Furthermore, the protein may be rendered inactive or non-specific, by misfolding or loss of tertiary structure (Zhang et al (2002) Anal. Biochem. 311:1-9).

[0016] Cysteine-engineered antibodies have been designed as FAB antibody fragments (thioFab) and expressed as full-length, IgG monoclonal (thioMab) antibodies (Junutula, J.R. et al. (2008) J Immunol Methods 332:41-52; US 2007/0092940, the contents of which are incorporated by reference). ThioFab and ThioMab antibodies have been conjugated through linkers at the newly introduced cysteine thiols with thiol-reactive linker reagents and drug-linker reagents to prepare antibody drug conjugates (Thio ADC).

[0017] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

SUMMARY

[0018] The disclosure provides anti-CD79b antibodies or functional fragments thereof, and their method of use in the treatment of hematopoietic tumors.

[0019] In one example, there is provided an antibody which binds, preferably specifically, to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, antibody fragment, including Fab, Fab', $F(ab')_2$, and Fv fragment, diabody, single domain antibody, chimeric antibody, humanized antibody, single-chain antibody or antibody that competitively inhibits the binding of an anti-CD79b polypeptide antibody to its respective antigenic epitope. Antibodies of the present disclosure may optionally be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, an auristatin, a maytansinoid, a dolostatin derivative or a calicheamicin, an antibiotic, a radioactive isotope, a nucleolytic enzyme, or the like. The antibodies of the present disclosure may optionally be produced in CHO cells or bacterial cells and preferably induce death of a cell to which they bind. For detection purposes, the antibodies of the present disclosure may be detectably labeled, attached to a solid support, or the like.

[0020] In one example, there is provided a humanized anti-CD79b antibody wherein the monovalent affinity (e.g affinity of the antibody as a Fab fragment to CD79b) or affinity in its bivalent form of the antibody to CD79b (e.g. affinity of the antibody as an IgG fragment to CD79b) is substantially the same as, lower than, or greater than, the monovalent affinity or affinity in its bivalent form, respectively, of a murine antibody (e.g. affinity of the murine antibody as a Fab fragment or as an IgG fragment to CD79b) or a chimeric antibody (e.g. affinity of the chimeric antibody as a Fab fragment or as an IgG fragment to CD79b), comprising, consisting or consisting essentially of a light chain and heavy chain variable domain sequence as depicted in Figures 7A-B (SEQ ID NO: 10) and Figures 8A-B (SEQ ID NO: 14).

[0021] In another example, there is provided a humanized anti-CD79b antibody wherein the affinity of the antibody in its bivalent form to CD79b (e.g., affinity of the antibody as an IgG to CD79b) is 0.4 nM, 0.2 nM or 0.5 nM.

[0022] In one example, an antibody that binds to CD79b is provided, wherein the antibody comprises at least one, two, three, four, five or six HVRs selected from the group consisting of:

(i) HVR-L1 comprising sequence A1-A15, wherein A1-A15 is KASQSVDYDGDSFLN (SEQ ID NO: 131)

(ii) HVR-L2 comprising sequence B1-B7, wherein B1-B7 is AASNLES (SEQ ID NO: 132)

(iii) HVR-L3 comprising sequence C1-C9, wherein C1-C9 is QQSNEDPLT (SEQ ID NO: 133)

(iv) HVR-H1 comprising sequence D1-D10, wherein D1-D10 is GYTFSSYWIE (SEQ ID NO: 134)

(v) HVR-H2 comprising sequence E1-E18, wherein E1-E18 is GEILPGGGDTNYNEIFKG (SEQ ID NO: 135) and

(vi) HVR-H3 comprising sequence F1-F10, wherein F1-F10 IS TRRVPVYFDY (SEQ ID NO: 136).

[0023] In one example, an antibody that binds to CD79b is provided, wherein the antibody comprises at least one variant HVR wherein the variant HVR sequence comprises modification of at least one residue of the sequence depicted in SEQ ID NOs: 131, 132, 133, 134, 135 or 136.

[0024] In one example, there is provided an antibody comprising a heavy chain variable domain comprising the HVR1-HC, HVR2-HC and/or HVR3-HC sequence depicted in Figure 15 (SEQ ID NO: 164-166).

[0025] In one example, there is provided an antibody comprising a light chain variable domain comprising HVR1-LC, HVR2-LC and/or HVR3-LC sequence depicted in Figure 15 (SEQ ID NO: 156-158).

[0026] In one example, there is provided an antibody comprising a heavy chain variable domain comprising the HVR1-HC, HVR2-HC and/or HVR3-HC sequence depicted in Figure 16 (SEQ ID NO: 183-185).

[0027] In one example, there is provided an antibody comprising a light chain variable domain comprising HVR1-LC, HVR2-LC and/or HVR3-LC sequence depicted in Figure 16 (SEQ ID NO: 175-177).

[0028] In one example, there is provided an antibody comprising a heavy chain variable domain comprising the HVR1-HC, HVR2-HC and/or HVR3-HC sequence depicted in Figure 17 (SEQ ID NO: 202-204).

[0029] In one example, there is provided an antibody comprising a light chain variable domain comprising HVR1-LC, HVR2-LC and/or HVR3-LC sequence depicted in Figure 17 (SEQ ID NO: 194-196).

[0030] In one example, there is provided an antibody comprising a heavy chain variable domain comprising the HVR1-HC, HVR2-HC and/or HVR3-HC sequence depicted in Figure 18 (SEQ ID NO: 221-223).

[0031] In one example, there is provided an antibody comprising a light chain variable domain comprising HVR1-LC, HVR2-LC and/or HVR3-LC sequence depicted in Figure 18 (SEQ ID NO: 213-215).

[0032] In one example, there is provided an anti-CD79b antibody comprising a heavy chain variable domain selected from SEQ ID NOs: 170, 189, 208 or 227. In another example, there is provided an anti-CD79b antibody comprising a light chain variable domain selected from SEQ ID NOs: 169, 188, 207 or 226.

[0032a] In a first aspect, there is provided an anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208.

[0033] In one example, there is provided a cysteine engineered anti-CD79b antibody comprising one or more free cysteine amino acids and a sequence selected from SEQ ID NOs: 251-298. The cysteine engineered anti-CD79b antibody may bind to a CD79b polypeptide. The cysteine engineered anti-CD79b antibody may be prepared by a process comprising replacing one or more amino acid residues of a parent anti-CD79b antibody by cysteine.

[0034] In one example, there is provided a cysteine engineered anti-CD79b antibody comprising one or more free cysteine amino acids wherein the cysteine engineered anti-CD79b antibody binds to a CD79b polypeptide and is prepared by a process comprising replacing one or more amino acid residues of a parent anti-CD79b antibody by cysteine wherein the parent antibody comprises at least one HVR sequence selected from:

(a) HVR-L1 comprising sequence A1-A15, wherein A1-A15 is KASQSVDYDGDSFLN (SEQ ID NO: 131) or KASQSVDYEGDSFLN (SEQ ID NO: 137);

(b) HVR-L2 comprising sequence B1-B7, wherein B1-B7 is AASNLES (SEQ ID NO: 132)

(c) HVR-L3 comprising sequence C1-C9, wherein C1-C9 is QQSNEDPLT (SEQ ID NO: 133)

(d) HVR-H1 comprising sequence D1-D10, wherein D1-D10 is GYTFSSYWIE (SEQ ID NO: 134)

(e) HVR-H2 comprising sequence E1-E18, wherein E1-E18 is GEILPGGGDTNYNEIFKG (SEQ ID NO: 135) and

(f) HVR-H3 comprising sequence F1-F10, wherein F1-F10 is TRRVPVYFDY (SEQ ID NO: 136) or TRRVPIRLDY (SEQ ID NO: 138).

[0035] The cysteine engineered anti-CD79b antibody may be a monoclonal antibody, antibody fragment, chimeric antibody, humanized antibody, single-chain antibody or antibody that competitively inhibits the binding of an anti-CD79b polypeptide antibody to its respective antigenic epitope. Antibodies of the present disclosure may optionally be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, an auristatin or maytansinoid. The antibodies of the present disclosure may optionally be produced in CHO cells or bacterial cells and preferably inhibit the growth or proliferation of or induce the death of a cell to which they bind. For diagnostic purposes, the antibodies of the present disclosure may be detectably labeled, attached to a solid support, or the like.

[0035a] In a second aspect, there is provided a polynucleotide encoding the anti-CD79b antibody of the first aspect.

[0035b] In a third aspect, there is provided a vector comprising the polynucleotide of the second aspect.

[0035c] In a fourth aspect, there is provided a host cell comprising the polynucleotide of the second aspect or the vector of the third aspect.

[0035d] In a fifth aspect, there is provided an immunoconjugate comprising the anti-CD79b antibody of the first aspect covalently attached to a cytotoxic agent.

[0035e] In a sixth aspect, there is provided an immunoconjugate comprising the formula: Ab-(L-D)$_p$, wherein:

a) Ab is the anti-CD79b antibody of the first aspect;

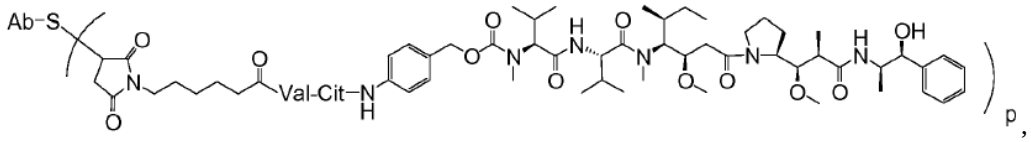
b) L is a linker moiety;

c) D is a drug moiety; and

d) p ranges from 1 to 8.

[0035f] In a seventh aspect, there is provided a composition comprising the anti-CD79b antibody of the first aspect or the immunoconjugate of the fifth or sixth aspect.

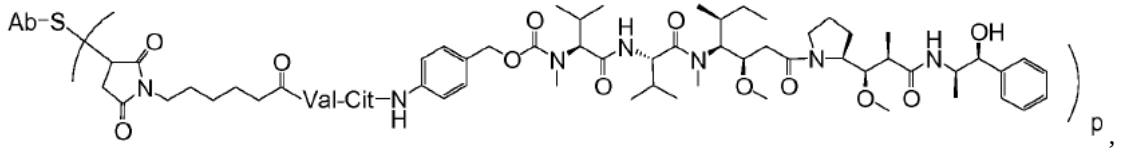
[0035g] In an eighth aspect, there is provided an immunoconjugate comprising the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and

Ab is an anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208.

[0035h] In a ninth aspect, there is provided an immunoconjugate comprising the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and

Ab is an anti-CD79b antibody comprising a light chain sequence of SEQ ID NO: 307 and a heavy chain sequence of SEQ ID NO: 308.

[0036] In one example, there is provided methods for making an antibody of the disclosure. For example, the disclosure provides a method of making a CD79b antibody (which, as defined herein includes full length and fragments thereof), said method comprising expressing in a suitable host cell a recombinant vector of the disclosure encoding said antibody (or fragment thereof), and recovering said antibody.

[0036a] In a tenth aspect, there is provided a method for making an immunoconjugate comprising the anti-CD79b antibody (Ab) of the first aspect and an auristatin or a maytansinoid drug moiety (D), wherein the anti-CD79b antibody is attached through one or more cysteine amino acids by a linker moiety (L) to D; the immunoconjugate comprising Formula I:

$$Ab–(L–D)p \qquad I$$

wherein p ranges from 1 to 8; the method comprising the steps of:

(a) reacting one or more cysteine amino acids of the anti-CD79b antibody with a linker reagent to form antibody-linker intermediate Ab-L; and

(b) reacting Ab-L with an activated drug moiety D; whereby the immunoconjugate is formed;

or comprising the steps of:

(c) reacting a nucleophilic group of a drug moiety with a linker reagent to form drug-linker intermediate D-L; and

(d) reacting D-L with one or more cysteine amino acids of the anti-CD79b antibody; whereby the immunoconjugate is formed.

[0037] In one example, there is provided a pharmaceutical formulation comprising an antibody of the disclosure or an antibody-drug conjugate of the disclosure, and a pharmaceutically acceptable diluent, carrier or excipient.

[0038] In one example, there is provided an article of manufacture comprising a container; and a composition contained within the container, wherein the composition comprises one or more CD79b antibodies of the disclosure.

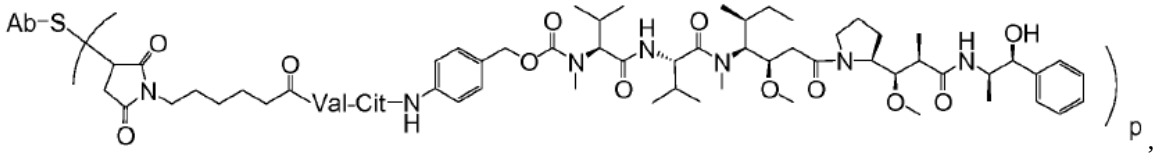
[0039] In one example, there is provided a kit comprising a first container comprising a composition comprising one or more CD79b antibodies of the disclosure; and a second container comprising a buffer.

[0040] In one example, there is provided use of a CD79b antibody of the disclosure in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor and/or a cell proliferative disorder.

[0040a] In an eleventh aspect, there is provided use of an effective amount of an immunoconjugate of the fifth or sixth aspect in the preparation of a medicament for treating a subject having a B cell proliferative disorder.

[0040b] In a twelfth aspect, there is provided use of an effective amount of an immunoconjugate in the preparation of a medicament for treating a subject having diffuse large B-cell lymphoma (DLBCL),

wherein the immunoconjugate comprises the formula:

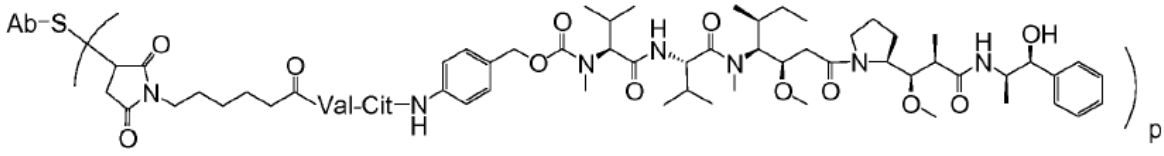


wherein Val is valine; Cit is citrulline; p is from 2 to 5; and Ab is an anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208; and

wherein the medicament is to be used in combination with an effective amount of each of i) rituximab, cyclophosphamide, doxorubicin, and prednisone, or ii) rituximab, cyclophosphamide, doxorubicin, and prednisolone.

[0040c] In a thirteenth aspect, there is provided use of an effective amount of an immunoconjugate in the preparation of a medicament for treating a subject having diffuse large B-cell lymphoma (DLBCL),

wherein the immunoconjugate comprises the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and Ab is an anti-CD79b antibody comprising a light chain sequence of SEQ ID NO: 307 and a heavy chain sequence of SEQ ID NO: 308; and

wherein the medicament is to be used in combination with an effective amount of each of i) rituximab, cyclophosphamide, doxorubicin, and prednisone, or ii) rituximab, cyclophosphamide, doxorubicin, and prednisolone.

[0041] In one example, there is provided use of an article of manufacture of the disclosure in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor and/or a cell proliferative disorder.

[0042] In one example, there is provided use of a kit of the disclosure in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a cancer, a tumor and/or a cell proliferative disorder.

[0043] In one example, there is provided a method of inhibiting the growth of a cell that expresses CD79b, said method comprising contacting said cell with an antibody of the disclosure thereby causing an

inhibition of growth of said cell. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

[0044] In one example, there is provided a method of therapeutically treating a mammal having a cancerous tumor comprising a cell that expresses CD79b, said method comprising administering to said mammal a therapeutically effective amount of an antibody of the disclosure, thereby effectively treating said mammal. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

[0045] In one example, there is provided a method for treating or preventing a cell proliferative disorder associated with increased expression of CD79b, said method comprising administering to a subject in need of such treatment an effective amount of an antibody of the disclosure, thereby effectively treating or preventing said cell proliferative disorder. In one example, said proliferative disorder is cancer. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

[0046] In one example, there is provided a method for inhibiting the growth of a cell, wherein growth of said cell is at least in part dependent upon a growth potentiating effect of CD79b, said method comprising contacting said cell with an effective amount of an antibody of the disclosure, thereby inhibiting the growth of said cell. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

[0047] In one example, there is provided a method of therapeutically treating a tumor in a mammal, wherein the growth of said tumor is at least in part dependent upon a growth potentiating effect of CD79b, said method comprising contacting said cell with an effective amount of an antibody of the disclosure, thereby effectively treating said tumor. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

[0048] In one example, there is provided a method of treating cancer comprising administering to a patient the pharmaceutical formulation comprising an immunoconjugate described herein, acceptable diluent, carrier or excipient.

[0049] In one example, there is provided a method of inhibiting B cell proliferation comprising exposing a cell to an immunoconjugate comprising an antibody of the disclosure under conditions permissive for binding of the immunoconjugate to CD79b.

[0050] In one example, there is provided a method of determining the presence of CD79b in a sample suspected of containing CD79b, said method comprising exposing said sample to an antibody of the disclosure, and determining binding of said antibody to CD79b in said sample wherein binding of said antibody to CD79b in said sample is indicative of the presence of said protein in said sample. In a fourteenth aspect, there is provided an *in vitro* method of determining the presence of CD79b in a biological sample suspected of containing CD79b, the method comprising *in vitro* exposing the biological sample to the anti-CD79b antibody of the first aspect or the immunoconjugate of the fifth or sixth aspect, and determining binding of the anti-CD79b antibody or the immunoconjugate to CD79b in the biological sample, wherein binding of the anti-CD79b antibody or the immunoconjugate to CD79b in the biological sample is indicative of the presence of CD79b in the biological sample.

[0051] In one example, there is provided a method of diagnosing a cell proliferative disorder associated with an increase in cells, such as B cells, expressing CD79b is provided, the method comprising contacting a test cells in a biological sample with any of the above antibodies; determining the level of antibody bound to test cells in the sample by detecting binding of the antibody to CD79b; and comparing the level of antibody bound to cells in a control sample, wherein the level of antibody bound is normalized to the number of CD79b-expressing cells in the test and control samples, and wherein a higher level of antibody bound in the test sample as compared to the control sample indicates the presence of a cell proliferative disorder associated with cells expressing CD79b.

[0052] In one example, there is provided a method of detecting soluble CD79b in blood or serum, the method comprising contacting a test sample of blood or serum from a mammal suspected of experiencing a B cell proliferative disorder with an anti-CD79b antibody of the disclosure and detecting a increase in soluble CD79b in the test sample relative to a control sample of blood or serum from a normal mammal.

[0053] In one example, there is provided a method of binding an antibody of the disclosure to a cell that expresses CD79b, said method comprising contacting said cell with an antibody of the disclosure. In one example, the antibody is conjugated to a cytotoxic agent. In one example, the antibody is conjugated to a growth inhibitory agent.

BRIEF DESCRIPTION OF THE DRAWINGS

[0054] Figure 1 shows a nucleotide sequence (SEQ ID NO: 1) of a PRO36249 cDNA, wherein SEQ ID NO: 1 is a clone designated herein as “DNA225786" (also referred here in as “CD79b"). The nucleotide sequence encodes for CD79b with the start and stop codons shown in bold and underlined.

[0055] Figure 2 shows the amino acid sequence (SEQ ID NO: 2) derived from the coding sequence of SEQ ID NO: 1 shown in Figure 1.

[0056] Figure 3 shows the nucleotide sequence (SEQ ID NO: 3) of the light chain of chimeric CD79b murine antibody (chMA79b) IgG1 (MA79b is a murine monoclonal anti-CD79b antibody). The nucleotide sequence encodes for the light chain of chMA79b with the start and stop codons shown in bold and underlined.

[0057] Figure 4 shows the amino acid sequence (SEQ ID NO: 4), missing the first 18 amino acid signal sequence, derived from the coding sequence of SEQ ID NO: 3 shown in Figure 3. Variable regions are regions not underlined.

[0058] Figure 5 shows the nucleotide sequence (SEQ ID NO: 5) of the heavy chain of chimeric murine antibody (chMA79b) IgG1 (MA79b is a murine monoclonal anti-CD79b antibody). The nucleotide sequence encodes for the heavy chain of chMA79b with the start and stop codons shown in bold and underlined.

[0059] Figure 6 shows the amino acid sequence (SEQ ID NO: 6), missing the first 18 amino acid signal sequence and the last lysine (K) prior to the stop codon, derived from the coding sequence of SEQ ID NO: 5 shown in Figure 5. Variable regions are regions not underlined.

[0060] Figures 7A-B show the alignment of sequences of the variable light chains for the following: light chain human kappa I consensus sequence (labeled as “huKI”; SEQ ID NO: 9) with VL-FR1, VL-FR2, VL-FR3, VL-FR4 (SEQ ID NOs: 139-142, respectively), murine anti-CD79b antibody (labeled as “MA79b”; SEQ ID NO: 10), MA79b-grafted “humanized” antibody (labeled as “huMA79b graft”; SEQ ID NO: 11), MA79b-grated “humanized” antibody variant 17 (labeled as “huMA79b.v17”; SEQ ID NO: 169), MA79b-grafted “humanized” antibody variant 18 (labeled as “huMA79b.v18”; SEQ ID NO: 188), MA79b-grafted “humanized” antibody variant 28 (labeled as “huMA79b.v28”; SEQ ID NO: 207) and MA79b-grafted “humanized” antibody variant 32 (labeled as “huMA79b.v32”; SEQ ID NO: 226). Positions are numbered according to Kabat and hypervariable regions (HVRs) grafted from MA79b to the variable light Kappa I consensus framework are boxed.

[0061] Figures 8A-B show the alignment of sequences of the variable heavy chains for the following: heavy chain human subgroup III consensus sequence (labeled as “humIII”; SEQ ID NO: 13) with VH-FR1, VH-FR2, VH-FR3, and VH-FR4 (SEQ ID NOs: 143-146), murine anti-CD79b antibody (labeled as “MA79b”; SEQ ID NO: 14), MA79b-grafted “humanized” antibody (labeled as “huMA79b graft”; SEQ ID NO: 15) (containing

What is claimed is:

1. An anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208.

2. The anti-CD79b antibody of claim 1, wherein the light chain comprises the sequence of SEQ ID NO: 307 and the heavy chain comprises the sequence of SEQ ID NO: 308.

3. The anti-CD79b antibody of claim 1 or 2, wherein the anti-CD79b antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody, a chimeric antibody, a humanized antibody, and any antibody fragments thereof.

4. The anti-CD79b antibody of any one of claims 1-3, wherein the anti-CD79b antibody is an antibody fragment.

5. A polynucleotide encoding the anti-CD79b antibody of any one of claims 1-4.

6. A vector comprising the polynucleotide of claim 5.

7. A host cell comprising the polynucleotide of claim 5 or the vector of claim 6.

8. The host cell of claim 7, wherein the host cell is an eukaryotic host cell.

9. An immunoconjugate comprising the anti-CD79b antibody of any one of claims 1-4 covalently attached to a cytotoxic agent.

10. The immunoconjugate of claim 9, wherein the cytotoxic agent is selected from the group consisting of a toxin, a therapeutic agent, a drug moiety, an antibiotic, a radioactive isotope, and a nucleolytic enzyme.

11. An immunoconjugate comprising the formula: Ab-$(L\text{-}D)_p$, wherein:

a) Ab is the anti-CD79b antibody of any one of claims 1-4;

b) L is a linker moiety;

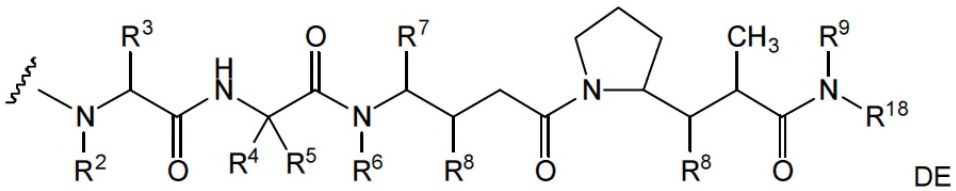
c) D is a drug moiety; and

d) p ranges from 1 to 8.

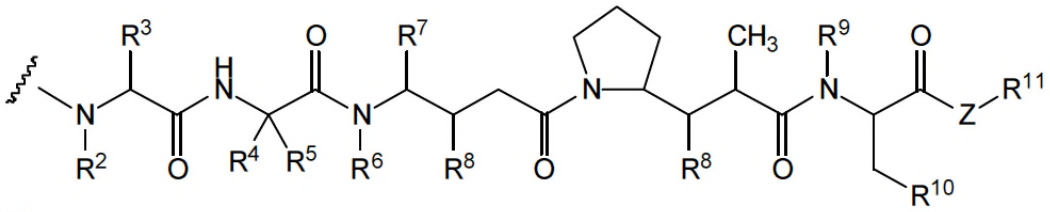
12. The immunoconjugate of claim 11, wherein L comprises a linker selected from one or more of 6-maleimidocaproyl (MC), maleimidopropanoyl (MP), valine-citrulline (val-cit), alanine-phenylalanine (ala-phe), p-aminobenzyloxycarbonyl (PAB), N-Succinimidyl 4-(2-pyridylthio) pentanoate (SPP), N-succinimidyl 4-(N-maleimidomethyl) cyclohexane-1 carboxylate (SMCC), 4-(2-Pyridyldithio)butyric acid-N-hydroxysuccinimide ester (SPDB), bis-maleimido-trioxyethylene glycol (BMPEO), and N-Succinimidyl (4-iodo-acetyl) aminobenzoate (SIAB).

13. The immunoconjugate of claim 11 or 12, wherein D is selected from the group consisting of a maytansinoid, an auristatin, and a dolastatin.

14. The immunoconjugate of claim 13, wherein D is an auristatin or a dolastatin, and wherein D is a drug moiety of formula DE or DF:



DE



DF

and wherein R^2 and R^6 are each methyl, R^3 and R^4 are each isopropyl, R^5 is H or methyl, R^7 is sec-butyl, each R^8 is independently selected from CH_3, O-CH_3, OH, and H; R^9 is H; R^{10} is aryl; Z is –O– or –NH–; R^{11} is H, C_1-C_8 alkyl, or $–(CH_2)_2–O–(CH_2)_2–O–(CH_2)_2–O–CH_3$; and R^{18} is $–C(R^8)_2–C(R^8)_2–$aryl.

15. The immunoconjugate of any one of claims 11-13, wherein D is MMAE or MMAF.

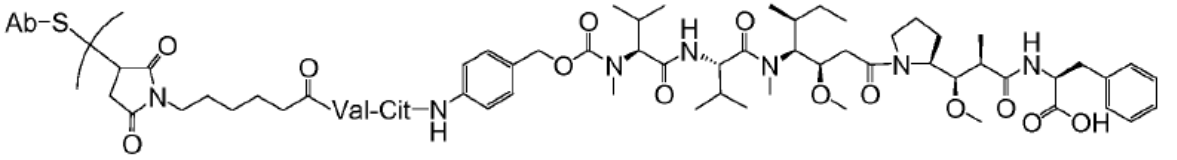
16. The immunoconjugate of any one of claims 11-15, wherein L comprises val-cit, MC, PAB, and/or MC-PAB.

17. The immunoconjugate of any one of claims 11-16, wherein L comprises MC-val-cit-PAB.

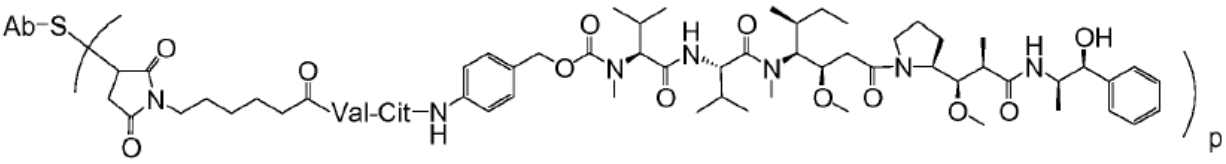
18. The immunoconjugate of any one of claims 11-13, wherein D is a maytansinoid.

19. The immunoconjugate of claim 18, wherein the maytansinoid is selected from DM1, DM3, and DM4.

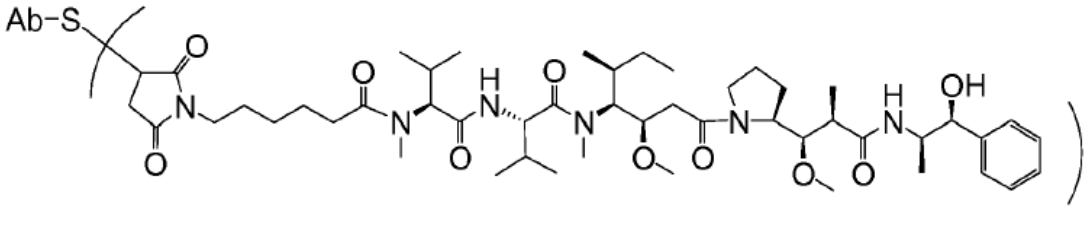
20. The immunoconjugate of any one of claims 11-19, wherein the immunoconjugate comprises a formula selected from the group consisting of:



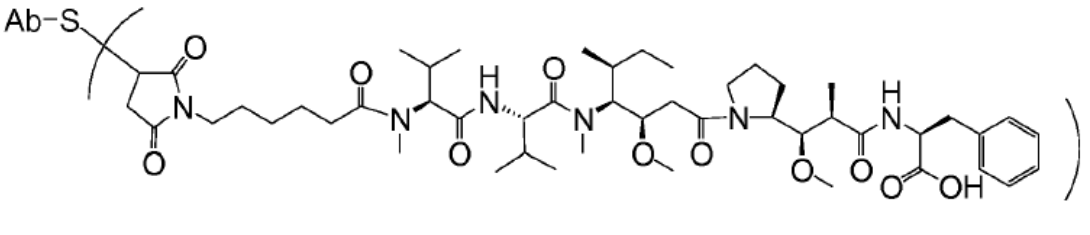
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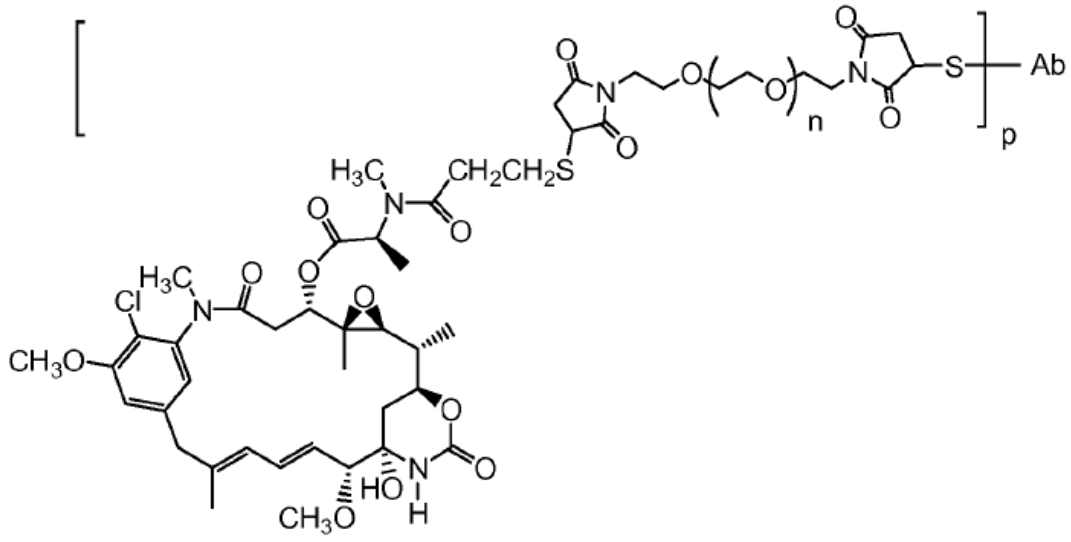
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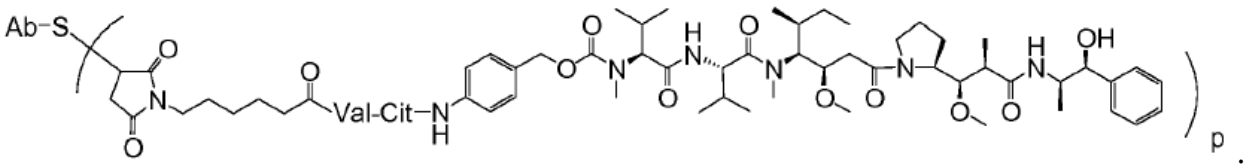
; and



;

wherein Val is valine and Cit is citrulline.

21. The immunoconjugate of claim 20, wherein the immunoconjugate comprises the formula:



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22. The immunoconjugate of any one of claims 11-21, wherein p is from 2 to 5.

23. The immunoconjugate of any one of claims 11-22, wherein p is from 3 to 4.

24. A composition comprising the anti-CD79b antibody of any one of claims 1-4 or the immunoconjugate of any one of claims 9-23.

25. Use of an effective amount of an immunoconjugate of any one of claims 9-23 in the preparation of a medicament for treating a subject having a B cell proliferative disorder.

26. The use of claim 25, wherein the B cell proliferative disorder is selected from the group consisting of lymphoma, myeloma, non-Hodgkin's lymphoma (NHL), diffuse large B-cell lymphoma (DLBCL), aggressive NHL, indolent lymphoma, follicular lymphoma (FL), relapsed aggressive NHL, relapsed indolent NHL, relapsed NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), and mantle cell lymphoma.

27. The use of claim 25 or 26, wherein the B cell proliferative disorder is NHL.

28. The use of claim 25 or 26, wherein the B cell proliferative disorder is DLBCL.

29. The use of claim 25 or 26, wherein the B cell proliferative disorder is relapsed NHL or refractory NHL.

30. The use of claim 25 or 26, wherein the B cell proliferative disorder is FL.

31. The use of any one of claims 25-30, wherein the medicament is to be used in combination with an effective amount of another therapeutic agent.

32. The use of claim 31, wherein the therapeutic agent is selected from the group consisting of an antibody, a chemotherapeutic agent, a cytotoxic agent, an anti-angiogenic agent, an immunosuppressive agent, a prodrug, a cytokine, a cytokine antagonist, cytotoxic radiotherapy, a corticosteroid, a cancer vaccine, and a growth-inhibitory agent.

33. The use of claim 31 or 32, wherein the therapeutic agent is selected from one or more of tamoxifen, letrozole, exemestane, anastrozole, irinotecan, cetuximab, fulvestrant, vinorelbine, erlotinib, bevacizumab, vincristine, imatinib mesylate, sorafenib, lapatinib, trastuzumab, cisplatin, gemcitabine, methotrexate, vinblastine, carboplatin, paclitaxel, 5-fluorouracil, doxorubicin, bortezomib, melphalan, prednisone, prednisolone, cyclophosphamide, hydroxydaunorubicin, and docetaxel.

34. The use of claim 31 or 32, wherein the therapeutic agent is an anti-CD20 antibody.

35. The use of claim 31 or 32, wherein the therapeutic agent is an anti-CD20 antibody, and wherein the B cell proliferative disorder is DLBCL.

36. The use of claim 31 or 32, wherein the therapeutic agent is an anti-CD20 antibody, and wherein the B cell proliferative disorder is FL.

37. The use of any one of claims 34-36, wherein the anti-CD20 antibody is rituximab.

38. The use of claim 31 or 32, wherein the therapeutic agent is a chemotherapeutic agent.

39. The use of claim 38, wherein the chemotherapeutic agent comprises one or more of i) cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone, or ii) cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone.

40. The use of claim 38 or 39, wherein the chemotherapeutic agent comprises i) cyclophosphamide, doxorubicin, and prednisone, or ii) cyclophosphamide, doxorubicin, and prednisolone.

41. The use of claim 34, wherein the medicament is to be used in further combination with an effective amount of a chemotherapeutic agent.

42. The use of claim 41, wherein the chemotherapeutic agent comprises i) cyclophosphamide, doxorubicin, and prednisone, or ii) cyclophosphamide, doxorubicin, and prednisolone.

43. The use of claim 42, wherein the proliferative disorder is NHL.

44. The use of claim 43, wherein the anti-CD20 antibody is rituximab.

45. The use of claim 42, wherein the proliferative disorder is DLBCL.

46. The use of claim 45, wherein the anti-CD20 antibody is rituximab.

47. An *in vitro* method of determining the presence of CD79b in a biological sample suspected of containing CD79b, the method comprising *in vitro* exposing the biological sample to the anti-CD79b antibody of any one of claims 1-4 or the immunoconjugate of any one of claims 9-23, and determining binding of the anti-CD79b antibody or the immunoconjugate to CD79b in the biological sample, wherein binding of the anti-CD79b antibody or the immunoconjugate to CD79b in the biological sample is indicative of the presence of CD79b in the biological sample.

48. A method for making an immunoconjugate comprising the anti-CD79b antibody (Ab) of any one of claims 1-4 and an auristatin or a maytansinoid drug moiety (D), wherein the anti-CD79b antibody is attached through one or more cysteine amino acids by a linker moiety (L) to D; the immunoconjugate comprising Formula I:

$$Ab–(L–D)_p \qquad \mathbf{I}$$

wherein p ranges from 1 to 8; the method comprising the steps of:
(a) reacting one or more cysteine amino acids of the anti-CD79b antibody with a linker reagent to form antibody-linker intermediate Ab-L; and

(b) reacting Ab-L with an activated drug moiety D; whereby the immunoconjugate is formed;

or comprising the steps of:

(c) reacting a nucleophilic group of a drug moiety with a linker reagent to form drug-linker intermediate D-L; and

(d) reacting D-L with one or more cysteine amino acids of the anti-CD79b antibody; whereby the immunoconjugate is formed.

49. The method of claim 48, further comprising the step of expressing the anti-CD79b antibody in Chinese hamster ovary (CHO) cells before step (a) or step (d).

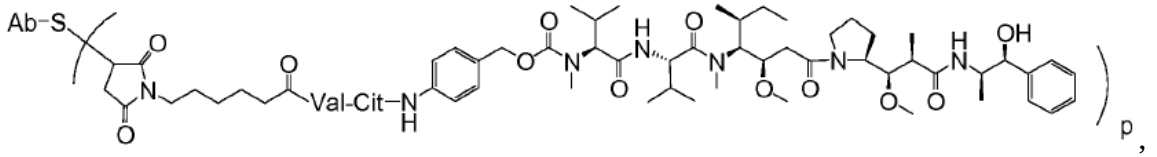
50. The method of claim 49, further comprising the step of treating the expressed anti-CD79b antibody with a reducing agent before step (a) or step (d).

51. The method of claim 50, wherein the reducing agent is TCEP or DTT.

52. The method of claim 50 or 51, further comprising the step of treating the expressed anti-CD79b antibody with an oxidizing agent after treating with the reducing agent.

53. The method of claim 52, wherein the oxidizing agent is selected from copper sulfate, dehydroascorbic acid, and air.

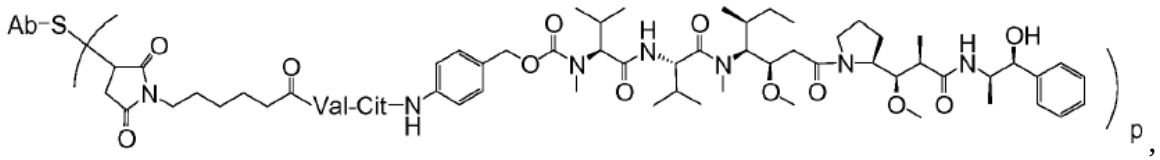
54. An immunoconjugate comprising the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and

Ab is an anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208.

55. An immunoconjugate comprising the formula:



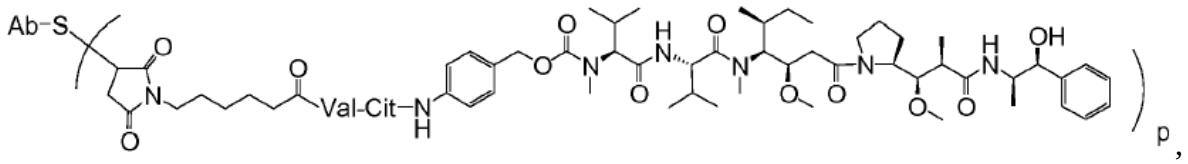
wherein Val is valine; Cit is citrulline; p is from 2 to 5; and

Ab is an anti-CD79b antibody comprising a light chain sequence of SEQ ID NO: 307 and a heavy chain sequence of SEQ ID NO: 308.

56. The immunoconjugate of claim 54 or 55, wherein p is from 3 to 4.

57. Use of an effective amount of an immunoconjugate in the preparation of a medicament for treating a subject having diffuse large B-cell lymphoma (DLBCL),

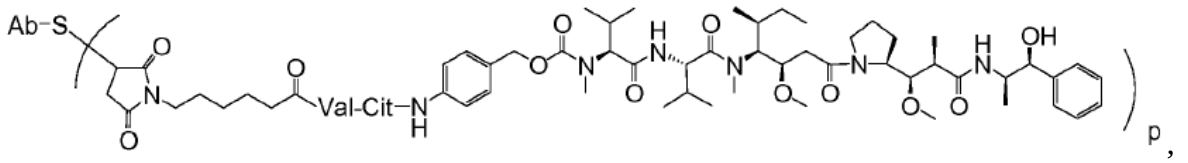
wherein the immunoconjugate comprises the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and Ab is an anti-CD79b antibody comprising a light chain variable domain sequence of SEQ ID NO: 207 and a heavy chain variable domain sequence of SEQ ID NO: 208; and
wherein the medicament is to be used in combination with an effective amount of each of i) rituximab, cyclophosphamide, doxorubicin, and prednisone, or ii) rituximab, cyclophosphamide, doxorubicin, and prednisolone.

58. Use of an effective amount of an immunoconjugate in the preparation of a medicament for treating a subject having diffuse large B-cell lymphoma (DLBCL),

wherein the immunoconjugate comprises the formula:



wherein Val is valine; Cit is citrulline; p is from 2 to 5; and Ab is an anti-CD79b antibody comprising a light chain sequence of SEQ ID NO: 307 and a heavy chain sequence of SEQ ID NO: 308; and

wherein the medicament is to be used in combination with an effective amount of each of i) rituximab, cyclophosphamide, doxorubicin, and prednisone, or ii) rituximab, cyclophosphamide, doxorubicin, and prednisolone.

59. The use of claim 57 or 58, wherein p is from 3 to 4.