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

[0007a] In one embodiment, there is provided the use of an agent in the manufacture of a medicament for stimulating the host immune defence mechanism in a subject to attack neoplastic cells 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 the subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:

a. a p62/SQSTM1 polypeptide; or,

b. a p62/SQSTM1 encoding nucleic acid.

[0007b] In one embodiment, there is provided the use of an agent in the manufacture of a medicament for stimulating the host immune defence mechanism in a subject to attack neoplastic cells 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 the 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.

[0007c] In one embodiment, there is provided the use of an agent in the manufacture of a medicament for stimulating the host immune defence mechanism in a subject to attack neoplastic cells 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 the subject; wherein said medicament is to be administered to said subject; and wherein said agent comprises:

a. at least 30 consecutive 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 consecutive amino acids of a p62/SQSTM1 polypeptide.

[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.