NP_003891.1. p62 has homology neither with ubiquitin C-terminal hydrolases nor with the S5a subunit of the 26 S proteasome complex, the only proteins known to bind to ubiquitin noncovalently. These results suggested that p62 belongs to a new class of ubiquitin-binding proteins.

**[0007]** p62 is a component of inclusion bodies found in protein aggregation diseases in the brain and liver: p62 is sequestered into cytoplasmic inclusion bodies, called sequestosomes. These p62-containing protein aggregates are degraded by autophagy. It was suggested that this function of p62 may have a protective effect on huntingtin-induced cell death (Bjørkøy et al., J Cell Biol., 171:603 (2005)). Mutations in p62 gene have been associated with sporadic and familial Paget disease (Jenny Chung et al., Semin Arthritis Rheum., 41:619 (2012)), a metabolic bone disease.

## SUMMARY OF THE INVENTION

[0008a] In one embodiment there is provided use of an agent for the manufacture of a medicament to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:

a. a p62 polypeptide; or,

b. a p62 encoding nucleic acid.

[0008b] In one embodiment there is provided, use of an agent for the manufacture of a medicament to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:

a. a p62/SQSTM1 polypeptide at least 90% identical to SEQ ID NO. 2; or,

b. a p62/SQSTM1 nucleic acid that encodes a polypeptide at least 90% identical to SEQ ID NO. 2.

[0008c] In one embodiment there is provided, use of an agent for the manufacture of a medicament to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:

a. at least 30 amino acids of a p62/SQSTM1 polypeptide; or,

b. a p62/SQSTM1 encoding nucleic acid, wherein said p62/SQSTM1 encoding nucleic acid encodes at least 30 amino acids of a p62/SQSTM1 polypeptide.

0008d] In one embodiment there is provided, an agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. a p62 polypeptide, or

b. a p62 encoding nucleic acid.

[0008e] In one embodiment there is provided, an agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. a p62/SQSTM1 polypeptide at least 90% identical to SEQ ID NO. 2; or

b. a p62/SQSTM1 nucleic acid that encodes a polypeptide at least 90% identical to SEQ ID NO: 2

[0008f] In one embodiment there is provided, an agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. at least 30 amino acids of a p62/SQSTM1 polypeptide; or,

b. a p62/SQSTM1 encoding nucleic acid, wherein said p62/SQSTM1 encoding nucleic acid encodes at least 30 amino acids of a p62/SQSTM1 polypeptide.

**[0008g]** Provided herein are methods to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject by administering to the subject an agent having (a) a p62 polypeptide or (b) a p62 encoding nucleic acid. The agent can have (a) one or more domain deletions, (b) a p62 encoding nucleic acid that is at least 95% identical to SEQ ID NO. 1, or (c) a p62 polypeptide that is at least 98% identical to SEQ ID NO: 2. The method domain deletions can be one or more of the following: PB1, ZZ, NLS2, TB, NLS1, NES, LIR, KIR, and UBA. The method can use a fusion polypeptide or nucleic acid encoding for a fusion polypeptide, respectively. The method can use a p62 polypeptide that is post-translationally modified.

**[0009]** The agent can be administered by any of the following routes: parenterally, orally, nasally, rectally, transdermally, intravaginally or inhalationally via an aerosol. The parenteral routes can be any of the following: intravascularly, intravenously, intraarterially, intramuscularly, intraocularly, intraperitoneally, intradermally and subcutaneously, or can be administered to an organ or to a tumor. The method can further include any and all of the following: administering of adjuvants, administering of co-stimulatory components, administering one or more molecules that block suppressive or negative regulatory immune mechanisms, or administering one or more anticancer therapies to said subject.

**[0010]** The method can be used to treat any cancer in a subject including: breast cancer, lung cancer, prostate cancer, gastric cancer, colorectal cancer, skin cancer, a cancer of the head and

neck, bronchus cancer, pancreatic cancer, urinary bladder cancer, brain cancer, central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cancer of the oral cavity or pharynx, liver cancer, kidney cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, ovarian cancer, uterine cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma, sarcoma and cancer of hematological tissues. The subject can be: a subject diagnosed with cancer, a subject previously treated for cancer, a subject with a family history of cancer, or a subject predisposed to cancer.

**[0011]** The method can include an agent that is a p62 encoding nucleic acid and the nucleic acid can be included in a plasmid or a viral vector. The method can also include a strategy for improving the efficiency of nucleic acid-based immunization.

## CLAIMS

What is claimed is:

1. Use of an agent for the manufacture of a medicament ~~A method~~ to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered ~~comprising administering~~ to said subject; and wherein said ~~an~~ agent ~~comprising~~comprises:
    a. a p62 polypeptide; or,
    b. a p62 encoding nucleic acid.
2. The ~~method~~ useof claim 1 wherein said agent comprises
    a. one or more domain deletions;
    b. ~~,~~wherein said p62 encoding nucleic acid is at least 95% identical to SEQ ID NO. 1; or
    c. wherein said p62 polypeptide is at least 98% identical to SEQ ID NO: 2
3. The ~~method~~ use of claim 2 wherein said one or more domain deletions is selected from the group consisting of PB1, ZZ, NLS2, TB, NLS1, NES, LIR, KIR, and UBA.
4. Use of an agent for the manufacture of a medicament to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:
    a. a p62/SQSTM1 polypeptide at least 90% identical to SEQ ID NO. 2; or,
    b. a p62/SQSTM1 nucleic acid that encodes a polypeptide at least 90% identical to SEQ ID NO: 2.
5. The use of claim 4 where said agent comprises one or more domain deletions.
6. The use of claim 5 wherein said one or more domain deletions is selected from the group consisting of PB1, ZZ, NLS2, TB, NLS1, NES, LIR, KIR, and UBA.
7. Use of an agent for the manufacture of a medicament to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:
    a. at least 30 amino acids of a p62/SQSTM1 polypeptide; or,
    b. a p62/SQSTM1 encoding nucleic acid, wherein said p62/SQSTM1 encoding nucleic acid encodes at least 30 amino acids of a p62/SQSTM1 polypeptide.
4~~,~~8. The ~~method~~ use of any of claims 1-~~3~~ 7 wherein said p62 polypeptide or p62 encoding nucleic acid further comprises a fusion polypeptide or nucleic acid encoding for a fusion polypeptide, respectively.

~~5. The method of any of claims 1-4 wherein said p62 polypeptide is post-translationally modified.~~

~~6. The method of claim 5 wherein said p62 polypeptide is post-translationally modified *in vitro*.~~

~~7. The method of any of claims 1-6 wherein said agent is administered by any of the routes selected from the group consisting of: parenterally, orally, nasally, rectally, transdermally, intravaginally or inhalationally via an aerosol.~~

~~8. The method of claim 7, wherein said agent is administered by any of the routes selected from the group consisting of: intravascularly, intravenously, intraarterially, intramuscularly, intraocularly, intradermally and subcutaneously.~~

~~9. The method of claim 7 wherein said agent is administered to an organ or to a tumor.~~

~~10.~~9. The ~~method~~ use of any of claims 1-~~9~~8, further comprising ~~administering~~ an to be administered adjuvant to said subject.

~~11.~~10. The ~~method~~ use of claim ~~10~~ 9 wherein said adjuvant is selected from the group consisting of: gel-type, microbial, particulate, oil-emulsion, surfactant-based, and synthetic adjuvants.

~~12.~~11. The ~~method~~ use of any of claims 1-~~11~~10, further comprising ~~administering~~ one or more co-stimulatory components to be administered to said subject.

~~13.~~12. The ~~method~~ use of claim ~~12~~11, wherein said one or more co-stimulatory components is selected from the group consisting of: a cell surface protein~~s~~, a cytokine~~s~~, a chemokine~~s~~, and a signaling molecule~~s~~.

~~14.~~13. The ~~method~~ use of any of claims 1-~~13~~12, further comprising ~~administering~~ one or more molecules that block suppressive or negative regulatory immune mechanisms to be administered to said subject.

~~15.~~14. The ~~method~~ use of claim ~~14~~ 13 wherein said one or more molecules that block suppressive or negative regulatory immune mechanisms is selected from the group consisting of: anti-CTLA-4 antibody, anti-CD25 antibody, anti-CD4 antibody, and ~~the fusion protein~~ IL13Ra2-Fc.

~~16.~~15. The ~~method~~ use of any of claims 1-~~15~~14, further comprising ~~administering~~ one or more anticancer therapies to be administered to said subject.

~~17.~~16. The ~~method~~ use of claim ~~16~~15 wherein said one or more anticancer therapies is selected from the group consisting of: a chemotherapeutic molecule, radiation, ~~and~~ an anti-angiogenic molecule, an antibody, and a biological agent.

~~18.~~17. The ~~method~~ use of claim ~~17~~16 wherein said chemotherapeutic molecule is selected from the group consisting of: cyclophosphamide, doxorubicin, paclitaxel, docetaxel, vinblastine, methotrexate, navelbine, capecitabine, ~~and~~ mitomycin C and 5-fluorouracil.

18. The use according of any claims 1-17, wherein said cancer is a solid tumor cancer.

19. The ~~method~~ use of ~~any of~~ claims 1-18, wherein said solid tumor cancer is selected from the group consisting of: breast cancer, lung cancer, prostate cancer, gastric cancer, colorectal cancer, skin cancer, a cancer of the head and neck, bronchus cancer, pancreatic cancer, urinary bladder cancer, brain cancer, central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cancer of the oral cavity or pharynx, liver cancer, kidney cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, ovarian cancer, uterine cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma, and sarcoma ~~and cancer of hematological tissues~~.

20. The use of any claims 1-17, wherein said cancer is cancer of the hematologic tissues.

~~20.~~21. The ~~method~~ use of claims 1-~~19~~20 wherein said subject is selected from the group consisting of: a subject diagnosed with a cancer, a subject previously treated for cancer, a subject with a family history of cancer, and a subject predisposed to cancer.

~~21.~~22. The method of any of claims 1-~~20~~21, wherein said agent comprises a p62 encoding nucleic acid, wherein said p62 ~~encoding nucleic acid~~ encoded polypeptide is at least ~~95~~90% identical to SEQ ID NO. ~~1~~2, and wherein said p62 encoding nucleic acid further comprises a plasmid or a viral vector.

~~22.~~23. The ~~method~~ use of any of claims 1-21, wherein said agent comprises a p62 encoding nucleic acid, and further comprising a strategy for improving the efficiency of nucleic acid-based immunization.

~~23.~~24. The ~~method~~ use of claim ~~22~~23 wherein said strategy is selected from the group consisting of: self-replicating viral replicons, optimizing at least one codon optimization, in vivo electroporation, incorporation of a CpG stimulatory motif~~s~~, including a sequence~~s~~ for targeting of the endocytic or ubiquitin-processing pathways, including a Marek's disease virus type 1 VP22 sequences, including a prime-boost regimen~~s~~, and the use of a mucosal delivery vector~~s~~.

25. An agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. a p62 polypeptide, or

b. a p62 encoding nucleic acid.

26. An agent of claim 25 wherein said agent comprises:

a. one or more domain deletions;

b. wherein said p62 encoding nucleic acid is at least 95% identical to SEQ ID NO. 1; or

c. wherein said p62 polypeptide is at least 98% identical to SEQ ID NO: 2.

~~24. An agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:~~

~~a. a p62 polypeptide or a p62 encoding nucleic acid, comprising at least one or more domain deletions, or~~

~~b. one or more domains of a p62 polypeptide or a nucleic acid encoding one or more domains of a p62.~~

27. An agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. a p62/SQSTM1 polypeptide at least 90% identical to SEQ ID NO. 2; or,

b. a p62/SQSTM1 nucleic acid that encodes a polypeptide at least 90% identical to SEQ ID NO: 2.

28. The agent of claim 27 wherein said agent comprises one or more domain deletions.

~~25.~~29. The agent of claim ~~24~~28 wherein said one or more domain deletions or domains, respectively, is selected from the group consisting of PB1, ZZ, NLS2, TB, NLS1, NES, LIR, KIR, and UBA.

30. An agent to treat, alleviate, ameliorate, relieve, delay onset of, inhibit progression of, reduce severity of, and/or reduce incidence of one or more symptoms of a cancer in a subject comprising:

a. at least 30 amino acids of a p62/SQSTM1 polypeptide; or,

b. a p62/SQSTM1 encoding nucleic acid, wherein said p62/SQSTM1 encoding nucleic acid encodes at least 30 amino acids of a p62/SQSTM1 polypeptide.

~~26.~~31. The agent of any of claims ~~24 or~~ 25-30 wherein said p62 polypeptide or p 62 encoding nucleic acid further comprises a fusion polypeptide or encoding nucleic acid, respectively.

~~28. The agent of any of claims 24-26 wherein said p62 polypeptide is post-translationally modified.~~

~~29. The agent of claim 27 wherein said p62 polypeptide is post-translationally modified *in vitro*.~~

~~30.~~32. The agent of any of claims ~~24-28~~25-31, further comprising an adjuvant.

~~31.~~33. The agent of claim ~~29~~ 32wherein said adjuvant is selected from the group consisting of: gel-type, microbial, particulate, oil-emulsion, surfactant-based, and synthetic adjuvants.

~~32.~~34. The agent of any of claims ~~24-30~~25-33, further comprising administering one or more co-stimulatory components.

~~33.~~35. The agent of claim ~~31~~34, wherein said one or more co-stimulatory components is selected from the group consisting of: a cell surface proteins, cytokines, a chemokines ~~and~~ a signaling molecules.

~~34.~~36. The agent of any of claims ~~24-32~~25-35, further comprising administering one or more molecules that block suppressive or negative regulatory immune mechanisms.

~~35.~~37. The agent of claim ~~33~~ 36wherein said one or more molecules that block suppressive or negative regulatory immune mechanisms is selected from the group consisting of: anti-CTLA-4 antibody, anti-CD25 antibody, anti-CD4 antibody, and ~~the fusion protein~~ IL13Ra2-Fc~~:~~.

~~36.~~38. The agent of any of claims ~~24-34~~ 25-37 further comprising a chemotherapeutic molecule or an anti-angiogenic molecule, an antibody, or a biological agent.

~~37.~~39. The agent of claim ~~35~~ 38wherein said chemotherapeutic molecule is selected from the group consisting of: cyclophosphamide, doxorubicin, paclitaxel, docetaxel, vinblastine, methotrexate, navelbine, capecitabine, ~~and~~ mitomycin C, and 5-fluorouracil.

~~38.~~40. The agent of any of claims ~~24-36~~25-39, wherein said agent comprises a p62/SQSTM1 encoding nucleic acid wherein said p62/SQSTM1 encoding nucleic acid further comprises a plasmid or a viral vector.

41. The agent of any of claims 25-40, wherein said agent is a nucleic acid and further includes a nucleic acid selected from the group consisting of: a self-replicating viral replicon, a codon-optimized sequence, a CpG stimulatory motif, a nucleic acid sequence for targeting of the endocytic or ubiquitin-processing pathways, a Marek's disease virus type 1 VP22 sequence, or a mucosal delivery vector.

~~39.~~42. ~~A composition comprising the agent of any of the claims 24-37 suitable for administration to a subject~~