In one aspect, there is provided a bispecific protein comprising:

a) antibody comprising a light chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO:8, a light chain complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO:9, a light chain complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO:10, a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:11, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:12, and a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:13; and

b) a peptide comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3; wherein the bispecific protein can bind to both B7-related protein 1 (B7RP1) and B-cell activating factor (BAFF).

Described herein is bispecific protein, wherein the protein can inhibit BAFF-mediated proliferation of human B cells and wherein the protein can inhibit B7RP1-mediated proliferation of human T cells. The bispecific protein can comprise an IgG antibody comprising two immunoglobulin heavy chains having different amino acid sequences and two immunoglobulin light chains having different amino acid sequences. The IgG antibody can inhibit BAFF-mediated proliferation of human B cells and B7RP1-mediated proliferation of human T cells The IgG antibody can be an IgG1, IgG2, IgG3, or IgG4 antibody and can be a human or humanized IgG antibody. The bispecific protein can comprise a light chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO:8, a light chain complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO:9, a light chain complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO:10, a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:11, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:12, and a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:13. Further, the bispecific protein can comprise a heavy chain variable region comprising SEQ ID NO:15 or a variant thereof and a light chain variable region comprising SEQ ID NO:14 or a variant thereof. Such variant sequences can comprise not more than 10 deletions, insertions of substitutions of a single amino acid per 100 amino acids relative to a reference sequence.

In an alternate example, a bispecific protein that can inhibit BAFF-mediated proliferation of human B cells and that can inhibit B7RP1-mediated proliferation of human T cells can comprise: (a) a polypeptide comprising an amino acid sequence having the following formula: A-L1-P-L2-P, wherein A is an immunoglobulin heavy chain of an IgG antibody, L1 is a first linker of that is absent or is 3 to 40 amino acids long, P is a BAFF-binding peptide that is 10 to 40 amino acids long, and L2 is a peptide linker that is absent or is 5 to 50 amino acids long; and (b) an immunoglobulin light chain. The immunoglobulin heavy chain of (a) and the immunoglobulin light chain of (b) can form an IgG antibody, comprising two molecules of the polypeptide of (a) and two molecules of the light chain of (b), that can bind B7RP1 and/or can inhibit B7RP1-mediated proliferation of human T cells. The immunoglobulin heavy chain may be missing a lysine at its C-terminal end just

upstream of L1. The IgG antibody can be a human or humanized IgG1, IgG2, IgG3, or IgG4 antibody. The BAFF-binding peptide P can have the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3. L1 can have the amino acid sequence of SEQ ID NO:4, 37, 38, 39, or 40. L2 can have the amino acid sequence of SEQ ID NO:5, 6, or 7. The bispecific protein can comprise a light chain CDR1 comprising the amino acid sequence of SEQ ID NO:8 (RASQGISNWLA), a light chain CDR2 comprising the amino acid sequence of SEQ ID NO:9 (AASSLQS), a light chain CDR3 comprising the amino acid sequence of SEQ ID NO:10 (QQYDSYPRT) , a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:11 (SYWMS), a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:12 (YIKQDGNEKYYVDSVKG), and a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:13 (EGILWFGDLPTF). The bispecific protein can comprise an immunoglobulin light chain variable region comprising the amino acid sequence of SEQ ID NO:14 and/or an immunoglobulin heavy chain variable region comprising the amino acid sequence of SEQ ID NO:15. The bispecific protein can comprise the amino acid sequence of SEQ ID NO:19 or a variant thereof and the amino acid sequence of SEQ ID NO:17 or 18 or variants thereof. Such variant sequences can comprise not more than 10 deletions, insertions of substitutions of a single amino acid per 100 amino acids relative to the reference sequence.

In a further aspect, herein is described a bispecific protein comprising: (a) a polypeptide comprising the amino acid sequence of SEQ ID NO:17 or SEQ ID NO:18 or variants thereof; and (b) another polypeptide comprising the amino acid sequence of SEQ ID NO:19 or a variant thereof; wherein the bispecific protein can bind to both B7-related protein 1 (B7RP1) and B-cell activating factor (BAFF). Such variant sequences can comprise not more than 10 deletions, insertions of substitutions of a single amino acid per 100 amino acids relative to the reference sequence. The bispecific protein can inhibit BAFF-mediated proliferation of human B cells and B7RP1-mediated proliferation of human T cells. The bispecific protein can be a tetramer comprising two molecules of the polypeptide of (a) and two molecules of the polypeptide of (b).

In another example, herein is provided a protein comprising a linker comprising the amino acid sequence of SEQ ID NO:6 or SEQ ID NO:7. In some examples, this protein can inhibit BAFF-mediated proliferation of human B cells and/or B7RP1-mediated proliferation of human T cells. Such a protein can comprise the amino acid sequences of SEQ ID NO:1, SEQ ID NO:14, and/or SEQ ID NO:15.

Such a protein can comprise an amino acid sequence comprising at least two copies of SEQ ID NO:1 separated by SEQ ID NO:6 or 7. In a further example, such a protein can include an immunoglobulin light chain and an immunoglobulin heavy, and SEQ ID NO:6 or 7 can be downstream from the C-terminus of the heavy chain. In such examples, SEQ ID NO:6 or 7 can be flanked by peptides that bind to a protein other than that bound by the heavy and light chains.

In another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of the bispecific protein as described herein and a physiologically acceptable excipient.

Further, herein is described a pharmaceutical composition comprising any of the bispecific proteins herein described or the protein comprising the amino acid sequence of SEQ ID NO:6 or 7 and a physiologically acceptable excipient.

Also described herein is a nucleic acid encoding any polypeptide included in one of bispecific proteins or the proteins comprising SEQ ID NO:6 or SEQ ID NO:7 herein described. Exemplary nucleic acids encoding a polypeptide included in a bispecific protein include, for example, SEQ ID NOs: 55, 56, 60, 61, 62, and 63, among others. Vectors comprising such nucleic acids and host cells containing such vectors and/or nucleic acids are described. Further described herein is method for making a bispecific protein comprising culturing the host cell containing a nucleic acid encoding any of the bispecific proteins described herein under conditions such that the nucleic acid is expressed and recovering the protein from the cell mass or the culture medium. The host cell can be a mammalian cell, for example, a CHO cell, or a bacterial cell such as *Eschericha coli*.

In another aspect, there is provided a method for making a bispecific protein comprising culturing the host cell containing one or more nucleic acids encoding the bispecific protein as described herein; and/or a vector comprising said one or more nucleic acids; under conditions such that the nucleic acid is expressed and recovering the bispecific protein from the cell mass or the culture medium.

Also described herein is a method for treating systemic lupus erythematosus, including lupus nephritis, comprising administering to a patient a therapeutically effective amount of any of the bispecific proteins described herein or a pharmaceutical composition comprising such a bispecific protein.

What is claimed is:

1. A bispecific protein comprising:

a) an antibody comprising a light chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO:8, a light chain complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO:9, a light chain complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO:10, a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:11, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:12, and a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:13; and

b) a peptide comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3; wherein the bispecific protein can bind to both B7-related protein 1 (B7RP1) and B-cell activating factor (BAFF).

2. The bispecific protein of claim 1, wherein the antibody is a human or humanized IgG antibody.

3. The bispecific protein of claim 1 or claim 2, which comprises a heavy chain variable region comprising SEQ ID NO:15 and a light chain variable region comprising SEQ ID NO:14.

4. The bispecific protein of claim 1, comprising:

(a) a polypeptide comprising an amino acid sequence having the following formula: A-L1-P-L2-P, wherein A is the an IgG antibody heavy chain, L1 is a first peptide linker that is absent or is 3 to 40 amino acids long, P is SEQ ID NO: 1, 2, or 3, and L2 is a second peptide linker that is absent or is 5 to 50 amino acids long, and

(b) an IgG antibody light chain.

5. The bispecific protein of claim 4, wherein the immunoglobulin heavy chain of (a) and the immunoglobulin light chain of (b) form an IgG antibody, comprising two molecules of the polypeptide of (a) and two molecules of the light chain of (b).

6. The bispecific protein of claim 4 or 5, wherein the immunoglobulin heavy chain is missing a lysine at its C-terminal end just upstream of L1.

7. The bispecific protein of any one of claims 4 to 6, wherein the IgG antibody is a human or humanized IgG1 antibody.

8. The bispecific protein of any one of claims 4 to 6, wherein the IgG antibody is a human or humanized IgG2 antibody.

9. The bispecific protein of any one of claims 4 to 6, wherein the IgG antibody is a human or humanized IgG4 antibody.

10. The bispecific protein of any one of claims 4 to 9, wherein P has the amino acid sequence of SEQ ID NO:1 (LPGCKWDLLIKQWVCDPL).

11. The bispecific protein of any one of claims 4 to 10, wherein L1 has the amino acid sequence of SEQ ID NO:40 (GGGGG).

12. The bispecific protein of any one of claims 4 to 11, wherein the L2 has the amino acid sequence of SEQ ID NO:5.

13. The bispecific protein of any of claims 4 to 11, wherein L2 has the amino acid sequence of SEQ ID NO:6.

14. The bispecific protein of any one of claims 4 to 13, comprising an immunoglobulin light chain variable region comprising the amino acid sequence of SEQ ID NO: 14.

15. The bispecific protein of any one of claims 4 to 14, comprising an immunoglobulin heavy chain variable region comprising the amino acid sequence of SEQ ID NO:15.

16. The bispecific protein of any one of claims 10 to 15, wherein the immunoglobulin light chain of (b) comprises the amino acid sequence of SEQ ID NO:19.

17. The bispecific protein of any one of claims 10 to 16, wherein the polypeptide of (a) comprises the amino acid sequence of SEQ ID NO:17 or 18.

18. A bispecific protein comprising

(a) a polypeptide comprising the amino acid sequence of SEQ ID NO:17 or SEQ ID NO:18 and

(b) another polypeptide comprising the amino acid sequence of SEQ ID NO:19; wherein the bispecific protein can bind to both B7-related protein 1 (B7RP1) and B-cell activating factor (BAFF).

19. The bispecific protein of claim 18, which is a tetramer comprising two molecules of the polypeptide of (a) and two molecules of the polypeptide of (b).

20. The bispecific protein of claim 17 or 18, wherein the polypeptide of (a) comprises the amino acid sequence of SEQ ID NO:17.

21. The bispecific protein of claim 17 or 18, wherein the polypeptide of (a) comprises the amino acid sequence of SEQ ID NO:18.

22. The bispecific protein of claim 1 comprising a linker comprising the amino acid sequence of SEQ ID NO:6 or SEQ ID NO:7.

23. The bispecific protein of claim 22, which comprises the amino acid sequences of SEQ ID NO:1, SEQ ID NO:14, and/or SEQ ID NO:15.

24. A pharmaceutical composition comprising a therapeutically effective amount of the bispecific protein of any one of claims 1 to 23 and a physiologically acceptable excipient.

25. A method for making a bispecific protein comprising

culturing a host cell containing one or more nucleic acids encoding the bispecific protein of any of claims 1 to 23; and/or a vector comprising said one or more nucleic acids; under conditions such that the nucleic acid is expressed and

recovering the bispecific protein from the cell mass or the culture medium.

26. The method of claim 25, wherein the host cell is a mammalian cell.

27. The method of claim 26, wherein the host cell is a CHO cell.

28. The method of claim 25, wherein the host cell is an *Eschericha coli* cell.