CLAIMS:

1. A modified Stimulator of Interferon Genes (STING) protein that has lower nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB) signaling activity than human STING and that comprises one or more mutations that result(s) in increased activation or that result(s) in constitutive activation of the STING protein to result in constitutive expression of type I interferon (IFN).

2. The modified STING protein of claim 1, wherein the modified STING protein is selected from among:

a) a modified non-human STING protein that has lower NF-κB signaling activity compared to the NF-κB signaling activity of human STING, wherein:

i) the non-human STING protein is modified to include a mutation or mutations so that it has increased type I interferon (IFN) pathway signaling activity or acts constitutively to induce type I IFN;

ii) the mutations are insertions, deletions, and/or replacements of amino acids; and

iii) the STING protein optionally has a deletion of the TRAF6 binding site;

b) the modified non-human STING protein of a) that is modified to constitutively induce type I IFN;

c) a chimeric STING protein that comprises a human STING and replacement of the C-terminal tail (CTT) of the human STING protein with the CTT from a non-human STING protein that has reduced NF-κB signaling activity compared to the NF-κB signaling activity of the human STING protein; and

d) a modified chimeric STING protein of c) that is modified to include a mutation or mutations so that it has increased type I interferon (IFN) pathway signaling activity or acts constitutively in the absence of cytosolic nucleic acids, wherein the mutations are insertions, deletions, and/or replacements of amino acids.

3. The modified STING protein of claim 2, wherein the non-human STING is a STING protein from a species selected from among Tasmanian devil, marmoset, cattle, cat, ostrich, boar, bat, manatee, crested ibis, coelacanth, zebrafish, and ghost shark.

4. The modified STING protein of claim 3, wherein the non-human STING protein is a Tasmanian devil STING protein of SEQ ID NO:331, or a variant thereof having at least 98% sequence identity to the STING protein of SEQ ID NO:331 and having lower NF-κB signaling activity than human STING.

5. The modified STING protein of any of claims 1-4, wherein:

the modified STING protein comprises a replacement corresponding to C206Y or R284G; and

corresponding residues are numbered by alignment to the sequence of human STING as set forth in any of SEQ ID NOs:305-309.

6. The modified STING protein of claim 5, wherein the modified STING protein comprises the sequence of amino acids set forth in SEQ ID NO: 332 or 333 or a protein having at least 98% sequence identity thereto, and comprising the replacement corresponding to C206Y and R284G, respectively.

7. The modified STING protein of any of claims 1-6, wherein the sequences of the non-human species STING proteins are those set forth in SEQ ID NOs: 331, 338 and 341-

350, or the non-human STING proteins are variants of any of the STING proteins set forth in SEQ ID NOs: 331, 338 and 341-350, having at least 98% sequence identity thereto.

8. The modified STING protein of any of claims 1-7 that is a modified non-human STING protein, or that is a chimeric STING protein, wherein:

the mutation(s) comprise one or more of an insertion, deletion, and replacement of an amino acid or amino acids;

the modified non-human STING protein comprises one or more mutations that result in constitutive expression of type I interferon (IFN) and the non-human STING protein has lower NF-κB signaling activity than human STING, whereby the resulting modified non-human STING protein has constitutive activity and has lower NF-κB signaling activity than human STING;

the chimeric STING protein comprises one or more mutations that result in constitutive expression of type I interferon (IFN), and has a C-terminal tail (CTT) from a non-human STING protein that has lower NF-κB signaling activity than human STING, whereby the resulting STING protein has constitutive activity and has lower NF-κB signaling activity than human STING; and

the TRAF6 binding site in the CTT optionally is deleted.

9. The modified STING protein of any of claims 1-8 that a comprises a non-human STING protein with a mutation that renders the activity of the STING protein constitutive.

10. The modified STING protein of any of claims 1-9 that is a chimeric modified STING protein.

11. The modified STING protein of claim 10, wherein the chimeric STING protein is a modified human STING protein with a replaced CTT from a non-human STING protein that has lower NF-κB signaling activity than human STING.

12. The modified STING protein of any of claims 1-5 and 7-11, wherein the modification(s) that confer(s) constitutive activity is one or more amino acid replacements that correspond(s) to one or more of R284G, S102P, V147L, V147M, N154S, V155M, G166E, C206Y, G207E, S102P/F279L, F279L, R281Q, R284S, R284M, R284K, R284T, R197A, D205A, R310A, R293A, T294A, E296A, R197A/D205A, S272A/Q273A, R310A/E316A, E316A, E316N, E316Q, S272A, R293A/T294A/E296A, D231A, R232A, K236A, Q273A, S358A/E360A/S366A, D231A/R232A/K236A/R238A, S358A, E360A, S366A, R238A, R375A, and S324A/S326A, with reference to the sequence of human STING, as set forth in any one of SEQ ID NOs:305-309.

13. The modified STING protein of any of claims 1-5 and 7-11, wherein the mutation or mutations confer constitutive activity and is/are any that correspond to those associated with the human auto-inflammatory disease STING-associated vasculopathy with onset in infancy (SAVI).

14. The modified STING protein of any of claims 1-13 that is a chimeric STING protein, wherein the replacing CTT is from a Tasmanian devil, marmoset, cattle, cat, ostrich, boar, bat, manatee, crested ibis, coelacanth, zebrafish, or ghost shark STING protein, and it replaces the human STING CTT.

15. The modified STING protein of any of claims 1-14 that is a chimeric STING protein, wherein the replacing CTT is selected from among the following species and has a sequence:

Tasmanian devil	RQEEFAIGPKRAMTVTTSSTLSQEPQLLISGMEQPLSLRTDGF	SEQ ID NO:353,
Marmoset	EEEEVTVGSLKTSEVPSTSTMSQEPELLISGMEKPLPLRSDLF	SEQ ID NO:354,
Cow	EREVTMGSTETSVMPGSSVLSQEPELLISGLEKPLPLRSDVF	SEQ ID NO:355,
Cat	EREVTVGSVGTSMVRNPSVLSQEPNLLISGMEQPLPLRTDVF	SEQ ID NO:356,
Ostrich	RQEEYTVCDGTLCSTDLSLQISESDLPQPLRSDCL	SEQ ID NO:357,
Boar	EREVTMGSAETSVVPTSSTLSQEPELLISGMEQPLPLRSDIF	SEQ ID NO:358,
Bat	EKEEVTVGTVGTYEAPGSSTLHQEPELLISGMDQPLPLRTDIF	SEQ ID NO:359,
Manatee	EREEVTVGSVGTSVVPSPSSPSTSSLSQEPKLLISGMEQPLPLR TDVF	SEQ ID NO:360,
Crested ibis	CHEEYTVYEGNQPHNPSTTLHSTELNLQISESDLPQPLRSDCF	SEQ ID NO:361,
Coelacanth (variant 1)	QKEEYFMSEQTQPNSSSTSCLSTEPQLMISDTDAPHTLKRQVC	SEQ ID NO:362,
Coelacanth (variant 2)	QKEEYFMSEQTQPNSSSTSCLSTEPQLMISDTDAPHTLKSGF	SEQ ID NO:363, or
Ghost shark	LTEYPVAEPSNANETDCMSSEPHLMISDDPKPLRSYCP	SEQ ID NO:365,

or variants of each of these sequences having at least 98% sequence identity thereto.

16. The modified STING protein of any of claims 1-15 that is a chimeric STING protein, wherein the human STING CTT is replaced with a CTT from Tasmanian devil STING.

17. The modified STING protein of any of claims 1-16 that comprises the sequence of amino acids set forth in SEQ ID NO:336 or sequence having at least 98% sequence identity thereto and comprising the replacement corresponding to R284G.

18. The modified STING protein of any of claims 1-17, wherein the full-length unmodified human non-chimeric STING protein comprises the sequence of amino acids set forth in any of SEQ ID NOs:305-309, or is a variant thereof with at least 98% sequence identity to the sequence of amino acids set forth in any of SEQ ID NOs:305-309.

19. A delivery vehicle, comprising a modified STING protein of any of claims 1-18 or nucleic acid encoding the modified STING protein.

20. An immunostimulatory bacterium, comprising a plasmid encoding a STING protein of any of claims 1-18.

21. The immunostimulatory bacterium of claim 20 that comprises, encoded on the plasmid, a combination of:

a) nucleic acid encoding the modified STING; and

b) nucleic acid encoding an immunostimulatory protein selected from among one or more of IL-2, IL-7, IL-12p70 (IL-12p40 + IL-12p35), IL-15, IL-15/IL-15R alpha chain complex, IL-2 that has attenuated binding to IL-2Ra, IL-2 modified so that it does not bind to IL-2Ra, IL-18, IL-36 gamma, CXCL9, CXCL10, CXCL11, CCL3, CCL4, CCL5, proteins that are involved in or that effect or potentiate recruitment/persistence of T cells, CD40, CD40 Ligand (CD40L), OX40, OX40 Ligand (OX40L), 4-1BB, 4-1BB Ligand (4-1BBL), members of the B7-CD28 family, a TGF-beta polypeptide antagonist, and members of the tumor necrosis factor receptor (TNFR) superfamily.

22. The immunostimulatory bacterium of claim 21 that comprises nucleic acid encoding a STING from a) and two of the proteins in b).

23. The immunostimulatory bacterium of any of claims 20-22, wherein the genome of the immunostimulatory bacterium is modified whereby:

the bacterium lacks flagella; or

the bacterium is *pagP*$^{-}$; or

the bacterium lacks flagella and is *pagP*$^{-}$; or

the bacterium is *msbB*$^{-}$/*pagP*$^{-}$; or

the bacterium lacks flagella and is *msbB*$^{-}$/*pagP*$^{-}$; and

the wild-type bacterium of the bacterium that lacks flagella is a species that has flagella.

24. The immunostimulatory bacterium of any of claims 20-23 that is auxotrophic for adenosine, or for adenosine and adenine.

25. The immunostimulatory bacterium of any of claims 20-24 that is auxotrophic for adenosine.

26. The immunostimulatory bacterium of any of claims 20-25, wherein the genome of the immunostimulatory bacterium is modified whereby the bacterium is *pagP*$^{-}$/*msbB*$^{-}$.

27. The immunostimulatory bacterium of any of claims 20-26 that is aspartate-semialdehyde dehydrogenase^{-} (*asd*$^{-}$), wherein the bacterium is *asd*$^{-}$ by virtue of disruption or deletion of all or a portion of the endogenous gene encoding aspartate-semialdehyde dehydrogenase (*asd*), whereby endogenous *asd* is not expressed.

28. The immunostimulatory bacterium of claim 27 that encodes aspartate-semialdehyde dehydrogenase (*asd*) on the plasmid under control of a bacterial promoter.

29. The immunostimulatory bacterium of any of claims 20-28 that is *asd*$^{-}$, *purI*$^{-}$, *msbB*$^{-}$, lacks flagella, and is *pagP*$^{-}$.

30. The immunostimulatory bacterium of any of claims 20-29 that is *csgD*$^{-}$.

31. The immunostimulatory bacterium of any of claims 20-30, wherein the nucleic acid encoding the modified STING protein and/or the immunostimulatory protein on the plasmid is operatively linked to nucleic acid encoding a secretory signal, whereby, upon expression in a host, the protein or proteins is/are secreted.

32. The immunostimulatory bacterium of any of claims 20-31, wherein one or more genes or operons involved in SPI-1-dependent invasion are deleted or inactivated, whereby the immunostimulatory bacterium does not invade or infect epithelial cells.

33. The immunostimulatory bacterium of any of claims 20-32 that is a Gram-negative bacterium.

34. The immunostimulatory bacterium of any of claims 20-33, wherein the bacterium is a strain of *Salmonella*, *Shigella*, *E. coli*, *Bifidobacteriae*, *Rickettsia*, *Vibrio*, *Listeria*, *Klebsiella*, *Bordetella*, *Neisseria*, *Aeromonas*, *Francisella*, *Cholera*, *Corynebacterium*, *Citrobacter*, *Chlamydia*, *Haemophilus*, *Brucella*, *Mycobacterium*, *Mycoplasma*, *Legionella*, *Rhodococcus*, *Pseudomonas*, *Helicobacter*, *Bacillus*, *Erysipelothrix*, *Yersinia*, or *Rochalimaea quintana*, or an attenuated strain thereof, or a modified strain thereof of any of the preceding list of bacterial strains.

35. The immunostimulatory bacterium of any of claims 20-34 that is a strain of *Salmonella*.

36. The immunostimulatory bacterium any of claims 20-35 that is a *Salmonella typhimurium* strain.

37. The immunostimulatory bacterium of any of claims 20-36, wherein the immunostimulatory bacterium is derived from an attenuated *Salmonella typhimurium* strain selected from among strains designated as AST-100, VNP20009, YS1646 (ATCC #202165), RE88, SL7207, χ 8429, χ 8431, and χ 8468, or is a wild-type bacterium that has all of the identifying characteristics of the strain deposited as ATCC Accession No. 14028, or is strain ATCC 14028.

38. A pharmaceutical composition, comprising the immunostimulatory bacterium of any of claims 20-37 or the delivery vehicle of claim 19 in a pharmaceutically acceptable vehicle.

39. The immunostimulatory bacterium of any of claims 20-37 for use for treatment of cancer.

40. Use of the immunostimulatory bacterium of any of claims 20-37 in the manufacture of a medicament for the treatment of cancer.

41. The delivery vehicle of claim 19 for use for treatment of cancer.

42. The immunostimulatory bacterium for use of claim 39, the use of claim 40, or the delivery vehicle for use of claim 41, wherein the cancer comprises a solid tumor.

43. The immunostimulatory bacterium for use of claim 39 or 42, the use of claim 40 or 42, or the delivery vehicle for use of claim 41 or 42, wherein the cancer is selected from among cancer of the breast, heart, lung, small intestine, colon, spleen, kidney, bladder, head and neck, colorectum, ovary, prostate, brain, pancreas, skin, bone, bone marrow, blood, thymus, uterus, testicles, cervix, and liver, gastric cancer, lymphoma, and leukemia.