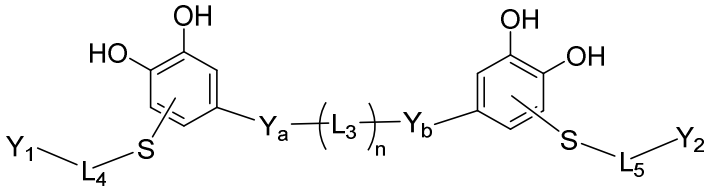
CLAIMS

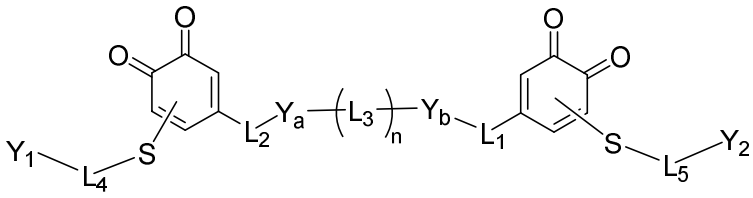
What is claimed is:

1. A conjugate of

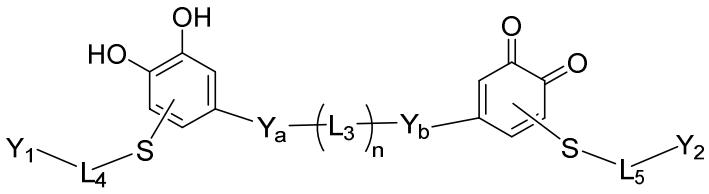
(i) Formula A', Formula B', Formula C', or Formula D':



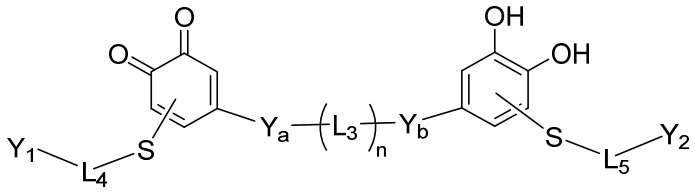
Formula A',



Formula B',



Formula C', or



Formula D',

wherein:

Y_a is a first polypeptide comprising a first terminal tag comprising $(X_1)_{m1}X_2X_3X_4X_5$, wherein X_1-X_5 is any amino acid provided that at least one amino acid of X_1-X_5 comprises a tyrosine or a portion thereof, and wherein m1 is an integer greater than or equal to 0, or $X_1X_2X_3$, wherein X_1-X_3 is any amino acid provided that at least one amino acid of X_1-X_3 is a tyrosine or a portion thereof, wherein Y_a is linked to "S" via the tyrosine or a portion thereof ;

Y_b is a second polypeptide comprising a second terminal tag different from the first terminal tag, the second terminal tag comprising $(X_6)_{m2}X_7X_8X_9X_{10}$, wherein X_6-X_{10} is any amino acid provided that at least one amino acid of X_6-X_{10} comprises a tyrosine or a portion thereof, and wherein m2 is an integer greater than or equal to 0, or $X_1X_2X_3$, wherein X_1-X_3 is any amino acid provided that at least one amino acid of X_1-X_3 is a tyrosine or a portion thereof, wherein Y_b is linked to "S" via the tyrosine or a portion thereof;

n is an integer greater than 0;

L_3 is an optional third linker;

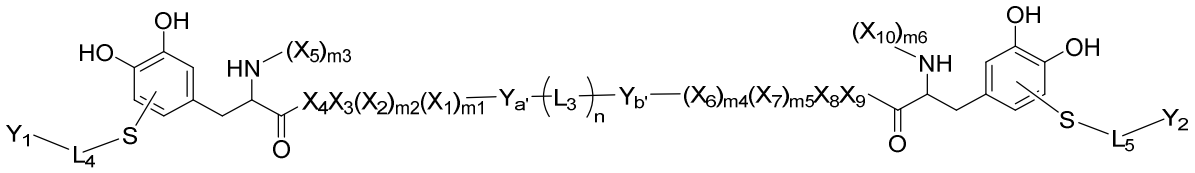
L_4 is an optional fourth linker;

L_5 is an optional fifth linker;

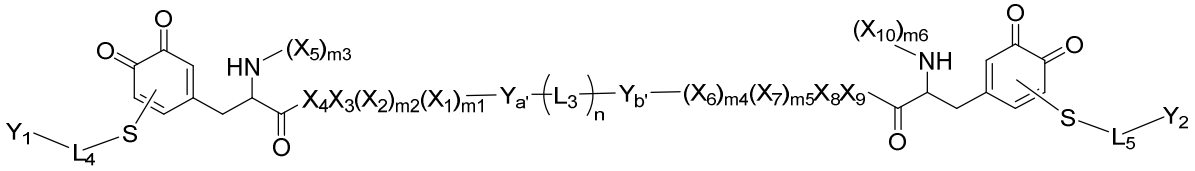
Y_1 is a first payload; and

Y_2 is a second payload;

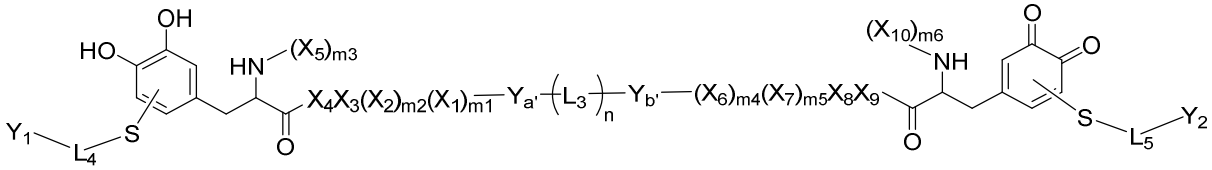
(ii) Formula A-I, Formula B-I, Formula C-I, or Formula D-I:



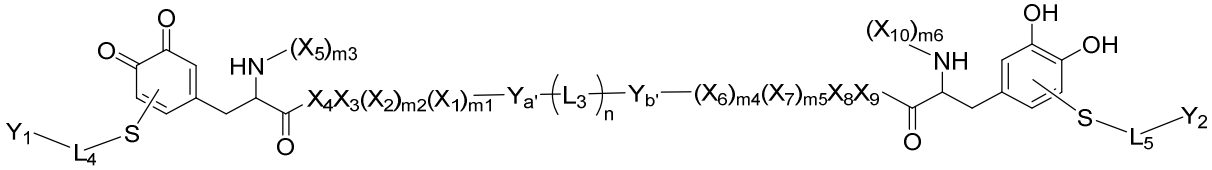
Formula A-I,



Formula B-I,



Formula C-I, or



Formula D-I; wherein:

$Y_{a'}$ is a first polypeptide,

each of X_1, X_2, X_3, X_4, and X_5 is independently any amino acid, wherein m1, m2, and m3 are each an integer greater than or equal to 0;

$Y_{b'}$ is a second polypeptide,

each of X_6, X_7, X_8, X_9, and X_{10} is independently any amino acid, wherein m4, m5, and m6 are each an integer greater than or equal to 0, and wherein the $-(X_1)_{m1}(X_2)_{m2}X_3X_4-$ moiety is different from the $-(X_6)_{m1}(X_7)_{m2}X_8\ X_9-$ moiety;

n is an integer greater than 0;

L_3 is an optional third linker;

L_4 is an optional fourth linker;

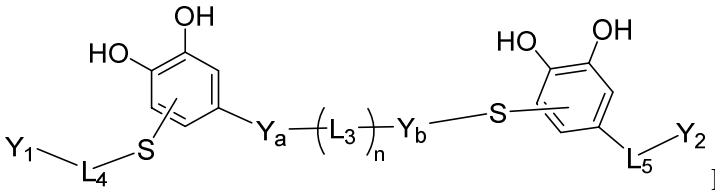
L_5 is an optional fifth linker;

Y_1 is a first payload; and

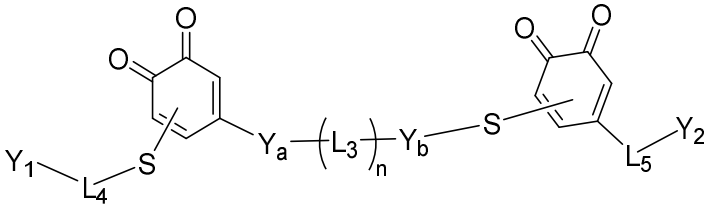
Y_2 is a second payload;

or

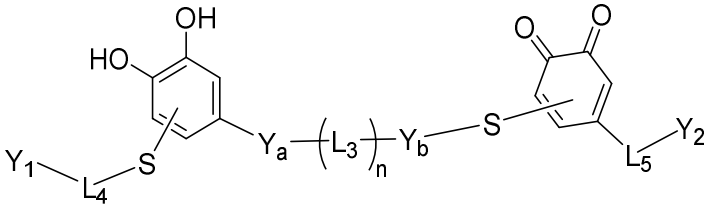
(iii) Formula E', Formula F', Formula G', Formula H', Formula J', or Formula K'



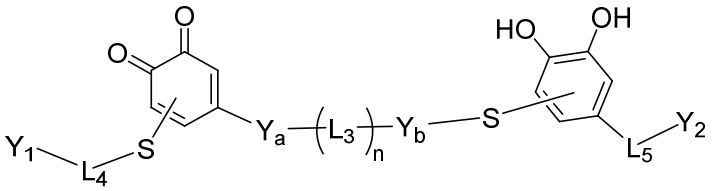
Formula E',



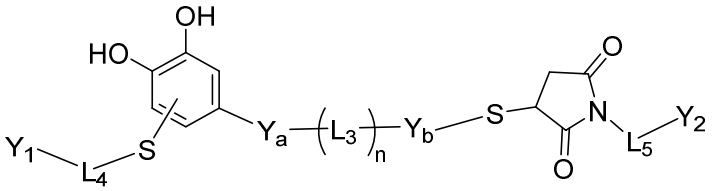
Formula F',



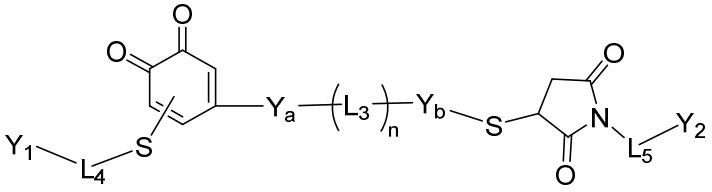
Formula G',



Formula H',



Formula J', or



Formula K',

wherein:

Y_a is a first polypeptide comprising a first terminal tag comprising $(X_1)_{m1}X_2X_3X_4X_5Y$, wherein X_1-X_5 is any amino acid provided that no more than two amino acids of X_2, X_3, X_4, and X_5 are aspartate or glutamate and wherein m1 is an integer greater than or equal to 0;

Y_b is a second polypeptide;

n is an integer greater than 0;

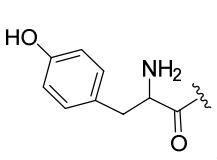
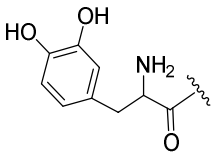
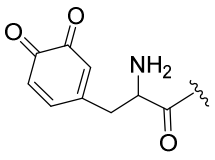
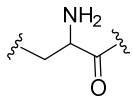
L_3 is an optional third linker;

L_4 is an optional fourth linker;

L_5 is an optional fifth linker;

Y_1 is a first payload; and

Y_2 is a second payload.

2. The conjugate of claim 1, wherein the tyrosine or a portion thereof is selected from the group consisting of , , , and .

3. The conjugate of claim 1-2, wherein the first terminal tag comprises at least two amino acids selected from the group consisting of aspartate (D), glutamate (E), arginine (R), and lysine (K).

4. The conjugate of any one of claims 1-3, wherein the second terminal tag comprises at least two amino acids selected from the group consisting of aspartate (D), glutamate (E), arginine (R), and lysine (K).

5. The conjugate of claim 1-2, wherein

(i) the first terminal tag comprises at least one of GGGGY, RGGGY, RGRGY, RRRGY, RRRRY, EGGGY, EGEGY, EEEGY, EEEEY, GGGWY, GGWGY, RRRWY, RRWRY, EEEWY, EEWEY, DDDDY, SGGY, SGY, KKKKY, RRKKY, RRRKY, EDEDY, EDDDY, EEDDY, RRKKY, KKGGY, DDGGY, EESY, ESSSY, SSSY, SNNY, SSNY, SEGY, SSSEY, EGGY, SSEEY, SESY, ESSY, ESY, SRY, SKY, SNY, ERY, EKY, EGY, SEYP, SHRKY, SARKY, SPPEY, SSEEY, SEEEY, and SSSSY; and/or

(ii) the second terminal tag comprises at least one of GGGGY, RGGGY, RGRGY, RRRGY, RRRRY, EGGGY, EGEGY, EEEGY, EEEEY, GGGWY, GGWGY, RRRWY, RRWRY, EEEWY, EEWEY, DDDDY, SGGY, SGY, KKKKY, RRKKY, RRRKY, EDEDY, EDDDY, EEDDY, RRKKY, KKGGY, DDGGY, EESY, ESSSY, SSSY, SNNY, SSNY, SEGY, SSSEY, EGGY, SSEEY, SESY, ESSY, ESY, SRY, SKY, SNY, ERY, EKY, EGY, SEYP, SHRKY, SARKY, SPPEY, SSEEY, SEEEY, and SSSSY;

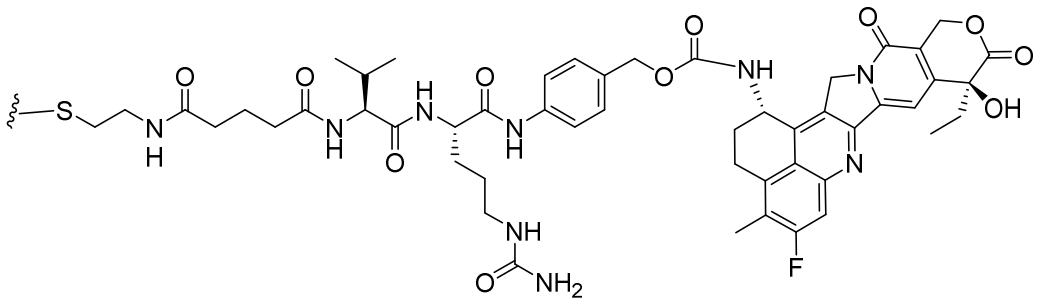
or

(ii) the -$(X_1)_{m1}(X_2)_{m2}X_3X_4$- moiety is selected from the group consisting of GGGG, RGGG, RGRG, RRRG, RRRR, EGGG, EGEG, EEEG, EEEE, GGGW, GGWG, RRRW, RRWR, EEEW, EEWE, DDDD, SGG, SG, KKKK, RRKK, RRRK, EDED, EDDD, EEDD, RRKK, KKGG, DDGG EES, ESSS, SSS, SNN, SSN, SEG, SSSE, EGG, SSEE, SES, ESS, ES, SR, SK, SN, ER, EK, EG, SE, SHRK, SARK, SPPE, SSEE, SEEE, and SSSS; and/or

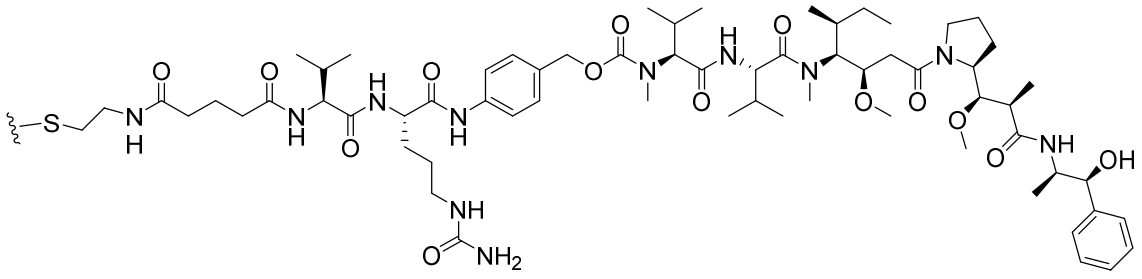
the -$(X_6)_{m1}(X_7)_{m2}X_8$ X_9- moiety is selected from the group consisting of GGGG, RGGG, RGRG, RRRG, RRRR, EGGG, EGEG, EEEG, EEEE, GGGW, GGWG, RRRW, RRWR, EEEW, EEWE, DDDD, SGG, SG, KKKK, RRKK, RRRK, EDED, EDDD, EEDD, RRKK, KKGG, DDGG, EES, ESSS, SSS, SNN, SSN, SEG, SSSE, EGG, SSEE, SES, ESS, ES, SR, SK, SN, ER, EK, EG, SE, SHRK, SARK, SPPE, SSEE, SEEE, and SSSS.

6. The conjugate of any one of claims 1-5, wherein at least one of L_3, L_4, or L_5 is a cleavable linker.

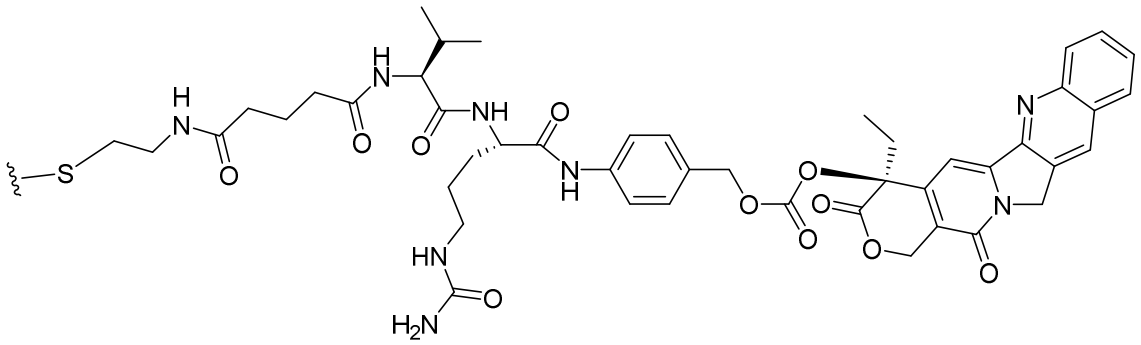
7. The conjugate of claim 6, wherein “Y1-L4-S-“ and/or “-S-L5-Y2” is selected from the group consisting of :



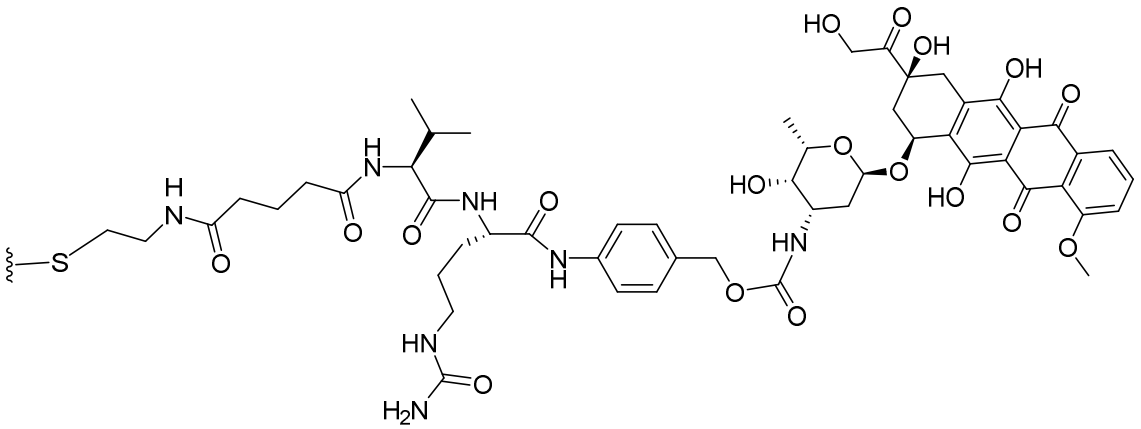
S-VC-PAB-DXD,



S-VC-PAB-MMAE,



S-VC-PAB-Camptothecin, and



S-VC-PAB-Doxorubicin.

8. The conjugate of any one of claims 1-6, wherein

(i) Y_a is a heavy chain variable region (VH), a light chain variable region (VL), a heavy chain, a light chain, a constant chain of an antibody or antibody fragment, a peptide, or a cyclic peptide and/or Y_b is a heavy chain variable region (VH), a light chain variable region (VL), a heavy chain, a light chain, a constant chain of an antibody, antibody fragment, a peptide, or a cyclic peptide; or

(ii) Ya' is a heavy chain variable region (VH), a light chain variable region (VL), a heavy chain, a light chain, a constant chain of an antibody or antibody fragment, a peptide, or a cyclic peptide; and/or Yb' is a heavy chain variable region (VH), a light chain variable region (VL), a heavy chain, a light chain, a constant chain of an antibody or antibody fragment, a peptide, or a cyclic peptide.

9. The conjugate of any one of claims 1-8, wherein Y_a and Y_b are attached via L_3; or $Y_{a'}$ and $Y_{b'}$ are attached via L_3.

10. The conjugate of any one of claims 1-8, wherein L_3 (i) comprises a peptide sequence, a dimerization and docking domain, a leucine zipper, or knobs-into-holes; or (ii) is a linker.

11. The conjugate of any one of claims 1-10, wherein

(i) Y_1, Y_2, or both Y_1 and Y_2 is a small molecule or

(ii) Y_1 and Y_2, or both Y_1 and Y_2 comprises a nucleic acid, an immune agonist, a peptide, a cytokine, or a binding domain.

12. The conjugate of claim 11, wherein the small molecule is selected from the group consisting of deruxtecan, exatecan, FL118, irinotecan, topotecan, SN-38, rubitecan, belotecan, lurototecan, gimatecan, diflomotecan, karenitecan, silatecan, namitecan, elomotecan, DRF-1042, delimotecan, NSC606985, chimmitecan, ZBH-1205, auristatin (MMAE, MMAF, MMAG, MMAH) calicheamicin, doxorubicin, taxol and taxol derivatives, maytansinoids (DM1-4), pyrolodiazepines (PBDs), tubulysins, eribulin, anthramycin, duocarmycin, anthracycline, and camptothecin (CPT), including the lactone and carboxylate forms of CPT.

13. The conjugate of claim 11, wherein the small molecule is selected from the group of a topoisomerase inhibitor and a tubulin inhibitor.