Claims

1. A bispecific heterodimeric diabody that specifically binds to an epitope of human P-cadherin and to an epitope of CD3 comprising a first polypeptide chain and a second polypeptide chain, wherein:

a. the first polypeptide comprises, in the N-terminal to C-terminal direction:

i. a Domain 1, comprising a sub-Domain 1A and a sub-Domain 1B, and

ii. a first heterodimer-promoting domain; and

b. the second polypeptide chain comprises, in the N-terminal to C-terminal direction:

i. a Domain 2, comprising a sub-Domain 2B and a sub-Domain 2A and

ii. a second heterodimer-promoting domain, and

wherein sub-Domain 1A and sub-Domain 2A form a P-cadherin VL/VH binding domain comprising a variable heavy (VH) domain of an anti-P-cadherin antibody (P-CAD VH) and a variable light (VL) domain of an anti-P-cadherin antibody (P-CAD VL), and sub-Domain 1B and sub-Domain 2B form a CD3 VL/VH binding domain comprising a VL domain of an anti-CD3 antibody (CD3 VL) and a VH binding domain of an anti-CD3 antibody (CD3 VH); or

wherein sub-Domain 1A and sub-Domain 2A form a CD3 VL/VH binding domain comprising a CD3 VL and a CD3 VH, and sub-Domain 1B and sub-Domain 2B form a P-cadherin VL/VH binding domain comprising a P-CAD VH and a P-CAD VL; and

wherein the first and second polypeptide chains comprise:

i) a P-CAD VL CDR1, a P-CAD VL CDR2, and a P-CAD VL CDR3 of a P-CAD VL comprising a sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 or 23;

ii) a CD3 VH CDR1, a CD3 VH CDR2, and a CD3 VH CDR3 of a CD3 VH comprising a sequence of SEQ ID NOS: 45 or 46;

iii) a CD3 VL CDR1, a CD3 VL CDR2, and a CD3 VL CDR3 of a CD3 VL comprising a sequence of SEQ ID NO: 47; and/or

iv) a P-CAD VH CDR1, a P-CAD VH CDR2, and a P-CAD VH CDR3 of a P-CAD VH comprising a sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24;

c. the sub-Domain 1A and the sub-Domain 1B are linked by a glycine-serine linker, Linker 1, and the sub-Domain 2B and the sub-Domain 2A are linked by a glycine-serine linker, Linker 1;

d. the first heterodimer-promoting domain comprises a cysteine linker, Linker 2, on sub-Domain 1B and/or the second heterodimer-promoting domain comprises a cysteine linker, Linker 2, on sub-Domain 2A; and

e. the first and second polypeptide chains are covalently bonded to one another by at least one disulfide bond.

2. The bispecific heterodimeric diabody of claim 1, wherein the sub-Domain 1A comprises a P-CAD VL or a CD3 VL, and the sub-Domain 1B comprises a P-CAD VH if the sub-Domain 1A comprises CD3 VL or the sub-Domain 1B comprises a CD3 VH if the sub-Domain 1A comprises P-CAD VL; and wherein the sub-Domain 2B comprises a P-CAD VL or a CD3 VL depending on the VL domain selected for sub-Domain 1A, and the sub-Domain 2A comprises P-CAD VH if the sub-Domain 2B comprises CD3 VL or the sub-Domain 1B comprises a CD3 VH if the sub-Domain 2B comprises P-CAD VL.

3. The bispecific heterodimeric diabody of claim 1 or claim 2, wherein the sub-Domain 1A comprises a P-CAD VL and the sub-Domain 1B comprises a CD3 VH, and the sub-Domain 2B comprises a CD3 VL and the sub-Domain 2A comprises a P-CAD VH.

4. The bispecific heterodimeric diabody of claim 1 or claim 2, wherein the sub-Domain 1A comprises a CD3 VL and the sub-Domain 1B comprises a P-CAD VH, and the sub-Domain 2B comprises a P-CAD VL and the sub-Domain 2A a CD3 VH.

5. The bispecific heterodimeric diabody of claim 1, wherein the sub-Domain 1A comprises a P-CAD VH or a CD3 VH, and the sub-Domain 1B comprises a P-CAD VL if the sub-Domain 1A comprises CD3 VH or the sub-Domain 1B comprises a CD3 VL if the sub-Domain 1A comprises a P-CAD VH; and wherein the sub-Domain 2B comprises a P-CAD VH or a CD3 VH depending on the VH domain selected for sub-Domain 1A, and the sub-Domain 2A comprises P-CAD VL if the sub-Domain 2B comprises a CD3 VH or the sub-Domain 2A comprises a CD3 VL if the sub-Domain 2B comprises a P-CAD VH.

6. The bispecific heterodimeric diabody of claim 1 or claim 5, wherein the sub-Domain 1A comprises a P-CAD VH and the sub-Domain 1B comprises a CD3 VL, and the sub-Domain 2B comprises a CD3 VH and the sub-Domain 2A comprises a P-CAD VL.

7. The bispecific heterodimeric diabody of claim 1 or claim 5, wherein the sub-Domain 1A comprises a CD3 VH and the sub-Domain 1B comprises a P-CAD VL, and the sub-Domain 2B comprises a P-CAD VH and the sub-Domain 2A comprises a CD3 VL.

8. The bispecific heterodimeric diabody of any one of claims 1 to 7, wherein the first heterodimer-promoting domain and the second heterodimer-promoting domain comprise an IgG Fc region comprising a CH2 and a CH3 domain, wherein the amino acid sequence of the CH2 domain and/or the CH3 domain comprises at least one amino acid modification, as compared to a wild-type IgG Fc region, to form a knob or a hole for knob-in-hole association.

9. The bispecific heterodimeric diabody of claim 8, wherein the first heterodimer-promoting domain and the second heterodimer-promoting domain are not both knobs or both holes; and/or wherein the first heterodimer-promoting domain and the second heterodimer-promoting domain form an IgG immunoglobulin Fc region.

10. The bispecific heterodimeric diabody of claim 8 or claim 9, wherein the IgG Fc region forming the knob comprises a sequence of SEQ ID NO: 63, and the IgG Fc region forming the hole comprises a sequence of SEQ ID NO: 64.

11. The bispecific heterodimeric diabody of any one of claims 1 to 10, wherein the glycine-serine linker, Linker 1, comprises a sequence of SEQ ID NO: 68 or SEQ ID NO: 69.

12. The bispecific heterodimeric diabody of any one of claims 1 to 11, wherein the sub-Domain 1A and the sub-Domain 1B do not associate to form a VL/VH epitope binding domain, and the sub-Domain 2B and the sub-Domain 2A do not associate to form a VL/VH epitope binding domain.

13. The bispecific heterodimeric diabody of any one of claims 1 to 12, wherein the Linker 2 of the first heterodimer-promoting domain and/or the second heterodimer-promoting domain further comprises atleast one glycine residue.

14. The bispecific heterodimeric diabody of claim 13, wherein the Linker 2 of the first heterodimer-promoting domain and/or the second heterodimer-promoting domain comprises a sequence of GFNRGEC (SEQ ID NO: 70), GVEPKSC (SEQ ID NO: 71), GGCGGG (SEQ ID NO: 72), GCPPCP (SEQ ID NO: 73), GGTGGCPPCP (SEQ ID NO: 74), GEPKSSDKTHTCPPCP (SEQ ID NO: 75) or GGTGGGEPKSSDKTHTCPPCP (SEQ ID NO: 76).

15. The bispecific heterodimer diabody of claim 14, wherein the Linker 2 of the first heterodimer-promoting domain comprises the sequence of GCPPCP (SEQ ID NO: 73), GGTGGCPPCP (SEQ ID NO: 74), GEPKSSDKTHTCPPCP (SEQ ID NO: 75) or GGTGGGEPKSSDKTHTCPPCP (SEQ ID NO: 76), and the Linker 2 of the second heterodimer-promoting domain comprises the sequence of GCPPCP (SEQ ID NO: 73), GGTGGCPPCP (SEQ ID NO: 74), GEPKSSDKTHTCPPCP (SEQ ID NO: 75) or GGTGGGEPKSSDKTHTCPPCP (SEQ ID NO: 76).

16. The bispecific heterodimer diabody of claim 14, wherein the Linker 2 of the first heterodimer-promoting domain comprises the sequence of GGCGGG (SEQ ID NO: 72), and the Linker 2 of the second heterodimer-promoting domain comprises the sequence of GGCGGG (SEQ ID NO: 72).

17. The bispecific heterodimeric diabody of claim 14, wherein the Linker 2 of the first heterodimer-promoting domain comprises the sequence of GFNRGEC (SEQ ID NO: 70) and the Linker 2 of the second heterodimer-promoting domain comprises the sequence of GVEPKSC (SEQ ID NO: 71), or the Linker 2 of the first heterodimer-promoting domain comprises the sequence of GVEPKSC (SEQ ID NO: 71) and the Linker 2 of the second heterodimer-promoting domain comprises the sequence of GFNRGEC (SEQ ID NO: 70).

18. The bispecific heterodimeric diabody of any one of claims 1 to 17, wherein the bispecific heterodimeric diabody:

a. binds to extracellular domain 3 (ECD3) of human P-cadherin,

b. binds to an epitope on human P-cadherin but does not bind to an epitope on E-cadherin or VE-cadherin, or

c. binds to an epitope on human P-cadherin but does not bind to an epitope on mouse P-cadherin,

d. demonstrates an extended serum and tumor half-life, or

e. demonstrates a lower EC50 in the presence of increased human P-cadherin expression levels or increased human P-cadherin receptor density levels.

19. A bispecific heterodimeric diabody that specifically binds to an epitope of human

P-cadherin and to an epitope of CD3 comprising a first polypeptide chain and a second polypeptide chain, wherein:

a. the first polypeptide comprises, in the N-terminal to C-terminal direction:

i. a Domain 1, comprising a sub-Domain 1A and a sub-Domain 1B, and

ii. a first heterodimer-promoting domain; and

b. the second polypeptide chain comprises, in the N-terminal to C-terminal direction:

i. a Domain 2, comprising a sub-Domain 2B and a sub-Domain 2A and

ii. a second heterodimer-promoting domain, and

wherein sub-Domain 1A and sub-Domain 2A form a P-cadherin VL/VH binding domain comprising a variable heavy (VH) domain of an anti-P-cadherin antibody (P-CAD VH) and a variable light (VL) domain of an anti-P-cadherin antibody (P-CAD VL), and sub-Domain 1B and sub-Domain 2B form a CD3 VL/VH binding domain comprising a VL domain of an anti-CD3 antibody (CD3 VL) and a VH binding domain of an anti-CD3 antibody (CD3 VH); or

wherein sub-Domain 1A and sub-Domain 2A form a CD3 VL/VH binding domain comprising a CD3 VL and a CD3 VH, and sub-Domain 1B and sub-Domain 2B form a P-cadherin VL/VH binding domain comprising a P-CAD VH and a P-CAD VL; and

wherein the first and second polypeptide chains comprise:

i. a P-CAD VL CDR1 sequence comprising $X_{L1.1}$-$X_{L1.2}$-$X_{L1.3}$-$X_{L1.4}$- $XL_{1.5}$- $X_{L1.6}$-$X_{L1.7}$-$X_{L1.8}$-$X_{L1.9}$-$X_{L1.10}$- $X_{L1.11}$-$X_{L1.2}$-$X_{L1.13}$, wherein

$X_{L1.1}$ is W, C, I, F, Y, T, H, N, M, Q, K, L, S, A, V, D, R, E, or G,

$X_{L1.2}$ is G,

$X_{L1.3}$ is R, Q, Y, L, K, F, M, N, W, C, I, T, V, S, E, A, H, D or G,

$X_{L1.4}$ is C, L, F, S, I, T, W, N, Y, V, D, A, K, Q, M, H, or R,

$X_{L1.5}$ is F, C, I, T, V, N, H, L, Y, S, R, Q, W, A, M, E, K, or D,

$X_{L1.6}$ is L, Q, F, M, N, C, K, H, or T,

$X_{L1.7}$ is I, Q, H, F, L, or V,

$X_{L1.8}$ is R, Q, L, T, G, C, E, D, M, Y, or S,

$X_{L1.9}$ is C, W, I, L, F, R, V, T, K, N, S, M, Q, Y, E, A, H, or D,

$X_{L1.10}$ is Q, F, N, L, C, Y, H, R, W, or M,

$X_{L1.11}$ is M, H, K, V, Q, L, Y, C, I, N, F, T, S, E, or W,

$X_{L1.12}$ is I, N, V, L, C, or T,

$X_{L1.13}$ is W, R, F, K, I, H, V, C, T, L, N, M, Q, Y, S, A, D, or E,

ii. a P-CAD VL CDR2 sequence comprising $X_{L2.1}$-$X_{L2.2}$-$X_{L2.3}$-$X_{L2.4}$-$X_{L2.5}$-$X_{L2.6}$- $X_{L2.7}$, wherein

$X_{L2.1}$ is I, L, V, F, Y, W, C, R, Q, N, M, H, E, T, P, K, D, S, A, or G,

$X_{L2.2}$ is W, L, F, I, C, N, R, V, Q, Y, E, D, H, or M,

$X_{L2.3}$ is C, Q, L, F, Y, W, E, R, M, H, A, N, T, K, D, S, I, V, or G,

$X_{L2.4}$ is R, K, I, L, C, Q, V, W, Y, M, F, or H,

$X_{L2.5}$ is R, Q, L, W, K, or H,

$X_{L2.6}$ is R, K, I, W, F, L, Q, C, M, Y, H, V, N, T, A, E, S, P, or D,

$X_{L2.7}$ is C, L, I, T, S, K, M, R, V, F, P, A, W, Q, D, N, G, or Y,

iii, a P-CAD VL CDR3 $X_{L3.1}$-$X_{L3.2}$-$X_{L3.3}$-$X_{L3.4}$-$X_{L3.5}$-$X_{L3.6}$- $X_{L3.7}$- $X_{L3.8}$-$X_{L3.9}$-$X_{L3.10}$- $X_{L3.11}$, wherein

$X_{L3.1}$ is W, R, Y, F, L, N, Q, C, M, I, H, T, A, D, E, S, K, V, or G,

$X_{L3.2}$ is N, C, V, T, S, or A,

$X_{L3.3}$ is W,

$X_{L3.4}$ is F, N, D, E, H, Q, Y, R, or W,

$X_{L3.5}$ is T, I, R, L, C, F, Y, W, Q, M, H, E, N, V, S, D, K, or A,

$X_{L3.6}$ is I, H, C, M, N, L, V, Q, E, S, T, A, K, D, F, Y, G, R, or W,

$X_{L3.7}$ is L, C, R, I, H, Q, E, T, V, M, K, F, or Y,

$X_{L3.8}$ is W, L, C, F, T, N, V, Y, I, M, H, Q, S, K, E, D, A, R, or G,

$X_{L3.9}$ is L, Y, Q, F, H, I, C, R, M, N, D, W, E, K, T, V, A, S, or G,

$X_{L3.10}$ is I, F, K, L, H, Y, M, V, Q, W, T, N, or C,

$X_{L3.11}$ is Q, W, R, F, T, C, Y, V, E, L, N, I, K, or M,

iv. a P-CAD VH CDR1 sequence comprising $X_{H1.1}$-$X_{H1.2}$-$X_{H1.3}$-$X_{H1.4}$- $X_{H1.5}$_$X_{H1.6}$-$X_{H1.7}$-$X_{H1.8}$-$X_{H1.9}$- $X_{H1.10}$ or $X_{H1.5}$, $X_{H1.6}$-$X_{H1.7}$-$X_{H1.8}$-$X_{H1.9}$- $X_{H1.10}$, wherein

$X_{H1.1}$ is R, Q, I, L, C, F, T, G, V, W, M, Y, N, E, P, K, H, D, S, or A,

$X_{H1.2}$ is H, R, C, Q, Y, I, F, K, M, V, L, N, or T,

$X_{H1.3}$ is N, C, R, V, L, T, I, S, K, Q, M, W, A, F, Y, H, or D,

$X_{H1.4}$ is F or Y,

$X_{H1.5}$ is W, R, I, C, K, Y, M, V, F, T, S, L, Q, E, A, N, H, D, or G,

$X_{H1.6}$ is R, I, M, N, Y, C, H, Q, L, K, F, V, T, E, A, S, D, W, or G,

$X_{H1.7}$ is K, R, L, H, F, Q, N, C, Y, M, I, T, V, or A,

$X_{H1.8}$ is P, R, F, W, H, C, Y, I, M, K, G, S, Q, A, L, N, T, or D,

$X_{H1.9}$ is Y, F, K, I, W, or L,

$X_{H1.10}$ is R, C, L, N, S, V, T, or A,

v. a P-CAD VH CDR2 sequence comprising $X_{H2.1}$-$X_{H2.2}$-$X_{H2.3}$-$X_{H2.4}$- $X_{H2.5}$-$X_{H2.6}$- $X_{H2.7}$-$X_{H2.8}$-$X_{H2.9}$-$X_{H2.10}$ or $X_{H2.1}$-$X_{H2.2}$-$X_{H2.3}$-$X_{H2.4}$- $X_{H2.5}$-$X_{H2.6}$- $X_{H2.7}$-$X_{H2.8}$-$X_{H2.9}$-$X_{H2.10}$-$X_{H2.11}$-$X_{H2.12}$-$X_{H2.13}$-$X_{H2.14}$-$X_{H2.15}$-$X_{H2.16}$-$X_{H2.17}$, wherein

$X_{H2.1}$ is W,

$X_{H2.2}$ is W, F, Y, I, V, H, L, or Q,

$X_{H2.3}$ is W, F, L, R, C, H, T, N, Y, Q, K, A, I, V, S, M, E, or D,

$X_{H2.4}$ is I, Y, V, Q, F, H, K, C, N, T, E, L, M, D, P, S, A, or W,

$X_{H2.5}$ is C, P, T, S, L, V, M, F, W, Q, K, G, I, A, N, H, E, D, Y, or R,

$X_{H2.6}$ is I, Q, W, V, C, L, K, E, T, M, F, Y, R, S, A, N, H, D, or G,

$X_{H2.7}$ is G, C, L, N, W, F, S, Y, T, D, I, or M,

$X_{H2.8}$ is Q, C, I, Y, W, L, T, V, K, M, H, F, S, R, A, E, N, D, or G,

$X_{H2.9}$ is F, L, V, W, H, C, Y, K, I, Q, R, T, M, N, A, S, or D,

$X_{H2.10}$ is R, W, K, F, C, T, L, Y, N, Q, V, H, M, A, S, or D,

$X_{H2.11}$ is L, F, W, N, Y, H, K, R, I, M, V, C, Q, or E,

$X_{H2.12}$ is W, F, I, Y, L, R, V, M, H, N, C, Q, K, T, D, E, A, or S,

$X_{H2.13}$ is P, R, Q, C, T, I, W, F, K, L, Y, S, V, M, D, or H,

$X_{H2.14}$ is W, C, I, F, T, R, Y, L, Q, S, V, D, N, M, K, A, H, E, or G,

$X_{H2.15}$ is W, I, L, V, F, K, R, H, Y, or M,

$X_{H2.16}$ is W, F, C, T, L, R, N, Q, A, S, M, K, E, H, Y, or G,

$X_{H2.17}$ is P, G, T, M, C, E, or V,

and

vi, a P-CAD VH CDR3 sequence comprising $X_{H3.1}$-$X_{H3.2}$-$X_{H3.3}$-$X_{H3.4}$- $X_{H3.5}$-$X_{H3.6}$- $X_{H3.7}$-$X_{H3.8}$-$X_{H3.9}$, wherein

$X_{H3.1}$ is F, Y, I, R, W, or L,

$X_{H3.2}$ is F, I, C, M, W, Q, L, H, V, N, R, T, D, S, E, A, Y, or K,

$X_{H3.3}$ is H, W, C, I, S, L, T, F, Q, Y, V, A, M, K, N, G, D, or E,

$X_{H3.4}$ is Y, I, M, W, R, H, V, F, C, K, N, Q, L, D, T, S, A, or E,

$X_{H3.5}$ is W, L, V, I, P, C, Y, M, H, T, N, F, D, A, or S,

$X_{H3.6}$ is F, W, C, H, N, R, Y, L, A, Q, E, M, T, I, S, K, or D,

$X_{H3.7}$ is Y, F, or W,

$X_{H3.8}$ is W, F, Y, I, L, Q, R, H, M, N, V, C, T, K, E, D, S, A, P, or G,

$X_{H3.9}$ is W, Y, F, R, I, L, C, V, H, N, K, T, Q, M, or D;

c. the sub-Domain 1A and the sub-Domain 1B are linked by a glycine-serine linker, Linker 1, and the sub-Domain 2B and the sub-Domain 2A are linked by a glycine-serine linker , Linker 1;

d. the first heterodimer-promoting domain comprises a cysteine linker, Linker 2, on sub-Domain 1B and/or the second heterodimer-promoting domain comprises a cysteine linker, Linker 2, on sub-Domain 2A; and

e. the first and second polypeptide chains are covalently bonded to one another by at least one disulfide bond.

20. The bispecific heterodimer diabody of claim 19, wherein $X_{L3.3}$ is W, $X_{H1.8}$ is G, $X_{H2.5}$ is Y, $X_{H3.1}$ is I, and $X_{H3.7}$ is F.

21. The bispecific heterodimer diabody of claim 19, wherein $X_{L3.3}$ is W, $X_{H2.5}$ is Y, $X_{H3.1}$ is I, $X_{H3.7}$ is F, $X_{L1.8}$ is G, $X_{L2.2}$ is N, $X_{L2.3}$ is N, $X_{L3.2}$ is T, $X_{H2.6}$ is N, $X_{H2.16}$ is Q, $X_{H3.5}$ is N and $X_{H3.9}$ is I.

22. The bispecific heterodimeric diabody of any one of claims 19, 20 or 21, comprising:

a. a P-CAD VL CDR1, a P-CAD VL CDR2, and a P-CAD VL CDR3 of a P-CAD VL comprising a sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 or 23;
b. a CD3 VH CDR1, a CD3 VH CDR2, and a CD3 VH CDR3 of a CD3 VH comprising a sequence of SEQ ID NOS: 45 or 46;
c. a CD3 VL CDR1, a CD3 VL CDR2, and a CD3 VL CDR3 of a CD3 VL comprising a sequence of SEQ ID NO: 47; and/or
d. a P-CAD VH CDR1, a P-CAD VH CDR2, and a P-CAD VH CDR3 of a P-CAD VH comprising a sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24.

23. The bispecific heterodimeric diabody of any one of claims 1 to 18 or 22, wherein:

a. the P-CAD VL CDR1 comprises a sequence of SEQ ID NOS: 35 or 36, the P-CAD VL CDR2 comprises a sequence of SEQ ID NOS: 37 or 38, and the P-CAD VL CDR3 comprises a sequence of SEQ ID NOS: 39, 40, 41, 42, 43 or 44;
b. the CD3 VH CDR1 comprises a sequence of SEQ ID NOS: 48, 52 or 53, the CD3 VH CDR2 comprises a sequence of SEQ ID NOS: 49, 50 or 54, and the CD3 VH CDR3 comprises a sequence of SEQ ID NO: 51;
c. the CD3 VL CDR1 comprises a sequence of SEQ ID NO: 55, the CD3 VL CDR2 comprises a sequence of SEQ ID NO: 56, and the CD3 VL CDR3 comprises a sequence of SEQ ID NO: 57; and/or

d. the P-CAD VH CDR1 comprises a sequence of SEQ ID NOS: 25 or 33, the P-CAD VH CDR2 comprises a sequence of SEQ ID NOS: 26 or 34, and a P-CAD VH CDR3 comprising a sequence of SEQ ID NOS: 27, 28, 29, 30, 31 or 32.

24. The bispecific heterodimeric diabody of claims 22 or claim 23, wherein the P-CAD VL CDR1 comprises the sequence of SEQ ID NO: 35, the P-CAD VL CDR2 comprises the sequence of SEQ ID NO: 37, the P-CAD VL CDR3 comprises the sequence of SEQ ID NO: 41, the P-CAD VH CDR1 comprises the sequence of SEQ ID NO: 25, the P-CAD VH CDR2 comprises the sequence of SEQ ID NO: 26, and the P-CAD VH CDR3 comprises the sequence of SEQ ID NO: 28.

25. The bispecific heterodimeric diabody of claim 22 or claim 23 wherein the P-CAD VL CDR1 comprises the sequence of SEQ ID NO: 35; the P-CAD VL CDR2 comprises the sequence of SEQ ID NO: 37; and the P-CAD VL CDR3 comprises the sequence of SEQ ID NO: 42, the P-CAD VH CDR1 comprises the sequence of SEQ ID NO: 25, the P-CAD VH CDR2 comprises the sequence of SEQ ID NO: 26, and the P-CAD VH CDR3 comprises the sequence of SEQ ID NO: 29.

26. The bispecific heterodimeric diabody of claim 22 or claim 23 wherein the P-CAD VL CDR1 comprises the sequence of SEQ ID NO: 35; the P-CAD VL CDR2 comprises the sequence of SEQ ID NO: 37, the P-CAD VL CDR3 comprises the sequence of SEQ ID NO: 43, the P-CAD VH CDR1 comprises the sequence of SEQ ID NO: 25, the P-CAD VH CDR2 comprises the sequence of SEQ ID NO: 26, and the P-CAD VH CDR3 comprises the sequence of SEQ ID NO: 30.

27. The bispecific heterodimeric diabody of claim 22 or claim 23, wherein the P-CAD VL CDR1 comprises the sequence of SEQ ID NO: 35; the P-CAD VL CDR2 comprises the sequence of SEQ ID NO: 37, the P-CAD VL CDR3 comprises the sequence of SEQ ID NO: 39, the P-CAD VH CDR1 comprises the sequence of SEQ ID NO: 25, the P-CAD VH CDR2 comprises the sequence of SEQ ID NO: 26, and the P-CAD VH CDR3 comprises the sequence of SEQ ID NO: 31.

28. The bispecific heterodimeric diabody of any one of claims 1 to 18, 22 to 27, wherein:

a) the P-CAD VL comprises a sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 or 23;
b) the CD3 VH comprises a sequence of SEQ ID NOS: 45 or 46;
c) the CD3 VL comprises the sequence of SEQ ID NO: 47; and
d) the P-CAD VH comprises a sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24.

29. The bispecific heterodimeric diabody of claim 28, wherein the P-CAD VL comprises the sequence of SEQ ID NO: 5, and the P-CAD VH comprises the sequence of SEQ ID NO: 6.

30. The bispecific heterodimeric diabody of claim 28, wherein the P-CAD VL comprises the sequence of SEQ ID NO: 7, and the P-CAD VH comprises the sequence of SEQ ID NO: 8.

31. The bispecific heterodimeric diabody of claim 28, wherein the P-CAD VL comprises the sequence of SEQ ID NO: 9 and the P-CAD VH comprises the sequence of SEQ ID NO: 10.

32. The bispecific heterodimeric diabody of claim 28, wherein the P-CAD VL comprises the sequence of SEQ ID NO: 15 and the P-CAD VH comprises the sequence of SEQ ID NO: 16.

33. A bispecific heterodimeric diabody that specifically binds to an epitope of human P-cadherin and to an epitope of CD3 comprising a first polypeptide chain and a second polypeptide chain, wherein the first polypeptide chain comprises a sequence of SEQ ID NO: 90 and the second polypeptide chain comprises a sequence of SEQ ID NO: 91.

34. A pharmaceutical composition comprising a therapeutically effective amount of the bispecific heterodimeric diabody of any one of claims 1 to 33 and a pharmaceutically acceptable carrier.

35. A bispecific heterodimeric diabody of any one of claims 1 to 33 or pharmaceutical composition of claim 34 for use in the treatment of a P-cadherin associated disorder.

36. The use of a bispecific heterodimeric diabody of any one of claims 1 to 33 or pharmaceutical composition of claim 34 in the manufacture of a medicament for the treatment of a P-cadherin associated disorder, wherein the P-cadherin associated disorder is cancer.

37. The use of claim 36, wherein the cancer is selected from the group consisting of breast, colorectal, ovarian, gastric, thyroid, prostate, cervical, pancreatic, lung, bladder, liver, endometrial, head and neck, testicular, and glioblastoma cancer.

38. The bispecific heterodimeric diabody of claim 35 or the use of claim 36, wherein upon administration, a cytolytic T cell response is activated.

39. The bispecific heterodimeric diabody of any one of claims 1 to 33 for use in therapy.

40. The bispecific heterodimeric diabody for the use of claim 39, wherein the therapy once provided, activates a cytolytic T cell response.

41. An isolated host cell that recombinantly produces the bispecific heterodimeric diabody of any one of claims 1 to 33.

42. An isolated polynucleotide comprising a nucleotide sequence encoding the bispecific heterodimeric diabody of any one of claims 1 to 33.

43. A vector comprising the polynucleotide of claim 42.

44. A method of producing a bispecific heterodimeric diabody, comprising culturing the host cell of claim 41 under conditions that result in production of the bispecific heterodimeric diabody, and purifying the bispecific heterodimeric diabody from the culture supernatant.

45. The bispecific heterodimeric diabody of any one of claims 1-33, wherein a crystal structure assembles into a compact spherical structure stabilized by a disulfide linkage between a pair of cysteine residues comprising a cysteine residue at position 239 (Cys^{239}) of sub-Domain 1B and a cysteine residue at position 246 (Cys^{246}) of sub-Domain 2A; and, wherein the crystal diffracts X-rays for determination of atomic coordinates to provide resolution of better than about 2.0 Angstroms.

46. An antibody that binds to P-cadherin, comprising:

i. P-CAD VL CDR1 sequence comprising $X_{L1.1}$-$X_{L1.2}$-$X_{L1.3}$-$X_{L1.4}$- $XL_{1.5}$- $X_{L1.6}$-$X_{L1.7}$-$X_{L1.8}$- $X_{L1.9}$-$X_{L1.10}$- $X_{L1.11}$-$X_{L1.2}$-$X_{L1.13}$, wherein

$X_{L1.1}$ is W, C, I, F, Y, T, H, N, M, Q, K, L, S, A, V, D, R, E, or G,

$X_{L1.2}$ is G,

$X_{L1.3}$ is R, Q, Y, L, K, F, M, N, W, C, I, T, V, S, E, A, H, D or G,

$X_{L1.4}$ is C, L, F, S, I, T, W, N, Y, V, D, A, K, Q, M, H, or R,

$X_{L1.5}$ is F, C, I, T, V, N, H, L, Y, S, R, Q, W, A, M, E, K, or D,

$X_{L1.6}$ is L, Q, F, M, N, C, K, H, or T,

$X_{L1.7}$ is I, Q, H, F, L, or V,

$X_{L1.8}$ is R, Q, L, T, G, C, E, D, M, Y, or S,

$X_{L1.9}$ is C, W, I, L, F, R, V, T, K, N, S, M, Q, Y, E, A, H, or D,

$X_{L1.10}$ is Q, F, N, L, C, Y, H, R, W, or M,

$X_{L1.11}$ is M, H, K, V, Q, L, Y, C, I, N, F, T, S, E, or W,

$X_{L1.12}$ is I, N, V, L, C, or T,

$X_{L1.13}$ is W, R, F, K, I, H, V, C, T, L, N, M, Q, Y, S, A, D, or E,

ii. a P-CAD VL CDR2 sequence comprising $X_{L2.1}$-$X_{L2.2}$-$X_{L2.3}$-$X_{L2.4}$-$X_{L2.5}$-$X_{L2.6}$- $X_{L2.7}$, wherein

$X_{L2.1}$ is I, L, V, F, Y, W, C, R, Q, N, M, H, E, T, P, K, D, S, A, or G,

$X_{L2.2}$ is W, L, F, I, C, N, R, V, Q, Y, E, D, H, or M,

$X_{L2.3}$ is C, Q, L, F, Y, W, E, R, M, H, A, N, T, K, D, S, I, V, or G,

$X_{L2.4}$ is R, K, I, L, C, Q, V, W, Y, M, F, or H,

$X_{L2.5}$ is R, Q, L, W, K, or H,

$X_{L2.6}$ is R, K, I, W, F, L, Q, C, M, Y, H, V, N, T, A, E, S, P, or D,

$X_{L2.7}$ is C, L, I, T, S, K, M, R, V, F, P, A, W, Q, D, N, G, or Y,

iii, a P-CAD VL CDR3 $X_{L3.1}$-$X_{L3.2}$-$X_{L3.3}$-$X_{L3.4}$-$X_{L3.5}$-$X_{L3.6}$- $X_{L3.7}$- $X_{L3.8}$-$X_{L3.9}$-$X_{L3.10}$- $X_{L3.11}$, wherein

$X_{L3.1}$ is W, R, Y, F, L, N, Q, C, M, I, H, T, A, D, E, S, K, V, or G,

$X_{L3.2}$ is N, C, V, T, S, or A,

$X_{L3.3}$ is W,

$X_{L3.4}$ is F, N, D, E, H, Q, Y, R, or W,

$X_{L3.5}$ is T, I, R, L, C, F, Y, W, Q, M, H, E, N, V, S, D, K, or A,

$X_{L3.6}$ is I, H, C, M, N, L, V, Q, E, S, T, A, K, D, F, Y, G, R, or W,

$X_{L3.7}$ is L, C, R, I, H, Q, E, T, V, M, K, F, or Y,

$X_{L3.8}$ is W, L, C, F, T, N, V, Y, I, M, H, Q, S, K, E, D, A, R, or G,

$X_{L3.9}$ is L, Y, Q, F, H, I, C, R, M, N, D, W, E, K, T, V, A, S, or G,

$X_{L3.10}$ is I, F, K, L, H, Y, M, V, Q, W, T, N, or C,

$X_{L3.11}$ is Q, W, R, F, T, C, Y, V, E, L, N, I, K, or M,

iv. a P-CAD VH CDR1 sequence comprising $X_{H1.1}$-$X_{H1.2}$-$X_{H1.3}$-$X_{H1.4}$- $X_{H1.5}$_$X_{H1.6}$-$X_{H1.7}$-$X_{H1.8}$-$X_{H1.9}$- $X_{H1.10}$ or $X_{H1.5}$, $X_{H1.6}$-$X_{H1.7}$-$X_{H1.8}$-$X_{H1.9}$- $X_{H1.10}$, wherein

$X_{H1.1}$ is R, Q, I, L, C, F, T, G, V, W, M, Y, N, E, P, K, H, D, S, or A,

$X_{H1.2}$ is H, R, C, Q, Y, I, F, K, M, V, L, N, or T,

$X_{H1.3}$ is N, C, R, V, L, T, I, S, K, Q, M, W, A, F, Y, H, or D,

$X_{H1.4}$ is F or Y,

$X_{H1.5}$ is W, R, I, C, K, Y, M, V, F, T, S, L, Q, E, A, N, H, D, or G,

$X_{H1.6}$ is R, I, M, N, Y, C, H, Q, L, K, F, V, T, E, A, S, D, W, or G,

$X_{H1.7}$ is K, R, L, H, F, Q, N, C, Y, M, I, T, V, or A,

$X_{H1.8}$ is P, R, F, W, H, C, Y, I, M, K, G, S, Q, A, L, N, T, or D,

$X_{H1.9}$ is Y, F, K, I, W, or L,

$X_{H1.10}$ is R, C, L, N, S, V, T, or A,

v.a P-CAD VH CDR2 sequence comprising $X_{H2.1}$-$X_{H2.2}$-$X_{H2.3}$-$X_{H2.4}$- $X_{H2.5}$-$X_{H2.6}$- $X_{H2.7}$-$X_{H2.8}$-$X_{H2.9}$-$X_{H2.10}$ or $X_{H2.1}$-$X_{H2.2}$-$X_{H2.3}$-$X_{H2.4}$- $X_{H2.5}$-$X_{H2.6}$- $X_{H2.7}$-$X_{H2.8}$-$X_{H2.9}$-$X_{H2.10}$-$X_{H2.11}$-$X_{H2.12}$-$X_{H2.13}$-$X_{H2.14}$-$X_{H2.15}$-$X_{H2.16}$-$X_{H2.17}$, wherein

$X_{H2,1}$ is W,

$X_{H2.2}$ is W, F, Y, I, V, H, L, or Q,

$X_{H2.3}$ is W, F, L, R, C, H, T, N, Y, Q, K, A, I, V, S, M, E, or D,

$X_{H2.4}$ is I, Y, V, Q, F, H, K, C, N, T, E, L, M, D, P, S, A, or W,

$X_{H2.5}$ is C, P, T, S, L, V, M, F, W, Q, K, G, I, A, N, H, E, D, Y, or R,

$X_{H2.6}$ is I, Q, W, V, C, L, K, E, T, M, F, Y, R, S, A, N, H, D, or G,

$X_{H2.7}$ is G, C, L, N, W, F, S, Y, T, D, I, or M,

$X_{H2.8}$ is Q, C, I, Y, W, L, T, V, K, M, H, F, S, R, A, E, N, D, or G,

$X_{H2.9}$ is F, L, V, W, H, C, Y, K, I, Q, R, T, M, N, A, S, or D,

$X_{H2.10}$ is R, W, K, F, C, T, L, Y, N, Q, V, H, M, A, S, or D,

$X_{H2.11}$ is L, F, W, N, Y, H, K, R, I, M, V, C, Q, or E,

$X_{H2.12}$ is W, F, I, Y, L, R, V, M, H, N, C, Q, K, T, D, E, A, or S,

$X_{H2.13}$ is P, R, Q, C, T, I, W, F, K, L, Y, S, V, M, D, or H,

$X_{H2.14}$ is W, C, I, F, T, R, Y, L, Q, S, V, D, N, M, K, A, H, E, or G,

$X_{H2.15}$ is W, I, L, V, F, K, R, H, Y, or M,

$X_{H2.16}$ is W, F, C, T, L, R, N, Q, A, S, M, K, E, H, Y, or G,

$X_{H2.17}$ is P, G, T, M, C, E, or V,

and

vi, a P-CAD VH CDR3 sequence comprising $X_{H3.1}$-$X_{H3.2}$-$X_{H3.3}$-$X_{H3.4}$- $X_{H3.5}$-$X_{H3.6}$- $X_{H3.7}$-$X_{H3.8}$-$X_{H3.9}$, wherein

$X_{H3.1}$ is F, Y, I, R, W, or L,

$X_{H3.2}$ is F, I, C, M, W, Q, L, H, V, N, R, T, D, S, E, A, Y, or K,

$X_{H3.3}$ is H, W, C, I, S, L, T, F, Q, Y, V, A, M, K, N, G, D, or E,

$X_{H3.4}$ is Y, I, M, W, R, H, V, F, C, K, N, Q, L, D, T, S, A, or E,

$X_{H3.5}$ is W, L, V, I, P, C, Y, M, H, T, N, F, D, A, or S,

$X_{H3.6}$ is F, W, C, H, N, R, Y, L, A, Q, E, M, T, I, S, K, or D,

$X_{H3.7}$ is Y, F, or W,

$X_{H3.8}$ is W, F, Y, I, L, Q, R, H, M, N, V, C, T, K, E, D, S, A, P, or G,

$X_{H3.9}$ is W, Y, F, R, I, L, C, V, H, N, K, T, Q, M, or D.

47. The antibody of claim 46, wherein $X_{L1.8}$ is G, $X_{L2.2}$ is N, $X_{L2.3}$ is N, $X_{L3.2}$ is T, $X_{H2.6}$ is N, $X_{H2.16}$ is Q, $X_{H3.5}$ is N and $X_{H3.9}$ is I.

48. The antibody of claim 46 or claim 47, comprising a P-CAD VL CDR1, a P-CAD VL CDR2, and a P-CAD VL CDR3 of a light chain variable region comprising the sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 or 23 and/or a P-CAD VH CDR1, a P-CAD VH CDR2, and a P-CAD VH CDR3 of a heavy chain variable region comprising the sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24.

49. The antibody of any one of claims 46 to 48, comprising:

a. a P-CAD VL CDR1 comprising the sequence of SEQ ID NO: 35 or 36,
b. a P-CAD VLCDR2 comprising the sequence of SEQ ID NO: 37 or 38,
c. a P-CAD VL CDR3 comprising the sequence of SEQ ID NO: 39, 40, 41, 42, 43 or 44,
d. a P-CAD VH CDR1 comprising the sequence of SEQ ID NO: 25 or 33,
e. a P-CAD VH CDR2 comprising the sequence of SEQ ID NO: 26 or 34, and
f. a P-CAD VH CDR3 comprising the sequence of SEQ ID NO: 27, 28, 29, 30, 31 or 32.

50. The antibody of any one of claims 46 to 49, comprising:

a. a P-CAD VL CDR1 comprising the sequence of SEQ ID NO: 35 or 36,
b. a P-CAD VL CDR2 comprising the sequence of SEQ ID NO: 37 or 38,

c. a P-CAD VL CDR3 comprising the sequence of SEQ ID NO: 39, 40, 41, 42, 43 or 44,
d. a P-CAD VH CDR1 comprising the sequence of SEQ ID NO: 25,
e. a P-CAD VH CDR2 comprising the sequence of SEQ ID NO: 26, and
f. a P-CAD VH CDR3 comprising the sequence of SEQ ID NO: 27, 28, 29, 30, 31 or 32.

51. The antibody of any one of claims 46 to 50, comprising:
a. a P-CAD VL CDR1 comprising the sequence of SEQ ID NO: 35,
b. a P-CAD VL CDR2 comprising the sequence of SEQ ID NO: 37,
c. a P-CAD VL CDR3 comprising the sequence of SEQ ID NO: 42,
d. a P-CAD VH CDR1 comprising the sequence of SEQ ID NO: 25,
e. a P-CAD VH CDR2 comprising the sequence of SEQ ID NO: 26, and
f. a P-CAD VH CDR3 comprising the sequence of SEQ ID NO: 29.

52. The antibody of any one of claims 46 to 51, comprising a light chain variable region comprising the sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 and 23, and/or a heavy chain variable region comprising the sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24.

53. The antibody of claim 52, comprising a light chain variable region amino acid comprising the sequence of SEQ ID NO: 5, and/or a heavy chain variable region comprising the sequence of SEQ ID NO: 6.

54. The antibody of claim 52, comprising a light chain variable region comprising the sequence of SEQ ID NO: 7, and/or a heavy chain variable region comprising the sequence of SEQ ID NO: 8.

55. The antibody of claim 52, comprising a light chain variable region comprising the sequence of SEQ ID NO: 9 and/or a heavy chain variable region comprising the sequence of SEQ ID NO: 10.

56. The antibody of claim 52, comprising a light chain variable region comprising the sequence of SEQ ID NO: 15 and/or a heavy chain variable region comprising the sequence of SEQ ID NO: 16.

57. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of any one of claims 46 to 56 and a pharmaceutically acceptable carrier.

58. Use of an antibody according to any one of claims 46 to 56 or a pharmaceutical composition of claim 57 in the manufacture of a medicament for the treatment of P-cadherin positive cancer.

59. The antibody of any one of claims 46 to 56 for use in therapy.

60. The use of an antibody of claim 58, wherein the P-cadherin associated positive cancer is selected from the group consisting of breast, colorectal, ovarian, gastric, thyroid, prostate, cervical, pancreatic, lung, bladder, liver, endometrial, head and neck, testicular, and glioblastoma cancer.

61. A nucleic acid that encodes the antibody according to any one of claims 46 to 56.

62. A vector comprising the nucleic acid of claim 61.

63. A host cell comprising the vector of claim 62.