THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An engineered T cell comprising a heterologous nucleotide sequence encoding at least one immunomodulatory factor, wherein the heterologous nucleotide sequence is introduced in-frame of an endogenous gene of the T cell, wherein expression of the endogenous gene is under the control of endogenous regulatory elements, wherein expression of the heterologous nucleotide sequence is controlled by the endogenous regulatory elements of the endogenous gene, and wherein the endogenous gene is selected from the group consisting of *RGS16, RGS1*, *RGS2,* and *CLU*, preferably *RGS16*.

2. The engineered T cell of claim 1, wherein one or more, or all of the following apply:
   (a) the heterologous nucleotide sequence is positioned adjacent to the translational start codon, or the stop codon of the endogenous gene;
   (b) the heterologous nucleotide sequence is positioned no more than about 20 base pairs upstream or downstream of the translational start codon, or stop codon of the endogenous gene; and
   (c) the heterologous nucleotide sequence further comprises one or more, or all of:
      (i) a stop codon;
      (ii) a nucleotide sequence encoding a poly(A) tail; and
      (iii) a linker, preferably a P2A linker or a T2A linker.

3. The engineered T cell of claim 2, wherein introduction of the heterologous nucleotide sequence disrupts expression of the endogenous gene.

4. The engineered T cell of claim 2 or claim 3, wherein the heterologous nucleotide sequence comprises a linker, and wherein the configuration of the heterologous nucleotide sequence is selected from the group consisting of:
   (a) 5' – linker – immunomodulatory factor – 3'; and
   (b) 5' – immunomodulatory factor – linker – 3'.

5. The engineered T cell of any one of claims 1 to 4, wherein the immunomodulatory factor is a cytokine selected from the group consisting of TNF, IFNγ, IFNα, IFNβ,

IL-2, IL-12, IL-15, IL-18, CXCL9, CXCL10, XCL1, CD40L, and combinations of the foregoing.

6. The engineered T cell of claim 5, wherein the heterologous nucleotide sequence comprises a sequence of any one of SEQ ID NOs: 25-34, or a sequence that is at least 80% identical to the sequence of any one of SEQ ID NOs: 25-34.

7. The engineered T cell of any one of claims 1 to 6, further comprising a genetic modification that disrupts the expression, function, or both the expression and function of a second endogenous gene of the T cell, wherein the second endogenous gene is selected from the group consisting of *NFKB1A*, *NR4A2*, *SOCS1* and *TNFAIP3*, preferably *TNFAIP3*.

8. The engineered T cell of any one of claims 1 to 7, further comprising a chimeric antigen receptor (CAR), wherein the CAR binds an antigen selected from the group consisting of CD19, CD20, CD22, CD30, ROR1, CD123, CD33, CD133, CD138, Claudin 18.2, Claudin 6, BCMA, GD2, Her2, Her1, mesothelin, MUC1, gp100, MART-1, MAGE-A3, MUC16, NY-ESO-1, L1-CAM, CEA, FAP, VEGFR2, WT1, TAG-72, CD171, α-FR, CAIX, PSMA, EGFRvIII CLL-1, GRP78, and Lewis Y, preferably Her2 and Lewis Y.

9. A pharmaceutical composition comprising the engineered T cell of any one of claims 1 to 8.

10. Use of the engineered T cell of any one of claims 1 to 8, or the pharmaceutical composition of claim 9 in the manufacture of a medicament for the treatment of cancer.

11. A genome editing system comprising:
    (a) a sgRNA comprising a sequence of at least 10 contiguous nucleotides that are complementary to a target nucleic acid sequence within an endogenous gene of a T cell, wherein the endogenous gene is selected from the group consisting of *RGS16*, *RGS1*, *RGS2*, and *CLU*, preferably *RGS16*;
    (b) a RNA-guided nuclease, preferably CRISPR-associated endonuclease 9 (Cas9); and

(c) a homology directed repair (HDR) template, wherein the HDR template comprises a nucleotide sequence encoding at least one immunomodulatory factor, preferably a cytokine, more preferably a cytokine selected from the group consisting of TNF, IFNγ, IFNα, IFNβ, IL-2, IL-12, IL-15, IL-18, CXCL9, CXCL10, XCL1, CD40L, and combinations of the foregoing.

12. The genome editing system of claim 11, wherein one or more, or all of the following apply:

(a) the target nucleic acid sequence comprises, or is adjacent to, the translational start codon, or the stop codon of the endogenous gene;

(b) the sgRNA comprises a sequence of any one of SEQ ID NOs: 1-9, or a sequence that is at least 90% identical to the sequence of SEQ ID NOs: 1-9; and

(c) the HDR template is within a vector, preferably an adeno-associated virus (AAV) vector, more preferably an AAV5 or AAV6 vector.

13. The genome editing system of claim 11 or claim 12, further comprising an inhibitor of non-homologous end-joining (NHEJ), preferably a DNA-PK inhibitor.

14. The genome editing system of any one of claims 11 to 13, wherein the HDR template further comprises one or more, or all of:

(a) a 5' homology arm comprising a sequence of from about 250 to about 1000 contiguous nucleotides that are homologous to a region 5' to the translation start site, or stop codon of the endogenous gene;

(b) a stop codon;

(c) a nucleotide sequence encoding a poly(A) tail;

(d) a linker;

(f) a 3' homology arm comprising a sequence of from about 250 to about 1000 contiguous nucleotides that are homologous to a region 3' to the translational start codon, or stop codon of the endogenous gene; and

(g) a sequence of any one of SEQ ID NOs: 25-34, or a sequence that is at least 80% identical to the sequence of any one of SEQ ID NOs: 25-34.

15. A method of enhancing the function of a T cell, the method comprising providing to the T cell the genome editing system of any one of claims 11 to 14.