEQ ID NO: 10.

~~10~~7. A DNA molecule comprising a polynucleotide sequence encoding a heavy chain polypeptide having the amino acid sequence SEQ ID NO: 9.

~~11~~8. An isolated polynucleotide encoding an antibody of any one of claims 1-~~8~~5.

~~12~~9. An isolated polynucleotide according to claim ~~11~~8, wherein the heavy chain variable region (HCVR) is encoded by SEQ ID NO: 11 and the light chain variable region (LCVR) is encoded by SEQ ID NO: 12.

~~13~~10. An isolated polynucleotide according to claim ~~11~~8 or ~~12~~9, wherein the heavy chain is encoded by SEQ ID NO: 13 and the light chain is encoded by SEQ ID NO: 14.

~~14~~11. A polynucleotide according to any one of claims ~~11~~8-~~13~~10, wherein said polynucleotide is operably linked to an expression control sequence.

~~15~~12. A vector comprising a polynucleotide according to claim ~~14~~11.

~~16~~13. A recombinant host cell comprising the DNA molecule of claim ~~96~~ and the DNA molecule of claim ~~107~~, which cell is capable of expressing an antibody comprising a heavy chain and a light chain, wherein the heavy chain comprises amino acid SEQ ID NO: 9 and the light chain comprises amino acid sequence SEQ ID NO: 10.

~~17~~14. A recombinant host cell transformed with the polynucleotide of any one of claims ~~11~~8-~~13~~10, which cell is capable of expressing an antibody comprising a heavy chain and a light chain, wherein the amino acid sequence of the heavy chain is SEQ ID NO: 9 and the amino acid sequence of the light chain is SEQ ID NO: 10.

~~18~~15. A recombinant host cell according to claim ~~16~~13 or claim ~~17~~14, where the host cell is a mammalian host cell selected from the group consisting of CHO, NS0, HEK293 and COS cells.

~~19~~16. A process for producing an antibody that binds to the p19 subunit of human IL-23 comprising a heavy chain and a light chain, wherein the heavy chain comprises amino acid sequence SEQ ID NO: 9 and light chain comprises amino acid sequences SEQ ID NO: 10, said process comprising the steps of:

a) Cultivating a recombinant host cell of any one of claims ~~16~~13-~~18~~15 under conditions such that said antibody is expressed; and

b) Recovering from said host cell the expressed antibody.

~~20~~17. A process for producing an antibody that binds to the p19 subunit of human IL-23 comprising a heavy chain and a light chain, wherein the amino acid sequence of the heavy chain is SEQ ID NO: 9 and the amino acid sequence of the light chain is SEQ ID NO: 10, said process comprising the steps of:

a) cultivating a recombinant host cell comprising a first polynucleotide sequence encoding the polypeptide sequence given by SEQ ID NO: 9 and a second polynucleotide sequence encoding the polypeptide sequence given by SEQ ID NO: 10, under conditions such that said polypeptide sequences are expressed; and

b) recovering from said host cell an antibody comprising a heavy chain and a light chain, wherein the polypeptide sequence of said heavy chain is given by SEQ ID NO: 9 and the polypeptide sequence of said light chain is given by SEQ ID NO: 10.

~~21~~18. An antibody produced by the process of claim ~~19~~16 or claim ~~20~~17.

~~22~~19. A pharmaceutical composition comprising an antibody according to any one of claims 1-~~8~~5 and ~~21~~18 and one or more pharmaceutically acceptable carriers, diluents or excipients.

~~23~~20. The use~~A method of treating or preventing an autoimmune or inflammatory condition in a patient, comprising administering to a patient in need thereof an effective amount~~ of an antibody according to any one of claims 1-~~8~~5 and ~~21~~18 in the manufacture of a medicament for the treatment or prevention of an autoimmune or inflammatory condition, wherein the condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, psoriasis, inflammatory bowel diseases, ankylosing spondylitis, graft-versus-host disease, lupus and metabolic syndrome.

~~24~~21. ~~A method of treating or preventing cancer in a patient, comprising administering to a patient in need thereof an effective amount~~The use of an antibody according to any one of claims 1-~~8~~5 and ~~21~~18 in the manufacture of a medicament for treating or preventing cancer.

~~25~~22. ~~A method of treating cancer in a patient~~The use according to claim ~~24~~21, wherein the cancer is melanoma, colon, ovarian, head and neck, lung, breast, or stomach cancer.

~~26~~23. An antibody according to any one of claims 1-~~8~~5 and ~~21~~18 for use in therapy.

~~27~~24. An antibody according to any one of claims 1-~~8~~5 and ~~21~~18 for use in the treatment of an autoimmune or inflammatory condition, wherein the condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, psoriasis, inflammatory bowel diseases, ankylosing spondylitis, graft-versus-host disease, lupus and metabolic syndrome.

~~28~~25. An antibody according to any one of claims 1-~~8~~5 and ~~21~~18 for use in the treatment of cancer.

~~29~~26. An antibody for use according to claim ~~28~~25, wherein the cancer is melanoma, colon, ovarian, head and neck, lung, breast, or stomach cancer.