

CLAIMS

1. An anti-CD93 construct comprising an antibody moiety comprising a heavy chain variable region (V_H) and a light chain variable region (V_L), wherein the antibody moiety competes for a binding epitope of CD93 with an antibody or antibody fragment comprising a second heavy chain variable region (V_{H-2}) and a second light chain variable region (V_{L-2}), wherein:

the V_{H-2} comprises the HC-CDR1 comprising the amino acid sequence of SEQ ID NO: 289, the HC-CDR2 comprising the amino acid sequence of SEQ ID NO: 290, and the HC-CDR3 comprising the amino acid sequence of SEQ ID NO: 291, and the V_{L-2} comprises the LC-CDR1 comprising the amino acid sequence of SEQ ID NO: 292, the LC-CDR2 comprising the amino acid sequence of SEQ ID NO: 293, and the LC-CDR3 comprising the amino acid sequence of SEQ ID NO: 294.

2. The anti-CD93 construct of claim 1, wherein:

the V_H comprises the HC-CDR1 comprising the amino acid sequence of SEQ ID NO: 289, the HC-CDR2 comprising the amino acid sequence of SEQ ID NO: 290, and the HC-CDR3 comprising the amino acid sequence of SEQ ID NO: 291, or a variant thereof comprising up to 5, 4, 3, 2, or 1 amino acid substitutions in the HC-CDRs; and the V_L comprises the LC-CDR1 comprising the amino acid sequence of SEQ ID NO: 292, the LC-CDR2 comprising the amino acid sequence of SEQ ID NO: 293, and the LC-CDR3 comprising the amino acid sequence of SEQ ID NO: 294, or a variant thereof comprising up to 5, 4, 3, 2, or 1 amino acid substitutions in the LC-CDRs.

3. The anti-CD93 construct of claim 1, wherein:

the V_H comprises the HC-CDR1 comprising the amino acid sequence of SEQ ID NO: 289, the HC-CDR2 comprising the amino acid sequence of SEQ ID NO: 290, and the HC-CDR3 comprising the amino acid sequence of SEQ ID NO: 291; and the V_L comprises the LC-CDR1 comprising the amino acid sequence of SEQ ID NO: 292, the LC-CDR2 comprising the amino acid sequence of SEQ ID NO: 293, and the LC-CDR3 comprising the amino acid sequence of SEQ ID NO: 294.

4. An anti-CD93 construct comprising an antibody moiety that specifically binds to CD93, comprising:

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 V_H chain region having the sequence set forth in any of SEQ ID NO: 287 and 319-321, and 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 V_L chain region having the sequence set forth in any of SEQ ID NO: 288 and 322-324.

5. The anti-CD93 construct of any one of claims 1-4, wherein:

the V_H comprises an amino acid sequence of SEQ ID NO: 287 and 319-321 or a variant comprising an amino acid sequence having at least about 80% sequence identity; and/or wherein the V_L comprises an amino acid sequence of SEQ ID NO: 288 and 322-324, or a variant comprising an amino acid sequence having at least about 80% sequence identity.

6. The anti-CD93 construct of any one of claims 1-5, wherein:

(a) the V_H comprises an amino acid sequence of SEQ ID NO: 287, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 288;

(b) the V_H comprises an amino acid sequence of SEQ ID NO: 287, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 322;

(c) the V_H comprises an amino acid sequence of SEQ ID NO: 287, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 323;

(d) the V_H comprises an amino acid sequence of SEQ ID NO: 287, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 324;

(e) the V_H comprises an amino acid sequence of SEQ ID NO: 319, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 288;

(f) the V_H comprises an amino acid sequence of SEQ ID NO: 319, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 322;

(g) the V_H comprises an amino acid sequence of SEQ ID NO: 319, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 323;

(h) the V_H comprises an amino acid sequence of SEQ ID NO: 319, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 324;

(i) the V_H comprises an amino acid sequence of SEQ ID NO: 320, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 288;

(j) the V_H comprises an amino acid sequence of SEQ ID NO: 320, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 322;

(k) the V_H comprises an amino acid sequence of SEQ ID NO: 320, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 323;

(l) the V_H comprises an amino acid sequence of SEQ ID NO: 320, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 324;

(m) the V_H comprises an amino acid sequence of SEQ ID NO: 321 and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 288;

(n) the V_H comprises an amino acid sequence of SEQ ID NO: 321, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 322;

(o) the V_H comprises an amino acid sequence of SEQ ID NO: 321, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 323;

(p) the V_H comprises an amino acid sequence of SEQ ID NO: 321, and wherein the V_L comprises an amino acid sequence of SEQ ID NO: 324.

7. The anti-CD93 construct of any one of claims 1-6, wherein the construct comprises a second moiety that binds to VEGF.

8. The anti-CD93 construct of claim 7, wherein the anti-CD93 antibody moiety is an anti-CD93 full-length antibody comprising two heavy chains and two light chains, and wherein the second moiety is fused to C-terminus of both of the heavy chains of the anti-CD93 full-length antibody.

9. The anti-CD93 construct of any one of claims 1-8, wherein the antibody moiety is an antibody or antigen-binding fragment thereof selected from the group consisting of a full-length antibody, a bispecific antibody, a single-chain Fv (scFv) fragment, a Fab fragment, a Fab' fragment, a F(ab')₂, an Fv fragment, a disulfide stabilized Fv fragment (dsFv), a (dsFv)₂, a Fv-Fc fusion, a scFv-Fc fusion, a scFv-Fv fusion, a diabody, a tribody, and a tetrabody.

10. The anti-CD93 construct of claim 9, wherein the antibody moiety is a full-length antibody.

11. The anti-CD93 construct of any one of claims 1-10, wherein the antibody moiety has an Fc fragment is selected from the group consisting of Fc fragments from IgG, IgA, IgD, IgE, IgM, and combinations and hybrids thereof.
12. The anti-CD93 construct of claim 11, wherein the Fc fragment is selected from the group consisting of Fc fragments from IgG1, IgG2, IgG3, IgG4, and combinations and hybrids thereof.
13. The anti-CD93 construct of claim 11 or claim 12, wherein the Fc fragment has:
 - a) a reduced effector function as compared to the corresponding wildtype Fc fragment; or
 - b) enhanced effector function as compared to the corresponding wildtype Fc fragment.
14. The anti-CD93 construct of any one of claims 1-13, wherein the antibody moiety blocks the binding of CD93 to IGFBP7 and/or MMRN2.
15. The anti-CD93 construct of any one of claims 1-10, wherein the CD93 is a human CD93.
16. A pharmaceutical composition comprising the anti-CD93 construct of any one of claims 1-15, and a pharmaceutical acceptable carrier.
17. An isolated nucleic acid encoding the anti-CD93 construct of any one of claims 1-15 or a portion thereof.
18. A vector comprising the isolated nucleic acid of claim 17.
19. An isolated host cell comprising the isolated nucleic acid of claim 17, or the vector of claim 18.
20. An immunoconjugate comprising the anti-CD93 construct of any one of claims 1-15, linked to a therapeutic agent or a label.
21. An effective amount of the anti-CD93 construct of any one of claims 1-15, or the pharmaceutical composition of claim 16 for use in treating a disease or condition in an individual.

22. Use of the anti-CD93 construct of any one of claims 1-15, or the pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a disease or condition in an individual.
23. The anti-CD93 construct or the pharmaceutical composition for use of claim 21 or the use of claim 22, wherein the disease or condition is associated with an abnormal vascular structure and/or the disease or condition is a cancer; and/or wherein the anti-CD93 construct is to be used parenterally and/or with a second therapy in treating the disease or condition.
24. The anti-CD93 construct or the pharmaceutical composition for use or the use of claim 23, wherein the cancer is a solid tumor; and/or wherein the cancer comprises CD93+ endothelial cells; and/or wherein the cancer comprises IGFBP7+ blood vessels and/or MMRN2+ blood vessels; and/or wherein the cancer is characterized by tumor hypoxia; and/or wherein the cancer is a locally advanced or metastatic cancer.
25. The anti-CD93 construct or the pharmaceutical composition for use or the use of claim 23 or claim 24, wherein the cancer is selected from the group consisting of a lymphoma, colon cancer, brain cancer, breast cancer, ovarian cancer, endometrial cancer, esophageal cancer, prostate cancer, cervical cancer, renal cancer, bladder cancer, gastric cancer, non-small cell lung cancer, melanoma, and pancreatic cancer.