therapeutic agent. The present compositions are useful for inhibiting abnormal cell growth or treating a proliferative disorder in a mammal (e.g., human).

[14] The present invention includes a method of inhibiting abnormal cell growth or treating a proliferative disorder in a mammal (e.g., human) comprising administering to said mammal a therapeutically effective amount of the conjugates or derivatives thereof, (and/or solvates and salts thereof) or a composition thereof, alone or in combination with a second therapeutic agent.

[15] The compounds of this invention, derivatives thereof, or conjugates thereof, and compositions comprising them, are useful for treating or lessening the severity of disorders, such as, characterized by abnormal growth of cells (e.g., cancer). Other applications for compounds or conjugates of this invention include, but are not limited to, treating osteoporosis, depression, anxiety, stress, phobias, panic, dysphoria, psychiatric disorders, and pain or as antiepileptics, antibacterials, diuretics and hypotensives, hypolipidemics, and anti-depressants.

therapeutic agent. The present compositions are useful for inhibiting abnormal cell growth or treating a proliferative disorder in a mammal (e.g., human).

[14] The present invention includes a method of inhibiting abnormal cell growth or treating a proliferative disorder in a mammal (e.g., human) comprising administering to said mammal a therapeutically effective amount of the conjugates or derivatives thereof, (and/or solvates and salts thereof) or a composition thereof, alone or in combination with a second therapeutic agent.

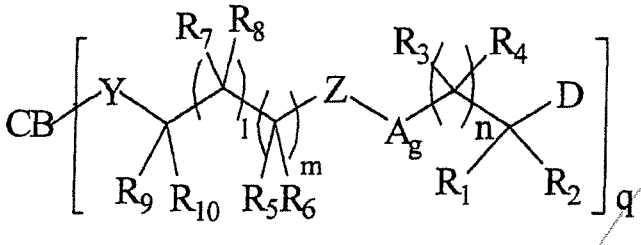
[15] The compounds of this invention, derivatives thereof, or conjugates thereof, and compositions comprising them, are useful for treating or lessening the severity of disorders, such as, characterized by abnormal growth of cells (e.g., cancer). Other applications for compounds or conjugates of this invention include, but are not limited to, treating osteoporosis, depression, anxiety, stress, phobias, panic, dysphoria, psychiatric disorders, and pain or as antiepileptics, antibacterials, diuretics and hypotensives, hypolipidemics, and anti-depressants.

BRIEF DESCRIPTION OF THE DRAWINGS

[16] Figure 1 shows the synthesis of sulfonic acid-containing cross-linking reagents that contain a nitropyridyldisulfide group and a reactive carboxylic acid ester. Hydroxyalkanoate esters are first converted into

The present invention also provides any one of the embodiments disclosed below and indicated with the numbers 1 to 16.

1. A cell-binding agent-drug conjugate of formula (II)



(II)

wherein:

CB represents a cell-binding agent;

D represents the drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-. X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl; wherein:

R_{11}, R_{12} and R_{13} are same or different and are H, linear alkyl having from 1 to 6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR14, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an

integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent;

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and q represents an integer from 1 to 20.

2. The conjugate of claim 1, wherein D is selected from thiotepa; cyclophosphamide (CYTOXAN$^{(TM)}$); alkyl sulfonates selected from busulfan, improsulfan and piposulfan; aziridines selected from benzodopa, carboquone, meturedopa, and uredopa; ethylenimines; and methylamelamines; acetogenins selected from bullatacin and bullatacinone; a camptothecin; bryostatin; callystatin; CC-1065; adozelesin, carzelesin or bizelesin synthetic analogues of CC-1065; cryptophycins; dolastatin; duocarmycin; KW-2189 or CBI-TMI synthetic analogues of duocarmycin,; eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards selected from chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; antibiotics such as the enediyne antibiotics (e.g. calicheamicin, especially calicheamicin gamma1 and calicheamicin theta I;

dynemicin, including dynemicin A; an esperamicin; neocarzinostatin chromophore and related chromoprotein enediyne antiobiotic chromomophores, aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, carminomycin, carzinophilin; chromomycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin epirubicin, esorubicin, idarubicin, marcellomycin, nitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites selected from methotrexate and 5-fluorouracil (5-FU); folic acid analogues selected from denopterin, methotrexate, pteropterin, trimetrexate; purine analogs selected from fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimnidine analogs selected from ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-FU; androgens selected from calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher selected from frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; maytansinoids selected from maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidamol;

nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK®; razoxane; rhizoxin; sizofiran; spirogermanium; tenuazonic acid; triaziquone; 2, 2',2"-trichlorotriethylamine; trichothecenes selected from T-2 toxin, verracurin A, roridin A and anguidine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxanes; chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs selected from cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylomithine (DMFO); retinoic acid; capecitabine; anti-hormonal agents selected from anti-estrogens including tamoxifen, raloxifene, aromatase inhibiting 4(5)-imidazoles, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and toremifene (Fareston); and anti-androgens selected from flutamide, nilutamide, bicalutamide, leuprolide, and goserelin, siRNA or a combination thereof; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

3. The conjugate of claim 1or 2, wherein D is selected from maytansinoids, CC-1065 analogs, morpholino doxorubicin, taxanes, calicheamicins, auristatins, pyrrolobenzodiazepine dimmer, siRNA or a

combination thereof, and pharmaceutically acceptable salts, acids or derivatives of any of the above.

4. The conjugate of claim 1, wherein the cell-binding agent binds to target cells selected from tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, myeloid cells, activated T-cells, B cells, or melanocytes, cells expressing one or more of IGF-IR, CanAg, EGFR, EphA2 receptor, MUC1, MUC16, VEGF, TF, MY9, anti-B4, EpCAM, CD2, CD3, CD4, CD5, CD6, CD11, CD 11a, CD18, CD19, CD20, CD22, CD26, CD30, CD33, CD37, CD38, CD40, CD44, CD56, CD79, CD105, CD138, EphA receptors, EphB receptors, EGFr, EGFRvIII, HER2/neu, HER3, mesothelin, cripto, $alpha_v beta_3$ integrin, $alpha_v beta_5$ integrin, $alpha_v beta_6$ integrin, Apo2, and C242 antigens; and cells expressing insulin growth factor receptor, epidermal growth factor receptor, or folate receptor.

5. The conjugate of claim 1, wherein the cell-binding agent is an antibody, a single chain antibody, an antibody fragment that binds to the target cell, a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment that binds the target cell, a chimeric antibody, a chimeric antibody fragment that binds to the target cell, a domain antibody, a domain antibody fragment that binds to the target cell, adnectins that mimic antibodies, DARPins, a lymphokine, a hormone, a vitamin, a growth factor, a colony stimulating factor, or a nutrient-transport molecule.

6. The conjugate of claim 5, wherein the antibody is a resurfaced antibody, a resurfaced single chain antibody, or a resurfaced antibody fragment thereof.

7. The conjugate of claim 5, wherein the antibody is a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment thereof.

8. The conjugate of claim 5, wherein the antibody is a human antibody, a humanized antibody or a resurfaced antibody, a humanized single chain antibody, or a humanized antibody fragment thereof.

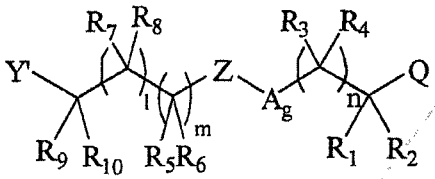
9. The conjugate of claim 5, wherein the antibody is a chimeric antibody, a chimeric antibody fragment, a domain antibody, or a domain antibody fragment thereof.

10. The conjugate of claim 8, wherein the antibody is My9-6, B4, C242, N901, DS6, EpCAM, EphA2 receptor, CD38, IGF-IR, CNTO 95, B-B4, trastuzumab, pertuzumab, bivatuzumab, sibrotuzumab, pertuzumab, or rituximab.

11. The conjugate of claim 4, wherein the tumor cells are selected from breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, and testicular cancer cells.

12. A method of treating a tumor comprising administering to a subject in need of treatment a therapeutically effective amount of a conjugate of claim 1.

13. A cross linker represented by formula (I)



(I)

wherein:

Y' represents a functional group that enables reaction with a cell-binding agent;

Q represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anionsselected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$,and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12} and R_{13} are same or different and are H, linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

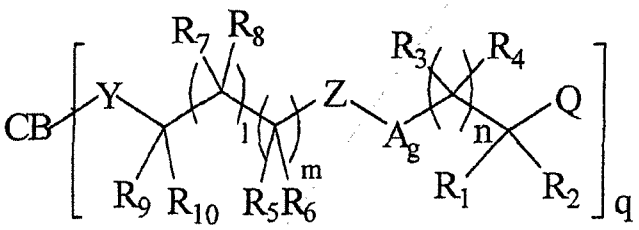
l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from anions selected from SO_3^-, $X\text{-}SO_3^-$, OPO_3^{2-}, $X\text{-}OPO_3^{2-}$, PO_3^{2-}, $X\text{-}PO_3^{2-}$, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$, and$X\text{-}N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1; and

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR14, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an

integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

14. A compound of formula (III):



(III)

wherein:

CB represents a cell-binding agent;

Q represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selcted from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12} and R_{13} are same or different and are H, linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

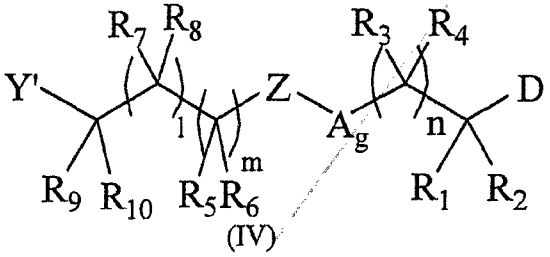
A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR14, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an

integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent; and

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and q represents an integer from 1 to 20.

15. A compound of formula (IV):



(IV)

wherein:

Y' represents a functional group that enables reaction with a cell-binding agent;

D represents the drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions

selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12} and R_{13} are same or different and are H, linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2-, a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ or X-$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1; and

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR14, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino

acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

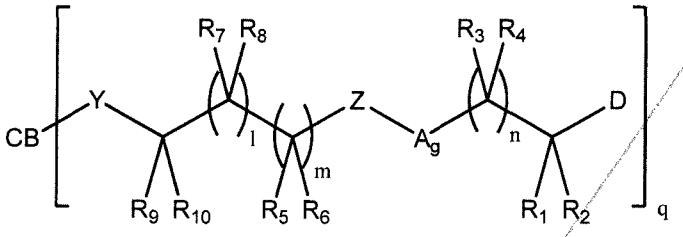
16. A pharmaceutical composition comprising an effective amount of the conjugate of claim 1, a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

BRIEF DESCRIPTION OF THE DRAWINGS

[16] Figure 1 shows the synthesis of sulfonic acid-containing cross-linking reagents that contain a nitropyridyldisulfide group and a reactive carboxylic acid ester. Hydroxyalkanoate esters are first converted into

Claims

1. A cell-binding agent-drug conjugate of formula (II)



(II)

wherein:

CB represents a cell-binding agent;

D represents the drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X--OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl; wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2^-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-

$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR_{14}, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent;

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and

q represents an integer from 1 to 20.

2. The conjugate of claim 1, wherein D is selected from thiotepa; cyclophosphamide (CYTOXAN™); alkyl sulfonates selected from busulfan, improsulfan and piposulfan; aziridines selected from benzodopa, carboquone, meturedopa, and uredopa; ethylenimines; methylamelamines; acetogenins selected from bullatacin and bullatacinone; camptothecin; bryostatin; callystatin; CC-1065; adozelesin, carzelesin or bizelesin synthetic analogues of CC-1065; cryptophycins; dolastatin; duocarmycin; KW-2189 or CBI-TMI synthetic analogues of duocarmycin; eleutherobin; pancratistatin; sarcodictyin; spongistatin; nitrogen mustards selected from chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard;

nitrosureas selected from: carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; antibiotics selected from: the enediyne antibiotics, calicheamicin, calicheamicin gammal and calicheamicin theta I; dynemicin, including dynemicin A; esperamicin; neocarzinostatin chromophore and related chromoprotein enediyne antiobiotic chromomophores, aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin; chromomycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin epirubicin, esorubicin, idarubicin, marcellomycin, nitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites selected from methotrexate and 5-fluorouracil (5-FU); folic acid analogues selected from denopterin, methotrexate, pteropterin, trimetrexate; purine analogs selected from fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimnidine analogs selected from ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens selected from calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals selected from: aminoglutethimide, mitotane, trilostane; folic acid replenisher selected from frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; maytansinoids selected from maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK®; razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2''-trichlorotriethylamine; trichothecenes selected from T-2 toxin, verracurin A, roridin A and anguidine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxanes;

chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs selected from cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylomithine (DMFO); retinoic acid; capecitabine; anti-hormonal agents selected from anti-estrogens including tamoxifen, raloxifene, aromatase inhibiting 4(5)-imidazoles, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and toremifene (Fareston); and anti-androgens selected from flutamide, nilutamide, bicalutamide, leuprolide, and goserelin, siRNA or a combination thereof; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

3. The conjugate of claim 1, wherein D is selected from maytansinoids, CC-1065 analogs, morpholino doxorubicin, taxanes, calicheamicins, auristatins, pyrrolobenzodiazepine dimmer, siRNA or a combination thereof, and pharmaceutically acceptable salts, acids or derivatives of any of the above.

4. The conjugate of claim 1, wherein the cell-binding agent binds to target cells selected from tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, myeloid cells, activated T-cells, B cells, or melanocytes, cells expressing one or more of IGF-IR, CanAg, EGFR, EphA2 receptor, MUC1, MUC16, VEGF, TF, MY9, anti-B4, EpCAM, CD2, CD3, CD4, CD5, CD6, CD11, CD11a, CD18, CD19, CD20, CD22, CD26, CD30, CD33, CD37, CD38, CD40, CD44, CD56, CD79, CD105, CD138, EphA receptors, EphB receptors, EGFr, EGFRvIII, HER2/neu, HER3, mesothelin, cripto, $alpha_v beta_3$, integrin, $alpha_v beta_5$ integrin, $alpha_v beta_6$ integrin, Apo2, and C242 antigens; and cells expressing insulin growth factor receptor, epidermal growth factor receptor, or folate receptor.

5. The conjugate of claim 1, wherein the cell-binding agent is an antibody, a single chain antibody, an antibody fragment that binds to the target cell, a

monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment that binds the target cell, a chimeric antibody, a chimeric antibody fragment that binds to the target cell, a domain antibody, a domain antibody fragment that binds to the target cell, adnectins that mimic antibodies, DARPins, a lymphokine, a hormone, a vitamin, a growth factor, a colony stimulating factor, or a nutrient-transport molecule.

6. The conjugate of claim 5, wherein the antibody is a resurfaced antibody, a resurfaced single chain antibody, or a resurfaced antibody fragment thereof.

7. The conjugate of claim 5, wherein the antibody is a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment thereof.

8. The conjugate of claim 5, wherein the antibody is a human antibody, a humanized antibody or a resurfaced antibody, a humanized single chain antibody, or a humanized antibody fragment thereof.

9. The conjugate of claim 5, wherein the antibody is a chimeric antibody, a chimeric antibody fragment, a domain antibody, or a domain antibody fragment thereof.

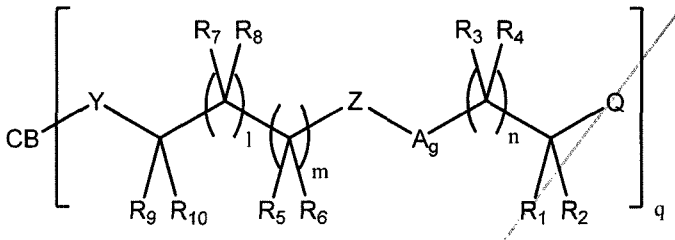
10. The conjugate of claim 8, wherein the antibody is My9-6, B4, C242, N901, DS6, EpCAM, EphA2 receptor, CD38, IGF-IR, CNTO 95, B-B4, trastuzumab, pertuzumab, bivatuzumab, sibrotuzumab, pertuzumab, or rituximab.

11. The conjugate of claim 4, wherein the tumor cells are selected from breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, and testicular cancer cells.

12. The conjugate of any one of the preceding claims for use in a method of treating a tumor.

13. Use of the conjugate of any one of the preceding claims for preparing a medicament for treating a tumor.

14. A compound of formula (III):



(III)

wherein:

CB represents a cell-binding agent;

Q represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-. X-SO_3^-, OPO_3^{2-}, X--OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2^-, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-

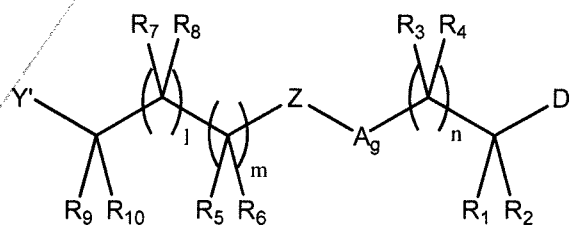
$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR_{14}, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent; and

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and

q represents an integer from 1 to 20.

15. A compound of formula (IV):



(IV)

wherein:

Y' represents a functional group that enables reaction with a cell-binding agent;

D represents the drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X--OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

A is a phenyl or substituted phenyl, wherein the substituent is a linear alkyl having from 1 to 6 carbon atoms, or a branched or cyclic alkyl having from 3 to 6 carbon atoms, or a charged substituent selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, CO_2^-, a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, wherein X has the same definition as above, and wherein g is 0 or 1; and

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000, or F1-E1-P-E2-F2 unit in which E1 and E2 are the same or different and are C=O, O, or NR_{14}, wherein R_{14} is H, a linear alkyl having from 1-6 carbon atoms, a branched or cyclic alkyl having from 3 to 6 carbon atoms, a linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms; P is a peptide unit between 2 and 20 amino acids in length, wherein E1 or E2 can be linked to the peptide through the terminal nitrogen, terminal carbon or through a side chain of one of the amino acids of the peptide; and F1 and F2 are the same or different and are an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p

is 0 or an integer from 2 to about 1000, provided that when Z is not F1-E1-P-E2-F2, at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent or when g is 1, at least one of A, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

16. A pharmaceutical composition comprising an effective amount of the conjugate of claim 1, a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

17. The conjugate of claim 1, wherein one of R_1, R_2, R_3, R_4, R_9, and R_{10} is a charged substituent selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, and the rest are H; l, g and m are each 0; and n is 1.

18. The conjugate of claim 17, wherein one of R_1, R_2, R_3, R_4, R_9, and R_{10} is SO_3^- or X-SO_3^-, the rest are H; l, g and m are each 0; and n is 1.

19. The conjugate of claim 17, wherein Z is absent when Z is the optional polyethylene unit and p=0.

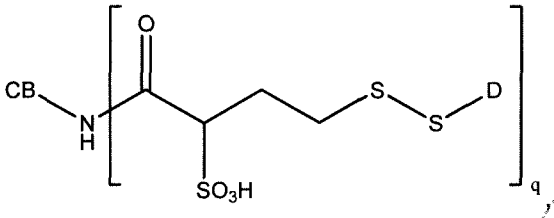
20. The conjugate of claim 1, wherein Z is an F1-E1-P-E2-F2 unit, wherein E1 and E2 are the same or different and are C=O or NR_{14}, wherein R_{14} is H, a linear alkyl having 1-6 carbon atoms or a branched or cyclic alkyl having from 3 to 6 carbon atoms; and P is a peptide unit between 2 and 8 amino acids.

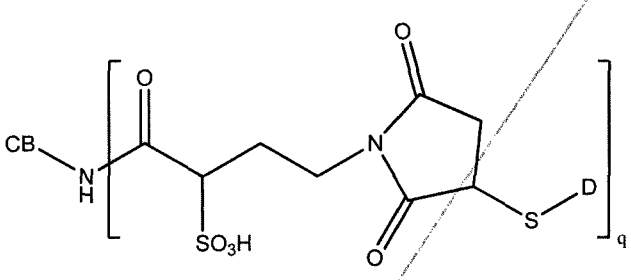
21. The conjugate of claim 20, wherein R_{14} is H or a linear alkyl having 1-6 carbon atoms; and P is a peptide unit between 2 and 5 amino acids; and F1 and F2 are the same or different and are optional polyethyleneoxy units of formula $(OCH_2CH_2)_p$, where p is 0 or an integer from 2 to 24.

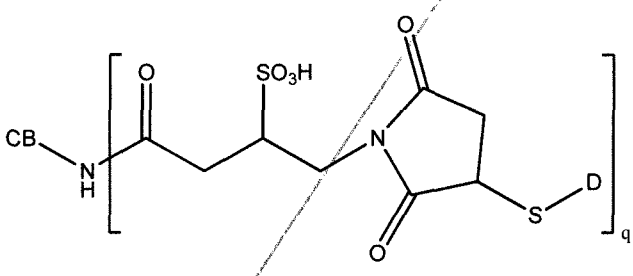
22. The conjugate of claim 21, wherein p is 0.

23. The conjugate of claim 22, wherein P is gly-gly-gly.

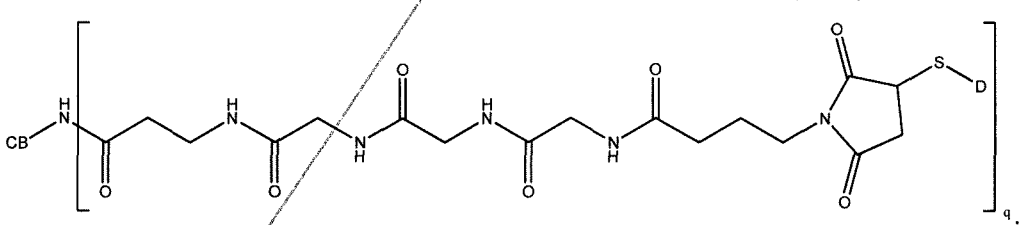
24. The conjugate of claim 1, which is represented by one of the following formulae:



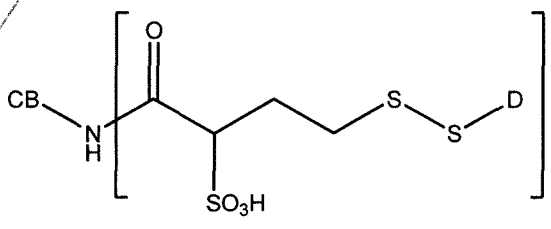




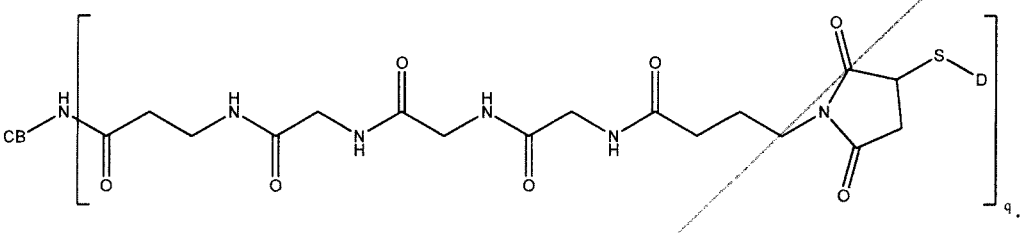
, and,



25. The conjugate of claim 24, which is represented by the following formula:

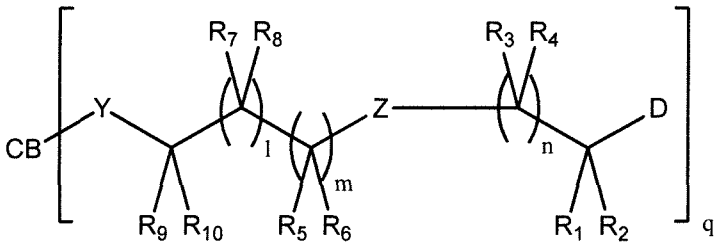


, or,


CB
H
N
O
N
H
O
N
H
O
N
H
O
N
H
O
O
N
O
S
D
q

Claims

1. A cell-binding agent-drug conjugate of formula (II)



(II)

wherein:

CB represents a cell-binding agent;

D represents a cytotoxic drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-, $X\text{-}SO_3^-$, OPO_3^{2-}, $X\text{-}OPO_3^{2-}$, PO_3^{2-}, $X\text{-}PO_3^{2-}$, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and $X\text{-}N^+R_{11}R_{12}R_{13}$, or a phenyl; wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000;

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and

q represents an integer from 1 to 20;

wherein at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

2. The conjugate of claim 1, wherein the cytotoxic drug is selected from thiotepa; cyclophosphamide; alkyl sulfonates selected from busulfan, improsulfan and piposulfan;

aziridines selected from benzodopa, carboquone, meturedopa, and uredopa; ethylenimines; methylamelamines; acetogenins selected from bullatacin and bullatacinone; camptothecin; bryostatin; callystatin; CC-1065; adozelesin, carzelesin or bizelesin synthetic analogues of CC-1065; cryptophycins; dolastatin; duocarmycin; KW-2189 or CBI-TMI synthetic analogues of duocarmycin; eleutherobin; pancratistatin; sarcodictyin; spongistatin; nitrogen mustards selected from chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas selected from: carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; antibiotics selected from: the enediyne antibiotics, calicheamicin, calicheamicin gammal and calicheamicin theta I; dynemicin, including dynemicin A; esperamicin; neocarzinostatin chromophore and related chromoprotein enediyne antiobiotic chromomophores, aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin; chromomycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin epirubicin, esorubicin, idarubicin, marcellomycin, nitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites selected from methotrexate and 5-fluorouracil (5-FU); folic acid analogues selected from denopterin, methotrexate, pteropterin, trimetrexate; purine analogs selected from fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimnidine analogs selected from ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens selected from calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals selected from: aminoglutethimide, mitotane, trilostane; folic acid replenisher selected from frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; maytansinoids selected from maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK®; razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2''-trichlorotriethylamine; trichothecenes selected from T-2 toxin, verracurin A, roridin A and anguidine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine;

arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxanes; chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs selected from cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylomithine (DMFO); retinoic acid; capecitabine; anti-hormonal agents selected from anti-estrogens including tamoxifen, raloxifene, aromatase inhibiting 4(5)-imidazoles, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and toremifene (Fareston); and anti-androgens selected from flutamide, nilutamide, bicalutamide, leuprolide, and goserelin, siRNA or a combination thereof; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

3. The conjugate of claim 1, wherein the cytotoxic drug is selected from maytansinoids, CC-1065 analogs, morpholino doxorubicin, taxanes, calicheamicins, auristatins, pyrrolobenzodiazepine dimmer, siRNA or a combination thereof, and pharmaceutically acceptable salts, acids or derivatives of any of the above.

4. The conjugate of claim 1, wherein the cell-binding agent binds to target cells selected from tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, myeloid cells, activated T-cells, B cells, or melanocytes, cells expressing one or more of IGF-IR, CanAg, EGFR, EphA2 receptor, MUC1, MUC16, VEGF, TF, MY9, anti-B4, EpCAM, CD2, CD3, CD4, CD5, CD6, CD11, CD11a, CD18, CD19, CD20, CD22, CD26, CD30, CD33, CD37, CD38, CD40, CD44, CD56, CD79, CD105, CD138, EphA receptors, EphB receptors, EGFr, EGFRvIII, HER2/neu, HER3, mesothelin, cripto, $alpha_v beta_3$, integrin, $alpha_v beta_5$ integrin, $alpha_v beta_6$ integrin, Apo2, and C242 antigens; and cells expressing insulin growth factor receptor, epidermal growth factor receptor, or folate receptor.

5. The conjugate of claim 1, wherein the cell-binding agent is an antibody, a single chain antibody, an antibody fragment that binds to the target cell, a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment that binds the target cell, a chimeric antibody, a chimeric antibody fragment that binds to the target cell, a domain antibody, a domain antibody fragment that binds to the target cell, adnectins that mimic antibodies, DARPins, a lymphokine, a hormone, a vitamin, a growth factor, a colony stimulating factor, or a nutrient-transport molecule.

6. The conjugate of claim 5, wherein the antibody is a resurfaced antibody, a resurfaced single chain antibody, or a resurfaced antibody fragment thereof.

7. The conjugate of claim 5, wherein the antibody is a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment thereof.

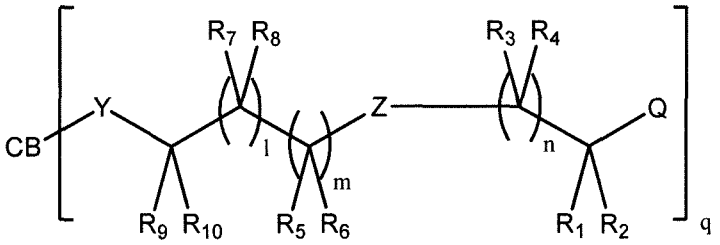
8. The conjugate of claim 5, wherein the antibody is a human antibody, a humanized antibody or a resurfaced antibody, a humanized single chain antibody, or a humanized antibody fragment thereof.

9. The conjugate of claim 5, wherein the antibody is a chimeric antibody, a chimeric antibody fragment, a domain antibody, or a domain antibody fragment thereof.

10. The conjugate of claim 8, wherein the antibody is My9-6, B4, C242, N901, DS6, EpCAM, EphA2 receptor, CD38, IGF-IR, CNTO 95, B-B4, trastuzumab, pertuzumab, bivatuzumab, sibrotuzumab, pertuzumab, or rituximab.

11. The conjugate of claim 4, wherein the tumor cells are selected from breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, and testicular cancer cells.

12. A compound of formula (III):



(III)

wherein:

CB represents a cell-binding agent;

Q represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-. X-SO_3^-, OPO_3^{2-}, X--OPO_3^{2-}, PO_3^{2-}, X-PO_3^{2-}, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

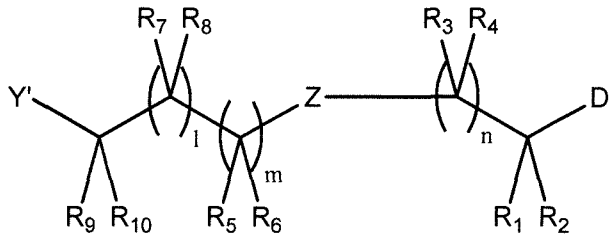
Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an integer from 2 to about 1000; and

Y represents a carbonyl, thioether, amide, disulfide, or hydrazone group; and

q represents an integer from 1 to 20;

wherein at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

13. A compound of formula (IV):



(IV)

wherein:

Y' represents a functional group that enables reaction with a cell-binding agent;

D represents a cytotoxic drug linked to the cell-binding agent by a disulfide, thioether, thioester, peptide, hydrazone, ester, ether, carbamate, or amide bond;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl having from 2 to 6 carbon atoms, a charged substituent selected from anions selected from SO_3^-, $X\text{-}SO_3^-$, OPO_3^{2-}, $X\text{-}OPO_3^{2-}$, PO_3^{2-}, $X\text{-}PO_3^{2-}$, and cations selected from a nitrogen containing heterocycle, $N^+R_{11}R_{12}R_{13}$ and $X\text{-}N^+R_{11}R_{12}R_{13}$, or a phenyl, wherein:

R_{11}, R_{12}, and R_{13} are the same or different and are linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms and X represents phenyl or a linear alkyl having from 1 to 6 carbon atoms, or branched or cyclic alkyl having from 3 to 6 carbon atoms;

l, m and n are 0 or an integer from 1 to 4;

Z is an optional polyethyleneoxy unit of formula $(OCH_2CH_2)_p$, wherein p is 0 or an

integer from 2 to about 1000,

wherein at least one of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} is a charged substituent.

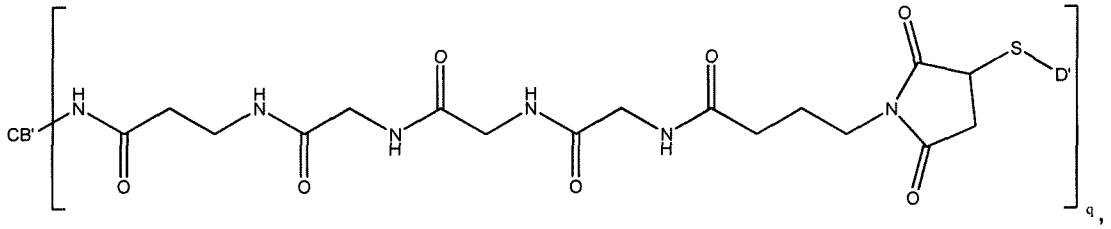
14. A pharmaceutical composition comprising an effective amount of the conjugate of claim 1, a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

15. The conjugate of claim 1, wherein one of R_1, R_2, R_3, R_4, R_9, and R_{10} is a charged substituent selected from SO_3^-, X-SO_3^-, OPO_3^{2-}, X-OPO_3^{2-}, $N^+R_{11}R_{12}R_{13}$ and X-$N^+R_{11}R_{12}R_{13}$, and the rest are H; l, g and m are each 0; and n is 1.

16. The conjugate of claim 15, wherein one of R_1, R_2, R_3, R_4, R_9, and R_{10} is SO_3^- or X-SO_3^-, the rest are H; l, g and m are each 0; and n is 1.

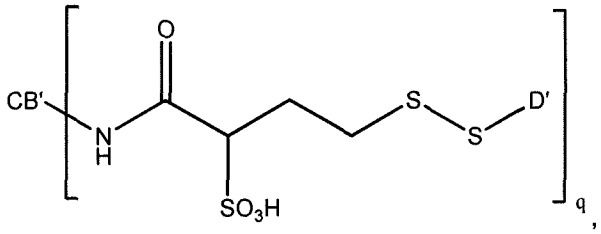
17. The conjugate of claim 15, wherein Z is absent.

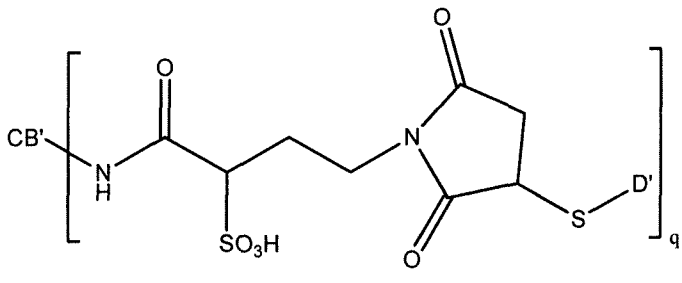
18. A cell-binding agent-drug conjugate represented by the following formula:



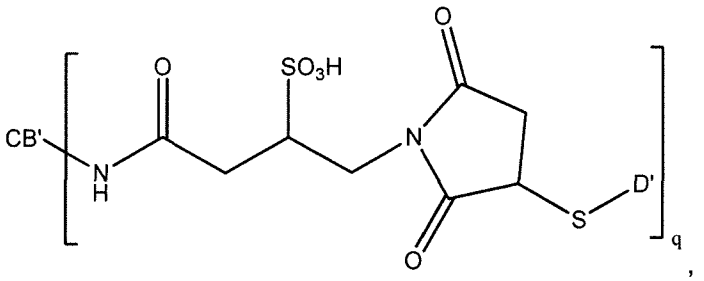
wherein D' is a cytotoxic drug, q represents an integer from 1 to 20, and CB'- represents a cell-binding agent.

19. The conjugate of claim 1, which is represented by one of the following formulae:



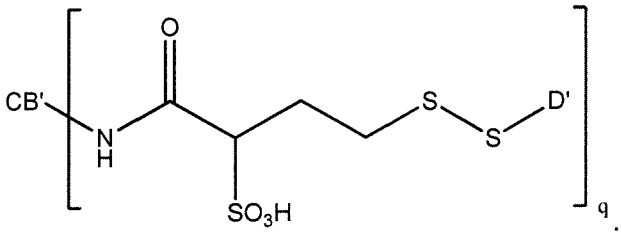


, and,



wherein D' is the cytotoxic drug, and CB'-NH- represents the cell-binding agent linked to Y.

20. The conjugate of claim 19, which is represented by the following formula:



21. The conjugate of claim 19, wherein the cytotoxic drug is a maytansinoid.

22. The conjugate of claim 19, wherein the cytotoxic drug is DM1 or DM4.

23. The conjugate of claim 20, wherein the cytotoxic drug is DM4.

24. The conjugate of claim 23, wherein the cell-binding agent is an antibody that binds to a folate receptor.

25. The conjugate of claim 24, wherein the folate receptor is FOLR1 (folate receptor 1).