

CLAIMS

1. A TACI polypeptide, having a sequence set forth in SEQ ID NO: 8, or being a truncated fragment of SEQ ID NO: 8 or a variant thereof, wherein,
5 the truncated fragment comprises amino acid residues at positions 48-85 of SEQ ID NO: 8;
the variant is a variant having one or more amino acid replacements at positions selected from the group consisting of positions 49, 52, 53, 57, 65, 82, and 83 in SEQ ID NO: 8 or the truncated fragment thereof, wherein the positions for the amino acid replacements are
10 amino acid residue positions numbered in natural order relative to the sequence SEQ ID NO: 8.
2. A TACI polypeptide, having a sequence set forth in SEQ ID NO: 8, or being a truncated fragment of SEQ ID NO: 8 or a variant thereof, wherein the truncated fragment comprises
15 amino acid residues at positions 51-85 of SEQ ID NO: 8, and the variant is a variant having one or more amino acid replacements at positions selected from the group consisting of positions 52, 53, 57, 65, 82, and 83 in SEQ ID NO: 8 or the truncated fragment thereof, wherein the positions for the amino acid replacements are amino acid residue positions numbered in natural order relative to the sequence SEQ ID NO: 8.
- 20 3. The TACI polypeptide according to claim 1 or 2, wherein the truncated fragment of the TACI polypeptide comprises:
amino acid residues at positions 48-86 of SEQ ID NO: 8;
amino acid residues at positions 48-87 of SEQ ID NO: 8;
25 amino acid residues at positions 48-88 of SEQ ID NO: 8;
amino acid residues at positions 50-85 of SEQ ID NO: 8; or
amino acid residues at positions 49-85 of SEQ ID NO: 8.
4. The TACI polypeptide according to any one of claims 1-3, wherein:
30 the variant is a variant having one or more amino acid replacements selected from the group consisting of 49T or 49R, 52S, 53E or 53Q, 57E, 65T or 65A, 82A or 82R, and 83Y in a sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO: 68, or
the variant is a variant having one or more amino acid replacements selected from the
35 group consisting of 52S, 53E or 53Q, 57E, 65T or 65A, 82A or 82R, and 83Y in a sequence of SEQ ID NO: 69 or SEQ ID NO: 70;
wherein the positions for the amino acid replacements are amino acid residue positions numbered in natural order relative to the sequence SEQ ID NO: 8;
preferably, the variant is:
40 a variant having any one amino acid replacement selected from the group consisting of 49T, 52S, 53E, 53Q, 57E, and 82A in a sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ

ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO: 68;
 a variant having any one amino acid replacement selected from the group consisting of 52S, 53E, 53Q, 57E, and 82A in a sequence of SEQ ID NO: 69 or SEQ ID NO: 70;
 a variant having amino acid replacements of 49R and 65T in a sequence of SEQ ID NO:
 5 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO:
 68;
 a variant having amino acid replacements of 49R and 65A in a sequence of SEQ ID NO:
 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO:
 68;
 10 a variant having amino acid replacements of 49R, 65T, and 82R in a sequence of SEQ ID
 NO: 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID
 NO: 68;
 a variant having amino acid replacements of 53E and 57E in a sequence of SEQ ID NO:
 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 68,
 15 SEQ ID NO: 69, or SEQ ID NO: 70;
 a variant having amino acid replacements of 52S, 53E, and 57E in a sequence of SEQ ID
 NO: 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO:
 68, SEQ ID NO: 69, or SEQ ID NO: 70;
 a variant having amino acid replacements of 49T and 82A in a sequence of SEQ ID NO:
 20 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO:
 68;
 a variant having amino acid replacements of 49T and 83Y in a sequence of SEQ ID NO:
 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO:
 68;
 25 a variant having amino acid replacements of 49T, 82A, and 83Y in a sequence of SEQ ID
 NO: 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID
 NO: 68; or
 a variant having amino acid replacements of 49T, 53E, 57E, and 82A in a sequence of
 SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or
 30 SEQ ID NO: 68;
 wherein the positions for the amino acid replacements are amino acid residue positions
 numbered in natural order relative to the sequence SEQ ID NO: 8.

5. The TACI polypeptide according to any one of claims 1-4, wherein the TACI
 35 polypeptide has a sequence set forth in any one of SEQ ID NO: 10, SEQ ID NOs: 13-15,
 SEQ ID NOs: 18-35, and SEQ ID NOs: 68-70; preferably, the TACI polypeptide has a
 sequence set forth in SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, or SEQ ID NO:
 35.

40 6. A TACI fusion protein comprising the TACI polypeptide according to any one of claims
 1-5.

7. The TACI fusion protein according to claim 6, comprising:
A) the TACI polypeptide according to any one of claims 1-5; and
B) an Fc region.

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8. The TACI fusion protein according to claim 7, wherein the Fc region is an Fc region of human IgG1;

preferably, the Fc region comprises a first subunit and a second subunit capable of associating with each other, wherein the first subunit and the second subunit have one or

10 more amino acid substitutions for reducing homodimerization; or

the first subunit and/or the second subunit of the Fc region comprises one or more amino acid substitutions, wherein the amino acid substitutions are capable of reducing the binding of the Fc region to an Fc receptor, and preferably, the amino acid substitutions are capable of reducing binding of the Fc region to an Fc γ receptor;

15 more preferably, the Fc region has a sequence set forth in SEQ ID NO: 11, SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 63, or a sequence having at least 90% sequence identity to SEQ ID NO: 11, SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 63.

9. The TACI fusion protein according to any one of claims 6-8, being a dimeric protein and comprising a polypeptide chain selected from the group consisting of polypeptide chains shown in a, b, and c:

20 a. from the N-terminus to the C-terminus: [TACI polypeptide]-[linker]-[subunit of Fc region];

b. from the N-terminus to the C-terminus: [subunit of Fc region]-[linker]-[TACI polypeptide]; and

25 c. from the N-terminus to the C-terminus: [TACI polypeptide 1]-[linker 1]-[subunit of Fc region]-[linker 2]-[TACI polypeptide 2], wherein linker 1 and linker 2 may be identical or different, and TACI polypeptide 1 and TACI polypeptide 2 may be identical or different;

30 wherein preferably, the linker in the polypeptide chain shown in a, b, or c is selected from the group consisting of a linker set forth in SEQ ID NO: 64 or is selected from the group consisting of a (G_xS)_y linker, wherein X is an integer selected from the group consisting of 1 to 5, and Y is an integer selected from the group consisting of 0 to 6; preferably, the linker is a linker set forth in SEQ ID NO: 65 or SEQ ID NO: 66;

35 more preferably, the TACI fusion protein comprises 2 identical polypeptide chains having sequences set forth in any one of SEQ ID NOs: 36-44.

10. A TACI fusion protein, being a fusion protein of TACI and an antibody and comprising a TACI polypeptide and an antibody, wherein:

40 A. the TACI polypeptide is the TACI polypeptide according to any one of claims 1-5; and

B. the antibody is an anti-IL23 antibody, an anti-IL12 antibody, or an anti-IL23/IL12 p40

subunit antibody.

11. The TACI fusion protein according to claim 10, wherein the antibody is an anti-IL23/IL12 p40 subunit antibody;

5 preferably, the antibody comprises a heavy chain variable region and a light chain variable region,

wherein the heavy chain variable region comprises a HCDR1, a HCDR2, and a HCDR3 set forth in SEQ ID NO: 52, SEQ ID NO: 53, and SEQ ID NO: 54, respectively; and

10 the light chain variable region comprises a LCDR1, a LCDR2, and a LCDR3 set forth in SEQ ID NO: 49, SEQ ID NO: 50, and SEQ ID NO: 51, respectively.

12. The TACI fusion protein according to claim 10 or 11, wherein the antibody comprises a heavy chain variable region set forth in SEQ ID NO: 45 and a light chain variable region set forth in SEQ ID NO: 46.

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13. The TACI fusion protein according to any one of claims 10-12, wherein the antibody comprises antibody heavy and light chain constant regions;

preferably, the heavy chain constant region is selected from the group consisting of human IgG1, IgG2, IgG3, and IgG4 constant regions, and the light chain constant region is selected from the group consisting of human antibody κ chain and λ chain constant regions;

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more preferably, the antibody comprises a heavy chain having at least 85% sequence identity to SEQ ID NO: 47 and a light chain having at least 85% sequence identity to SEQ ID NO: 48;

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most preferably, the antibody comprises a heavy chain set forth in SEQ ID NO: 47 and a light chain set forth in SEQ ID NO: 48.

14. The TACI fusion protein according to any one of claims 10-13, comprising a polypeptide chain as described in d or e:

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d. a first polypeptide chain comprising [antibody heavy chain]-[linker]-[TACI polypeptide] from the N-terminus to the C-terminus, and a second polypeptide chain being an antibody light chain;

e. a first polypeptide chain comprising [antibody heavy chain]-[linker]-[TACI polypeptide] from the N-terminus to the C-terminus, and

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a second polypeptide chain comprising [TACI polypeptide]-[linker]-[antibody light chain] from the N-terminus to the C-terminus;

wherein preferably, the linker can be selected from the group consisting of a $(G_xS)_y$ linker, wherein X is an integer selected from the group consisting of 1 to 5, and Y is an integer selected from the group consisting of 0 to 6; preferably, the linker is a linker set forth in SEQ ID NO: 65, SEQ ID NO: 66, or SEQ ID NO: 67.

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15. The TACI fusion protein according to any one of claims 10-14, wherein the TACI fusion protein comprises two identical first polypeptide chains set forth in SEQ ID NO: 55 and two identical second polypeptide chains set forth in SEQ ID NO: 56; or the TACI fusion protein comprises two identical first polypeptide chains set forth in SEQ ID NO: 57 and two identical second polypeptide chains set forth in SEQ ID NO: 58.
16. A pharmaceutical composition, comprising:
the TACI polypeptide according to any one of claims 1-5 or the TACI fusion protein according to any one of claims 6-15, and
one or more pharmaceutically acceptable carriers, diluents, or excipients.
17. A nucleic acid molecule encoding the TACI polypeptide according to any one of claims 1-5 or the TACI fusion protein according to any one of claims 6-15.
18. A host cell, comprising the nucleic acid molecule according to claim 17.
19. Use of a therapeutically effective amount of the TACI polypeptide according to any one of claims 1-5, a therapeutically effective amount of the TACI fusion protein according to any one of claims 6-15, or a therapeutically effective amount of the pharmaceutical composition according to claim 16 in the manufacture of a medicament for treating or ameliorating a B cell disorder or an autoimmune disease.
20. The use of claim 19, wherein the B cell disorder or the autoimmune disease is a disease or condition associated with TACI expression.
21. The use of claim 19 or 20, wherein:
the autoimmune disease is selected from the group consisting of: systemic lupus erythematosus, myasthenia gravis, multiple sclerosis, insulin-dependent diabetes mellitus, Crohn's disease, rheumatoid arthritis, polyarticular juvenile rheumatoid arthritis, and psoriatic arthritis; and
the B cell disorder is selected from the group consisting of: tumors, chronic leukocytic leukemia, multiple myeloma, non-Hodgkin's lymphoma, post-transplant lymphoproliferative disorder, and light chain gammopathy.
22. The use of any one of claims 19 to 21, wherein the autoimmune disease is systemic lupus erythematosus.