

[0004] Folate receptor alpha (FolR α or FOLR1) is a glycosylphosphatidylinositol linked cell-surface glycoprotein that has high affinity for folates. Except for low levels in kidney and lung, most normal tissues do not express FOLR1, but high levels of FOLR1 have been found in serous and endometrioid epithelial ovarian cancer, endometrial adenocarcinoma, non-small cell lung carcinoma (NSCLC) of the adenocarcinoma subtype, and triple-negative breast cancer (TNBC). FOLR1 expression is maintained in metastatic foci and recurrent carcinomas in ovarian cancer patients, and FOLR1 expression has been observed after chemotherapy in epithelial ovarian and endometrial cancers. These properties, together with the highly restricted expression of FOLR1 on normal tissues, make FOLR1 a highly promising target for cancer therapy. As such, the folate receptor provides a potential target for diagnostics and therapeutics for cancers and inflammatory conditions. New antibodies are needed for specific binding and targeting of these folate receptors.

[0005] There is a need for improved methods of modulating the immune regulation of folate receptor alpha (FOLR1) and the downstream signaling processes activated by folate receptor alpha (FOLR1). Moreover, given the specific expression of folate receptor alpha (FOLR1) in cancer- and carcinoma-transformed cells and lower expression in non-cancer tissue, there is a need for improved therapeutics that can specifically target cells and tissues that overexpress folate receptor alpha (FOLR1). Antibody conjugates to FOLR1 could be used to deliver therapeutic or diagnostic payload moieties to target cells expressing folate receptor alpha for the treatment or diagnosis of such diseases.

SUMMARY

[0006] Provided herein are antibody conjugates that selectively bind folate receptor alpha (FOLR1). The antibody conjugates comprise an antibody that binds folate receptor alpha (FOLR1) linked to one or more payload moieties. The antibody can be linked to the payload directly by a covalent bond or indirectly by way of a linker. Folate receptor alpha (FOLR1) antibodies are described in detail herein, as are useful payload moieties, and useful linkers.

[0006a] In one aspect, provided is an antibody conjugate comprising an antibody that specifically binds to folate receptor alpha (FOLR1) linked site-specifically to at least one payload moiety, wherein the antibody comprises one or more non-natural amino acids at sites selected from the group consisting of: HC-F404, HC-K121, HC-Y180, HC-F241, HC-221, LC-T22, LC-S7, LC-N152, LC-K42, LC-E161, LC-D170, HC-S136, HC-S25, HC-A40, HC-

S119, HC-S190, HC-K222, HC-R19, HC-Y52, or HC-S70, according to the Kabat, Chothia, or EU numbering scheme.

[0006b] In another aspect, provided is a kit comprising an antibody conjugate as described herein, and instructions for use of the antibody conjugate.

[0006c] In another aspect, provided is a pharmaceutical composition comprising the antibody conjugate as described herein and a pharmaceutically acceptable carrier.

[0007] Provided are compositions comprising the antibody conjugates. In some examples, the compositions are pharmaceutical compositions. Any suitable pharmaceutical composition may be used. In some examples, the pharmaceutical

composition is a composition for parenteral administration. Provided herein are kits comprising the antibody conjugates or pharmaceutical compositions.

[0007a] In another aspect, provided is use of an antibody conjugate as described herein, or a pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease or condition in a subject in need thereof, wherein the disease or condition is a cancer.

[0007b] In another aspect, provided is use of an antibody conjugate as described herein, or a pharmaceutical composition as described herein in the manufacture of a medicament for diagnosing a disease or condition in a subject in need thereof, wherein the disease or condition is a cancer.

[0007c] In another aspect, provided is an antibody conjugate as described herein, or a pharmaceutical composition as described herein for use as a medicament.

[0008] Provide herein are methods of using the anti-FOLR1 antibody conjugates. In some examples, the methods are methods of delivering one or more payload moieties to a target cell or tissue expressing folate receptor alpha. In some examples, the methods are methods of treatment. In some examples, the methods are diagnostic methods. In some examples, the methods are analytical methods. In some examples, the antibody conjugates are used to treat a disease or condition. In some examples, the disease or condition is selected from a cancer, autoimmune disease, and infection.

[0009] In some examples, the antibody conjugates bind human folate receptor alpha. In some examples, the antibody conjugates also bind homologs of human folate receptor alpha. In some examples, the antibody conjugates also bind homologs of cynomolgus monkey and/or mouse folate receptor alpha.

BRIEF DESCRIPTION OF THE FIGURES

[0010] **FIG. 1** provides a comparison of the Kabat and Chothia numbering systems for CDR-H1. *Adapted from* Martin A.C.R. (2010). Protein Sequence and Structure Analysis of Antibody Variable Domains. In R. Kontermann & S. Dübel (Eds.), *Antibody Engineering* vol. 2 (pp. 33-51). Springer-Verlag, Berlin Heidelberg.

[0011] **FIGS. 2-4** provide alignments of the VH sequences (SEQ ID NOs: 308-366) from the variant antibodies provided herein. CDRs according to Chothia are highlighted, and CDRs according to Kabat are boxed.

[0012] **FIG. 5** provides alignments of the VL sequences (SEQ ID NOs: 367-369) from trastuzumab and the variant antibodies provided herein. CDRs according to Chothia are highlighted, and CDRs according to Kabat are underlined.

[0013] **FIG. 6** is a graph illustrating body weight change in mice implanted with KB cervical carcinoma cells after being administered a single dose of different FOLR1 antibody-drug conjugates as disclosed herein.

[0014] **FIG. 7 (A, B)** are graphs illustrating tumor growth curves and tumor size at day 25 in mice implanted with KB cervical carcinoma cells after being administered a single dose of different FOLR1 antibody-drug conjugates as disclosed herein.

WHAT IS CLAIMED IS:

1. An antibody conjugate comprising an antibody that specifically binds to folate receptor alpha (FOLR1) linked site-specifically to at least one payload moiety, wherein the antibody comprises one or more non-natural amino acids at sites selected from the group consisting of: HC-F404, HC-K121, HC-Y180, HC-F241, HC-221, LC-T22, LC-S7, LC-N152, LC-K42, LC-E161, LC-D170, HC-S136, HC-S25, HC-A40, HC-S119, HC-S190, HC-K222, HC-R19, HC-Y52, or HC-S70, according to the Kabat, Chothia, or EU numbering scheme.

2. The antibody conjugate of claim 1, wherein the one or more non-natural amino acids is selected from the group consisting of p-acetyl-L-phenylalanine, O-methyl-L-tyrosine, an -3-(2-naphthyl)alanine, 3-methyl-phenylalanine, O-4-allyl-L-tyrosine, 4-propyl-L-tyrosine, a tri-O-acetyl-GlcNAc β -serine, L-Dopa, fluorinated phenylalanine, isopropyl-L-phenylalanine, p-azido-L-phenylalanine, p-azido-methyl-L-phenylalanine, compound 56, p-acyl-L-phenylalanine, p-benzoyl-L-phenylalanine, L-phosphoserine, phosphoserine, phosphotyrosine, p-iodo-phenylalanine, p-bromophenylalanine, p-amino-L-phenylalanine, isopropyl-L-phenylalanine, and p-propargyloxy-phenylalanine.

3. The antibody conjugate of claim 2, wherein a residue of the one or more non-natural amino acids is linked to the payload moiety via a linker that is hydrolytically stable.

4. The antibody conjugate of claim 2, wherein a residue of the one or more non-natural amino acids is linked to the payload moiety via a linker that is cleavable.

5. The antibody conjugate of any one of claims 2 to 4 wherein the non-natural amino acid residue is a residue of compound (30) or compound (56).

6. The antibody conjugate of any one of the preceding claims wherein the payload moiety is selected from the group consisting of maytansines, hemiasterlins, amanitins, and auristatins.

7. The antibody conjugate of any one of the preceding claims wherein the payload moiety is selected from the group consisting of DM1, hemiasterlin, amanitin, MMAF, and MMAE.

8. The antibody conjugate of any one of the preceding claims, wherein the antibody comprises:

- (i) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 58 and 117; a CDR-H2 comprising one of SEQ ID NOs: 176 and 235; and a CDR-H3 comprising SEQ ID NO: 294;
- (ii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 19 and 78; a CDR-H2 comprising one of SEQ ID NOs: 137 and 196; and a CDR-H3 comprising SEQ ID NO: 255;
- (iii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 4 and 63; a CDR-H2 comprising one of SEQ ID NOs: 122 and 181; and a CDR-H3 comprising SEQ ID NO: 240;
- (iv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 5 and 64; a CDR-H2 comprising one of SEQ ID NOs: 123 and 182; and a CDR-H3 comprising SEQ ID NO: 241;
- (v) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 6 and 65; a CDR-H2 comprising one of SEQ ID NOs: 124 and 183; and a CDR-H3 comprising SEQ ID NO: 242;
- (vi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 7 and 66; a CDR-H2 comprising one of SEQ ID NOs: 125 and 184; and a CDR-H3 comprising SEQ ID NO: 243;
- (vii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 8 and 67; a CDR-H2 comprising one of SEQ ID NOs: 126 and 185; and a CDR-H3 comprising SEQ ID NO: 244;
- (viii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 9 and 68; a CDR-H2 comprising one of SEQ ID NOs: 127 and 186; and a CDR-H3 comprising SEQ ID NO: 245;
- (ix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 10 and 69; a CDR-H2 comprising one of SEQ ID NOs: 128 and 187; and a CDR-H3 comprising SEQ ID NO: 246;
- (x) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 11 and 70; a CDR-H2 comprising one of SEQ ID NOs: 129 and 188; and a CDR-H3 comprising SEQ ID NO: 247;

(xi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 12 and 71; a CDR-H2 comprising one of SEQ ID NOs: 130 and 189; and a CDR-H3 comprising SEQ ID NO: 248;

(xii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 13 and 72; a CDR-H2 comprising one of SEQ ID NOs: 131 and 190; and a CDR-H3 comprising SEQ ID NO: 249;

(xiii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 14 and 73; a CDR-H2 comprising one of SEQ ID NOs: 132 and 191; and a CDR-H3 comprising SEQ ID NO: 250;

(xiv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 15 and 74; a CDR-H2 comprising one of SEQ ID NOs: 133 and 192; and a CDR-H3 comprising SEQ ID NO: 251;

(xv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 16 and 75; a CDR-H2 comprising one of SEQ ID NOs: 134 and 193; and a CDR-H3 comprising SEQ ID NO: 252;

(xvi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 17 and 76; a CDR-H2 comprising one of SEQ ID NOs: 135 and 194; and a CDR-H3 comprising SEQ ID NO: 253;

(xvii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 18 and 77; a CDR-H2 comprising one of SEQ ID NOs: 136 and 195; and a CDR-H3 comprising SEQ ID NO: 254;

(xviii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 20 and 79; a CDR-H2 comprising one of SEQ ID NOs: 138 and 197; and a CDR-H3 comprising SEQ ID NO: 256;

(xix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 21 and 80; a CDR-H2 comprising one of SEQ ID NOs: 139 and 198; and a CDR-H3 comprising SEQ ID NO: 257;

(xx) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 22 and 81; a CDR-H2 comprising one of SEQ ID NOs: 140 and 199; and a CDR-H3 comprising SEQ ID NO: 258;

(xxi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 23 and 82; a CDR-H2 comprising one of SEQ ID NOs: 141 and 200; and a CDR-H3 comprising SEQ ID NO: 259;

(xxii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 24 and 83; a CDR-H2 comprising one of SEQ ID NOs: 142 and 201; and a CDR-H3 comprising SEQ ID NO: 260;

(xxiii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 25 and 84; a CDR-H2 comprising one of SEQ ID NOs: 143 and 202; and a CDR-H3 comprising SEQ ID NO: 261;

(xxiv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 26 and 85; a CDR-H2 comprising one of SEQ ID NOs: 144 and 203; and a CDR-H3 comprising SEQ ID NO: 262;

(xxv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 27 and 86; a CDR-H2 comprising one of SEQ ID NOs: 145 and 204; and a CDR-H3 comprising SEQ ID NO: 263;

(xxvi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 28 and 87; a CDR-H2 comprising one of SEQ ID NOs: 146 and 205; and a CDR-H3 comprising SEQ ID NO: 264;

(xxvii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 29 and 88; a CDR-H2 comprising one of SEQ ID NOs: 147 and 206; and a CDR-H3 comprising SEQ ID NO: 265;

(xxviii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 30 and 89; a CDR-H2 comprising one of SEQ ID NOs: 148 and 207; and a CDR-H3 comprising SEQ ID NO: 266;

(xxix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 31 and 90; a CDR-H2 comprising one of SEQ ID NOs: 149 and 208; and a CDR-H3 comprising SEQ ID NO: 267;

(xxx) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 32 and 91; a CDR-H2 comprising one of SEQ ID NOs: 150 and 209; and a CDR-H3 comprising SEQ ID NO: 268;

(xxxi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 33 and 92; a CDR-H2 comprising one of SEQ ID NOs: 151 and 210; and a CDR-H3 comprising SEQ ID NO: 269;

(xxxii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 34 and 93; a CDR-H2 comprising one of SEQ ID NOs: 152 and 211; and a CDR-H3 comprising SEQ ID NO: 270;

(xxxiii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 35 and 94; a CDR-H2 comprising one of SEQ ID NOs: 153 and 212; and a CDR-H3 comprising SEQ ID NO: 271;

(xxxiv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 36 and 95; a CDR-H2 comprising one of SEQ ID NOs: 154 and 213; and a CDR-H3 comprising SEQ ID NO: 272;

(xxxv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 37 and 96; a CDR-H2 comprising one of SEQ ID NOs: 155 and 214; and a CDR-H3 comprising SEQ ID NO: 273;

(xxxvi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 38 and 97; a CDR-H2 comprising one of SEQ ID NOs: 156 and 215; and a CDR-H3 comprising SEQ ID NO: 274;

(xxxvii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 39 and 98; a CDR-H2 comprising one of SEQ ID NOs: 157 and 216; and a CDR-H3 comprising SEQ ID NO: 275;

(xxxviii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 40 and 99; a CDR-H2 comprising one of SEQ ID NOs: 158 and 217; and a CDR-H3 comprising SEQ ID NO: 276;

(xxxix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 41 and 100; a CDR-H2 comprising one of SEQ ID NOs: 159 and 218; and a CDR-H3 comprising SEQ ID NO: 277;

(xl) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 42 and 101; a CDR-H2 comprising one of SEQ ID NOs: 160 and 219; and a CDR-H3 comprising SEQ ID NO: 278;

(xli) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 43 and 102; a CDR-H2 comprising one of SEQ ID NOs: 161 and 220; and a CDR-H3 comprising SEQ ID NO: 279;

(xlii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 44 and 103; a CDR-H2 comprising one of SEQ ID NOs: 162 and 221; and a CDR-H3 comprising SEQ ID NO: 280;

(xliii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 45 and 104; a CDR-H2 comprising one of SEQ ID NOs: 163 and 222; and a CDR-H3 comprising SEQ ID NO: 281;

(xliv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 46 and 105; a CDR-H2 comprising one of SEQ ID NOs: 164 and 223; and a CDR-H3 comprising SEQ ID NO: 282;

(xlv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 47 and 106; a CDR-H2 comprising one of SEQ ID NOs: 165 and 224; and a CDR-H3 comprising SEQ ID NO: 283;

(xlvi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 48 and 107; a CDR-H2 comprising one of SEQ ID NOs: 166 and 225; and a CDR-H3 comprising SEQ ID NO: 284;

(xlvii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 49 and 108; a CDR-H2 comprising one of SEQ ID NOs: 167 and 226; and a CDR-H3 comprising SEQ ID NO: 285;

(xlviii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 50 and 109; a CDR-H2 comprising one of SEQ ID NOs: 168 and 227; and a CDR-H3 comprising SEQ ID NO: 286;

(xlix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 51 and 110; a CDR-H2 comprising one of SEQ ID NOs: 169 and 228; and a CDR-H3 comprising SEQ ID NO: 287;

(l) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 52 and 111; a CDR-H2 comprising one of SEQ ID NOs: 170 and 229; and a CDR-H3 comprising SEQ ID NO: 288;

(li) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 53 and 112; a CDR-H2 comprising one of SEQ ID NOs: 171 and 230; and a CDR-H3 comprising SEQ ID NO: 289;

(lii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 54 and 113; a CDR-H2 comprising one of SEQ ID NOs: 172 and 231; and a CDR-H3 comprising SEQ ID NO: 290;

(liii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 55 and 114; a CDR-H2 comprising one of SEQ ID NOs: 173 and 232; and a CDR-H3 comprising SEQ ID NO: 291;

(liv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 56 and 115; a CDR-H2 comprising one of SEQ ID NOs: 174 and 233; and a CDR-H3 comprising SEQ ID NO: 292;

(lv) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 57 and 116; a CDR-H2 comprising one of SEQ ID NOs: 175 and 234; and a CDR-H3 comprising SEQ ID NO: 293;

(lvi) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 59 and 118; a CDR-H2 comprising one of SEQ ID NOs: 177 and 236; and a CDR-H3 comprising SEQ ID NO: 295;

(lvii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 60 and 119; a CDR-H2 comprising one of SEQ ID NOs: 178 and 237; and a CDR-H3 comprising SEQ ID NO: 296;

(lviii) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 61 and 120; a CDR-H2 comprising one of SEQ ID NOs: 179 and 238; and a CDR-H3 comprising SEQ ID NO: 297; or

(lix) a V_H comprising: a CDR-H1 comprising one of SEQ ID NOs: 62 and 121; a CDR-H2 comprising one of SEQ ID NOs: 180 and 239; and a CDR-H3 comprising SEQ ID NO: 298.

9. The antibody conjugate of any one of the preceding claims, wherein the antibody comprises:

(a) a V_L comprising: a CDR-L1 comprising SEQ ID NO: 300; a CDR-L2 comprising SEQ ID NO: 303; and a CDR-L3 comprising SEQ ID NO: 306; or

(b) a V_L comprising: a CDR-L1 comprising SEQ ID NO: 301; a CDR-L2 comprising SEQ ID NO: 304; and a CDR-L3 comprising SEQ ID NO: 307.

10. The antibody conjugate of any one of the preceding claims, wherein the antibody comprises:

(i) the V_H region is SEQ ID NO: 362, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(ii) the V_H region is SEQ ID NO: 323, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(iii) the V_H region is SEQ ID NO: 308, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(iv) the V_H region is SEQ ID NO: 309, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

- (v) the V_H region is SEQ ID NO: 310, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (vi) the V_H region is SEQ ID NO: 311, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (vii) the V_H region is SEQ ID NO: 312, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (viii) the V_H region is SEQ ID NO: 313, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (ix) the V_H region is SEQ ID NO: 314, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (x) the V_H region is SEQ ID NO: 315, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xi) the V_H region is SEQ ID NO: 316, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xii) the V_H region is SEQ ID NO: 317, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xiii) the V_H region is SEQ ID NO: 318, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xiv) the V_H region is SEQ ID NO: 319, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xv) the V_H region is SEQ ID NO: 320, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xvi) the V_H region is SEQ ID NO: 321, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xvii) the V_H region is SEQ ID NO: 322, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xviii) the V_H region is SEQ ID NO: 324, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xix) the V_H region is SEQ ID NO: 325, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xx) the V_H region is SEQ ID NO: 326, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof; or
- (xxi) the V_H region is SEQ ID NO: 327, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

- (xxii) the V_H region is SEQ ID NO: 328, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxiii) the V_H region is SEQ ID NO: 329, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxiv) the V_H region is SEQ ID NO: 330, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxv) the V_H region is SEQ ID NO: 331, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxvi) the V_H region is SEQ ID NO: 332, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxvii) the V_H region is SEQ ID NO: 333, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxviii) the V_H region is SEQ ID NO: 334, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxix) the V_H region is SEQ ID NO: 335, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxx) the V_H region is SEQ ID NO: 336, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxi) the V_H region is SEQ ID NO: 337, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxii) the V_H region is SEQ ID NO: 338, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxiii) the V_H region is SEQ ID NO: 339, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxiv) the V_H region is SEQ ID NO: 340, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxv) the V_H region is SEQ ID NO: 341, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxvi) the V_H region is SEQ ID NO: 342, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxvii) the V_H region is SEQ ID NO: 343, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;
- (xxxviii) the V_H region is SEQ ID NO: 344, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xxxix) the V_H region is SEQ ID NO: 345, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xl) the V_H region is SEQ ID NO: 346, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xli) the V_H region is SEQ ID NO: 347, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlii) the V_H region is SEQ ID NO: 348, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xliii) the V_H region is SEQ ID NO: 349, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xliv) the V_H region is SEQ ID NO: 350, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlv) the V_H region is SEQ ID NO: 351, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlvi) the V_H region is SEQ ID NO: 352, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlvii) the V_H region is SEQ ID NO: 353, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlviii) the V_H region is SEQ ID NO: 354, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(xlix) the V_H region is SEQ ID NO: 355, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(l) the V_H region is SEQ ID NO: 356, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(li) the V_H region is SEQ ID NO: 357, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(lii) the V_H region is SEQ ID NO: 358, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(liii) the V_H region is SEQ ID NO: 359, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(liv) the V_H region is SEQ ID NO: 360, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(lv) the V_H region is SEQ ID NO: 361, or a variant thereof, and the V_L region is SEQ ID NO: 367, or a variant thereof;

(lvi) the V_H region is SEQ ID NO: 363, or a variant thereof, and the V_L region is SEQ ID NO: 368, or a variant thereof;

(lvii) the V_H region is SEQ ID NO: 364, or a variant thereof, and the V_L region is SEQ ID NO: 368, or a variant thereof;

(lviii) the V_H region is SEQ ID NO: 365, or a variant thereof, and the V_L region is SEQ ID NO: 369, or a variant thereof; or

(lix) the V_H region is SEQ ID NO: 366, or a variant thereof, and the V_L region is SEQ ID NO: 369, or a variant thereof.

11. The antibody conjugate of claim 10, wherein the antibody comprises one or more non-natural amino acids at sites selected from the group of: HC-F404, HC-Y180, and LC-K42 according to the Kabat or EU numbering scheme of Kabat.

12. The antibody conjugate of claim 11, wherein the antibody comprises a non-natural amino acid at site HC-F404.

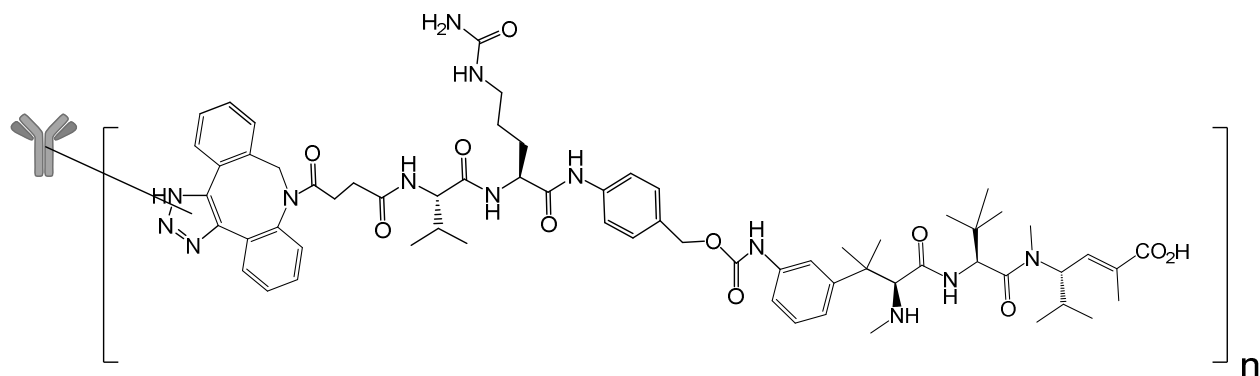
13. The antibody conjugate of claim 11, wherein the antibody comprises non-natural amino acids at sites HC-F404 and HC-Y180.

14. The antibody conjugate of claim 11, wherein the antibody comprises non-natural amino acids at sites HC-F404 and LC-K42.

15. The antibody conjugate of claim 11, wherein the antibody comprises non-natural amino acids at sites HC-Y180 and LC-K42.

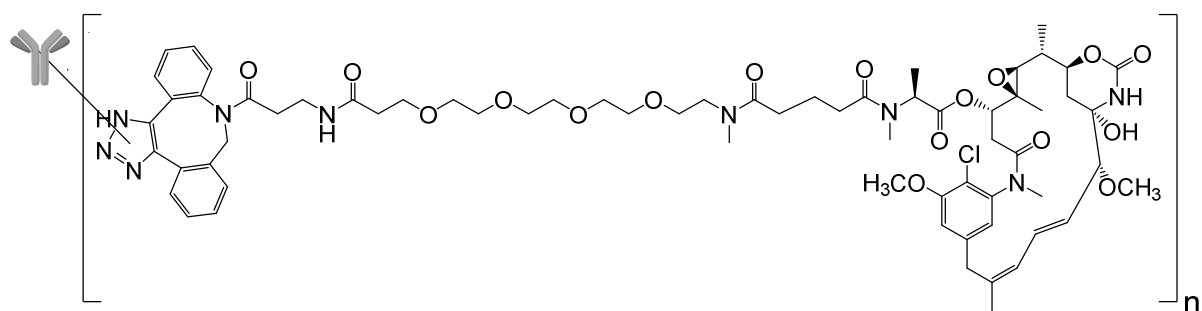
16. The antibody conjugate of any one of claims 12 to 15, wherein one or both non-natural amino acids is selected from the group consisting of para-azidomethylphenylalanine and p-azido-methyl-L-phenylalanine.

17. The antibody conjugate of any one of claims 1 to 16, wherein the antibody conjugate has the structure of **Conjugate P**:



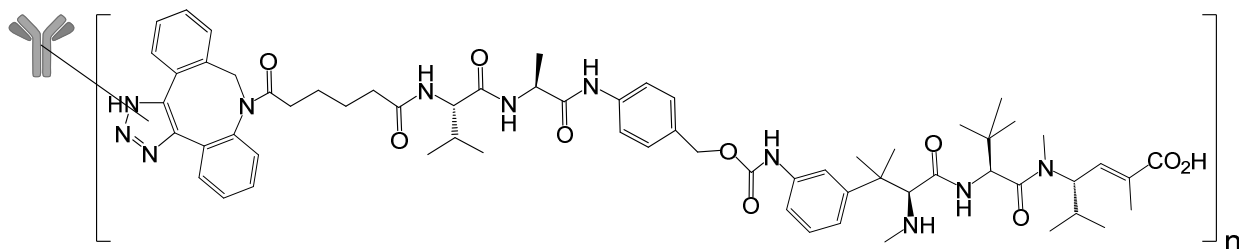
wherein **n** is an integer from 1 to 6.

18. The antibody conjugate of any one of claims 1 to 16, wherein the antibody conjugate has the structure of **Conjugate M**:



wherein **n** is an integer from 1 to 6.

19. The antibody conjugate of any one of claims 1 to 16, wherein the antibody conjugate has the structure of **Conjugate Q**:



wherein **n** is an integer from 1 to 6.

20. The antibody conjugate of any one of the preceding claims, wherein the antibody comprises a V_H region of SEQ ID NO: 362, or a variant thereof 7 or fewer amino acid

substitutions, and a V_L region of SEQ ID NO: 367, or a variant thereof having 7 or fewer amino acid substitutions.

21. The antibody conjugate of any one of the preceding claims, wherein the antibody comprises a V_H region of SEQ ID NO: 323, or a variant thereof 7 or fewer amino acid substitutions, and a V_L region of SEQ ID NO: 367, or a variant thereof having 7 or fewer amino acid substitutions.

22. The antibody of claim 20 or 21, wherein the amino acid substitutions are conservative amino acid substitutions.

23. The antibody conjugate of any one of the preceding claims, further comprising at least one constant region domain.

24. The antibody conjugate of claim 23, wherein the constant region comprises a sequence selected from SEQ ID NOs: 370, 371, and 372.

25. The antibody conjugate of any one of the preceding claims, wherein the antibody is a monoclonal antibody.

26. The antibody conjugate of any one of the preceding claims, wherein the antibody is an IgA, an IgD, an IgE, an IgG, or an IgM.

27. The antibody conjugate of any one of the preceding claims, wherein the antibody is humanized or human.

28. The antibody conjugate of any one of the preceding claims, wherein the antibody is aglycosylated.

29. The antibody conjugate of any one of the preceding claims, wherein the antibody is an antibody fragment.

30. The antibody conjugate of claim 29, wherein the antibody fragment is selected from an Fv fragment, a Fab fragment, a F(ab')₂ fragment, a Fab' fragment, an scFv (sFv) fragment, and an scFv-Fc fragment.

31. The antibody conjugate of claim 30, wherein the antibody is an scFv fragment.
32. The antibody conjugate of claim 31, wherein the scFv fragment comprises a sequence selected from SEQ ID NOs: 379-380.
33. The antibody conjugate of claim 30, wherein the antibody is an scFv-Fc fragment.
34. The antibody conjugate of claim 33, wherein the scFv-Fc fragment comprises SEQ ID NO: 381 or SEQ ID NO: 382.
35. The antibody conjugate of any one of the preceding claims, wherein the antibody has a k_a of about $2.90 \times 10^5 \text{ M}^{-1} \times \text{sec}^{-1}$ to about $9.64 \times 10^9 \text{ M}^{-1} \times \text{sec}^{-1}$ when associating with human folate receptor at a temperature of 25°C .
36. The antibody conjugate of any one of the preceding claims, wherein the antibody has a k_d of about $2.28 \times 10^{-4} \text{ sec}^{-1}$ to about $4.82 \times 10^1 \text{ sec}^{-1}$ when dissociating from human folate receptor at a temperature of 25°C .
37. The antibody conjugate of any one of the preceding claims, wherein the antibody has a K_D of about $2.26 \times 10^{-11} \text{ M}$ to about $7.20 \times 10^{-9} \text{ M}$ when bound to human folate receptor at a temperature of 25°C .
38. The antibody conjugate of any one of the preceding claims, wherein the antibody specifically binds cynomolgus folate receptor.
39. The antibody conjugate of claim 38, wherein the antibody has a K_D of about $0.19 \times 10^{-9} \text{ M}$ to about $2.84 \times 10^{-9} \text{ M}$ when bound to cynomolgus folate receptor at a temperature of 25°C .
40. The antibody conjugate of any one of the preceding claims, wherein the antibody specifically binds mouse folate receptor.

41. The antibody conjugate of claim 40, wherein the antibody has a K_D of about 0.5×10^{-9} M to about 9.07×10^{-8} M when bound to mouse folate receptor at a temperature of 25°C.
42. A kit comprising an antibody conjugate of any one of the preceding claims, and instructions for use of the antibody conjugate.
43. The kit of claim 42, wherein the antibody conjugate is lyophilized.
44. The kit of claim 43, further comprising a fluid for reconstitution of the lyophilized antibody.
45. A pharmaceutical composition comprising the antibody conjugate of any one of claims 1 to 41 and a pharmaceutically acceptable carrier.
46. Use of an antibody conjugate of any one of claims 1 to 41, or a pharmaceutical composition of claim 45 in the manufacture of a medicament for treating or preventing a disease or condition in a subject in need thereof, wherein the disease or condition is a cancer.
47. Use of an antibody conjugate of any one of claims 1 to 41, or a pharmaceutical composition of claim 45 in the manufacture of a medicament for diagnosing a disease or condition in a subject in need thereof, wherein the disease or condition is a cancer.
48. The use of claim 46 or 47, wherein the disease or condition is breast cancer.
49. The use of claim 46 or 47, wherein the disease or condition is triple-negative breast cancer (TNBC).
50. The use of claim 46 or 47, wherein the disease or condition is ovarian cancer.
51. The use of claim 46 or 47, wherein the disease or condition is lung cancer.
52. The use of claim 46 or 47, wherein the disease or condition is non-small cell lung cancer (NSCLC).
53. The use of claim 46 or 47, wherein the disease or condition is endometrial cancer.

54. An antibody conjugate of any one of claims 1 to 41, or a pharmaceutical composition of claim 45 for use as a medicament.