Claims

1. A nucleic acid encoding a bispecific antibody construct comprising a first binding domain which binds to human delta-like 3 (DLL3) on the surface of a target cell and a second binding domain which binds to human and macaque CD3 on the surface of a T cell, wherein the first binding domain binds to an epitope of DLL3 within the amino acid sequence of SEQ ID NO: 258.

2. The nucleic acid of claim 1, wherein the first binding domain further binds to macaque DLL3.

3. The nucleic acid of claim 2, wherein the macaque DLL3 is *Macaca fascicularis* DLL3.

4. The nucleic acid of claim 1, wherein the second binding domain binds to human CD3 epsilon and to *Callithrix jacchus*, *Saguinus Oedipus* or *Saimiri sciureus* CD3 epsilon.

5. The nucleic acid of claim 1, wherein the antibody construct is in a format selected from the group consisting of: (scFv)2, diabodies and oligomers of the foregoing formats.

6. The nucleic acid of claim 1, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of:
   a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 31, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 32, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 33, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 34, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 35, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 36;
   b) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 41, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 42, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 43, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 44, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 46;
   c) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 51, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 52, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 53, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 54, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 55, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 56;
   d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 61, CDR-H2

comprising the amino acid sequence of SEQ ID NO: 62, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 63, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 64, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 65, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 66;

e) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 71, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 72, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 73, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 74, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 75, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 76;

f) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 81, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 82, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 83, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 84, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 85, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 86;

g) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 91, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 92, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 93, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 94, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 95, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 96;

h) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 101, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 102, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 103, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 104, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 105, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 106; and

i) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 111, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 112, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 113, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 114, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 115, and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 116.

7. The nucleic acid of claim 6, wherein the first binding domain comprises a VL region comprising CDR-H1, CDR-H2 and CDR-H3 and a VH region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of:

a) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 342, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 343, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 344; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 345, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 346, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 347;

b) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 351, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 352, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 353; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 354, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 355, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 356;

c) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 360, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 361, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 362; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 363, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 364, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 365;

d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 369, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 370, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 371; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 372, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 373, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 374;

e) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 378, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 379, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 380; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 381, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 382, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 383;

f) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 387, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 388, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 389; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 392;

g) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 397, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 398; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 399, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 400, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 401;

h) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 405, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 406, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 407; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 408, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 409, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 410; and

i) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 414, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 415, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 416; CDR-H1 comprising the amino acid sequence of

SEQ ID NO: 417, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 418, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 419; and

j) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.

8. The nucleic acid of claim 6, wherein the second binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 348, SEQ ID NO: 357, SEQ ID NO: 366, SEQ ID NO: 375, SEQ ID NO: 384, SEQ ID NO: 393, SEQ ID NO: 402, SEQ ID NO: 411, SEQ ID NO: 420, and SEQ ID NO: 429.

9. The nucleic acid of claim 6, wherein the second binding domain comprises a VL region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 349, SEQ ID NO: 358, SEQ ID NO: 367, SEQ ID NO: 376, SEQ ID NO: 385, SEQ ID NO: 394, SEQ ID NO: 403, SEQ ID NO: 412, SEQ ID NO: 421, and SEQ ID NO: 430.

10. The nucleic acid of claim 6, wherein the second binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences, respectively, selected from the group consisting of: SEQ ID NOs: 348 and 349; SEQ ID NOs: 357 and 358; SEQ ID NOs: 366 and 367; SEQ ID NOs: 375 and 376; SEQ ID NOs: 384 and 385; SEQ ID NOs: 393 and 394; SEQ ID NOs: 402 and 403; SEQ ID NOs: 411 and 412; SEQ ID NOs: 420 and 421; and SEQ ID NOs: 429 and 430.

11. The nucleic acid of claim 6, wherein the second binding domain comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 350, SEQ ID NO: 359, SEQ ID NO: 368, SEQ ID NO: 377, SEQ ID NO: 386, SEQ ID NO: 395, SEQ ID NO: 404, SEQ ID NO: 413, SEQ ID NO: 422, and SEQ ID NO: 431.

12. The nucleic acid of claim 6, wherein the first binding domain comprises a VH region comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 31, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 32, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 33, and a VL region comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 36, and wherein the second binding domain comprises a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423,

a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425, and a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.

13. The nucleic acid of claim 12, wherein the first binding domain comprises a VH region comprising the amino acid sequence of SEQ ID NO: 435 and a VL region comprising the amino acid sequence of SEQ ID NO: 436, and wherein the second binding domain comprises a VH region comprising the amino acid sequence of SEQ ID NO: 429 and a VL region comprising the amino acid sequence of SEQ ID NO: 430.

14. The nucleic acid of claim 13, wherein the first binding domain comprises the amino acid sequence of SEQ ID NO: 437, and wherein the second binding domain comprises the amino acid sequence of SEQ ID NO: 431.

15. The nucleic acid of claim 1, wherein the first binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 37, SEQ ID NO: 47, SEQ ID NO: 57, SEQ ID NO: 67, SEQ ID NO: 77, SEQ ID NO: 87, SEQ ID NO: 97, SEQ ID NO: 107, SEQ ID NO: 117, SEQ ID NO: 435, and SEQ ID NO: 529.

16. The nucleic acid of claim 1, wherein the first binding domain comprises a VL region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 38, SEQ ID NO: 48, SEQ ID NO: 58, SEQ ID NO: 68, SEQ ID NO: 78, SEQ ID NO: 88, SEQ ID NO: 98, SEQ ID NO: 108, SEQ ID NO: 118, SEQ ID NO: 436, and SEQ ID NO: 530.

17. The nucleic acid of claim 1, wherein the first binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences, respectively, selected from the group consisting of: SEQ ID NOs: 37+38; SEQ ID NOs: 47+48; SEQ ID NOs: 57+58; SEQ ID NOs: 67+68; SEQ ID NOs: 77+78; SEQ ID NOs: 87+88; SEQ ID NOs: 97+98; SEQ ID NOs: 107+108; SEQ ID NOs: 117+118; SEQ ID NOs: 435+436; and SEQ ID NOs: 529+530.

18. The nucleic acid of claim 1, wherein the first binding domain comprises a polypeptide comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 39, SEQ ID NO: 49, SEQ ID NO: 59, SEQ ID NO: 69, SEQ ID NO: 79, SEQ ID NO: 89,

SEQ ID NO: 99, SEQ ID NO: 109, SEQ ID NO: 119, SEQ ID NO: 437, and SEQ ID 531.

19. The nucleic acid of claim 1, wherein the nucleic acid comprises a nucleotide sequence encoding a polypeptide comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 40, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 70, SEQ ID NO: 80, SEQ ID NO: 90, SEQ ID NO: 100, SEQ ID NO: 110, SEQ ID NO: 120, SEQ ID NO: 211, SEQ ID NO: 212, SEQ ID NO: 213, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 216, SEQ ID NO: 217, SEQ ID NO: 438, and SEQ ID NO: 532.

20. The nucleic acid of claim 1, wherein the nucleic acid comprises a nucleotide sequence encoding a polypeptide comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 517, SEQ ID NO: 518, SEQ ID NO: 519, SEQ ID NO: 520, SEQ ID NO: 521, SEQ ID NO: 522, SEQ ID NO: 523, and SEQ ID NO: 524.

21. A vector comprising the nucleic acid of claim 1.

22. An isolated host cell transformed or transfected with the vector of claim 21.

23. A process for producing a bispecific antibody construct comprising culturing the host cell of claim 22 under conditions allowing the expression of the antibody construct and, optionally, recovering the antibody construct from the culture.

24. An isolated host cell transformed or transfected with the nucleic acid of claim 1.