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 and/or cancer in a patient in need thereof.

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 and/or an anti-cancer drug.

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 and/or cancer in a patient in need thereof.

In a fourth aspect, there is provided a pharmaceutical composition comprising a telomerase inhibitor and a pharmaceutically acceptable excipient, for use in treating an inflammatory disease and/or cancer.

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 and/or cancer in a patient in need thereof.

2. Use of a telomerase inhibitor in the manufacture of a medicament for sensitizing a patient to treatment with an anti-inflammatory drug and/or an anti-cancer drug.

3. Use of a telomerase inhibitor in the manufacture of a medicament for preventing recurrence of an inflammatory disease and/or cancer in a patient in need thereof.

4. The use according to any one of claims 1 to 3, wherein the telomerase inhibitor is selected from the group consisting of: interfering nucleic acid agent, an antibody, a small organic molecule, and a peptide nucleic acid (PNA).

5. The use according to claim 4, wherein the interfering nucleic acid agent is selected from the group consisting of a double stranded RNA (dsRNA), an antisense RNA, and a ribozyme.

6. The use according to claim 5, wherein the dsRNA is selected from the group consisting of short hairpin RNA (shRNA), small interfering (siRNA), and micro RNA (miRNA).

7. The use according to claim 6, wherein the shRNA is selected from the group consisting of SEQ ID NO: 48 and SEQ ID NO: 49.

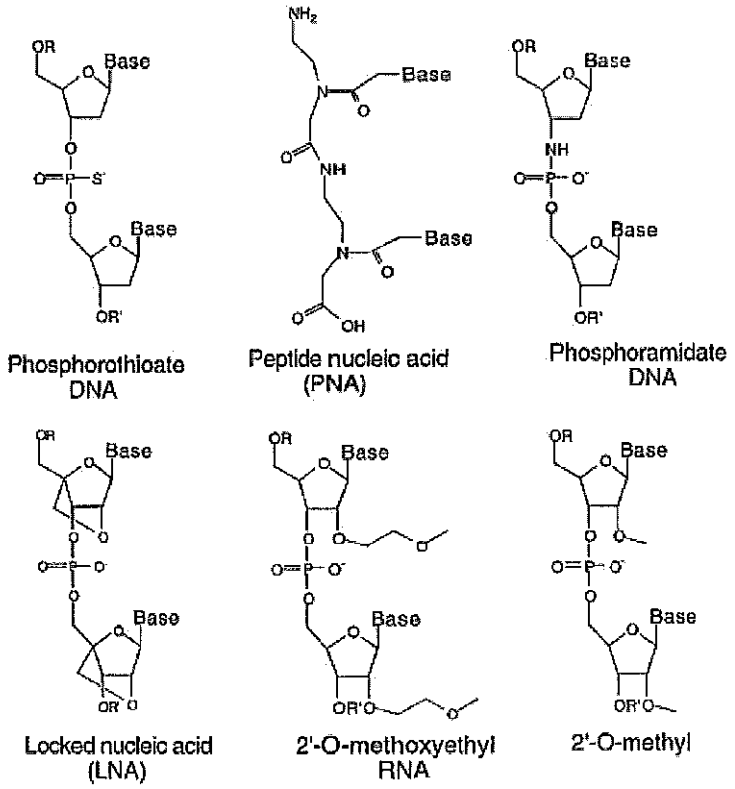
8. The use according to claim 6, wherein the siRNA is directed against hTERT.

9. The use according to claim 8, wherein the siRNA is selected from the group consisting of SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, and SEQ ID NO: 53.

10. The use according to claim 4, wherein the interfering nucleic acid agent is a 2'-O-alkyl oligonucleotide inhibitor.

11. The use according to claim 4, wherein the small organic molecule inhibitor is selected from the group consisting of N,N'-1,3-Phenylenebis-[2,3-dihydroxy-benzamide] (MST-312), BIBR 1532 (2-[(E)-3-naphtalen-2-yl-but-2-enoylamino]-benzoic acid), and costunolide ((3aS,6E,10E,11aR)-6,10-dimethyl-3-methylene-3,3a,4,5,8,9-hexahydrocyclodeca[b]furan-2(11aH)-one).

12. The use according to claim 4, wherein the telomerase inhibitor is based on a compound selected from the group consisting of:



13. The use according to any one of the preceding claims, wherein the medicament is to be administered with an inhibitor of NFκB.

14. The use according to claim 13, wherein the NFκB inhibitor is 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).

15. 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.

16. The use according to any one of the preceding claims, wherein the cancer is selected from the group consisting of: acute and chronic leukaemia, bone tumor, breast

cancer, colon cancer, lung cancer, prostate cancer, and stomach cancer.

17. A pharmaceutical composition comprising a telomerase inhibitor and a pharmaceutically acceptable excipient, for use in treating an inflammatory disease and/or cancer.