

WHAT IS CLAIMED IS:

1. An isolated antigen binding protein (ABP), comprising a heavy chain variable (VH) domain comprising from N-terminus to C-terminus, CDR-H1, CDR-H2, and CDR-H3; and a light chain variable (VL) domain comprising from N-terminus to C-terminus CDR-L1, CDR-L2, and CDR-L3, wherein the CDRs of the VH and VL comprise the following six CDR sequences:

- a. CDR-H3 having the sequence A-R-D-G-V-L-X₁-L-N-K-R-S-F-D-I, wherein X₁ is A or T (SEQ ID NO: 128);
- b. CDR-H2 having the sequence S-I-Y-Y-S-G-X₂-T-Y-Y-N-P-S-L-K-S, wherein X₂ is S, Q or G (SEQ ID NO: 129);
- c. CDR-H1 having the sequence G-S-I-X₃-S-G-X₄-Y-Y-W-G, wherein X₃ is E or A, and X₄ is L, V or S (SEQ ID NO: 130);
- d. CDR-L3 having the sequence QQHTVRPPLT (SEQ ID NO: 64);
- e. CDR-L2 having the sequence GASSRAT (SEQ ID NO: 68); and
- f. CDR-L1 having the sequence RASQSVSSSYLA (SEQ ID NO: 71), wherein the ABP specifically binds human TIGIT (hTIGIT; SEQ ID NO:1).

2. The ABP of claim 1, wherein the ABP comprises:

a CDR-H3 of SEQ ID NO: 32, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.

3. The ABP of claim 1, wherein the ABP comprises:

- a. a V_H sequence of SEQ ID NO: 13 and a V_L sequence of SEQ ID NO: 26;
- b. a V_H sequence of SEQ ID NO: 12 and a V_L sequence of SEQ ID NO: 26;
- c. a V_H sequence of SEQ ID NO: 14 and a V_L sequence of SEQ ID NO: 26;
- d. a V_H sequence of SEQ ID NO: 15 and a V_L sequence of SEQ ID NO: 26;
- e. a V_H sequence of SEQ ID NO: 9 and a V_L sequence of SEQ ID NO: 26;
- f. a V_H sequence of SEQ ID NO: 10 and a V_L sequence of SEQ ID NO: 26; or
- g. a V_H sequence of SEQ ID NO: 11 and a V_L sequence of SEQ ID NO: 26.

4. The ABP of claim 3, wherein:

a. the ABP of claim 3 (a) comprises (i) a heavy chain of SEQ ID NO: 99 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 100 and a light chain of SEQ ID NO: 92;

b. the ABP of claim 3 (b) comprises (i) a heavy chain of SEQ ID NO: 97 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 98 and a light chain of SEQ ID NO: 92;

c. the ABP of claim 3 (c) comprises (i) a heavy chain of SEQ ID NO: 101 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 102 and a light chain of SEQ ID NO: 92;

d. the ABP of claim 3 (d) comprises (i) a heavy chain of SEQ ID NO: 103 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 104 and a light chain of SEQ ID NO: 92;

e. the ABP of claim 3 (e) comprises (i) a heavy chain of SEQ ID NO: 90 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 91 and a light chain of SEQ ID NO: 92;

f. the ABP of claim 3 (f) comprises (i) a heavy chain of SEQ ID NO: 93 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 94 and a light chain of SEQ ID NO: 92; or

g. the ABP of claim 3 (g) comprises (i) a heavy chain of SEQ ID NO: 95 and a light chain of SEQ ID NO: 92; or (ii) a heavy chain of SEQ ID NO: 96 and a light chain of SEQ ID NO: 92.

5. The ABP of claim 1, wherein the ABP:

a. competes for binding to TIGIT with an antibody selected from MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, MAB15, MAB16, MAB17, MAB18, MAB19, MAB20, or MAB21, each as provided in Table 5 of this disclosure;

b. inhibits binding of CD155 to TIGIT;

c. inhibits binding of CD112 to TIGIT;

d. inhibits association of CD226 with TIGIT;

e. activates an effector T cell or a natural killer (NK) cell;

f. decreases the number of regulatory T cells in a tissue or in circulation;

g. inhibits the suppression of an effector T cell by a regulatory T cell;

h. does not bind specifically to any of PVRL1, PVRL2, PVRL3, or PVRL4; or

- i. is capable of any combination of (a)-(h).
6. The ABP of claim 1, wherein the ABP:
- a. binds hTIGIT (SEQ ID NO: 1) with a K_D of less than about 10 nM, 5 nM, or 2 nM, as measured by biolayer interferometry, and
 - b. shows no significant binding to mTIGIT (SEQ ID NO:3) in a biolayer interferometry assay and/or binds to cell surface mTIGIT with a K_D of greater than about 10 nM.
7. An isolated nucleotide sequence or set of isolated nucleotide sequences encoding the ABP of claim 1.
8. The ABP of claim 1, wherein the ABP comprises:
- a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 54, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.
9. The ABP of claim 1, wherein the ABP comprises:
- a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 39, a CDR-H1 of SEQ ID NO: 51, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.
10. The ABP of claim 1, wherein the ABP comprises:
- a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 40, a CDR-H1 of SEQ ID NO: 52, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.
11. The ABP of claim 1, wherein the ABP comprises:
- a CDR-H3 of SEQ ID NO: 31, a CDR-H2 of SEQ ID NO: 41, a CDR-H1 of SEQ ID NO: 53, a CDR-L3 of SEQ ID NO: 64, a CDR-L2 of SEQ ID NO: 68, and a CDR-L1 of SEQ ID NO: 71.
12. A pharmaceutical composition comprising a therapeutically effective amount of the ABP of claim 1 and a pharmaceutically acceptable excipient.

13. The ABP of claim 2, wherein the ABP comprises a V_H sequence of SEQ ID NO: 13 and a V_L sequence of SEQ ID NO: 26.

14. The ABP of claim 2, wherein the ABP comprises a heavy chain of SEQ ID NO: 99 and a light chain of SEQ ID NO: 92.

15. The ABP of claim 2, wherein the ABP comprises a heavy chain of SEQ ID NO: 100 and a light chain of SEQ ID NO: 92.

16. An isolated nucleotide sequence or set of isolated nucleotide sequences encoding the ABP of claim 13.

17. An isolated nucleotide sequence or set of isolated nucleotide sequences encoding the ABP of claim 14.

18. A pharmaceutical composition comprising a therapeutically effective amount of the ABP of claim 13 and a pharmaceutically acceptable excipient.

19. A pharmaceutical composition comprising a therapeutically effective amount of the ABP of claim 14 and a pharmaceutically acceptable excipient.

20. A pharmaceutical composition comprising a therapeutically effective amount of the ABP of claim 15 and a pharmaceutically acceptable excipient.