chaperones such as ELKS and NEMO (IKKγ)[63]. Phosphorylated IκB proteins are ubiquitinated and degraded[52,57] largely in the cytoplasm[64]. NFκB subunits free from IκB proteins accumulate in the nucleus and bind DNA at NFκB sites[65]. Uncontrolled activation of NFκB and its effects such as chronic inflammation are hallmarks of many human cancers but the mechanism of how NFκB activity is sustained in cancers is unknown. Activation of additional co-signalling modules involved in carcinogenesis which feed forward NFκB dependent signalling could be one possible explanation.

There is a need to provide methods for inhibiting NFκB activation to thereby prevent and treat inflammation and progression to cancer, and its recurrence.

Summary

The present disclosure is based on the surprising finding that telomerase inhibitors inhibit regulatory elements of NFκB mediated inflammation. The ability of telomerase inhibitors to block inflammation enables their use in the treatment of inflammatory diseases as well as cancer, which is often characterized by inflammation.

In a first aspect, there is provided use of a telomerase inhibitor in the manufacture of a medicament for treating an inflammatory disease in a patient in need thereof, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

Advantageously, telomerase only affects about 13% of NFκB target genes, and hence the use of telomerase inhibitors confers specificity towards these target genes. It was also found that telomerase strongly inhibits IL6 and TNF which are key cytokines involved in human diseases ranging from inflammation to cancer and

metabolic syndromes. In addition, blocking telomerase which is expressed to undetectable levels in most human cells except stem cells of highly proliferating organs, avoids off target effects. Toxicity seen with anti-inflammatory drugs (e.g. NSAIDs) can also be avoided with use of telomerase inhibitors.

In a second aspect, there is provided use of a telomerase inhibitor in the manufacture of a medicament for sensitizing a patient to treatment with an anti-inflammatory drug, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

In a third aspect, there is provided use of a telomerase inhibitor in the manufacture of a medicament for preventing recurrence of an inflammatory disease in a patient in need thereof, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

In a fourth aspect, there is provided a pharmaceutical composition comprising N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312) and a pharmaceutically acceptable excipient, for use in treating an inflammatory disease.

Disclosed is a telomerase inhibitor for use in treating or preventing recurrence of an inflammatory disease and/or cancer in a patient in need thereof, or for sensitizing a patient to treatment with an anti-inflammatory drug and/or an anti-cancer drug.

Disclosed is a use of a telomerase inhibitor in the manufacture of a medicament for treating or preventing recurrence of an inflammatory disease and/or cancer in a patient in need thereof, or for sensitizing a patient to treatment with an anti-inflammatory drug and/or an anti-cancer drug.

CLAIMS

1. Use of a telomerase inhibitor in the manufacture of a medicament for treating an inflammatory disease in a patient in need thereof, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

2. Use of a telomerase inhibitor in the manufacture of a medicament for sensitizing a patient to treatment with an anti-inflammatory drug, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

3. Use of a telomerase inhibitor in the manufacture of a medicament for preventing recurrence of an inflammatory disease in a patient in need thereof, wherein the telomerase inhibitor is N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312).

4. The use according to any one of the preceding claims, wherein the medicament is to be administered with an inhibitor of NFκB
selected from the group consisting of p65 shRNA (sc-29410-SH), sc-3060 (sequence: AAVALLPAVLLALLAPVQRKRQKLMP, SEQ ID NO: 47), 2-(1,8-naphthyridin-2-yl)-Phenol, 5-Aminosalicylic acid, BAY 11-7082, BAY 11-7085, CAPE (Caffeic Acid Phenethylester), Diethylmaleate, IMD 0354, Lactacystin, MG-132 [Z-Leu-Leu-Leu-CHO], parthenolide, phenylarsine oxide, PPM-18, Pyrrolidinedithiocarbamic acid ammonium salt, (E)-3-(4-methylphenylsulfonyl)-2-propenenitrile, tetrahydrocurcuminoids, sulfasalazine, sulindac, clonidine, helenalin, wedelolactone, pyrollidinedithiocarbamate (PDTC), Calbiochem IKK-2

inhibitor VI, and Calbiochem IKK inhibitor III (BMS-345541).

5. The use according to any one of the preceding claims, wherein the inflammatory disease is selected from the group consisting of: an inflammatory disease of the joints, an inflammatory disease of the skin, an inflammatory disease of the eyes, an inflammatory disease of the peripheral or central nervous system, an inflammatory disease of the airways or the lung, and an inflammatory disease of the gastrointestinal tract.

6. The use according to any one of the preceding claims, wherein the inflammatory disease is selected from the group consisting of: mild cognitive impairment, rheumatoid arthritis, atherosclerosis, restenosis, pancreatitis, sepsis and peritonitis.

7. The use according to claim 5, wherein the inflammatory disease of the peripheral or central nervous system is selected from the group consisting of: depression, bipolar or manic depression, acute and chronic anxiety states, schizophrenia, Alzheimer's disease, Parkinson's disease, acute and chronic multiple sclerosis, acute and chronic pain, and injuries to the brain caused by stroke, hypoxia or craniocerebral trauma.

8. The use according to claim 5, wherein the inflammatory disease of the airways or the lung is selected from the group consisting of: diseases of the airways that are accompanied by increased mucus production, and inflammations and/or obstructive diseases of the upper and lower respiratory tract.

9. The use according to claim 8, wherein the inflammatory disease of the airways or the lung is selected from the group consisting of: acute, allergic or chronic bronchitis, chronic obstructive bronchitis (COPD), coughing, pulmonary emphysema, allergic or non-allergic rhinitis or sinusitis, chronic rhinitis or sinusitis, asthma, alveolitis, idiopathic pulmonary fibrosis, fibrosing alveolitis, Crohn's disease, ulcerative colitis, Farmer's disease, hyperreactive airways, infectious bronchitis or pneumonitis, paediatric asthma, bronchiectases, pulmonary fibrosis, ARDS (acute adult respiratory distress syndrome), bronchial oedema, pulmonary oedema, bronchitis, pneumonia or interstitial pneumonia triggered by various causes (such as aspiration, inhalation of toxic gases, or bronchitis), pneumonia or interstitial pneumonia as a result of heart failure, irradiation, chemotherapy, cystic fibrosis or mucoviscidosis, and alphal-antitrypsin deficiency.

10. The use according to claim 5, wherein the inflammatory disease of the gastrointestinal tract is selected from the group consisting of acute or chronic inflammatory changes in gall bladder inflammation, Crohn's disease, ulcerative colitis, inflammatory pseudopolyps, juvenile polyps, colitis cystica profunda, pneumatosis cystoides intestinales, and diseases of the bile duct and gall bladder (such as gallstones and conglomerates).

11. The use according to any one of the preceding claims, wherein the inflammatory disease is one that is mediated by NFκB, optionally selected from a group consisting of muscular dystrophy, arthritis, traumatic brain injury, spinal cord injury, sepsis, rheumatic disease, atherosclerosis, type 1 diabetes, type 2 diabetes,

leptospiriosis renal disease, glaucoma, retinal disease, ageing, headache, pain, complex regional pain syndrome, cardiac hypertrophy, muscle wasting, catabolic disorders, obesity, fetal growth retardation, hypercholesterolemia, heart disease, chronic heart failure, ischemia/reperfusion, stroke, cerebral aneurysm, angina pectoris, pulmonary disease, cystic fibrosis, acid-induced lung injury, pulmonary hypertension, asthma, chronic obstructive pulmonary disease, Sjogren's syndrome, hyaline membrane disease, kidney disease, glomerular disease, alcoholic liver disease, gut diseases, peritoneal endometriosis, skin diseases, nasal sinusitis, mesothelioma, anhidrotic ecodermal dysplasia-ID, behcet's disease, incontinentia pigmenti, tuberculosis, asthma, crohn's disease, colitis, ocular allergy, appendicitis, paget's disease, pancreatitis, periodonitis, endometriosis, inflammatory bowel disease, inflammatory lung disease, silica-induced diseases, sleep apnea, AIDS, HIV-1, autoimmune diseases, antiphospholipid syndrome, lupus, lupus nephritis, familial mediterranean fever, hereditary periodic fever syndrome, psychosocial stress diseases, neuropathological diseases, familial amyloidotic polyneuropathy, inflammatory neuropathy, parkinson's disease, multiple sclerosis, alzheimer's disease, amyotropic lateral sclerosis, huntington's disease, cataracts, and hearing loss.

12. A pharmaceutical composition comprising N,N'-1,3-phenylenebis-[2,3-dihydroxy-benzamide] (MST-312) and a pharmaceutically acceptable excipient, for use in treating an inflammatory disease.