What is claimed is:

1. A modified primary human T cell comprising: at least one nucleic acid sequence comprising at least one heterologous gene non-virally inserted into one or both of:
an endogenous T cell receptor alpha subunit constant gene (TRAC); and
an endogenous T cell receptor beta subunit constant gene (TRBC),
wherein the at least one heterologous gene encodes at least one antigen-specific receptor that specifically binds the target antigen expressed by a cancer, and wherein the at least one nucleic acid sequence is at least 500 bp in size.

2. The T cell of claim 1, wherein the modified human T cell does not comprise a viral vector.

3. The T cell of claim 1 or 2, wherein the at least one nucleic acid sequence is at least 1.5 kb in size.

4. The T cell of any one of claims 1-3, wherein the at least one nucleic acid sequence is non-virally inserted into an exon of the T cell receptor alpha subunit constant gene (TRAC) or into an exon of the T cell receptor beta subunit constant gene (TRBC).

5. The T cell of any one of claims 1-4, wherein the at least one heterologous gene comprises at least one of: (a) a variable region of a heterologous T cell receptor alpha (TCR-α) chain and (b) a variable region of a heterologous T cell receptor beta (TCR-β) chain.

6. The T cell of any one of claims 1-5, wherein the at least one heterologous gene comprises at least one of:
(1) a) a variable region of a heterologous T cell receptor alpha (TCR-α) chain or b) a variable region and constant region of the heterologous TCR-α chain; and
(2) a) a variable region of a heterologous T cell receptor beta (TCR-β) chain or b) a variable region and constant region of the heterologous TCR-β chain.

7. The T cell of claim 6, wherein the at least one heterologous gene comprises each of:
(1) the a) variable region of the heterologous TCR-α chain or b) variable region and constant region of the heterologous TCR-α chain; and

(2) the a) variable region of the heterologous TCR-β chain or b) variable region and constant region of the heterologous TCR-β chain.

8. The T cell of claim 7, wherein one or more coding sequences for the heterologous TCR-α chain and the heterologous TCR-β chain are linked by a linker sequence or a multicistronic element.

9. The T cell of claim 8, wherein the linker sequence is a cleavable linker sequence that is cleaved to generate the heterologous TCR-α chain gene and the heterologous TCR-β chain gene.

10. The T cell of claim 8, wherein the heterologous gene encodes the TCR-α chain and the heterologous TCR-β chain and wherein the heterologous gene is inserted into TRAC.

11. The T cell of any one of claims 1-5, wherein the at least one heterologous gene is non-virally inserted into an endogenous TRAC, wherein the at least one heterologous gene comprises each of:
(1) a) a variable region of the heterologous TCR-α chain or b) a variable region and constant region of the heterologous TCR-α chain; and
(2) a) a variable region of the heterologous TCR-β chain or b) a variable region and constant region of the heterologous TCR-β chain,
wherein the heterologous TCR-α chain and the heterologous TCR-β chain are operably linked by a cleavable linker sequence that is cleaved to generate the heterologous TCR-α chain and the heterologous TCR-β chain, and wherein the heterologous TCR-α chain and the heterologous TCR-β form an antigen-specific T cell receptor (TCR) that recognizes the target antigen expressed by the cancer.

12. The T cell of any one of claims 1-11, wherein expression of the at least one heterologous gene is under the control of an endogenous promoter.

13. The T cell of any one of claims 1-12, wherein the modified human T cell is a CD8+ T cell or a CD4+ T cell.

14. The T cell of claim 13, wherein the CD8+ T cell or CD4+ T cell is an effector T cell or a naïve T cell.

15. The T cell of any one of claims 1-14, wherein the primary human T cell is obtained from a subject having cancer and modified to comprise the at least one nucleic acid sequence comprising at least one heterologous gene.

16. A population of cells comprising a plurality of the primary human T cell of any one of claims 1-15.

17. The T cell of any one of claims 1-15 or the population of cells of claim 16 for use in therapy.

18. Use of the T cell of any one of claims 1-15 or the population of cells of claim 16 in the manufacture of a medicament for treating a cancer that expresses the target antigen.