What is claimed is:

1. A method of eliciting an anti-tumor T cell response in a subject having a tumor or cancer, comprising the step of administering to said subject a recombinant Listeria strain comprising a recombinant nucleic acid, said nucleic acid molecule comprising a first open reading frame encoding a recombinant polypeptide and a second open reading frame second open reading frame encoding a metabolic, wherein said recombinant polypeptide comprises a truncated LLO protein fused to a heterologous antigen or fragment thereof, wherein said Listeria comprises a mutation in the endogenous alanine racemase gene (dal), D-amino acid transferase gene (dat), and actA genes, and wherein said T-cell response comprises increasing a ratio of T effector cells to regulatory T cells (Tregs), thereby eliciting an anti-tumor T cell response in said subject.
2. The method of claim 1, wherein said tumor-associated antigen is a human papilloma virus E7 antigen.
3. The method of any one of claims 1-2, wherein said truncated LLO protein is an N-terminal LLO.
4. The method of claim 2, wherein said LLO is set forth in SEQ ID NO: 2.
5. The method of any one of claims claim 1-4, wherein said heterologous antigen is a tumor-associated antigen.
6. The method of any one of claims 1-4, wherein said tumor-associated antigen is an angiogenic antigen.
7. The method of any one of claims 1-6, wherein said Listeria lacks antibiotic resistance genes.
8. The method of any one of claims 1-7, wherein said recombinant nucleic acid is in a plasmid in said Listeria.
9. The method of claim 8, wherein said plasmid is an episomal plasmid.
10. The method of claim 9, wherein said plasmid is a multicopy plasmid.
11. The method of claim 8, wherein said plasmid is an integrative plasmid.
12. The method of any one of claims 1-11, wherein said metabolic enzyme is an amino acid metabolism enzyme.
13. The method of claim 12, wherein said metabolic enzyme is a D-amino acid transferase enzyme or a alanine racemase enzyme.

14. The method of any one of claims 1-13, further comprising administering to said subject an adjuvant.
15. The method of claim 14, wherein said adjuvant comprises a granulocyte/macrophage colony-stimulating factor (GM-CSF), a saponin QS21, a monophosphoryl lipid Aa CpG-containing oligonucleotide, or a bacterial toxin.
16. The method of any one of claims 1-15, further comprising co-administering with, prior to or following the administration of said recombinant Listeria an immune checkpoint protein inhibitor.
17. The method of claim 16, wherein said immune checkpoint protein is programmed cell death protein 1 (PD1), T cell membrane protein 3 (TIM3), adenosine A2a receptor (A2aR) and lymphocyte activation gene 3 (LAG3), killer immunoglobulin receptor (KIR) or cytotoxic T-lymphocyte antigen-4 (CTLA-4).
18. The method of any one of claims 1-15, or 1-16, further comprising co-administering a cytokine that enhances said anti-tumor immune response.
19. The method of claim 18, wherein said cytokine is: a type I interferon (IFN-α / IFN-β), TNF-α, IL-1, IL-4, IL-12, INF-γ.
20. The method of any one of claims 1-19, wherein said method induces the expansion of T effector cells in peripheral lymphoid organs leading to an enhanced presence of T effector cells at the tumor site.
21. The method of claim 20, wherein said expansion of T effector cells leads to an increased ratio of T effector cells to regulatory T cells in the periphery and at the tumor site without affecting the number of Tregs.
22. The method of claim 21, wherein said T effector cells are CD4+FoxP3- and CD8+ T-cells.
23. The method of claim 21, wherein said T effector cells are CD4+FoxP3- T cells.
24. The method of claim 21, wherein said regulatory T cells are CD4+FoxP+ T cells.
25. A method for increasing the ratio of T effector cells to regulatory T cells (Tregs) in the spleen of a subject, the method comprising the step of administering to said subject a recombinant Listeria strain comprising a recombinant nucleic acid encoding a truncated LLO protein, wherein said Listeria comprises a mutation in the endogenous alanine racemase gene (dal), D-amino acid transferase gene (dat), and actA genes, wherein said T-cell response comprises increasing a ratio of T effector cells to regulatory T cells (Tregs).

26. The method of claim 25, wherein said tumor-associated antigen is a human papilloma virus E7 antigen.
27. The method of any one of claims 25-26, wherein said truncated LLO protein is an N-terminal LLO.
28. The method of any one of claims 25-27, wherein said LLO is set forth in SEQ ID NO: 2.
29. The method of any one of claims 25-28, wherein said Listeria lacks an antibiotic resistance genes.
30. The method of any one of claims 25-29, wherein said nucleic acid is in a plasmid in said Listeria.
31. The method of claim 30, wherein said plasmid is an episomal plasmid.
32. The method of claim 31, wherein said plasmid is a multicopy plasmid.
33. The method of claim 30, wherein said plasmid is an integrative plasmid.
34. The method of any one of claims 25-33, further comprising administering to said subject an adjuvant.
35. The method of any one of claims 25-34, wherein said adjuvant comprises a granulocyte/macrophage colony-stimulating factor (GM-CSF), a saponin QS21, a monophosphoryl lipid A, a CpG-containing oligonucleotide, or a bacterial toxin.
36. The method of any one of claims 25-35, further comprising co-administering with, prior to or following the administration of said recombinant Listeria an immune checkpoint protein inhibitor.
37. The method of claim 36, wherein said immune checkpoint protein is programmed cell death protein 1 (PD1), T cell membrane protein 3 (TIM3), adenosine A2a receptor (A2aR) and lymphocyte activation gene 3 (LAG3), killer immunoglobulin receptor (KIR) or cytotoxic T-lymphocyte antigen-4 (CTLA-4).
38. The method of any one of claims 25-35, or 25-36, further comprising co-administering a cytokine that enhances said anti-tumor immune response.
39. The method of claim 38, wherein said cytokine is: a type I interferon (IFN-α / IFN-β), TNF-α, IL-1, IL-4, IL-12, INF-γ.
40. The method of any one of claims 25-39, wherein said method induces the expansion of T effector cells in peripheral lymphoid organs.
41. The method of claim 40, wherein said expansion of T effector cells leads to an increased ratio of T effector cells to regulatory T cells in the periphery without affecting the number of Tregs.

42. The method of claim 41, wherein said T effector cells are CD4+FoxP3- and CD8+ T-cells.
43. The method of claim 41, wherein said T effector cells are CD4+FoxP3- T cells.
44. The method of claim 41, wherein said regulatory T cells are CD4+FoxP+ T cells.
45. The method of any one of claims 1-24, wherein eliciting an anti-tumor T cell response in a subject having a tumor or cancer allows treating said tumor or cancer in said subject.
46. The method of any one of claims 25-44, wherein eliciting an anti-tumor T cell response in a subject having a tumor or cancer allows treating said tumor or cancer in said subject.

Claims

1. The use of a recombinant Listeria strain in the manufacture of a medicament for the treatment of eliciting an anti-tumor T cell response in a subject having a tumor or cancer, wherein the recombinant Listeria strain comprising a recombinant nucleic acid, said nucleic acid molecule comprising a first open reading frame encoding a recombinant polypeptide and a second open reading frame second open reading frame encoding a metabolic, wherein said recombinant polypeptide comprises a truncated LLO protein fused to a heterologous antigen or fragment thereof, wherein said Listeria comprises a mutation in the endogenous alanine racemase gene (dal), D-amino acid transferase gene (dat), and actA genes, and wherein said T-cell response comprises increasing a ratio of T effector cells to regulatory T cells (Tregs), thereby eliciting an anti-tumor T cell response in said subject.
2. The use of a recombinant Listeria strain of claim 1, wherein said tumor-associated antigen is a human papilloma virus E7 antigen.
3. The use of a recombinant Listeria strain of any one of claims 1-2, wherein said truncated LLO protein is an N-terminal LLO.
4. The use of a recombinant Listeria strain of claim 2, wherein said LLO is set forth in SEQ ID NO: 2.
5. The use of a recombinant Listeria strain of any one of claims claim 1-4, wherein said heterologous antigen is a tumor-associated antigen.
6. The use of a recombinant Listeria strain of any one of claims 1-4, wherein said tumor-associated antigen is an angiogenic antigen.
7. The use of a recombinant Listeria strain of any one of claims 1-6, wherein said Listeria lacks antibiotic resistance genes.
8. The use of a recombinant Listeria strain of any one of claims 1-7, wherein said recombinant nucleic acid is in a plasmid in said Listeria.
9. The use of a recombinant Listeria strain of claim 8, wherein said plasmid is an episomal plasmid.
10. The use of a recombinant Listeria strain of claim 9, wherein said plasmid is a multicopy plasmid.
11. The use of a recombinant Listeria strain of claim 8, wherein said plasmid is an integrative plasmid.

12. The use of a recombinant Listeria strain of any one of claims 1-11, wherein said metabolic enzyme is an amino acid metabolism enzyme.
13. The use of a recombinant Listeria strain of claim 12, wherein said metabolic enzyme is a D-amino acid transferase enzyme or a alanine racemase enzyme.
14. The use of a recombinant Listeria strain of any one of claims 1-13, further comprising administering to said subject an adjuvant.
15. The use of a recombinant Listeria strain of claim 14, wherein said adjuvant comprises a granulocyte/macrophage colony-stimulating factor (GM-CSF), a saponin QS21, a monophosphoryl lipid Aa CpG-containing oligonucleotide, or a bacterial toxin.
16. The use of a recombinant Listeria strain of any one of claims 1-15, further comprising co-administering with, prior to or following the administration of said recombinant Listeria an immune checkpoint protein inhibitor.
17. The use of a recombinant Listeria strain of claim 16, wherein said immune checkpoint protein is programmed cell death protein 1 (PD1), T cell membrane protein 3 (TIM3), adenosine A2a receptor (A2aR) and lymphocyte activation gene 3 (LAG3), killer immunoglobulin receptor (KIR) or cytotoxic T-lymphocyte antigen-4 (CTLA-4).
18. The use of a recombinant Listeria strain of any one of claims 1-15, or 1-16, further comprising co-administering a cytokine that enhances said anti-tumor immune response.
19. The use of a recombinant Listeria strain of claim 18, wherein said cytokine is: a type I interferon (IFN-α / IFN-β), TNF-α, IL-1, IL-4, IL-12, INF-γ.
20. The use of a recombinant Listeria strain of any one of claims 1-19, wherein said method induces the expansion of T effector cells in peripheral lymphoid organs leading to an enhanced presence of T effector cells at the tumor site.
21. The use of a recombinant Listeria strain of claim 20, wherein said expansion of T effector cells leads to an increased ratio of T effector cells to regulatory T cells in the periphery and at the tumor site without affecting the number of Tregs.
22. The use of a recombinant Listeria strain of claim 21, wherein said T effector cells are CD4+FoxP3- and CD8+ T-cells.
23. The use of a recombinant Listeria strain of claim 21, wherein said T effector cells are CD4+FoxP3- T cells.
24. The use of a recombinant Listeria strain of claim 21, wherein said regulatory T cells are CD4+FoxP+ T cells.
25. The use of a recombinant Listeria strain in the manufacture of a medicament for the treatment of increasing the ratio of T effector cells to regulatory T cells (Tregs) in the

spleen of a subject, wherein the recombinant Listeria strain comprising a recombinant nucleic acid encoding a truncated LLO protein, wherein said Listeria comprises a mutation in the endogenous alanine racemase gene (dal), D-amino acid transferase gene (dat), and actA genes, wherein said T-cell response comprises increasing a ratio of T effector cells to regulatory T cells (Tregs).

26. The use of a recombinant Listeria strain of claim 25, wherein said tumor-associated antigen is a human papilloma virus E7 antigen.
27. The use of a recombinant Listeria strain of any one of claims 25-26, wherein said truncated LLO protein is an N-terminal LLO.
28. The use of a recombinant Listeria strain of any one of claims 25-27, wherein said LLO is set forth in SEQ ID NO: 2.
29. The use of a recombinant Listeria strain of any one of claims 25-28, wherein said Listeria lacks an antibiotic resistance genes.
30. The use of a recombinant Listeria strain of any one of claims 25-29, wherein said nucleic acid is in a plasmid in said Listeria.
31. The use of a recombinant Listeria strain of claim 30, wherein said plasmid is an episomal plasmid.
32. The use of a recombinant Listeria strain of claim 31, wherein said plasmid is a multicopy plasmid.
33. The use of a recombinant Listeria strain of claim 30, wherein said plasmid is an integrative plasmid.
34. The use of a recombinant Listeria strain of any one of claims 25-33, further comprising administering to said subject an adjuvant.
35. The use of a recombinant Listeria strain of any one of claims 25-34, wherein said adjuvant comprises a granulocyte/macrophage colony-stimulating factor (GM-CSF), a saponin QS21, a monophosphoryl lipid A, a CpG-containing oligonucleotide, or a bacterial toxin.
36. The use of a recombinant Listeria strain of any one of claims 25-35, wherein the recombinant Listeria strain is co-administered with an immune checkpoint protein inhibitor, prior to or following the admistration of said recombinant Listeria strain.
37. The use of a recombinant Listeria strain of claim 36, wherein said immune checkpoint protein is programmed cell death protein 1 (PD1), T cell membrane protein 3 (TIM3), adenosine A2a receptor (A2aR) and lymphocyte activation gene 3 (LAG3), killer immunoglobulin receptor (KIR) or cytotoxic T-lymphocyte antigen-4 (CTLA-4).

38. The use of a recombinant Listeria strain of any one of claims 25-35, or 25-36, wherein the recombinant Listeria strain is co-administered with a cytokine that enhances said anti-tumor immune response.
39. The use of a recombinant Listeria strain of claim 38, wherein said cytokine is: a type I interferon (IFN-α / IFN-β), TNF-α, IL-1, IL-4, IL-12, INF-γ.
40. The use of a recombinant Listeria strain of any one of claims 25-39, wherein the use of a recombinant Listeria strain induces the expansion of T effector cells in peripheral lymphoid organs.
41. The use of a recombinant Listeria strain of claim 40, wherein said expansion of T effector cells leads to an increased ratio of T effector cells to regulatory T cells in the periphery without affecting the number of Tregs.
42. The use of a recombinant Listeria strain of claim 41, wherein said T effector cells are CD4+FoxP3- and CD8+ T-cells.
43. The use of a recombinant Listeria strain of claim 41, wherein said T effector cells are CD4+FoxP3- T cells.
44. The use of a recombinant Listeria strain of claim 41, wherein said regulatory T cells are CD4+FoxP+ T cells.
45. The use of a recombinant Listeria strain of any one of claims 1-24, wherein eliciting an anti-tumor T cell response in a subject having a tumor or cancer allows treating said tumor or cancer in said subject.
46. The use of a recombinant Listeria strain of any one of claims 25-44, wherein eliciting an anti-tumor T cell response in a subject having a tumor or cancer allows treating said tumor or cancer in said subject.