WHAT IS CLAIMED IS:

1. ~~A method of killing or reducing the number of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor in the manufacture of a medicament for killing or reducing the number of naturally-occurring and/or treatment-induced senescent cells in a subject.

2. ~~A method of decreasing the accumulation of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor in the manufacture of a medicament for decreasing the accumulation of naturally-occurring and/or treatment-induced senescent cells in a subject.

3. ~~A method of decreasing a level of a marker of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor in the manufacture of a medicament for decreasing a level of a marker of naturally-occurring and/or treatment-induced senescent cells in a subject.

4. ~~A method of reducing the activity of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor in the manufacture of a medicament for reducing the activity of naturally-occurring and/or treatment-induced senescent cells in a subject.

5. ~~A method of decreasing levels and/or activity of one or more SASP factor(s) derived from naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor in the manufacture of a medicament for decreasing levels and/or activity of one or more SASP factor(s) derived from naturally-occurring and/or treatment-induced senescent cells in a subject.

6. The ~~method~~ use of any one of claims 1-5, wherein the subject has been previously diagnosed or identified as having an aging-related disease or an inflammatory disease.

7. The ~~method~~ use of claim 6, wherein the aging-related disease is inflamm-aging related.

8. The ~~method~~ use of claim 6, wherein the aging-related disease is selected from the group consisting of: Alzheimer's disease, aneurysm, cystic fibrosis, fibrosis in pancreatitis, glaucoma, hypertension, inflammatory bowel disease, intervertebral disc degeneration, osteoarthritis, type 2 diabetes mellitus, adipose atrophy, lipodystrophy, atherosclerosis, cataracts, COPD, idiopathic pulmonary fibrosis, kidney transplant failure, liver fibrosis, loss of bone mass, myocardial infarction, sarcopenia, wound healing, alopecia, cardiomyocyte hypertrophy, osteoarthritis, Parkinson's disease, age-associated loss of lung tissue elasticity, age-related macular degeneration, cachexia, glomerulosclerosis, liver cirrhosis, NAFLD, osteoporosis, amyotrophic lateral sclerosis, Huntington's disease, spinocerebellar ataxia, multiple sclerosis, neurodegeneration, stroke, cancer, dementia, vascular disease, infection susceptibility, chronic inflammation, and renal dysfunction.

9. The ~~method~~ use of claim 6, wherein the aging-related disease is a cancer selected from the group consisting of: solid tumor, hematological tumor, sarcoma,

osteosarcoma, glioblastoma, neuroblastoma, melanoma, rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, B-cell neoplasms, multiple myeloma, B-cell lymphoma, B-cell non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma, retinoblastoma, stomach cancer, urothelial carcinoma, lung cancer, renal cell carcinoma, gastric and esophageal cancer, pancreatic cancer, prostate cancer, breast cancer, colorectal cancer, ovarian cancer, non-small cell lung carcinoma, squamous cell head and neck carcinoma, endometrial cancer, cervical cancer, liver cancer, and hepatocellular carcinoma.

10. The ~~method~~ use of claim 6, wherein the inflammatory disease is selected from the group consisting of: rheumatoid arthritis, inflammatory bowel disease, lupus erythematosus, lupus nephritis, diabetic nephropathy, CNS injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Crohn's disease, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, ulcerative colitis, nonalcoholic steatohepatitis, mood disorders and cancer treatment-related cognitive impairment.

11. The ~~method~~ use of any one of claims 1-10, wherein the treatment-induced senescent cells are chemotherapy-induced senescent cells.

12. The ~~method~~ use of any one of claims 1-11, wherein the administration of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor results in a decrease in the number or activity of naturally-occurring senescent cells and/or treatment-induced senescent cells in a target tissue in the subject.

~~13. The method of claim 12, wherein the target tissue is selected from the group consisting of: adipose tissue, pancreatic tissue, liver tissue, kidney tissue, lung tissue, heart tissue, vasculature, bone tissue, central nervous system (CNS) tissue, eye tissue, skin tissue, muscle tissue, and secondary lympho-organ tissue.~~

~~14. The method of any one of claims 1-13, wherein the TGFβ receptor is a TGF-β receptor II (TGF-βRII).~~

~~15. The method of any one of claims 1-13, wherein the TGFβ receptor is a TGF-βRIII.~~

~~16~~13. The ~~method~~ use of any one of claims 1-~~15~~12, wherein at least one of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor is a soluble TGF-β receptor, an extracellular domain of TGF-β receptor, an antibody that binds specifically to TGF-β, an antagonistic antibody that binds to a TGF-β receptor, an agent that binds to a LAP, or an agent that binds to a TGF-β/LAP complex.

~~17~~14. The ~~method~~ use of claim ~~16~~13, wherein the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor decrease(s) the activation of a TGF-β receptor through binding to a LAP, or to a TGF-β/LAP complex.

~~18~~15. The ~~method~~ use of any one of claims 1-~~15~~12, wherein at least one of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor is a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a first domain of a pair of affinity domains;

(b) a second chimeric polypeptide comprising:

(i) a second domain of a pair of affinity domains; and

(ii) a second target-binding domain,

wherein one or both of the first target-binding domain and the second target-binding domain binds specifically to a ligand of a TGF-β receptor; or

one or both of the first target-binding domain and the second target-binding domain is an antagonistic antigen-binding domain that binds specifically to a TGF-β receptor.

~~19. The method of claim 18, wherein the TGF-β receptor is TGF-βRII.~~

~~20. The method of claim 18, wherein the TGF-β receptor is TGF-βRIII.~~

~~21. The method of any one of claims 18-20, wherein the first target-binding domain and the soluble tissue factor domain directly abut each other in the first chimeric polypeptide.~~

~~22. The method of any one of claims 18-20, wherein the first chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the soluble tissue factor domain in the first chimeric polypeptide.~~

~~23. The method of any one of claims 18-22, wherein the soluble tissue factor domain and the first domain of the pair of affinity domains directly abut each other in the first chimeric polypeptide.~~

~~24. The method of any one of claims 18-22, wherein the first chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.~~

~~25. The method of any one of claims 18-24, wherein the second domain of the pair of affinity domains and the second target-binding domain directly abut each other in the second chimeric polypeptide.~~

~~26. The method of any one of claims 18-24, wherein the second chimeric polypeptide further comprises a linker sequence between the second domain of the pair of~~

affinity domains and the second target-binding domain in the second chimeric polypeptide.

27. The method of any one of claims 18-26, wherein the first target-binding domain and the second target-binding domain bind specifically to the same antigen.

28. The method of any one of claims 18-26, wherein the first target-binding domain and the second target-binding domain bind specifically to different antigens.

29. The method of any one of claims 18-28, wherein the first chimeric polypeptide further comprises one or more additional target-binding domain(s).

30. The method of any one of claims 18-29, wherein the second chimeric polypeptide further comprises one or more additional target-binding domain(s).

31. The method of any one of claims 18-30, wherein the soluble tissue factor domain is a soluble human tissue factor domain.

32. The method of claim 31, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 93.

33. The method of any one of claims 18-32, wherein the pair of affinity domains is a sushi domain from an alpha chain of human IL-15 receptor (IL15Rα) and a soluble IL-15.

34. The method of claim 33, wherein the soluble IL-15 has a D8N or D8A amino acid substitution.

~~35. The method of any one of claims 33-34, wherein the soluble IL-15 comprises a mutation to reduce or eliminate IL-15 activity.~~

~~36. The method of any one of claims 18-32, wherein the pair of affinity domains is selected from the group consisting of: barnase and barnstar, a PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.~~

~~37. The method of any one of claims 18-32, wherein the first domain or the second domain of a pair of affinity domains is a soluble common gamma-chain family cytokine or an antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor.~~

~~38. The method of any one of claims 18-37, wherein the first target-binding domain and/or the second target-binding domain comprise a soluble TGF-β receptor.~~

~~39. The method of claim 38, wherein the soluble TGF-β receptor is a soluble TGF-βRII.~~

~~40. The method of claim 39, wherein the soluble TGF-βRII comprises a first sequence that is at least 80% identical to SEQ ID NO: 183, and a second sequence that is at least 80% identical to SEQ ID NO: 183, wherein the first and second sequence are separated by a linker.~~

~~41. The method of claim 40, wherein the soluble TGF-βRII comprises a first sequence that is at least 90% identical to SEQ ID NO: 183, and a second sequence that is at least 90% identical to SEQ ID NO: 183.~~

42. The method of claim 41, wherein the soluble TGF-βRII comprises a first sequence of SEQ ID NO: 183, and a second sequence of SEQ ID NO: 183.

43. The method of claim 40, wherein the linker comprises a sequence of SEQ ID NO: 102.

44. The method of claim 39, wherein the soluble TGF-βRII comprises a sequence that is at least 80% identical to SEQ ID NO: 188.

45. The method of claim 44, wherein the soluble TGF-βRII comprises a sequence that is at least 90% identical to SEQ ID NO: 188.

46. The method of claim 45, wherein the soluble TGF-βRII comprises a sequence of SEQ ID NO: 188.

47. The method of claim 18, wherein the first chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 236.

48. The method of claim 47, wherein the first chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 236.

49. The method of claim 48, wherein the first chimeric polypeptide comprises a sequence of SEQ ID NO: 236.

50. The method of claim 18, wherein the second chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 193.

51. The method of claim 50, wherein the first chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 236.

~~52. The method of claim 51, wherein the second chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 193.~~

~~53. The method of claim 52, wherein the second chimeric polypeptide comprises a sequence of SEQ ID NO: 193.~~

~~54. The method of claim 53, wherein the first chimeric polypeptide comprises a sequence of SEQ ID NO: 236.~~

~~55~~16. The ~~method~~ use of any one of claims 1-~~15~~12, wherein at least one of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor is a single-chain chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a second target-binding domain,

wherein one or both of the first target-binding domain and the second target-binding domain binds specifically to a ligand of a TGF-β receptor; or

one or both of the first target-binding domain and the second target-binding domain is an antagonistic antigen-binding domain that binds specifically to a TGF-β receptor.

~~56. The method of claim 55, wherein the TGF-β receptor is TGF-βRII.~~

~~57. The method of claim 55, wherein the TGF-β receptor is TGF-βRIII.~~

~~58. The method of any one of claims 55-57, wherein the first target-binding domain and the soluble tissue factor domain directly abut each other.~~

~~59. The method of any one of claims 55-57, wherein the single-chain chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the soluble tissue factor domain.~~

~~60. The method of any one of claims 55-59, wherein the soluble tissue factor domain and the second target-binding domain directly abut each other.~~

~~61. The method of any one of claims 55-59, wherein the single-chain chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the second target-binding domain.~~

~~62. The method of any one of claims 55-61, wherein the first target-binding domain and the second target-binding domain bind specifically to the same antigen.~~

~~63. The method of any one of claims 55-61, wherein the first target-binding domain and the second target-binding domain bind specifically to different antigens.~~

~~64. The method of any one of claims 55-63, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~65. The method of claim 64, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 93.~~

~~66. The method of any one of claims 55-65, wherein the single-chain chimeric polypeptide further comprises one or more additional target-binding domains at its N- and/or C-terminus.~~

~~67. The method of any one of claims 55-66, wherein the first target-binding domain and/or the second target-binding domain comprise a soluble TGF-β receptor.~~

68. The method of claim 67, wherein the soluble TGF-β receptor is a soluble TGF-βRII.

69. The method of claim 68, wherein the soluble TGF-βRII comprises a first sequence that is at least 80% identical to SEQ ID NO: 183, and a second sequence that is at least 80% identical to SEQ ID NO: 183, wherein the first and second sequence are separated by a linker.

70. The method of claim 69, wherein the soluble TGF-βRII comprises a first sequence that is at least 90% identical to SEQ ID NO: 183, and a second sequence that is at least 90% identical to SEQ ID NO: 183.

71. The method of claim 70, wherein the soluble TGF-βRII comprises a first sequence of SEQ ID NO: 183, and a second sequence of SEQ ID NO: 183.

72. The method of claim 69, wherein the linker comprises a sequence of SEQ ID NO: 102.

73. The method of claim 72, wherein the soluble TGF-βRII comprises a sequence that is at least 80% identical to SEQ ID NO: 188.

74. The method of claim 73, wherein the soluble TGF-βRII comprises a sequence that is at least 90% identical to SEQ ID NO: 188.

75. The method of claim 74, wherein the soluble TGF-βRII comprises a sequence of SEQ ID NO: 188.

76. The method of any one of claims 1-75, wherein the method comprises administering two or more doses of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor to the subject.

~~77. The method of claim 76, wherein any two consecutive doses of the two or more doses are administered about 1 week to about one year apart.~~

~~78. The method of claim 77, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 6 months apart.~~

~~79. The method of claim 78, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 2 months apart.~~

~~80. The method of claim 79, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 1 month apart.~~

~~81. The method of any one of claims 76-80, wherein the two or more doses are administered by subcutaneous administration.~~

~~82. The method of any one of claims 76-80, wherein the two or more doses are administered by intramuscular administration.~~

~~83. The method of any one of claims 76-82, wherein the two or more doses are administered over a period of time of about 1 year to about 60 years.~~

~~84. The method of claim 83, wherein the two or more doses are administered over a period of time of about 1 year to about 50 years.~~

~~85. The method of claim 84, wherein the two or more doses are administered over a period of time of about 1 year to about 40 years.~~

~~86. The method of claim 85, wherein the two or more doses are administered over a period of time of about 1 year to about 30 years.~~

~~87. The method of claim 86, wherein the two or more doses are administered over a period of time of about 1 year to about 20 years.~~

~~88. The method of claim 87, wherein the two or more doses are administered over a period of time of about 1 year to about 10 years.~~

~~89. The method of any one of claims 1-88, wherein a first dose of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor begins when the subject reaches an age of at least 30 years.~~

~~90. The method of claim 89, wherein a first dose of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor begins when the subject reaches an age of at least 40 years.~~

~~91. The method of claim 90, wherein a first dose of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor begins when the subject reaches an age of at least 50 years.~~

~~92. The method of claim 91, wherein a first dose of the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor begins when the subject reaches an age of at least 60 years.~~

~~93. The method of any one of claims 1-92, wherein each of the two or more doses are administered at a dosage of about 0.01 mg of each agent that results in a decrease in the activation of a TGF-β receptor/kg to about 10 mg of each agent that results in a decrease in the activation of a TGF-β receptor/kg.~~

~~94. The method of claim 93, wherein each of the two or more doses are administered at a dosage of about 0.02 mg of each agent that results in a decrease in the~~

~~activation of a TGF-β receptor/kg to about 5 mg of each agent that results in a decrease in the activation of a TGF-β receptor/kg.~~

~~95. The method of any one of claims 1-3 and 9-94, wherein the subject is not diagnosed or identified as having an aging-related disease or an inflammatory disease.~~

~~96. The method of any one of claims 1-3 and 9-95, wherein the subject has not been previously treated with a chemotherapeutic agent.~~

~~97. The method of any one of claims 1-3 and 9-95, wherein the subject has not been previously treated with a therapeutic agent that induces cellular senescence.~~

~~98~~17. ~~A method of killing or reducing the number of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more common gamma-chain family cytokine receptor activating agent(s) in the manufacture of a medicament for killing or reducing the number of naturally-occurring and/or treatment-induced senescent cells in a subject.

~~99~~18. ~~A method of decreasing the accumulation of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more common gamma-chain family cytokine receptor activating agent(s) in the manufacture of a medicament for decreasing the accumulation of naturally-occurring and/or treatment-induced senescent cells in a subject.

~~100~~19. ~~A method of decreasing a level of a marker of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more common gamma-chain family cytokine receptor activating agent(s) in the manufacture of a medicament for

decreasing a level of a marker of naturally-occurring and/or treatment-induced senescent cells in a subject.

~~101~~20. ~~A method of reducing the activity of naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more common gamma-chain family cytokine receptor activating agent(s) in the manufacture of a medicament for reducing the activity of naturally-occurring and/or treatment-induced senescent cells in a subject.

~~102~~21. ~~A method of decreasing levels or activity of SASP factors derived from naturally-occurring and/or treatment-induced senescent cells in a subject, the method comprising administering to the subject~~ Use of ~~a therapeutically effective amount of~~ one or more common gamma-chain family cytokine receptor activating agent(s) in the manufacture of a medicament for decreasing levels or activity of SASP factors derived from naturally-occurring and/or treatment-induced senescent cells in a subject.

~~103~~22. The ~~method~~ use of any one of claims ~~98~~17-~~102~~21, wherein the subject has been previously diagnosed or identified as having an aging-related disease or an inflammatory disease.

~~104. The method of claim 103, wherein the aging-related disease is inflamm-aging related.~~

~~105. The method of claim 103, wherein the aging-related disease is selected from the group consisting of: Alzheimer's disease, aneurysm, cystic fibrosis, fibrosis in pancreatitis, glaucoma, hypertension, inflammatory bowel disease, intervertebral disc degeneration, osteoarthritis, type 2 diabetes mellitus, adipose atrophy, lipodystrophy, atherosclerosis, cataracts, COPD, idiopathic pulmonary fibrosis, kidney transplant failure, liver fibrosis, loss of bone mass, myocardial infarction, sarcopenia, wound healing, alopecia, cardiomyocyte hypertrophy, osteoarthritis, Parkinson's disease, age-associated~~

~~loss of lung tissue elasticity, age-related macular degeneration, cachexia, glomerulosclerosis, liver cirrhosis, NAFLD, osteoporosis, amyotrophic lateral sclerosis, Huntington's disease, spinocerebellar ataxia, multiple sclerosis, neurodegeneration, stroke, blood brain barrier impairments, cancer, dementia, vascular disease, infection susceptibility, chronic inflammation, and renal dysfunction.~~

~~106. The method of claim 103, wherein the aging-related disease is a cancer selected from the group consisting of: solid tumor, hematological tumor, sarcoma, osteosarcoma, glioblastoma, neuroblastoma, melanoma, rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, B-cell neoplasms, multiple myeloma, B-cell lymphoma, B-cell non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma, retinoblastoma, stomach cancer, urothelial carcinoma, lung cancer, renal cell carcinoma, gastric and esophageal cancer, pancreatic cancer, prostate cancer, breast cancer, colorectal cancer, ovarian cancer, non-small cell lung carcinoma, squamous cell head and neck carcinoma, endometrial cancer, cervical cancer, liver cancer, and hepatocellular carcinoma.~~

~~107. The method of claim 103, wherein the inflammatory disease is selected from the group consisting of: rheumatoid arthritis, inflammatory bowel disease, lupus erythematosus, lupus nephritis, diabetic nephropathy, CNS injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Crohn's disease, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, ulcerative colitis, nonalcoholic steatohepatitis, mood disorders and cancer treatment-related cognitive impairment.~~

~~108. The method of any one of claims 98-107, wherein the treatment-induced senescent cells are chemotherapy-induced senescent cells.~~

~~109. The method of any one of claims 98-108, wherein the administration of the one or more common gamma-chain family cytokine receptor activating agent(s) results in a decrease in the number of naturally-occurring senescent cells and/or treatment-induced senescent cells in a target tissue in the subject.~~

~~110. The method of claim 109, wherein the target tissue is selected from the group consisting of: adipose tissue, pancreatic tissue, liver tissue, kidney tissue, lung tissue, heart tissue, vasculature, bone tissue, central nervous system (CNS) tissue, eye tissue, skin tissue, muscle tissue, and secondary lympho-organ tissue.~~

~~111~~23. The ~~method~~ use of any one of claims ~~98~~17-~~110~~22, wherein at least one of the one or more common gamma-chain family cytokine receptor activating agent(s) is a complex of a common gamma-chain family cytokine or a functional fragment thereof and an antibody or antibody fragment that binds specifically to the common gamma-chain family cytokine or the functional fragment thereof.

~~112~~24. The ~~method~~ use of any one of claims ~~98~~17-~~110~~22, wherein at least one of the one or more common gamma-chain family cytokine receptor activating agent(s) is a single-chain chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a second target-binding domain,

wherein one or both of the first target-binding domain and the second target-binding domain is a soluble common gamma-chain family cytokine, an agonistic antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor, a soluble common gamma-chain family cytokine receptor, or an antigen-binding domain that binds specifically to a common gamma-chain family cytokine.

~~113. The method of claim 112, wherein one or both of the first target-binding domain and the second target-binding domain comprises a soluble common gamma-chain family cytokine.~~

~~114. The method of claim 113, wherein the soluble common gamma-chain family cytokine is selected from the group consisting of: soluble IL-2, soluble IL-4, soluble IL-7, soluble IL-9, soluble IL-15, and soluble IL-21.~~

~~115. The method of claim 114, wherein one or both of the first target-binding domain and the second target-binding domain comprises an agonistic antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor.~~

~~116. The method of claim 115, wherein the common gamma-chain family cytokine receptor is a receptor for one or more of IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21.~~

~~117. The method of claim 115 or 116, wherein the agonistic antigen-binding domain is an scFv, a VHH, or a VNAR.~~

~~118. The method of any one of claims 112-117, wherein the first target-binding domain and the soluble tissue factor domain directly abut each other.~~

~~119. The method of any one of claims 112-117, wherein the single-chain chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the soluble tissue factor domain.~~

~~120. The method of any one of claims 112-119, wherein the soluble tissue factor domain and the second target-binding domain directly abut each other.~~

~~121. The method of any one of claims 112-119, wherein the single-chain chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the second target-binding domain.~~

~~122. The method of any one of claims 112-121, wherein the first target-binding domain and the second target-binding domain bind specifically to the same antigen.~~

~~123. The method of claim 122, wherein the first target-binding domain and the second target-binding domain bind specifically to the same epitope.~~

~~124. The method of claim 123, wherein the first target-binding domain and the second target-binding domain comprise the same amino acid sequence.~~

~~125. The method of any one of claims 112-121, wherein the first target-binding domain and the second target-binding domain bind specifically to different antigens.~~

~~126. The method of any one of claims 112-125, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~127. The method of claim 126, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 93.~~

~~128. The method of any one of claims 112-127, wherein the single-chain chimeric polypeptide further comprises one or more additional target-binding domains at its N- and/or C-terminus.~~

~~129~~25. The ~~method~~ use of any one of claims ~~98~~17-~~110~~22, wherein at least one of the one or more common gamma-chain family cytokine receptor activating agent(s) is a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a first domain of a pair of affinity domains;

(b) a second chimeric polypeptide comprising:

(i) a second domain of a pair of affinity domains; and

(ii) a second target-binding domain,

wherein one or both of the first target-binding domain and the second target-binding domain is a soluble common gamma-chain family cytokine, an agonistic antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor, a soluble common gamma-chain family cytokine receptor, or an antigen-binding domain that binds specifically to a common gamma-chain family cytokine.

~~130. The method of claim 129, wherein one or both of the first target-binding domain and the second target-binding domain comprises a soluble common gamma-chain family cytokine.~~

~~131. The method of claim 130, wherein the soluble common gamma-chain family cytokine is selected from the group consisting of: soluble IL-2, soluble IL-4, soluble IL-7, soluble IL-9, soluble IL-15, and soluble IL-21.~~

~~132. The method of claim 129, wherein one or both of the first target-binding domain and the second target-binding domain comprises an agonistic antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor.~~

~~133. The method of claim 132, wherein the common gamma-chain family cytokine receptor is a receptor for one or more of IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21.~~

~~134. The method of claim 132 or 133, wherein the agonistic antigen-binding domain is an scFv, a VHH, or a VNAR.~~

~~135. The method of any one of claims 129-134, wherein the first target-binding domain and the soluble tissue factor domain directly abut each other in the first chimeric polypeptide.~~

~~136. The method of any one of claims 129-134, wherein the first chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the soluble tissue factor domain in the first chimeric polypeptide.~~

~~137. The method of any one of claims 129-136, wherein the soluble tissue factor domain and the first domain of the pair of affinity domains directly abut each other in the first chimeric polypeptide.~~

~~138. The method of any one of claims 129-136, wherein the first chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.~~

~~139. The method of any one of claims 129-138, wherein the second domain of the pair of affinity domains and the second target-binding domain directly abut each other in the second chimeric polypeptide.~~

~~140. The method of any one of claims 129-138, wherein second chimeric polypeptide further comprises a linker sequence between the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide.~~

~~141. The method of any one of claims 129-140, wherein the first target-binding domain and the second target-binding domain bind specifically to the same antigen.~~

~~142. The method of any one of claims 129-140, wherein the first target-binding domain and the second target-binding domain bind specifically to different antigens.~~

~~143. The method of any one of claims 129-142, wherein the first chimeric polypeptide further comprises one or more additional target-binding domain(s).~~

~~144. The method of any one of claims 129-143, wherein the second chimeric polypeptide further comprises one or more additional target-binding domains.~~

~~145. The method of any one of claims 129-144, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~146. The method of claim 145, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 93.~~

~~147. The method of any one of claims 129-146, wherein the pair of affinity domains is a sushi domain from an alpha chain of human IL-15 receptor (IL15Rα) and a soluble IL-15.~~

~~148. The method of any one of claims 129-146, wherein the pair of affinity domains is selected from the group consisting of: barnase and barnstar, a PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.~~

~~149. The method of any one of claims 129-146, wherein the first domain or the second domain of a pair of affinity domains is a soluble common gamma-chain family cytokine or an antigen-binding domain that binds specifically to a common gamma-chain family cytokine receptor.~~

~~150. The method of any one of claims 98-110, wherein at least one of the one or more common gamma-chain family cytokine receptor activating agent(s) is soluble IL-15 or an IL-15 agonist.~~

~~151. The method of claim 150, wherein the soluble IL-15 is at least 90% identical to SEQ ID NO: 82.~~

~~152. The method of claim 150, wherein the IL-15 agonist comprises a complex of IL-15 and all or a portion of a soluble IL-15 receptor (IL-15R).~~

~~153. The method of claim 152, wherein the portion of the soluble IL-15R is a portion of IL-15Rα.~~

~~154. The method of claim 153, wherein the portion of the soluble IL-15Rα is a sushi domain of IL-15Rα.~~

~~155. The method of any one of claims 152-154, wherein the IL-15 agonist further comprises an Fc domain.~~

~~156. The method of claim 150, wherein the IL-15 agonist comprises a fusion protein comprising IL-15 and a sushi domain from an IL-15Rα.~~

~~157~~26. The ~~method~~ use of any one of claims ~~98~~17-~~110~~22, wherein one of the one or more common gamma-chain family cytokine receptor activating agent(s) is a soluble IL-2 or an IL-2 agonist.

~~158~~27. The ~~method~~ use of any one of claims ~~98~~17-~~110~~22, wherein one of the one or more common gamma-chain family cytokine receptor activating agent(s) is an antibody or an antigen-binding antibody fragment that binds specifically to a common gamma-chain family cytokine.

~~159. The method of any one of claims 98-158, wherein the method comprises administering one, two or more doses of the one or more common gamma-chain family cytokine receptor activating agent(s) to the subject.~~

~~160. The method of claim 159, wherein any two consecutive doses of the two or more doses are administered about 1 week to about one year apart.~~

~~161. The method of claim 160, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 6 months apart.~~

~~162. The method of claim 161, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 2 months apart.~~

~~163. The method of claim 162, wherein any two consecutive doses of the two or more doses are administered about 1 week to about 1 month apart.~~

~~164. The method of any one of claims 159-163, wherein the one, two or more doses are administered by subcutaneous administration.~~

~~165. The method of any one of claims 159-163, wherein the two or more doses are administered by intramuscular administration.~~

~~166. The method of any one of claims 159-165, wherein the two or more doses are administered over a period of time of about 1 year to about 60 years.~~

~~167. The method of claim 166, wherein the two or more doses are administered over a period of time of about 1 year to about 50 years.~~

~~168. The method of claim 167, wherein the two or more doses are administered over a period of time of about 1 year to about 40 years.~~

~~169. The method of claim 168, wherein the two or more doses are administered over a period of time of about 1 year to about 30 years.~~

~~170. The method of claim 169, wherein the two or more doses are administered over a period of time of about 1 year to about 20 years.~~

~~171. The method of claim 170, wherein the two or more doses are administered over a period of time of about 1 year to about 10 years.~~

~~172. The method of any one of claims 98-171, wherein each of the two or more doses are administered at a dosage of about 0.01 mg of each common gamma-chain family cytokine receptor activating agent/kg to about 10 mg of each common gamma-chain family cytokine receptor activating agent/kg.~~

~~173. The method of claim 172, wherein each of the two or more doses are administered at a dosage of about 0.02 mg of each common gamma-chain family cytokine receptor activating agent/kg to about 5 mg of each common gamma-chain family cytokine receptor activating agent/kg.~~

~~174. The method of any one of claims 98-173, wherein a first dose of the one or more common gamma-chain family cytokine receptor activating agent(s) begins when the subject reaches an age of at least 30 years.~~

~~175. The method of claim 174, wherein a first dose of the one or more common gamma-chain family cytokine receptor activating agent(s) begins when the subject reaches an age of at least 40 years.~~

~~176. The method of claim 175, wherein a first dose of the one or more common gamma-chain family cytokine receptor activating agent(s) begins when the subject reaches an age of at least 50 years.~~

~~177. The method of claim 176, wherein a first dose of the one or more common gamma-chain family cytokine receptor activating agent(s) begins when the subject reaches an age of at least 60 years.~~

~~178. The method of any one of claims 98-102 and 108-177, wherein the subject is not diagnosed or identified as having an aging-related disease or an inflammatory disease.~~

~~179. The method of any one of claims 98-102 and 108-178, wherein the subject has not been previously treated with a chemotherapeutic agent.~~

~~180. The method of any one of claims 98-102 and 108-178, wherein the subject has not been previously treated with a therapeutic agent that induces cellular senescence.~~

~~1812~~8. The ~~method~~ use of any one of claims ~~98~~17-~~180~~27, wherein ~~the method further comprises administering to the subject~~ at least one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor is to be further administered to the subject.

~~1822~~9. The ~~method~~ use of claim ~~1812~~8, wherein the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β receptor is a soluble TGF-β receptor, an extracellular domain of TGF-β receptor, an antibody that binds specifically to TGF-β, an antagonistic antibody that binds to a TGF-β receptor, an agent that binds to a LAP, or an agent that binds to a TGF-β/LAP complex.

~~1833~~0. The ~~method~~ use of claim ~~1822~~9, wherein the one or more agent(s) that result(s) in a decrease in the activation of a TGF-β decrease(s) the activation of a TGF-β receptor through binding to a LAP, or to a TGF-β/LAP complex.

~~184. The method of any one of claims 31, 32, 64, 65, 126, 127, 145, and 146, wherein the soluble human tissue factor domain does not initiate blood coagulation.~~

~~185~~31. The ~~method~~ use of any one of claims 1-~~184~~30, wherein ~~the method further comprises administering~~ an additional therapeutic agent selected from the group of: combinations of agents, such as checkpoint inhibitors, chemotherapy drugs, and therapeutic antibodies, is to be further administered.

~~186. The method of any one of claims 55-75, wherein the single-chain chimeric polypeptide is stable in human serum for at least 10 days at 37 °C.~~

~~187. The method of any one of claims 18-54, wherein the multi-chain chimeric polypeptide is stable in human serum for at least 10 days at 37 °C.~~

~~188. The method of any one of claims 112-128, wherein the single-chain chimeric polypeptide does not have significant clotting activity.~~

~~189. The method of any one of claims 129-149, wherein the multi-chain chimeric polypeptide does not have significant clotting activity.~~

~~190. The method of any one of claims 1-189, wherein the method results in rejuvenation of aged immune cells in the subject~~

~~191. The method of claim 190, wherein the rejuvenation of the aged immune cells results in a reduction of number of diseased cells or infectious agents in the subject.~~

~~192. The method of claim 190 or 191, wherein the aged immune cells include one or more of aged NK cells, aged NKT cells, aged T cells, aged B cells, aged monocytes, aged macrophages, aged neutrophils, aged basophils, aged eosinophils, aged Kupffer cells, and aged microgial cells.~~

~~193. The methods of claim 191, wherein the diseased cells include cancer cells, virally-infected cells, and intracellularly-bacterially-infected cells.~~

~~194. The methods of claim 191, wherein the infectious agents include virus, bacterium, fungus, and parasite.~~