

In another aspect, the present disclosure refers to the antibody or the pharmaceutical composition disclosed herein for use in therapy.

In another aspect of the present disclosure, there is provided a use of the antibody disclosed herein in the manufacture of a medicament for the treatment of rheumatic
5 disease, wherein the rheumatic disease is at least one of lupus nephritis, systemic lupus erythematosus, and rheumatoid arthritis.

In a further aspect of the present disclosure, there is provided a use of the disclosed herein in the manufacture of a medicament for the treatment of neural disease, wherein the neural disease is multiple sclerosis.

10 In another aspect of the present disclosure, there is provided a use of the antibody disclosed herein in the manufacture of a medicament for the treatment of dermatology disease, wherein the dermatology disease is at least one of atopic dermatitis and psoriasis.

In yet another aspect, the present disclosure refers to a DNA molecule comprising a polynucleotide that encodes the amino acid sequence of SEQ ID NO: 1, 2, 5, 6, 9 or 10.

15 In a further aspect, the present disclosure refers to a DNA molecule comprising a polynucleotide sequence that encodes the antibody heavy chain having the amino acid sequence of SEQ ID NO: 1, 5, or 9 and a polynucleotide sequence that encodes the antibody light chain having the amino acid sequence of SEQ ID NO: 2, 6, or 10.

20 In another aspect, the present disclosure refers to a mammalian cell comprising the DNA molecule as disclosed herein.

In yet another aspect, the present disclosure refers to a process for producing an antibody, the process comprises: a) cultivating the mammalian cell as disclosed herein under conditions such that the antibody is expressed, and b) recovering the expressed antibody.

Description

The antibodies of the present invention seek to provide alternative BTLA agonist antibodies. Such BTLA agonist antibodies may be useful in the treatment of autoimmune diseases such as lupus. Such BTLA agonist antibodies are able to bind BTLA from multiple species such as human, cynomolgus monkey, and/or murine BTLA. In addition, such BTLA agonist antibodies demonstrate increased *in vitro* activity compared to an antibody having the same heavy chain variable region and light chain variable region as Mab8D5. The antibodies of the present inventions possess at least one of these desirable characteristics.

One such BTLA agonist antibody is able to bind human, cynomolgus monkey, and murine BTLA. Surprisingly, this antibody has this desired cross-reactivity because it mimics HVEM binding to BTLA. This antibody also has a higher binding affinity to BTLA as compared to HVEM binding BTLA. This may provide a benefit for patients having disease states with transient levels of HVEM, wherein it may desirable to have a BTLA-mimicking agonist antibody on-board during times when the patient has a reduction in HVEM.

The present inventions provide antibodies that bind to BTLA and activate and/or enhance BTLA-mediated signaling (BTLA agonist antibodies). The present inventions provide an antibody that comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, and wherein the amino acid sequence of LCDR1 is SEQ ID NO: 22, the amino acid sequence of LCDR2 is SEQ ID NO: 25, the amino acid

WE CLAIM:

1. An antibody that binds BTLA, comprising HCDR1 having the amino acid sequence of SEQ ID NO: 13, HCDR2 having the amino acid sequence of SEQ ID NO: 16, HCDR3 having the amino acid sequence of SEQ ID NO: 19, LCDR1 having the amino acid sequence of SEQ ID NO: 22, LCDR2 having the amino acid sequence of SEQ ID NO: 25, and LCDR3 having the amino acid sequence of SEQ ID NO: 28.
2. The antibody of Claim 1, comprising a heavy chain variable region (HCVR) having the amino acid sequence of SEQ ID NO: 3, and a light chain variable region (LCVR) having the amino acid sequence of SEQ ID NO: 4.
3. The antibody of Claim 1 or 2, comprising a heavy chain (HC) having the amino acid sequence of SEQ ID NO: 1, and a light chain (LC) having the amino acid sequence of SEQ ID NO: 2.
4. An antibody that binds BTLA, comprising HCDR1 having the amino acid sequence of SEQ ID NO: 14, HCDR2 having the amino acid sequence of SEQ ID NO: 17, HCDR3 having the amino acid sequence of SEQ ID NO: 20, LCDR1 having the amino acid sequence of SEQ ID NO: 23, LCDR2 having the amino acid sequence of SEQ ID NO: 26, and LCDR3 having the amino acid sequence of SEQ ID NO: 29.
5. The antibody of Claim 4, comprising a heavy chain variable region (HCVR) having the amino acid sequence of SEQ ID NO: 7, and a light chain variable region (LCVR) having the amino acid sequence of SEQ ID NO: 8.
6. The antibody of Claims 4 or 5, comprising a heavy chain (HC) having the amino acid sequence of SEQ ID NO: 5, and a light chain (LC) having the amino acid sequence of SEQ ID NO: 6.
7. An antibody that binds BTLA, comprising HCDR1 having the amino acid sequence of SEQ ID NO: 15, HCDR2 having the amino acid sequence of SEQ ID NO: 18, HCDR3 having the amino acid sequence of SEQ ID NO: 21, LCDR1 having the amino acid sequence of SEQ ID NO: 24, LCDR2 having the amino acid sequence of SEQ ID NO: 27, and LCDR3 having the amino acid sequence of SEQ ID NO: 30.

8. The antibody of Claim 7, comprising a heavy chain variable region (HCVR) having the amino acid sequence of SEQ ID NO: 11, and a light chain variable region (LCVR) having the amino acid sequence of SEQ ID NO: 12.
9. The antibody of Claim 7 or 8, comprising a heavy chain (HC) having the amino acid sequence of SEQ ID NO: 9, and a light chain (LC) having the amino acid sequence of SEQ ID NO: 10.
10. A pharmaceutical composition comprising the antibody of any one of Claims 1 to 9, and one or more pharmaceutically acceptable carriers, diluents, or excipients.
11. The antibody of any one of Claims 1 to 9 or the pharmaceutical composition of Claim 10 for use in therapy.
12. Use of the antibody of any one of Claims 1 to 9 in the manufacture of a medicament for the treatment of rheumatic disease, wherein the rheumatic disease is at least one of lupus nephritis, systemic lupus erythematosus, and rheumatoid arthritis.
13. Use of the antibody of any one of Claims 1 to 9 in the manufacture of a medicament for the treatment of neural disease, wherein the neural disease is multiple sclerosis.
14. Use of the antibody of any one of Claims 1 to 9 in the manufacture of a medicament for the treatment of dermatology disease, wherein the dermatology disease is at least one of atopic dermatitis and psoriasis.
15. A DNA molecule comprising a polynucleotide that encodes the amino acid sequence of SEQ ID NO: 1, 2, 5, 6, 9 or 10.
16. A DNA molecule comprising a polynucleotide sequence that encodes the antibody heavy chain having the amino acid sequence of SEQ ID NO: 1, 5, or 9 and a polynucleotide sequence that encodes the antibody light chain having the amino acid sequence of SEQ ID NO: 2, 6, or 10.
17. A mammalian cell comprising the DNA molecule of Claim 16.
18. A process for producing an antibody, the process comprises: a) cultivating the mammalian cell of Claim 18 under conditions such that the antibody is expressed, and b) recovering the expressed antibody.