Claims

1. A polynucleotide molecule comprising a nucleotide sequence encoding a chimeric antigen receptor (CAR) or a fragment thereof i) comprising an extracellular domain comprising an antigen-binding region which binds to epidermal growth factor receptor variant III (EGFRvIII); or ii) comprising an extracellular domain comprising an antigen-binding region which binds to CD19; wherein the nucleotide sequence encoding the CAR is operably linked to a promoter and wherein the polynucleotide molecule further comprises a nucleotide sequence encoding a heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP).

2. The polynucleotide molecule of claim 1, wherein the polynucleotide molecule further comprises a nucleotide sequence encoding a self-cleaving peptide.

3. The polynucleotide molecule of claim 2, wherein the polynucleotide molecule comprises in the following order from the 5' to the 3' end:
a) a promoter;
b) a nucleotide sequence encoding a chimeric antigen receptor (CAR) or a fragment thereof i) comprising an extracellular domain comprising an antigen binding region which binds to epidermal growth factor receptor variant III (EGFRvIII); or ii) comprising an extracellular domain comprising an antigen binding region which binds to CD19; wherein the nucleotide sequence encoding the chimeric antigen receptor (CAR) or a fragment thereof is operably linked to the promoter of a);
c) a nucleotide sequence encoding a self-cleaving peptide; and
d) a nucleotide sequence encoding a heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP).

4. The polynucleotide molecule of any one of claims 1-3, wherein the heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP) is a signal peptide selected from the group consisting of interleukin 2 (IL-2) signal peptide, interleukin 4 (IL-4) signal peptide, interleukin 9 (IL-9) signal peptide and interferon gamma (IFNγ) signal peptide, preferably selected from the group consisting of human

IL-2 signal peptide, human IL-4 signal peptide, human IL-9 signal peptide and human IFNγ signal peptide.

5. The polynucleotide molecule of any one of claims 1-3, wherein the heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP) is a human interleukin 2 (IL-2) signal peptide.

6. The polynucleotide molecule of any one of claims 1-5, wherein the heterologous signal peptide is fused to the N-terminal region of the signal regulatory protein gamma (SIRPγ)-related protein (SGRP).

7. The polynucleotide molecule of any one of claims 1-6, wherein the promoter which is operably linked to the nucleotide sequence encoding the chimeric antigen receptor (CAR) or a fragment thereof is the elongation factor 1 alpha (EF1A) promoter or the elongation factor 1 alpha short (EFS) promoter, preferably the EF1A promoter.

8. The polynucleotide molecule of any one of claims 1-7, wherein the chimeric antigen receptor (CAR) or a fragment thereof comprises i) an extracellular domain comprising an antigen binding region which binds to epidermal growth factor receptor variant III (EGFRvIII); or ii) an extracellular domain comprising an antigen binding region which binds to CD19; wherein the CAR or a fragment thereof further comprises a CD8α leader, CD8α hinge and transmembrane domains, a TNF receptor superfamily member 9 (4-1BB) costimulatory domain and a CD3ζ signaling domain.

9. The polynucleotide molecule of claim 8, wherein i) the extracellular domain comprising an antigen binding region which binds to epidermal growth factor receptor variant III (EGFRvIII) is a single-chain variable fragment (scFv); or ii) the extracellular domain comprising an antigen binding region which binds to CD19 is a single-chain variable fragment (scFv).

10. The polynucleotide molecule of any one of claims 1-9, comprising the sequence as shown in SEQ ID NO: 1 or the sequence as shown in SEQ ID NO: 2.

11. An amino sequence comprising a chimeric antigen receptor (CAR) or a fragment thereof comprising an extracellular domain comprising an antigen-binding region which binds to epidermal growth factor receptor variant III (EGFRvIII); wherein the nucleotide sequence encoding the chimeric antigen receptor (CAR) is operably linked to a promoter and wherein the polynucleotide molecule further comprises a nucleotide sequence encoding a heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP) comprising the sequence as shown in SEQ ID NO: 3.

12. An amino sequence comprising a chimeric antigen receptor (CAR) or a fragment thereof comprising an extracellular domain comprising an antigen-binding region which binds to CD19; wherein the nucleotide sequence encoding the CAR is operably linked to a promoter and wherein the polynucleotide molecule further comprises a nucleotide sequence encoding a heterologous signal peptide fused to a signal regulatory protein gamma (SIRPγ)-related protein (SGRP) comprising the sequence as shown in SEQ ID NO: 4.

13. A construct comprising the polynucleotide molecule of any one of claims 1-10.

14. A chimeric antigen receptor (CAR)-T cell comprising T cells expressing the polynucleotide molecule of any one of claims 1-10 and/or the construct of claim 13.

15. Use of the chimeric antigen receptor (CAR)-T cell of claim 14 in the manufacture of a medicament for the treatment of an epidermal growth factor receptor (EGFR)-associated cancer or a CD19-associated cancer.

16. The chimeric antigen receptor (CAR)-T cell of claim 14 for use in therapy.