CLAIMS

1. An *in vitro* method of activating and expanding γδ T cells comprising

isolating γδ T cells from a blood sample of a human subject,

activating the isolated γδ T cells in the presence of an aminobisphosphonate, human recombinant interleukin 2 (IL-2), and human recombinant interleukin 15 (IL-15), and

expanding the activated γδ T cells in the absence of an aminobisphosphonate and in the presence of human recombinant interleukin 2 (IL-2) and human recombinant interleukin 15 (IL-15),

wherein the fold-expansion of the expanded γδ T cells is from 3000-fold to 35,000-fold.

2. The method of claim 1, wherein the γδ T cells are isolated from a leukapheresis human sample.

3. The method of claim 1 or 2, wherein the aminobisphosphonate comprises pamidronic acid, alendronic acid, zoledronic acid, risedronic acid, ibandronic acid, incadronic acid, a salt thereof and/or a hydrate thereof.

4. The method of any one of claims 1-3, wherein the aminobisphosphonate is zoledronic acid.

5. The method of any one of claims 1-4, wherein activation is in the presence of zoledronic acid and a cytokine composition consisting of IL-2 and IL-15.

6. The method of any one of claims 1-5, wherein the activation is further in the presence of a Toll-like receptor 2 (TLR2) ligand.

7. The method of claim 6, wherein the TLR2 ligand is selected from the group consisting of Amphotericin B, L-theanine, tannin, and polyphenols.

8. The method of any one of claims 1-7, wherein the activation is further in the presence of N-acetyl cysteine (NAC).

9. The method of any one of claims 1-8, wherein the activation is further in the presence of a COX-2 inhibitor.

10. The method of claim 9, wherein the COX-2 inhibitor is Ibuprofen.

11. The method of any one of claims 1 – 10, wherein activation is in the presence of zoledronic acid at a concentration of 1 μM to 10 μM.

12. The method of any one of claims 1 – 11, wherein activation is in the presence of IL-2 at a concentration of 10 IU/ml to 100 IU/ml.

13. The method of any one of claims 1 – 10, wherein activation is in the presence of zoledronic acid at a concentration of 1 μM to 100 μM, IL-2 at a concentration from 10 IU/ml to 200 IU/ml, and IL-15 at a concentration of 10 – 500 ng/ml.

14. The method of any one of claims 1 – 10 and 13, wherein expansion is in the presence of IL-2 at a concentration from 10 IU/ml to 100 IU/ml and~~/or~~ IL-15 at a concentration of 50 – 200 ng/ml.

15. An *in vitro* method of activating and expanding γδ T cells comprising

isolating γδ T cells from peripheral blood mononuclear cells (PBMC) of a human subject, wherein the isolating comprises

contacting the PBMC with anti-α and anti-β T cell receptor (TCR) antibodies,

depleting α- and/or β-TCR positive cells from the PBMC,

activating the isolated γδ T cells in the presence of an aminobisphosphonate, human recombinant interleukin 2 (IL-2), and human recombinant interleukin 15 (IL-15), and

expanding the activated γδ T cells in the absence of an aminobisphosphonate and in the presence of human recombinant interleukin 2 (IL-2) and human recombinant interleukin 15 (IL-15),

wherein the fold-expansion of the expanded γδ T cells is from 3000-fold to 35,000-fold.

16. The method of any one of claims 1-15, further comprising transducing the activated γδ T cells with a recombinant viral vector or a transposon.

17. The method of claim 16, wherein the viral vector is a retroviral vector, a lentiviral vector, or an adeno-associated virus (AAV)~~, or a transposon~~.

18. The method of claim 16 or 17, wherein the viral vector is a lentiviral vector.

19. The method of any one of claims 16-18, wherein the viral vector comprises a RD114TR gene having at least 95% identity to SEQ ID NO: 1 encoding an envelope protein.

20. The method of any one of claims 16-19, wherein the viral vector encodes CD8 and/or an αβ-TCR.

21. The method of any one of claims 16-20, wherein the transducing is in the presence of a transduction enhancer.

22. The method of claim 21, wherein the transduction enhancer is a fibronectin fragment coated onto plates or a soluble cationic peptide.

23. The method of any one of claims 1- 22, wherein the activation is further in the presence of a phosphoantigen selected from the group consisting of (E)-4-hydroxy-3-methyl-but-2-enyl pyrophosphate (HMBPP), isoprenoid pyrophosphates (farnesyl pyrophosphate (FPP), geranylgeranyl pyrophosphate (GGPP), isopentenyl pyrophosphate (IPP), and dimethylallyl diphosphate (DMAPP).

24. The method of claim 4, wherein the fold-expansion of the expanded γδ T cells is from 10,000-fold to 35,000-fold.

25. The method of any one of claims 1-24, wherein the activated γδ T cells are expanded in the absence of a phosphoantigen.

26. The method of any one of claim ~~25~~1-24, wherein the activated γδ T cells are expanded in the absence of a phosphoantigen ~~is~~ selected from the group consisting of (E)-4-hydroxy-3-methyl-but-2-enyl pyrophosphate (HMBPP), isoprenoid pyrophosphates (farnesyl pyrophosphate (FPP), geranylgeranyl pyrophosphate (GGPP), isopentenyl pyrophosphate (IPP), and dimethylallyl diphosphate (DMAPP).