

## CLAIMS

1. An isolated polynucleotide comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises:
  - (a) an extracellular domain comprising at least one antigen binding domain that specifically binds folate receptor 1 (FOLR1);
  - (b) a hinge region;
  - (c) a transmembrane region; and
  - (d) an intracellular signaling domain.
2. The isolated polynucleotide of claim 1, wherein the antigen binding domain comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequences of:
  - (1) SEQ ID NOs: 29, 30, 31, 53, 54 and 55, respectively, or SEQ ID NOs: 77, 78, 79, 101, 102 and 103, respectively;
  - (2) SEQ ID NOs: 17, 18, 19, 41, 42 and 43, respectively, or SEQ ID NOs: 65, 66, 67, 89, 90 and 91, respectively;
  - (3) SEQ ID NOs: 20, 21, 22, 44, 45 and 46, respectively, or SEQ ID NOs: 68, 69, 70, 92, 93 and 94, respectively;
  - (4) SEQ ID NOs: 23, 24, 25, 47, 48 and 49, respectively, or SEQ ID NOs: 71, 72, 73, 95, 96 and 97, respectively;
  - (5) SEQ ID NOs: 26, 27, 28, 50, 51 and 52, respectively, or SEQ ID NOs: 74, 75, 76, 98, 99 and 100, respectively;
  - (6) SEQ ID NOs: 32, 33, 34, 56, 57 and 58, respectively, or SEQ ID NOs: 80, 81, 82, 104, 105 and 106, respectively;
  - (7) SEQ ID NOs: 35, 36, 37, 59, 60 and 61, respectively, or SEQ ID NOs: 83, 84, 85, 107, 108 and 109, respectively; or
  - (8) SEQ ID NOs: 38, 39, 40, 62, 63 and 64, respectively, or SEQ ID NOs: 86, 87, 88, 110, 111 and 112, respectively;wherein the antigen binding domain specifically binds FOLR1, preferably human FOLR1.

3. The isolated polynucleotide of claim 1 or 2, wherein the antigen binding domain comprises a heavy chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 120, 9, 1, 3, 5, 7, 11, 13, 15, 113, 114, 115, 116, 119, 124, 125, 128, 129, 130, 136, 137, 138, 142, 143, 144, 148, 149, 150, 154, 155, 156, or 171-184, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 122, 10, 2, 4, 6, 8, 12, 14, 16, 117, 118, 121, 123, 126, 127, 131, 132, 133, 134, 139, 140, 141, 145, 146, 147, 151, 152, 153, 157, 158, or 185-198.

4. The isolated polynucleotide of any one of claims 1-3, wherein the antigen binding domain comprises:

- (1) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:120, and a light chain variable region having the polypeptide sequence of SEQ ID NO:122;
- (2) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:9, and a light chain variable region having the polypeptide sequence of SEQ ID NO:10;
- (3) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:1, and a light chain variable region having the polypeptide sequence of SEQ ID NO:2;
- (4) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:3, and a light chain variable region having the polypeptide sequence of SEQ ID NO:4;
- (5) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:5, and a light chain variable region having the polypeptide sequence of SEQ ID NO:6;
- (6) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:7, and a light chain variable region having the polypeptide sequence of SEQ ID NO:8;
- (7) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:11, and a light chain variable region having the polypeptide sequence of SEQ ID NO:12;
- (8) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:13, and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;
- (9) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:15, and a light chain variable region having the polypeptide sequence of SEQ ID NO:16;
- (10) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:113, and a light chain variable region having the polypeptide sequence of SEQ ID NO:117;

- (11) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:113,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:118;
- (12) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:114,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:117;
- (13) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:114,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:118;
- (14) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:115,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:117;
- (15) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:115,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:118;
- (16) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:116,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:117;
- (17) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:116,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:118;
- (18) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:119,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:121;
- (19) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:119,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:122;
- (20) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:119,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:123;

- (21) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:120,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:121;
- (22) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:120,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:123;
- (23) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:124,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:126;
- (24) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:124,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:127;
- (25) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:128,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:131;
- (26) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:128,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:132;
- (27) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:128,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:133;
- (28) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:128,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:134;
- (29) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:129,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:131;
- (30) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:129,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:132;

- (31) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:129,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:133;
- (32) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:129,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:134;
- (33) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:130,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:131;
- (34) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:130,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:132;
- (35) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:130,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:133;
- (36) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:130,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:134;
- (37) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:136,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:139;
- (38) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:136,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:140;
- (39) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:136,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:141;
- (40) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:137,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:139;

- (41) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:137,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:140;
- (42) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:137,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:141;
- (43) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:138,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:139;
- (44) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:138,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:140;
- (45) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:138,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:141;
- (46) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:142,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:145;
- (47) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:142,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:146;
- (48) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:142,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:147;
- (49) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:143,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:145;
- (50) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:143,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:146;

- (51) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:143,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:147;
- (52) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:144,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:145;
- (53) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:144,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:146;
- (54) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:144,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:147;
- (55) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:148,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:151;
- (56) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:150,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:153;
- (57) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:171,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:185;
- (58) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:171,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:186;
- (59) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:171,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:187;
- (60) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:185;

- (61) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:186;
- (62) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:187;
- (63) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:182,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:190;
- (64) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:195;
- (65) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:196;
- (66) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:197;
- (67) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:198;
- (68) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:195;
- (69) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:196;
- (70) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184,  
and a light chain variable region having the polypeptide sequence of SEQ ID  
NO:197; or

- (71) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184,  
and a light chain variable region having the polypeptide sequence of SEQ ID NO:198.
5. The isolated polynucleotide of any one of claims 1-4, wherein the antigen binding domain is a single chain variable fragment (scFv) that specifically binds FOLR1, preferably human FOLR1, optionally, wherein the single chain variable fragment (scFv) is humanized.
  6. The isolated polynucleotide of claim 5, wherein the single chain variable fragment (scFv) comprises a polypeptide sequence at least 95% identical to any one of SEQ ID NOs: 159-170.
  7. The isolated polynucleotide of any one of claims 1-6, wherein the chimeric antigen receptor (CAR) comprises one or more antigen binding domains, and/or wherein the intracellular signaling domain comprises one or more costimulatory domains and one or more activating domains.
  8. A chimeric antigen receptor (CAR) encoded by the isolated polynucleotide of any one of claims 1-7.
  9. A vector comprising the isolated polynucleotide of any one of claims 1-7.
  10. A host cell comprising the vector of claim 9, optionally, wherein the host cell is a T cell or NK cell, preferably a human T cell or human NK cell.
  11. A method of making a host cell expressing a chimeric antigen receptor (CAR), the method comprising transducing a T cell or NK cell with the vector of claim 9.
  12. A method of producing a chimeric antigen receptor (CAR)-T cell or a chimeric antigen receptor (CAR)-NK cell, the method comprising culturing T cells or NK cells comprising the isolated polynucleotide comprising a nucleic acid encoding a chimeric antigen receptor (CAR) of any one of claims 1-7 under conditions to produce the CAR-T cell or CAR-NK cell and recovering the CAR-T cell or CAR-NK cell.
  13. A method of generating a cell comprising a chimeric antigen receptor (CAR), the method comprising contacting a cell with the isolated polynucleotide comprising a nucleic acid encoding a chimeric antigen receptor (CAR) of any one of claims 1-7, wherein the isolated polynucleotide is an *in vitro* transcribed RNA or synthetic RNA.
  14. The host cell of claim 10 for use in a method of treating cancer in a subject in need thereof, wherein the host cell is to be administered to the subject in need thereof.
  15. Use of the host cell of claim 10 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to the subject.

16. The host cell for use of claim 14, or the use of claim 15, wherein the cancer is selected from a lung cancer, a gastric cancer, a colon cancer, a hepatocellular carcinoma, a renal cell carcinoma, a bladder urothelial carcinoma, a metastatic melanoma, a breast cancer, an ovarian cancer, a cervical cancer, a head and neck cancer, a pancreatic cancer, a glioma, a glioblastoma, and other solid tumors, and a non-Hodgkin's lymphoma (NHL), an acute lymphocytic leukemia (ALL), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a multiple myeloma (MM), an acute myeloid leukemia (AML), and other liquid tumors.

17. The host cell for use of claim 14 or 16, or the use of claim 15 or 16, further comprising an agent that increases the efficacy of a cell expressing a CAR, an agent that ameliorates one or more side effects associated with administration of a cell expressing a CAR, or an agent that treats the disease associated with FOLR1, to be administered to the subject in need thereof.

18. A humanized anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region having a polypeptide sequence at least 95% identical to any one of SEQ ID NO: 120, 113, 114, 115, 116, 119, 124, 125, 128, 129, 130, 136, 137, 138, 142, 143, 144, 148, 149, 150, 154, 155, 156 or 171-184, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 122, 117, 118, 121, 123, 126, 127, 131, 132, 133, 134, 139, 140, 141, 145, 146, 147, 151, 152, 153, 157, 158 or 185-198.

19. The humanized anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof of claim 18, wherein the antibody or antigen-binding fragment thereof comprises:

- (1) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:120, and a light chain variable region having the polypeptide sequence of SEQ ID NO:122;
- (2) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:113, and a light chain variable region having the polypeptide sequence of SEQ ID NO:117;
- (3) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:113, and a light chain variable region having the polypeptide sequence of SEQ ID NO:118;
- (4) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:114, and a light chain variable region having the polypeptide sequence of SEQ ID NO:117;
- (5) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:114, and a light chain variable region having the polypeptide sequence of SEQ ID NO:118;







- (51) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:171, and a light chain variable region having the polypeptide sequence of SEQ ID NO:187;
  - (52) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173, and a light chain variable region having the polypeptide sequence of SEQ ID NO:185;
  - (53) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173, and a light chain variable region having the polypeptide sequence of SEQ ID NO:186;
  - (54) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:173, and a light chain variable region having the polypeptide sequence of SEQ ID NO:187;
  - (55) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:182, and a light chain variable region having the polypeptide sequence of SEQ ID NO:190;
  - (56) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:195;
  - (57) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:196;
  - (58) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:197;
  - (59) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:198;
  - (60) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:195;
  - (61) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:196;
  - (62) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:197; or
  - (63) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:198.
20. The humanized anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof of claim 18 or 19, wherein the monoclonal antibody or antigen-binding fragment thereof is capable of binding FOLR1, inducing effector-mediated tumor cell lysis, mediating the recruitment of conjugated drugs, and/or forming a bispecific antibody with another monoclonal antibody or antigen-binding fragment with a cancer-killing effect.

21. An isolated nucleic acid encoding the anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20.
22. A vector comprising the isolated nucleic acid of claim 21.
23. A host cell comprising the vector of claim 22.
24. A pharmaceutical composition, comprising the anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20 and a pharmaceutically acceptable carrier.
25. The pharmaceutical composition of claim 24 for use in a method of targeting FOLR1 on a cancer cell surface or treating cancer in a subject in need thereof, wherein the composition is to be administered to the subject in need thereof.
26. Use of the pharmaceutical composition of claim 24 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to the subject in need thereof.
27. The pharmaceutical composition for use of claim 24, or the use of claim 26, wherein the cancer is selected from a lung cancer, a gastric cancer, a colon cancer, a hepatocellular carcinoma, a renal cell carcinoma, a bladder urothelial carcinoma, a metastatic melanoma, a breast cancer, an ovarian cancer, a cervical cancer, a head and neck cancer, a pancreatic cancer, a glioma, a glioblastoma, and other solid tumors, and a non-Hodgkin's lymphoma (NHL), an acute lymphocytic leukemia (ALL), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a multiple myeloma (MM), an acute myeloid leukemia (AML), and other liquid tumors.
28. A method of producing the anti-FOLR1 monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20, comprising culturing a cell comprising a nucleic acid encoding the monoclonal antibody or antigen-binding fragment under conditions to produce the monoclonal antibody or antigen-binding fragment, and recovering the antibody or antigen-binding fragment from the cell or culture.
29. A method of producing the pharmaceutical composition of claim 24, comprising combining the monoclonal antibody or antigen-binding fragment thereof with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.