CLAIMS

1. A multispecific construct comprising:

(1) a first antibody moiety that specifically binds to claudin-6 ("CLDN6"); and

(2) a second antibody moiety that specifically binds to 4-1BB.

2. The multispecific construct of claim 1, wherein the first antibody moiety is selected from the group consisting of a full-length antibody, Fab, Fab', $F(ab')_2$, scFv, and sdAb.

3. The multispecific construct of claim 1 or 2, wherein the first antibody moiety comprises:

(1) a HC-CDR1, a HC-CDR2, and a HC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a heavy variable region (VH) comprising the sequence set forth in SEQ ID No: 7; and

(2) a LC-CDR1, a LC-CDR2, and a LC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a light chain variable region (VL) comprising the sequence set forth in SEQ ID No: 8.

4. The multispecific construct of any one of claims 1-3, wherein the first antibody moiety comprises a heavy variable region (VH) and a light chain variable region (VL), wherein:

(a) the VH comprises:

(i) a HC-CDR1 comprising an amino acid sequence of SEQ ID NO: 1,

(ii) a HC-CDR2 comprising an amino acid sequence of SEQ ID NO: 2, and

(iii) a HC-CDR3 comprising an amino acid sequence of SEQ ID NO: 3, and;

(b) the VL comprises:

(i) a LC-CDR1 comprising an amino acid sequence of SEQ ID NO: 4,

(ii) a LC-CDR2 comprising an amino acid sequence of SEQ ID NO: 5, and

(iii) a LC-CDR3 comprising an amino acid sequence of SEQ ID NO: 6.

5. The multispecific construct of any one of claims 1-4, wherein the first antibody moiety comprises a heavy variable region (VH) and a light chain variable region (VL), and wherein:

(1) the VH comprises the amino acid sequence of SEQ ID NO: 7, or a variant thereof comprising at least about 80% sequence identity to SEQ ID NO: 7; and/or

(2) the VL comprises the amino acid sequence of SEQ ID NO: 8, or a variant thereof comprising at least about 80% sequence identity to SEQ ID NO: 8.

6. The multispecific construct of any one of claims 1-2, wherein the first antibody moiety comprises:

(1) a HC-CDR1, a HC-CDR2, and a HC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a heavy variable region (VH) comprising the sequence set forth in SEQ ID No: 18; and

(2) a LC-CDR1, a LC-CDR2, and a LC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a light chain variable region (VL) comprising the sequence set forth in SEQ ID NO: 19.

7. The multispecific construct of any one of claims 1-2 and 6, wherein the first antibody moiety comprises a heavy variable region (VH) and a light chain variable region (VL), wherein:

(1) the VH comprises:

(i) a HC-CDR1 comprising an amino acid sequence of SEQ ID NO: 12,

(ii) a HC-CDR2 comprising an amino acid sequence of SEQ ID NO: 13, and

(iii) a HC-CDR3 comprising an amino acid sequence of SEQ ID NO: 14, and;

(2) the VL comprises:

(i) a LC-CDR1 comprising an amino acid sequence of SEQ ID NO: 15,

(ii) a LC-CDR2 comprising an amino acid sequence of SEQ ID NO: 16, and

(iii) a LC-CDR3 comprising an amino acid sequence of SEQ ID NO: 17.

8. The multispecific construct of any one of claims 1-2 and 6-7, wherein the first antibody moiety comprises a heavy variable region (VH) and a light chain variable region (VL), and wherein:

(1) the VH comprises the amino acid sequence of SEQ ID NO: 18, or a variant thereof having at least about 80% sequence identity to SEQ ID NO: 18; and/or

(2) the VL comprises the amino acid sequence of SEQ ID NO: 19, or a variant thereof having at least about 80% sequence identity to SEQ ID NO: 19.

9. The multispecific construct of any one of claims 1-8, wherein binding of the first antibody moiety with CLDN6 triggers the second antibody moiety to activate 4-1BB.

10. The multispecific construct of claim 9, wherein the second antibody moiety specifically binds to CRD 3/4 region of 4-1BB.

11. The multispecific construct of any one of claims 1-10, wherein the second antibody moiety is selected from the group consisting of a full-length antibody, Fab, Fab', $F(ab')_2$, scFv, and sdAb.

12. The multispecific construct of claim 11, wherein the second antibody moiety is a sdAb.

13. The multispecific construct of claim 12, wherein the sdAb comprises a sdAb-CDR1, a sdAb-CDR2, and a sdAb-CDR3, respectively comprising the amino acid sequence of a CDR1, a CDR2, and a CDR3 within a single monomeric variable antibody domain comprising the amino acid sequence set forth in SEQ ID NOs: 27.

14. The multispecific construct of claim 12, wherein the sdAb comprises:
(1) a sdAb-CDR1 comprising an amino acid sequence of SEQ ID NO: 24;
(2) a sdAb-CDR2 comprising an amino acid sequence of SEQ ID NO: 25; and
(3) a sdAb-CDR3 comprising an amino acid sequence of SEQ ID NO: 26.

15. The multispecific construct of any one of claims 1-14, wherein the second antibody moiety comprises the amino acid sequence of SEQ ID NO:27, or a variant thereof having at least about 80% sequence identity to SEQ ID NOs: 27.

16. The multispecific construct of any one of claims 1-15, wherein the multispecific construct is a bispecific antibody or a bispecific binding fragment.

17. The multispecific construct of any one of claims 1-5 and 9-16, wherein:

(1) the first antibody moiety comprises:

(a) a HC-CDR1, a HC-CDR2, and a HC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a heavy variable region (VH) comprising the sequence set forth in SEQ ID No: 7;

(b) a LC-CDR1, a LC-CDR2, and a LC-CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a light chain variable region (VL) comprising the sequence set forth in SEQ ID No: 8, and

(2) the second antibody moiety comprises a sdAb-CDR1, a sdAb-CDR2, and a sdAb CDR3, respectively comprising the amino acid sequence of a CDR1, a CDR2, and a CDR3 within a single monomeric variable antibody domain comprising the amino acid sequence set forth in SEQ ID NOs: 27.

18. A pharmaceutical composition comprising the multispecific construct of any one of claims 1-17, and a pharmaceutical acceptable carrier.

19. A nucleic acid encoding the multispecific construct of any one of claims 1-17.

20. A vector comprising the nucleic acid of claim 19.

21. A host cell comprising the nucleic acid of claim 19, or the vector of claim 20.

22. Use of the multispecific construct of any one of claims 1-17, or the pharmaceutical composition of claim 18, in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

23. The use of claim 22, wherein the disease or condition is cancer.

24. A multispecific construct comprising:

(1) a first antibody moiety that specifically binds to a tumor antigen; and

(2) a second antibody moiety that specifically binds to 4-1BB, wherein binding of the first antibody moiety with the tumor antigen triggers the second antibody moiety to activate 4-1BB.

25. The multispecific construct of claim 24, wherein the activation of 4-1BB by the second antibody moiety is enhanced by at least 10 folds after binding of the first antibody moiety with the tumor antigen.

26. The multispecific construct of claim 24 or 25, wherein the second antibody moiety specifically binds to CRD 3/4 region of 4-1BB.

27. The multispecific construct of any one of claims 24-26, wherein the second antibody moiety is a sdAb.

28. The multispecific construct of claim 26, wherein the sdAb comprises a sdAb-CDR1, a sdAb-CDR2, and a sdAb-CDR3, respectively comprising the amino acid sequence of a CDR1, a CDR2, and a CDR3 within a single monomeric variable antibody domain comprising the amino acid sequence set forth in SEQ ID NOs: 27.

29. The multispecific construct of claim 26, wherein the sdAb comprises:

(1) a sdAb-CDR1 comprising an amino acid sequence of SEQ ID NO: 24;

(2) a sdAb-CDR2 comprising an amino acid sequence of SEQ ID NO: 25; and

(3) a sdAb-CDR3 comprising an amino acid sequence of SEQ ID NO: 26.

30. The multispecific construct of any one of claims 24-29, wherein the tumor antigen is CLDN6.

31. A multispecific construct, comprising two heavy chain components and two light chain components, wherein:

(a) each heavy chain component comprises a sequence set forth in SEQ ID NO: 28 and each light chain component comprises a sequence set forth in SEQ ID NO: 29;

(b) each heavy chain component comprises a sequence set forth in SEQ ID NO: 30 and each light chain component comprises a sequence set forth in SEQ ID NO: 31;

(c) each heavy chain component comprises a sequence set forth in SEQ ID NO: 32 and each light chain component comprises a sequence set forth in SEQ ID NO: 33;

(d) each heavy chain component comprises a sequence set forth in SEQ ID NO: 34 and each light chain component comprises a sequence set forth in SEQ ID NO: 35;

(e) each heavy chain component comprises a sequence set forth in SEQ ID NO: 36 and each light chain component comprises a sequence set forth in SEQ ID NO: 37; or

(f) each heavy chain component comprises a sequence set forth in SEQ ID NO: 38 and each light chain component comprises a sequence set forth in SEQ ID NO: 39.