

28. The engineered polynucleotide according to claim 27, wherein the polynucleotide is in a vector.
29. An engineered cell comprising the polypeptide according to any one of claims 15-26.
30. An engineered cell comprising the polynucleotide according to any one of claims 24-25.
- 5 31. The engineered cell according to any one of claims 29-30, wherein the engineered cell comprises T-cells or Natural Killer cells.
32. The engineered cell according to any one of claims 31, wherein the cell is a T-cell or Natural Killer cell.
33. The engineered cell according to any one of claims 32, wherein the T-cell is a CD4 T-cell  
10 or CD8 T-cell.
34. The engineered cell according to any one of claims 31, wherein the Natural Killer cell is a NKT cell or NK-92 cell.
35. Use of an engineered cell according to any one of claims 1-15 and 29-34 in the manufacture of a medicament for treating B-cell lymphoma.
- 15 36. Use of an engineered cell according to any one of claims 1-15 and 29-34 in the manufacture of a medicament for treating T-cell lymphoma.
37. Use of an engineered cell according to any one of claims 1-15 and 29-34 in the manufacture of a medicament for treating multiple myeloma.
38. Use of an engineered cell according to any one of claims 1-15 and 29-34 in the  
20 manufacture of a medicament for treating chronic myeloid leukemia, wherein the

target of the first antigen recognition domain comprises CD33; and the target of the second antigen recognition domain comprises CD123.

39. Use of an engineered cell according to any one of claims 1-15 in the manufacture of a medicament for treating B-cell acute lymphoblastic leukemia (B-ALL), wherein the target of the first antigen recognition domain comprises CD19; and the target of the second antigen recognition domain comprises CD123.

40. Use of an engineered cell according to any one of claims 1-6 in the manufacture of a medicament for treating multiple myeloma, wherein the target of the first antigen recognition domain is selected from the group consisting of CD38, CS1, BCMA, and CD38; and the target of the second antigen recognition domain is selected from the group consisting of CD38, CS1, BCMA, and CD38.

41. Use of an engineered cell according to any one of claims 1-15 in the manufacture of a medicament for treating a cell proliferative disease, wherein the target of the first antigen recognition domain is selected from the group consisting of BCMA, TAC1, CS1, and BAFF-R; and the target of the second antigen recognition domain is selected from the group consisting of BCMA, TAC1, CS1, and BAFF-R.

42. The use according to claim 41, wherein the cell proliferative disease is selected from the group consisting of lymphomas, leukemias, and plasma cell neoplasms.

43. The use according to claim 42, wherein plasma cell neoplasms is selected from plasma cell leukemia, multiple myeloma, plasmacytoma, amyloidosis, waldestrom's macroglobulinema, heavy chain diseases, solitary bone plamacytoma,

monoclonal gammopathy of undetermined significance (MGUS), and smoldering multiple myeloma.

44. Use of an engineered cell according to any one of claims 30-34 in the manufacture of a medicament for treating a cell proliferative disease.

5 45. Use of an engineered cell comprising a chimeric antigen receptor polypeptide having an antigen recognition domain selective for a target selected from the group consisting of interleukin 6 receptor, NY-ESO-1, alpha fetoprotein (AFP), glypican-3 (GPC3), BCMA, BAFF-R, TACI, LeY, CD5, CD13, CD14, CD15, CD45, CD19, CD20, CD22, CD33, CD41, CD61, CD64, CD68, CD117, CD123, CD138, CD267, CD269, CD38, Flt3 receptor, and CS1; and CAR  
10 enhancing agent in the manufacture of a medicament for treating a cell proliferative disease.

46. The use according to claim 45, wherein said CAR enhancing agent is selected from the group consisting of agents that target immune-checkpoint pathways, inhibitors of colony stimulating factor-1 receptor (CSF1R), PD-1, PD-L1, IL-2, IL-12, IL-15, CSF1R, CTAL-4, TIM-3, and TGFR beta.

15 47. Use of an engineered cell comprising an engineered polypeptide according to any one of claims 13-23 in the manufacture of a medicament for treating a cell proliferative disease.

48. An engineered chimeric antigen receptor polypeptide, the polypeptide comprising: a signal peptide, a CD45 antigen recognition domain, a hinge region, a transmembrane domain, at least one co-stimulatory domain, and a signaling domain.

NKG2C, NKG2D, B7-H3, a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS, and 4-1BB (CD137), active fragments thereof, and combinations thereof.

55. An engineered polynucleotide that encodes a polypeptide according to any one of claims 48-54.

5 56. The engineered polynucleotide according to claim 55, wherein the polynucleotide is in a vector.

57. An engineered cell comprising the polynucleotide according to any one of claims 55-56.

58. An engineered cell comprising the polypeptide according to any one of claims 48-54.

59. The engineered cell according to any one of claims 57-58, wherein the cell is a T-cell or  
10 Natural Killer cell.

60. The engineered cell according to claim 59, wherein the T-cell is a CD4 T-cell or CD8 T-cell.

61. The engineered cell according to claim 59, wherein the Natural Killer cell is a NKT cell or NK-92cell.

15 62. An *in vitro* method of reducing the number of target cells, the method comprising the steps of:

i. contacting said target cells with an effective amount of an engineered cell according to any one of claims 1-14, 29-34, and 57-61; and

ii. optionally, assaying for the reduction in the number of said cells;

20 wherein said target cells comprise at least one cell surface antigen selected from the group consisting of interleukin 6 receptor, NY-ESO-1, alpha fetoprotein (AFP), glypican-3 (GPC3), BCMA, BAFF-R, TACI, LeY, CD5, CD13, CD14, CD15 CD19, CD20, CD22, CD33, CD41,