CLAIMS

What is Claimed:

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule comprises at least one of:

a) a variable heavy chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 17, 51, 73, and 95,

b) a variable heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 18, 52, 74, and 96,

c) a variable heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 19, 53, 75, and 97,

d) a variable light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 56, 78, and 100,

e) a variable light chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 23, 57, 79, and 101,

f) a variable light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 24, 58, 80, and 102.

2. The chimeric antigen receptor according to claim 1 having no more than 8 amino acid substitutions.

3. The chimeric antigen receptor according to claim 1 further comprising at least one costimulatory domain.

4. The chimeric antigen receptor according to claim 1 further comprising at least one activating domain.

5. The chimeric antigen receptor according to claim 3 wherein the costimulatory domain is a signaling region (or other suitable portion) of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CDl la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-

2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

6. The chimeric antigen receptor according to claim 5 wherein the costimulatory domain comprises CD28.

7. The chimeric antigen receptor according to claim 6 wherein the CD28 costimulatory domain comprises a sequence selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, and SEQ ID NO. 8.

8. The chimeric antigen receptor according to claim 5 wherein the CD8 costimulatory domain comprises SEQ ID NO. 14.

9. The chimeric antigen receptor according to claim 4 wherein the activating domain comprises CD3.

10. The chimeric antigen receptor according to claim 9 wherein the CD3 comprises CD3 zeta.

11. The chimeric antigen receptor according to claim 10 wherein the CD3 zeta comprises SEQ ID NO. 10.

12. The chimeric antigen receptor according to claim 1 further comprising SEQ ID NO. 2 and SEQ ID NO. 10.

13. An isolated polynucleotide encoding the chimeric antigen receptor of claim 1.

14. A vector comprising the polynucleotide of claim 13.

15. The vector according to claim 14 which is a retroviral vector, a DNA vector, a plasmid, a RNA vector, an adenoviral vector, an adenovirus associated vector, a lentiviral vector, or any combination thereof.

16. An immune cell comprising the vector of claim 14.

17. The immune cell according to claim 16, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.

18. The immune cell according to claim 17, wherein the cell is an autologous T cell.

19. The immune cell according to claim 17, wherein the cell is an allogeneic T cell.

20. A chimeric antigen receptor having at least 90% identity to the sequence of the antigen binding molecule of claim 1.

21. A chimeric antigen receptor having at least 95% identity to the sequence of the antigen binding molecule of claim 1.

22. A pharmaceutical composition comprising the T cell of claim 17, 18, or 19.

23. A chimeric antigen receptor comprising at least one of:

(a) a VH region comprising the amino acid sequence of SEQ ID NO: 16 and a VL region comprising the amino acid sequence of SEQ ID NO: 21;

(b) a VH region comprising the amino acid sequence of SEQ ID NO: 50 and a VL region comprising the amino acid sequence of SEQ ID NO: 55;

(c) a VH region comprising the amino acid sequence of SEQ ID NO: 72 and a VL region comprising the amino acid sequence of SEQ ID NO: 77;

(d) a VH region comprising the amino acid sequence of SEQ ID NO: 94 and a VL region comprising the amino acid sequence of SEQ ID NO: 99;

wherein the VH and VL region is linked by at least one linker.

24. The chimeric antigen receptor according to claim 23 having no more than 8 amino acid substitutions.

25. The chimeric antigen receptor according to claim 23, wherein the linker comprises at least one of SEQ ID NO. 130 and SEQ ID NO. 132.

26. The chimeric antigen receptor according to claim 23, further comprising at least one costimulatory domain.

27. The chimeric antigen receptor according to claim 23, further comprising at least one activating domain.

28. The chimeric antigen receptor according to claim 26 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30,

CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CDl la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

29. An immune cell comprising the chimeric antigen receptor of claim 23.

30. The immune cell according to claim 29, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.

31. The T cell of claim 30 that is an autologous T cell.

32. The T cell of claim 30 that is an allogeneic T cell.

33. A pharmaceutical composition comprising the immune cell of claim 29.

~~34. An isolated polynucleotide comprising at least one of:~~

- ~~SEQ ID NO. 27; SEQ ID NO. 31; SEQ ID NO. 35; SEQ ID NO. 39; SEQ ID NO. 43; SEQ ID NO. 47; SEQ ID NO. 61; SEQ ID NO. 65; SEQ ID NO. 69; SEQ ID NO. 83; SEQ ID NO. 87; SEQ ID NO. 91; SEQ ID NO. 105; SEQ ID NO. 109; SEQ ID NO. 113; SEQ ID NO. 117; SEQ ID NO. 121; and SEQ ID NO. 125.~~

~~35. A vector comprising the polynucleotide according to claim 34.~~

~~36. An immune cell comprising the vector of claim 33.~~

~~37. The immune cell according to claim 36, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR expressing cell, dendritic cell, or NK T cell.~~

~~38. The T cell of claim 37 that is an autologous T cell.~~

~~39. The T cell of claim 37 that is an allogeneic T cell.~~

~~40. An isolated polypeptide comprising the amino acid sequence set forth in at least one of:~~

- ~~SEQ ID NO. 28; SEQ ID NO. 32; SEQ ID NO. 36; SEQ ID NO. 40; SEQ ID NO. 44; SEQ ID NO. 48; SEQ ID NO. 62; SEQ ID NO. 66; SEQ ID NO. 70; SEQ ID NO. 84; SEQ ID NO. 88; SEQ ID NO. 92; SEQ ID NO. 106; SEQ ID NO. 110; SEQ ID NO. 114; SEQ ID NO. 118; SEQ ID NO. 122; and SEQ ID NO. 126.~~

~~41. The isolated polypeptide according to claim 40 having no more than 8 amino acid substitutions.~~

~~42. A vector encoding the polypeptide of claim 40.~~

~~43. An immune cell comprising the vector of claim 42.~~

~~44. The immune cell according to claim 43, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR expressing cell, dendritic cell, or NK T cell.~~

~~45. The T cell of claim 44 that is an autologous T cell or an allogeneic T cell.~~

~~46.~~34. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule comprises a variable heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 19, 53, 75, and 97.

~~47.~~35. The polynucleotide according to claim ~~46~~ 34 further comprising an activating domain.

~~48.~~36. The polynucleotide according to claim ~~47~~ 35 wherein the activating domain is CD3.

~~49.~~37. The polynucleotide according to claim ~~48~~ 36 wherein the CD3 is CD3 zeta.

~~50.~~38. The polynucleotide according to claim ~~49~~ 37 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO. 9.

~~51.~~39. The polynucleotide according to claim ~~46~~ 34 further comprising a costimulatory domain.

~~52.~~40. The polynucleotide according to claim ~~51~~ 39 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CDl la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

~~53.~~41. The polynucleotide according to claim ~~52~~ 40 wherein the CD28 costimulatory domain encodes the amino acid sequence set forth in SEQ ID NO 2.

~~54.~~42. A vector comprising the polynucleotide of claim ~~46~~34.

~~55.~~43. An immune cell comprising the vector of claim ~~54~~42.

~~56.~~44. The immune cell of claim ~~50~~43, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.

~~57.~~45. The immune~~T~~ cell of claim ~~51~~ 44, wherein the immune cell is a T cell that is an autologous T cell, or an allogeneic T cell.

~~58.~~46. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR), said CAR or TCR comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule comprises a variable light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 58, 80, and 102.

~~59.~~47. The polynucleotide according to claim ~~58~~ 46 further comprising an activating domain.

~~60.~~48. The polynucleotide according to claim ~~59~~ 47 wherein the activating domain is CD3.

~~61.~~49. The polynucleotide according to claim ~~60~~ 48 wherein the CD3 is CD3 zeta.

~~62.~~50. The polynucleotide according to claim ~~61~~ 49 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO. 9.

~~63.~~51. The polynucleotide according to claim ~~58~~ 46 further comprising a costimulatory domain.

~~64.~~52. The polynucleotide according to claim ~~63~~ 51 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CDl la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

~~65.~~53. The polynucleotide according to claim ~~64~~ 52 wherein the CD28 costimulatory domain comprises the nucleotide sequence set forth in SEQ ID NO 3 or in SEQ ID NO 1.

~~66.~~54. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO. 17), CDR2

(SEQ ID NO. 18), and CDR3 (SEQ ID NO. 19) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO. 22), CDR2 (SEQ ID NO. 23), and CDR3 (SEQ ID NO. 24).

~~67.~~55. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO. 51), CDR2 (SEQ ID NO. 52), and CDR3 (SEQ ID NO. 53) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO. 56), CDR2 (SEQ ID NO. 57), and CDR3 (SEQ ID NO. 58).

~~68.~~56. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO. 73), CDR2 (SEQ ID NO. 74), and CDR3 (SEQ ID NO. 75) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO. 78), CDR2 (SEQ ID NO. 79), and CDR3 (SEQ ID NO. 80).

~~69.~~57. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO. 95), CDR2 (SEQ ID NO. 96), and CDR3 (SEQ ID NO. 97) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO. 100), CDR2 (SEQ ID NO. 101), and CDR3 (SEQ ID NO. 102).

~~70.~~58. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to CLL-1, wherein the antigen binding molecule comprises:

(a) a heavy chain variable region (VH) complementarity determining region (CDR) 1 comprising the amino acid sequence $GX_2X_3X_4X_5X_6X_7X_8X_9$ (SEQ ID NO: 134), wherein:

X_2 is G, F, or Y;

X_3 is S or T;

X_4 is I, F, or L;

X_5 is S or T;

X_6 is not present or S;

X_7 is not present or G;

X_8 is not present or E or G; and

X_9 is F, L, or Y;

(b) a heavy chain variable region (VH) complementarity determining region (CDR) 2 comprising the amino acid sequence $X_1X_2X_3X_4X_5X_6$ (SEQ ID NO: 135), wherein:

X_1 is D, H, S, or Y;

X_2 is H, P, or Y;

X_3 is D, E, or S;

X_4 is D or G;

X_5 is G or S; and

X_6 is not present of D or E;

(c) a heavy chain variable region (VH) complementarity determining region (CDR) 3, comprising the amino acid sequence $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}$DY (SEQ ID NO: 136), wherein:

X_1 is E or L;

X_2 is R, S, or V;

X_3 is R or Y;

X_4 is C, G, or S;

X_5 is not present or G or I;

X_6 is not present or G;

X_7 is not present or D;

X_8 is not present or C;

X_9 is not present or W or Y;

X_{10} is not present or P or S;

X_{11} is not present or G or Y; and

X_{12} is F or R;

(d) a light chain variable region (VL) CDR1 comprising the amino acid sequence X_1ASQ$X_5X_6X_7X_8X_9$LX_{11} (SEQ ID NO: 137), wherein

X_1 is Q or R;

X_5 is D or S;

X_6 is I or V;

X_7 is N or S;

X_8 is N or S;

X_9 is F, L, or Y; and

X_{11} is N or T;

(e) a light chain variable region (VL) CDR2 comprising the amino acid sequence $X_1ASX_4X_5X_6X_7$ (SEQ ID NO: 138), wherein

X_1 is D or G;

X_4 is N, S, or T;

X_5 is L or R;

X_6 is A, E, or K; and

X_7 is S or T; and/or

(f) a light chain variable region (VL) CDR3 comprising the amino acid sequence $QQX_3X_4X_5X_6PX_8T$ (SEQ ID NO: 139), wherein

X_3 is S or Y;

X_4 is D, G, or Y;

X_5 is N, S, or T;

X_6 is L, T, or Y; and

X_8 is F or I.

~~71.~~59. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polynucleotide according to any of claims ~~46~~34, ~~58~~46, ~~66~~54, ~~67~~55, ~~68~~56, ~~69~~57, or ~~70~~58.

~~72. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polypeptide according to 40.~~

~~73.~~60. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the chimeric antigen receptor according to any of claims 1, 20, 21, and 23.

~~74.~~61. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the cells according any of claims 16, 29, ~~36,~~ 43, 44, and ~~55~~45.

~~75.~~62. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the composition according to claim 22 and 33.

~~76.~~63. The method according to any of claims ~~71-75~~59-62 wherein the disease or disorder is cancer.

~~77.~~64. The method according to claim ~~76~~ 63 wherein the cancer is leukemia, lymphoma, or myeloma.

~~78.~~65. The method according to any of claims ~~71-75~~59-62 wherein the disease or disorder is at least one of acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia, atypical chronic myeloid leukemia, acute promyelocytic leukemia (APL), acute monoblastic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia, myelodysplastic syndrome (MDS), myeloproliferative disorder, myeloid neoplasm, myeloid sarcoma), Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN), and inflammatory/autoimmune disease.

~~79.~~66. The method according to claim ~~78~~ 65 wherein the inflammatory/autoimmune disease is at least one of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalga, mastocytosis, and Celiac disease.

~~80.~~67. The lentiviral vector according to claim 15 that comprises pGAR, or a derivative thereof.