10:6606-6611. CD74 expression is also known to be a key factor associated with the progression of pancreatic cancer. Zhang *et al*., *Hepatobiliary Pancreat. Dis. Int.*, 2014, 13:81-86.

[0005] In view of the role of CD74 in multiple disease processes, there is a need for improved methods of modulating the interaction of CD74 with its ligands and the downstream signaling processes activated by CD74. Moreover, given the upregulation of CD74 in several diseases, there is also a need for therapeutics that specifically target cells and tissues overexpressing CD74. Antibody conjugates to CD74 could be used to deliver therapeutic or diagnostic payload moieties to target cells expressing CD74 for the treatment or diagnosis of such diseases.

SUMMARY

[0006] Provided herein are antibody conjugates that selectively bind CD74. The antibody conjugates comprise an antibody that binds CD74 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. CD74 antibodies are described in detail herein, as are useful payload moieties, and useful linkers.

[0007] Also provided are compositions comprising the antibody conjugates. In some embodiments, the compositions are pharmaceutical compositions. Any suitable pharmaceutical composition may be used. In some embodiments, the pharmaceutical composition is a composition for parenteral administration.Further provided herein are kits comprising the antibody conjugates or pharmaceutical compositions.

[0008] Also provided herein are methods of using the anti-CD74 antibody conjugates. In some embodiments, the methods are methods of delivering one or more payload moieties to a target cell or tissue expressing CD74. In some embodiments, the methods are methods of treatment. In some embodiments, the methods are diagnostic methods. In some embodiments, the methods are analytical methods. In some embodiments, the antibody conjugates are used to treat a disease or condition. In some embodiments, the disease or condition is selected from a cancer, an autoimmune disease, an infectious disease, or an inflammatory condition. In some embodiments, the disease or condition is a B-cell lymphoma. In some embodiments, the disease or condition is non-Hodgkin’s lymphoma. In some embodiments, the disease or condition is leukemia. In some embodiments, the disease or condition is pancreatic cancer. In some embodiments, the disease or condition is multiple myeloma.

[0008a] According to an aspect, there is provided an antibody conjugate comprising an antibody that specifically binds to CD74 linked site-specifically to at least one payload moiety, wherein the antibody comprises a non-natural amino acid at a site 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 and wherein the antibody further comprises:

a. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 1 and 33; a CDR-H2 comprising at least one of SEQ ID NOs: 65 and 97; and a CDR-H3 comprising SEQ ID NO: 129;

b. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 2 and 34; a CDR-H2 comprising at least one of SEQ ID NOs: 66 and 98; and a CDR-H3 comprising SEQ ID NO: 130;

c. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 3 and 35; a CDR-H2 comprising at least one of SEQ ID NOs: 67 and 99; and a CDR-H3 comprising SEQ ID NO: 131;

d. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 4 and 36; a CDR-H2 comprising at least one of SEQ ID NOs: 68 and 100; and a CDR-H3 comprising SEQ ID NO: 132;

e. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 5 and 37; a CDR-H2 comprising at least one of SEQ ID NOs: 69 and 101; and a CDR-H3 comprising SEQ ID NO: 133;

f. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 6 and 38; a CDR-H2 comprising at least one of SEQ ID NOs: 70 and 102; and a CDR-H3 comprising SEQ ID NO: 134;

g. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 7 and 39; a CDR-H2 comprising at least one of SEQ ID NOs: 71 and 103; and a CDR-H3 comprising SEQ ID NO: 135;

h. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 8 and 40; a CDR-H2 comprising at least one of SEQ ID NOs: 72 and 104; and a CDR-H3 comprising SEQ ID NO: 136;

i. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 9 and 41; a CDR-H2 comprising at least one of SEQ ID NOs: 73 and 105; and a CDR-H3 comprising SEQ ID NO: 137;

j. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 10 and 42; a CDR-H2 comprising at least one of SEQ ID NOs: 74 and 106; and a CDR-H3 comprising SEQ ID NO: 138;

k. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 11 and 43; a CDR-H2 comprising at least one of SEQ ID NOs: 75 and 107; and a CDR-H3 comprising SEQ ID NO: 139;

l. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 12 and 44; a CDR-H2 comprising at least one of SEQ ID NOs: 76 and 108; and a CDR-H3 comprising SEQ ID NO: 140;

m. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 13 and 45; a CDR-H2 comprising at least one of SEQ ID NOs: 77 and 109; and a CDR-H3 comprising SEQ ID NO: 141;

n. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 14 and 46; a CDR-H2 comprising at least one of SEQ ID NOs: 78 and 110; and a CDR-H3 comprising SEQ ID NO: 142;

o. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 15 and 47; a CDR-H2 comprising at least one of SEQ ID NOs: 79 and 111; and a CDR-H3 comprising SEQ ID NO: 143;

p. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 16 and 48; a CDR-H2 comprising at least one of SEQ ID NOs: 80 and 112; and a CDR-H3 comprising SEQ ID NO: 144;

q. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 17 and 49; a CDR-H2 comprising at least one of SEQ ID NOs: 81 and 113; and a CDR-H3 comprising SEQ ID NO: 145;

r. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 18 and 50; a CDR-H2 comprising at least one of SEQ ID NOs: 82 and 114; and a CDR-H3 comprising SEQ ID NO: 146;

s. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 19 and 51; a CDR-H2 comprising at least one of SEQ ID NOs: 83 and 115; and a CDR-H3 comprising SEQ ID NO: 147;

t. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 20 and 52; a CDR-H2 comprising at least one of SEQ ID NOs: 84 and 116; and a CDR-H3 comprising SEQ ID NO: 148;

u. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 21 and 53; a CDR-H2 comprising at least one of SEQ ID NOs: 85 and 117; and a CDR-H3 comprising SEQ ID NO: 149;

v. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 22 and 54; a CDR-H2 comprising at least one of SEQ ID NOs: 86 and 118; and a CDR-H3 comprising SEQ ID NO: 150;

w. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 23 and 55; a CDR-H2 comprising at least one of SEQ ID NOs: 87 and 119; and a CDR-H3 comprising SEQ ID NO: 151;

x. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 24 and 56; a CDR-H2 comprising at least one of SEQ ID NOs: 88 and 120; and a CDR-H3 comprising SEQ ID NO: 152;

y. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 25 and 57; a CDR-H2 comprising at least one of SEQ ID NOs: 89 and 121; and a CDR-H3 comprising SEQ ID NO: 153;

z. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 26 and 58; a CDR-H2 comprising at least one of SEQ ID NOs: 90 and 122; and a CDR-H3 comprising SEQ ID NO: 154;

aa. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 27 and 59; a CDR-H2 comprising at least one of SEQ ID NOs: 91 and 123; and a CDR-H3 comprising SEQ ID NO: 155; or

bb. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 28 and 60; a CDR-H2 comprising at least one of SEQ ID NOs: 92 and 124; and a CDR-H3 comprising SEQ ID NO: 156.

[0008b] According to another aspect there is provided a kit comprising an antibody conjugate described herein, and instructions for use of the antibody conjugate.

[0008c] According to another aspect there is provided a pharmaceutical composition comprising the antibody conjugate described herein and a pharmaceutically acceptable carrier.

[0008d] According to another aspect there is provided an antibody conjugate described herein, or a pharmaceutical composition described herein for use in treating or preventing a disease or condition in a subject

[0008e] According to another aspect there is provided an antibody conjugate described herein, or a pharmaceutical composition described herein for use in diagnosing a disease or condition in a subject.

5.2.1.3.Kabat CDR-H1

[00185] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 33-60.

5.2.1.4.Kabat CDR-H3 + Kabat CDR-H2

[00186] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 129-156 and a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 97-124. In some aspects, the Kabat CDR-H3 sequence and the Kabat CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H3 and Kabat CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 230-251 and 273-280.

5.2.1.5.Kabat CDR-H3 + Kabat CDR-H1

[00186.1] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 129-156 and a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 33-60. In some aspects, the Kabat CDR-H3 sequence and the Kabat CDR-H1 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H3 and Kabat CDR-H1 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 230-251 and 273-280.

5.2.1.6.Kabat CDR-H1 + Kabat CDR-H2

[00187] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 33-60 and a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 97-124. In some aspects, the Kabat CDR-H1 sequence and the Kabat CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H1 and Kabat CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 230-251 and 273-280.

WHAT IS CLAIMED IS:

1. An antibody conjugate comprising an antibody that specifically binds to CD74 linked site-specifically to at least one payload moiety, wherein the antibody comprises a non-natural amino acid at a site 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 and wherein the antibody further comprises:

a. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 1 and 33; a CDR-H2 comprising at least one of SEQ ID NOs: 65 and 97; and a CDR-H3 comprising SEQ ID NO: 129;

b. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 2 and 34; a CDR-H2 comprising at least one of SEQ ID NOs: 66 and 98; and a CDR-H3 comprising SEQ ID NO: 130;

c. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 3 and 35; a CDR-H2 comprising at least one of SEQ ID NOs: 67 and 99; and a CDR-H3 comprising SEQ ID NO: 131;

d. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 4 and 36; a CDR-H2 comprising at least one of SEQ ID NOs: 68 and 100; and a CDR-H3 comprising SEQ ID NO: 132;

e. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 5 and 37; a CDR-H2 comprising at least one of SEQ ID NOs: 69 and 101; and a CDR-H3 comprising SEQ ID NO: 133;

f. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 6 and 38; a CDR-H2 comprising at least one of SEQ ID NOs: 70 and 102; and a CDR-H3 comprising SEQ ID NO: 134;

g. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 7 and 39; a CDR-H2 comprising at least one of SEQ ID NOs: 71 and 103; and a CDR-H3 comprising SEQ ID NO: 135;

h. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 8 and 40; a CDR-H2 comprising at least one of SEQ ID NOs: 72 and 104; and a CDR-H3 comprising SEQ ID NO: 136;

i. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 9 and 41; a CDR-H2 comprising at least one of SEQ ID NOs: 73 and 105; and a CDR-H3 comprising SEQ ID NO: 137;

j. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 10 and 42; a CDR-H2 comprising at least one of SEQ ID NOs: 74 and 106; and a CDR-H3 comprising SEQ ID NO: 138;

k. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 11 and 43; a CDR-H2 comprising at least one of SEQ ID NOs: 75 and 107; and a CDR-H3 comprising SEQ ID NO: 139;

l. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 12 and 44; a CDR-H2 comprising at least one of SEQ ID NOs: 76 and 108; and a CDR-H3 comprising SEQ ID NO: 140;

m. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 13 and 45; a CDR-H2 comprising at least one of SEQ ID NOs: 77 and 109; and a CDR-H3 comprising SEQ ID NO: 141;

n. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 14 and 46; a CDR-H2 comprising at least one of SEQ ID NOs: 78 and 110; and a CDR-H3 comprising SEQ ID NO: 142;

o. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 15 and 47; a CDR-H2 comprising at least one of SEQ ID NOs: 79 and 111; and a CDR-H3 comprising SEQ ID NO: 143;

p. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 16 and 48; a CDR-H2 comprising at least one of SEQ ID NOs: 80 and 112; and a CDR-H3 comprising SEQ ID NO: 144;

q. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 17 and 49; a CDR-H2 comprising at least one of SEQ ID NOs: 81 and 113; and a CDR-H3 comprising SEQ ID NO: 145;

r. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 18 and 50; a CDR-H2 comprising at least one of SEQ ID NOs: 82 and 114; and a CDR-H3 comprising SEQ ID NO: 146;

s. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 19 and 51; a CDR-H2 comprising at least one of SEQ ID NOs: 83 and 115; and a CDR-H3 comprising SEQ ID NO: 147;

t. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 20 and 52; a CDR-H2 comprising at least one of SEQ ID NOs: 84 and 116; and a CDR-H3 comprising SEQ ID NO: 148;

u. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 21 and 53; a CDR-H2 comprising at least one of SEQ ID NOs: 85 and 117; and a CDR-H3 comprising SEQ ID NO: 149;

v. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 22 and 54; a CDR-H2 comprising at least one of SEQ ID NOs: 86 and 118; and a CDR-H3 comprising SEQ ID NO: 150;

w. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 23 and 55; a CDR-H2 comprising at least one of SEQ ID NOs: 87 and 119; and a CDR-H3 comprising SEQ ID NO: 151;

x. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 24 and 56; a CDR-H2 comprising at least one of SEQ ID NOs: 88 and 120; and a CDR-H3 comprising SEQ ID NO: 152;

y. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 25 and 57; a CDR-H2 comprising at least one of SEQ ID NOs: 89 and 121; and a CDR-H3 comprising SEQ ID NO: 153;

z. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 26 and 58; a CDR-H2 comprising at least one of SEQ ID NOs: 90 and 122; and a CDR-H3 comprising SEQ ID NO: 154;

aa. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 27 and 59; a CDR-H2 comprising at least one of SEQ ID NOs: 91 and 123; and a CDR-H3 comprising SEQ ID NO: 155; or

bb. a V_H comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 28 and 60; a CDR-H2 comprising at least one of SEQ ID NOs: 92 and 124; and a CDR-H3 comprising SEQ ID NO: 156.

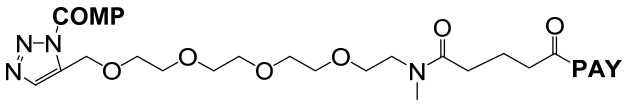
2. The antibody conjugate of claim 1, wherein the non-natural amino acid is selected from the group consisting of p-acetyl-L-phenylalanine, O-methyl-L-tyrosine, an -3-(2-naphthyl)alanine, 3-methyl-phenylalanine, O-4-allyl-L-tyrosine, 4-propyl-L-tyrosine, a tri-O-acetyl-GlcNAcβ-serine, L-Dopa, fluorinated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

3. The antibody conjugate of claim 2, wherein the antibody is linked to the payload moiety via a linker that is hydrolytically stable.

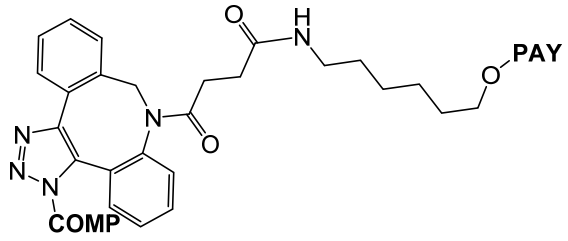
4. The antibody conjugate of claim 2, wherein the antibody is linked to the payload moiety via a linker that is cleavable.

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

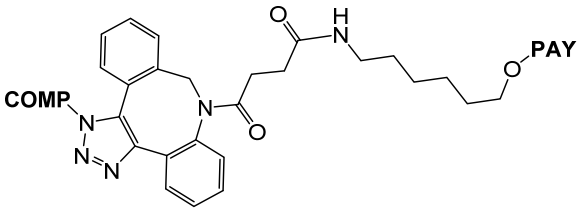
6. The antibody conjugate of any of the preceding claims according to any of formulas 101a-104b:



(103b)



(104a)



(104b)

wherein **COMP** is an amino acid residue of the antibody bearing the indicated bond and **PAY** is a payload moiety.

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

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

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

a. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 161; a CDR-L2 comprising SEQ ID NO: 181; and a CDR-L3 comprising SEQ ID NO: 201;

b. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 162; a CDR-L2 comprising SEQ ID NO: 182; and a CDR-L3 comprising SEQ ID NO: 202;

c. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 163; a CDR-L2 comprising SEQ ID NO: 183; and a CDR-L3 comprising SEQ ID NO: 203;

d. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 164; a CDR-L2 comprising SEQ ID NO: 184; and a CDR-L3 comprising SEQ ID NO: 204;

e. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 165; a CDR-L2 comprising SEQ ID NO: 185; and a CDR-L3 comprising SEQ ID NO: 205;

f. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 166; a CDR-L2 comprising SEQ ID NO: 186; and a CDR-L3 comprising SEQ ID NO: 206;

g. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 167; a CDR-L2 comprising SEQ ID NO: 187; and a CDR-L3 comprising SEQ ID NO: 207;

h. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 168; a CDR-L2 comprising SEQ ID NO: 188; and a CDR-L3 comprising SEQ ID NO: 208;

i. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 169; a CDR-L2 comprising SEQ ID NO: 189; and a CDR-L3 comprising SEQ ID NO: 209;

j. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 170; a CDR-L2 comprising SEQ ID NO: 190; and a CDR-L3 comprising SEQ ID NO: 210;

k. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 171; a CDR-L2 comprising SEQ ID NO: 191; and a CDR-L3 comprising SEQ ID NO: 211;

l. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 172; a CDR-L2 comprising SEQ ID NO: 192; and a CDR-L3 comprising SEQ ID NO: 212;

m. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 173; a CDR-L2 comprising SEQ ID NO: 193; and a CDR-L3 comprising SEQ ID NO: 213;

n. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 174; a CDR-L2 comprising SEQ ID NO: 194; and a CDR-L3 comprising SEQ ID NO: 214;

o. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 175; a CDR-L2 comprising SEQ ID NO: 195; and a CDR-L3 comprising SEQ ID NO: 215;

p. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 176; a CDR-L2 comprising SEQ ID NO: 196; and a CDR-L3 comprising SEQ ID NO: 216;

q. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 177; a CDR-L2 comprising SEQ ID NO: 197; and a CDR-L3 comprising SEQ ID NO: 217;

r. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 178; a CDR-L2 comprising SEQ ID NO: 198; and a CDR-L3 comprising SEQ ID NO: 218; or

s. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 179; a CDR-L2 comprising SEQ ID NO: 199; and a CDR-L3 comprising SEQ ID NO: 219.

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

a. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 256, or the variant thereof;

b. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 257, or the variant thereof;

c. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 265, or the variant thereof;

d. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 264, or the variant thereof;

e. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 267, or the variant thereof;

f. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 268, or the variant thereof;

g. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 269, or the variant thereof;

h. the V_H region is SEQ ID NO: 236, or the variant thereof, and the V_L region is SEQ ID NO: 270, or the variant thereof;

i. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 256, or the variant thereof;

j. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 257, or the variant thereof;

k. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 265, or the variant thereof;

l. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 264, or the variant thereof;

m. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 267, or the variant thereof;

n. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 268, or the variant thereof;

o. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 269, or the variant thereof;

p. the V_H region is SEQ ID NO: 237, or the variant thereof, and the V_L region is SEQ ID NO: 270, or the variant thereof;

q. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 256, or the variant thereof;

r. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 257, or the variant thereof;

s. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 265, or the variant thereof;

t. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 264, or the variant thereof;

u. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 267, or the variant thereof;

v. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 268, or the variant thereof;

w. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 269, or the variant thereof;

x. the V_H region is SEQ ID NO: 238, or the variant thereof, and the V_L region is SEQ ID NO: 270, or the variant thereof;

y. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 256, or the variant thereof;

z. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 257, or the variant thereof;

aa. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 265, or the variant thereof;

bb. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 264, or the variant thereof;

cc. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 267, or the variant thereof;

dd. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 268, or the variant thereof;

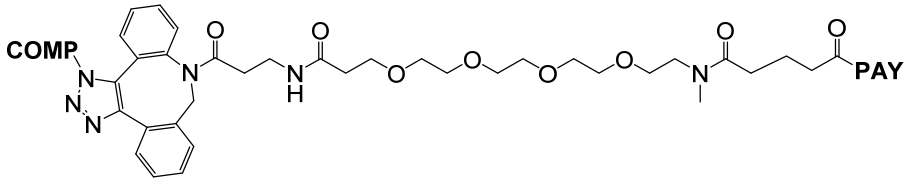
ee. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 269, or the variant thereof; or

ff. the V_H region is SEQ ID NO: 239, or the variant thereof, and the V_L region is SEQ ID NO: 270, or the variant thereof.

11. The antibody conjugate of claim 10, wherein the antibody comprises a non-natural amino acid at site HC-F404 according to the EU numbering scheme of Kabat.

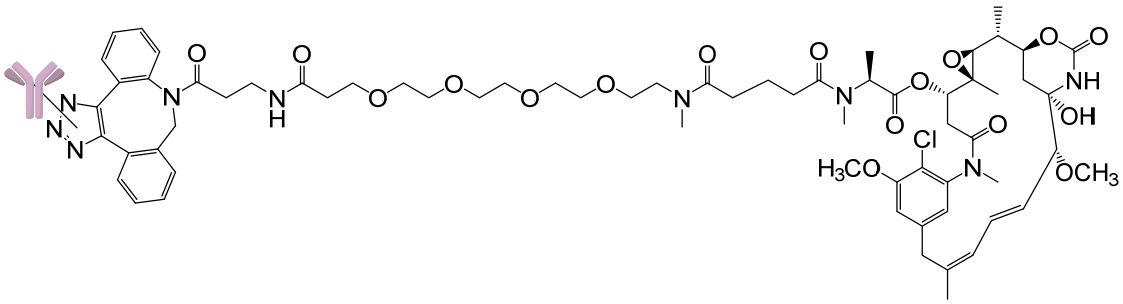
12. The antibody conjugate of claim 11, wherein the non-natural amino acid is para-azidomethylphenylalanine or p-azidomethyl-L-phenylalanine.

13. The antibody conjugate of claim 12, wherein the antibody conjugate has the formula of (102b):



wherein **COMP** is the non-natural amino acid residue of the antibody bearing the indicated bond and **PAY** is DM1.

14. The antibody conjugate of claim 13, wherein the antibody conjugate has the structure of **Conjugate A**:



and the antibody comprises a V_H region comprising SEQ ID NO: 236 and a V_L region comprising SEQ ID NO: 256.

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

16. The antibody conjugate of claim 15, wherein the constant region comprises a sequence selected from SEQ ID NOs: 304-305.

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

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

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

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

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

22. The antibody conjugate of claim 21, 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.

23. The antibody conjugate of claim 22, wherein the antibody is an scFv fragment.

24. The antibody conjugate of claim 23, wherein the scFv fragment comprises a sequence selected from SEQ ID NOs: 221-228.

25. The antibody conjugate of claim 22, wherein the antibody is an scFv-Fc fragment.

26. The antibody conjugate of claim 25, wherein the scFv-Fc fragment comprises SEQ ID NO: 229.

27. The antibody conjugate of any of the preceding claims, wherein the antibody has a k_a of at least about 10^5 $M^{-1}\times sec^{-1}$ at a temperature of 25°C.

28. The antibody conjugate of any of the preceding claims, wherein the antibody has a k_d of 10^{-3} sec^{-1} or less at a temperature of 25°C.

29. The antibody conjugate of any of the preceding claims, wherein the antibody has a K_D of 10^{-9} M or less at a temperature of 25°C.

30. The antibody conjugate of any of the preceding claims, wherein the antibody is internalized after binding to CD74 on the surface of a cell.

31. The antibody conjugate of any of the preceding claims, wherein the Tm2 of the antibody is at least 75°C, 75.5°C, 76°C, 76.5°C, 77°C, 77.5°C, 78°C, 78.5°C, or 79°C.

32. The antibody conjugate of any of the preceding claims, wherein the Tm1 of the antibody is less than 61°C or less than 60°C.

33. A kit comprising an antibody conjugate of any of the preceding claims, and instructions for use of the antibody conjugate.

34. The kit of claim 33, wherein the antibody conjugate is lyophilized.

35. The kit of claim 34, further comprising a fluid for reconstitution of the lyophilized antibody conjugate.

36. A pharmaceutical composition comprising the antibody conjugate of any of claims 1 to 32 and a pharmaceutically acceptable carrier.

37. An antibody conjugate of any one of claims 1 to 32, or a pharmaceutical composition of claim 36 for use in treating or preventing a disease or condition in a subject.

38. An antibody conjugate of any one of claims 1 to 32, or a pharmaceutical composition of claim 36 for use in diagnosing a disease or condition in a subject.

39. The antibody conjugate or pharmaceutical composition of any of claims 37 or 38, wherein the disease or condition is selected from a cancer, an autoimmune disease, an inflammatory disease, or an infection.

40. The antibody conjugate or pharmaceutical composition of claim 39, wherein the cancer is selected from multiple myeloma or pancreatic cancer.

41. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is B-cell lymphoma.

42. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is non-Hodgkin’s lymphoma.

43. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is leukemia.