CLAIMS

1. A vector comprising: a nucleotide sequence encoding a first shRNA that inhibits expression of Programmed Cell Death 1 (PD-1), a nucleotide sequence encoding a second shRNA that inhibits expression of T cell immunoreceptor with Ig and ITIM domains (TIGIT), and a nucleotide sequence encoding a chimeric antigen receptor (CAR).

2. The vector of claim 1, wherein the expression of the first shRNA is regulated by a first promoter and the second shRNA is regulated by a second promoter.

3. The vector of claim 2, wherein the first and the second promoters are RNA polymerase III promoters.

4. The vector of claim 2 or 3, wherein the RNA polymerase III promoters are U6 promoters.

5. The vector of any one of claims 2-4, wherein the two promoters are oriented in different directions from each other on the vector.

6. The vector of claim 5, wherein the two promoters are oriented in head to head orientation.

7. The vector of claim 5, wherein the two promoters are oriented in tail to tail orientation.

8. An immune cell comprising the vector of any one of claims 1-7.

9. The immune cell of claim 8, wherein the target antigen is a cancer antigen whose expression is increased in or on the surface of a cancer cell, a cancer tissue, and/or a tumor microenvironment.

10. The immune cell of claim 8 or 9 , wherein the target antigen is CD19 or CD22.

11. The immune cell of any one of claims 8-10, wherein the immune cell is a human-derived T cell, a dendritic cell or natural killer (NK) cell.

12. The immune cell of any one of claims 8-11 , wherein the immune cell is a human-derived T cell.

13. The immune cell of any one of claims 8-12, wherein the intracellular signal transduction domain of the CAR further comprises a costimulatory molecule selected from the group consisting of ICOS, OX40, CD137 (4-1BB), CD27, and CD28.

14. A pharmaceutical composition comprising the immune cell of any one of claims 1-13 and a pharmaceutically acceptable carrier.

15. The pharmaceutical composition of claim 14 for use in a method of treating cancer in a human subject.