

CLAIMS

1. A system for inducible expression of a polynucleotide comprising:
 - (a) a first nucleic acid comprising a first promoter which comprises the nucleotide sequence set forth in SEQ ID NO:41, wherein the first nucleic acid is operably linked to a polynucleotide;
 - (b) a second nucleic acid comprising a second promoter operably linked to a nucleic acid encoding a transcriptional activator for the first promoter; and
 - (c) an agent selected from the group consisting of tamoxifen, a metabolite of tamoxifen, and an analog of tamoxifen.
2. The system of claim 1, further comprising: (d) an activating stimulator selected from the group consisting of an anti-CD3 antibody, an anti-CD28 antibody, and an antigen binding fragment thereof.
3. The system of claim 1, wherein the agent is selected from 4-hydroxytamoxifen or 4-hydroxy-N-desmethyltamoxifen.
4. The system of claim 1, wherein the second promoter is a constitutive promoter.
5. The system of claim 4, wherein the second promoter is an EF1 α promoter.
6. The system of claim 1, wherein the transcriptional activator comprises a 4-hydroxytamoxifen (4-OHT)-dependent transcriptional regulator (HEA-3) polypeptide.
7. The system of claim 1, wherein the transcriptional activator comprises the amino acid sequence set forth in SEQ ID NO:40.
8. The system of claim 1, wherein a first vector comprises the first nucleic acid, and a second vector comprises the second nucleic acid.
9. The system of claim 8, wherein the first vector and the second vector are packaged in a viral vector.
10. The system of claim 9, wherein the viral vector comprises a lentiviral vector.
11. The system of claim 1, wherein the first nucleic acid or the second nucleic acid further comprises a nucleotide sequence encoding a selectable marker.
12. The system of claim 1, wherein the first promoter is in an opposite orientation to the second promoter.

13. The system of claim 1, wherein the polypeptide comprises a cytokine, a chemokine receptor, or a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain, a spacer, a transmembrane domain, and an intracellular signaling domain.

14. The system of any one of claims 1-13, further comprising an *ex vivo* host cell comprising the first nucleic acid and the second nucleic acid.

15. The system of claim 14, wherein the host cell is a T cell.

16. The system of claim 14, wherein the host cell is selected from the group consisting of a CD4⁺ T cell, a CD8⁺ T cell, a precursor T cell, and a hematopoietic stem cell.

17. The system of claim 14, wherein the host cell is a CD8⁺ cytotoxic T lymphocyte cell selected from the group consisting of a naïve CD8⁺ T cell, a central memory CD8⁺ T cell, an effector memory CD8⁺ T cell, and a bulk CD8⁺ T cell.

18. The system of claim 14, wherein the host cell is a CD4⁺ helper T lymphocyte cell selected from the group consisting of a naïve CD4⁺ T cell, a central memory CD4⁺ T cell, an effector memory CD4⁺ T cell, and a bulk CD4⁺ T cell.

19. A pharmaceutical composition for use in the treatment of a cancer or a viral infection, comprising the system of claim 14, and a pharmaceutically acceptable excipient.

20. The pharmaceutical composition of claim 19, wherein the cancer comprises a solid tumor.

21. The pharmaceutical composition of claim 19, wherein the cancer is a breast cancer, a brain cancer, a lung cancer, a colon cancer, a renal cancer, a pancreatic cancer, a prostate cancer, an ovarian cancer, or a hematologic malignancy.

22. An *in vitro* method for preparing a population of cells for infusion, the method comprising:

(a) providing the system of any one of claims 1-13;

(b) introducing the first nucleic acid and the second nucleic acid into an isolated T cell population; and

(c) culturing the T cell population in the presence of the agent.

23. The method of claim 22, wherein (c) further comprises culturing the T cell population in the presence of an activating stimulator selected from the group consisting of an anti-CD3 antibody, an anti-CD28 antibody, and an antigen binding fragment thereof.

24. The method of claim 22, wherein the T cell population comprises a cell selected from the group consisting of a CD4⁺ T cell, a CD8⁺ T cell, a precursor T cell, and a hematopoietic stem cell.

25. The method of claim 24, wherein the cell is a CD8⁺ cytotoxic T lymphocyte cell selected from the group consisting of a naïve CD8⁺ T cell, a central memory CD8⁺ T cell, an effector memory CD8⁺ T cell, and a bulk CD8⁺ T cell; or wherein the cell is a CD4⁺ helper T lymphocyte cell selected from the group consisting of a naïve CD4⁺ T cell, a central memory CD4⁺ T cell, an effector memory CD4⁺ T cell, and a bulk CD4⁺ T cell..