CLAIMS

What is claimed is:

1. A method of treating or preventing frailty in a patient, said method comprising

(a) identifying a patient desiring or in need of frailty treatment or prevention, and

(b) administering to said patient a recombinant TLR5 agonist, wherein said TLR5 agonist is not fused to a pathogenic protein antigen.

2. The method of claim 1, wherein frailty comprises an accumulation of deficiencies in major physiological functions, reduction of regeneration capabilities, impaired wound healing and/or increased risk of age-related diseases or disorders.

3. The method of either claim 1 or 2, wherein frailty is measured according to the Physiological Frailty Index.

4. The method of claim 3, wherein the Physiological Frailty Index comprises assessment of one or more parameters selected from grip strength, systolic blood pressure, diastolic blood pressure, blood flow volume, number of blood neutrophils, percentage of blood neutrophils, number of blood monocytes, percentage of blood monocytes, number of lymphocytes, number of red blood cells, hemoglobin levels, hematocrit levels, mean corpuscular volume, mean corpuscular hemoglobin levels, mean corpuscular hemoglobin concentration and keratinocyte-derived cytokine levels.

5. The method of any one of the above claims, wherein the TLR5 agonist is a flagellin or a derivative thereof.

6. The method of claim 5, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 1.

7. The method of claim 6, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence that is SEQ ID NO: 1.

8. The method of claim 5, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence having at least 95% sequence identity to one of SEQ ID NOs: 2-27.

9. The method of claim 8, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence of one of SEQ ID NOs: 2-27.

10. The method of any one of the above claims, wherein the patient's Physiological Frailty Index is reduced by about 25% to about 75%.

11. The method of claim 10, wherein the patient's Physiological Frailty Index is reduced by at least about 75%, or about 50%, or about 35%, or about 25%.

12. The method of claim 10, wherein the frailty is associated with aging.

13. The method of any one of the above claims, wherein the patient is middle-aged.

14. The method of claim 13, wherein the patient is between about 36 and about 55 years old.

15. The method of any one of the above claims, wherein the patient is elderly.

16. The method of claim 15, wherein the patient is between about 56 and about 85 years old.

17. The method of any one of the above claims, wherein the biological sex of the patient is male.

18. The method of any one of claims 1-17, wherein the biological sex of the patient is female.

19. A method of treating or preventing an age-related disease or disorder in a patient, said method comprising

(a) identifying a patient desiring or in need of treatment or prevention of an age-related disease or disorder, and

(b) administering to said patient a recombinant TLR5 agonist, wherein said TLR5 agonist is not fused to a pathogenic protein antigen.

20. The method of claim 19, wherein the age-related disease or disorder is characterized by increased cellular senescence.

21. The method of either claim 19 or 20, wherein the age-related disease or disorder is selected from accelerated aging, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, cardiac diastolic dysfunction, benign prostatic hypertrophy, aortic aneurysm, emphysema, atherosclerosis, diabetes, pulmonary fibrosis, blindness, dementia, Alzheimer's disease, kidney dysfunction, osteoarthritis, low grade chronic sterile inflammation, herniated intervertebral disc, frailty, hair loss, hearing loss, vision loss, muscle fatigue, skin conditions,

skin nevi, wrinkly skin, hyperpigmentation, scarring, keloid, rosacea, vitiligo, ichthyosis vulgaris, dermatomyositis, actinic keratosis, and sarcopenia.

22. The method of claim 21, wherein the age-related disease or disorder is accelerated aging.

23. The method of claim 22, wherein the accelerate aging is a a Progeroid syndrome, or symptom thereof.

24. The method of claim 23, wherein the Progeroid syndrome is selected from Hutchinson-Gilford progeria syndrome (HGPS), Werner syndrome (WS), Bloom syndrome (BS), Rothmund-Thomson syndrome (RTS), Cockayne syndrome (CS), xeroderma pigmentosum (XP), trichothiodystrophy (TTD), combined xeroderma pigmentosum-Cockayne syndrome (XP-CS), and restrictive dermopathy (RD).

25. The method of claim 22, wherein the accelerated aging is indueed by a cancer or a cancer treatment.

26. The method of claim 25, wherein the cancer treatment is selected from one or more of radiotherapy, hormonal therapy, tyrosine kinase inhibitor, anthracycline, alkylating agent, topoisomerase inhibitor, antimetabolites/cytotoxic drug, BRAF inhibitor, antitumor antibiotic, isoquinololine alkaloid, Bcl-2 inhibitor, hematopoietic cell transplantation (HCT), telomerase inhibitor, nucleoside analogue reverse-transcriptase inhibitor, DNA cross-linking agent, ribonucleotide reductase inhibitor, microtubule inhibitor, and miRNA.

27. The method of any one of claims 25-26, wherein the patient was previously afflicted with a cancer.

28. The method of claim 27, wherein the patient is cancer survivor.

29. The method of claim 28, wherein the cancer survivor has completed a cancer treatment and has no apparent evidence of active disease.

30. The method of any one of claims 25-29, wherein the cancer is slectbasal cell carcinoma, biliary tract cancer; bladder cancer; bone cancer; brain and central nervous system cancer; breast cancer; cancer of the peritoneum; cervical cancer; choriocarcinoma; colon and rectum cancer; connective tissue cancer; cancer of the digestive system; endometrial cancer; esophageal cancer; eye cancer; cancer of the head and neck; gastric cancer (including gastrointestinal cancer); glioblastoma; hepatic carcinoma; hepatoma; intra-epithelial neoplasm; kidney or renal cancer; larynx cancer; leukemia; liver cancer; lung cancer (*e.g.*, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of

the lung); melanoma; myeloma; neuroblastoma; oral cavity cancer (lip, tongue, mouth, and pharynx); ovarian cancer; pancreatic cancer; prostate cancer; retinoblastoma; rhabdomyosarcoma; rectal cancer; cancer of the respiratory system; salivary gland carcinoma; sarcoma; skin cancer; squamous cell cancer; stomach cancer; testicular cancer; thyroid cancer; uterine or endometrial cancer; cancer of the urinary system; vulval cancer; lymphoma including Hodgkin's and non-Hodgkin's lymphoma, as well as B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL); small lymphocytic (SL) NHL; intermediate grade/follicular NHL; intermediate grade diffuse NHL; high grade immunoblastic NHL; high grade lymphoblastic NHL; high grade small non-cleaved cell NHL; bulky disease NHL; mantle cell lymphoma; AIDS-related lymphoma; and Waldenstrom's Macroglobulinemia; chronic lymphocytic leukemia (CLL); acute lymphoblastic leukemia (ALL); Hairy cell leukemia; chronic myeloblastic leukemia; as well as other carcinomas and sarcomas; and post-transplant lymphoproliferative disorder (PTLD), as well as abnormal vascular proliferation associated with phakomatoses, edema (*e.g.* that associated with brain tumors), and Meigs' syndrome.

31. The method of any one of claims 19-30, wherein the patient is middle-aged.

32. The method of claim 31, wherein the patient is between about 36 and about 55 years old.

33. The method of any one of claims 19-30, wherein the patient is elderly.

34. The method of claim 33, wherein the patient is between about 56 and about 85 years old.

35. The method of any one of claims 25-34, wherein the patient received the cancer treatment before the age of about 18, before the age of about 16, before the age of about 14, before the age of about 12, before the age of about 10, before the age of about 8, before the age of about 6, before the age of about 4, or before the age of about 2.

36. The method of any one of claims 25-35, wherein the TLR5 agonist is administered to the patient for at least one week, or at least one month, or at least six months, or at least one year, or at least two years, or at least three years, or at least four years, or at least five years after the patient received the cancer treatment.

37. The method of any one of claims 25-36, wherein the patient no longer has cancer or the patient is in remission at the time the TLR5 agonist is administered.

38. The method of any one of claims 19-37, wherein administering the TLR5 agonist to the patient treats or prevents the age-related disease or disorder by decreasing cellular senescence.

39. The method of any one of claims 19-38, wherein the TLR5 agonist is flagellin or a derivative thereof.

40. The method of claim 39, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 1.

41. The method of claim 40, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence that is SEQ ID NO: 1.

42. The method of claim 39, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence having at least 95% sequence identity to one of SEQ ID NOs: 2-27.

43. The method of claim 42, wherein the TLR5 agonist comprises a polypeptide having an amino acid sequence of one of SEQ ID NOs: 2-27.

44. The method of any one of claims 19-43, wherein the biological sex of the patient is male.

45. The method of any one of claims 19-43, wherein the biological sex of the patient is female.

46. The method of any one of the preceding claims, wherein the TLR5 agonist is administered in one or more cycles.

47. The method of claim 46, wherein the cycle involves dosing a patient once per day for one day, once a day for two days, once a day for three days, once a day for four days, or once a day for five days.

48. The method of claim 47, wherein no more than 5 cycles, or no more than 3 cycles, or no more than 2 cycles are administered per year.

49. A TLR5 agonist for use in the treatment or prevention of frailty.

50. Use of aTLR5 agonist in the manufacture of a medicament for treatment or prevention of frailty.

51. A TLR5 agonist for use in the treatment or prevention of an age-related disease or disorder.

52. Use of aTLR5 agonist in the manufacture of a medicament for treatment or prevention of an age-related disease or disorder.