CLAIMS

1. A nucleic acid sequence for targeting a single point mutation within the p53 tumour suppressor gene wherein:

(a) the single point mutation is selected from R249S (p53), R249G (p53) and R249M (p53) and the nucleic acid sequence is an siRNA sequence selected from SEQ ID NOs 16 and 17 or an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 16 and 17;

(b) the single point mutation is selected from R248W (p53) and R248Q (p53) and the nucleic acid sequence is an siRNA sequence which is SEQ ID NO: 13 or an shRNA sequence having an siRNA sequence which is SEQ ID NO: 13; or

(c) the single point mutation is selected from R273H (p53) and R273L (p53) and the nucleic acid sequence is an siRNA sequence which is SEQ ID NO: 21 or an shRNA sequence having an siRNA sequence which is SEQ ID NO: 21.

~~(a) the site of the point mutation is selected from the group consisting of R249 (p53), R248 (p53) and R273 (p53), and wherein the nucleic acid sequence is:~~

~~(a) an siRNA sequence selected from SEQ ID NOs 17, 13, 16 and 21; or~~

~~(b) an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 17, 13, 16 and 21.~~

~~2. The nucleic acid sequence of claim 1, wherein the point mutation is:~~

~~(a) a substitution mutation; or~~

~~(b) selected from the group consisting of R249S (p53), R249G (p53), R249M (p53), R248W (p53), R248Q (p53), R273H (p53) and R273L (53).~~

~~3~~2. The nucleic acid sequence of ~~any one of the preceding claims~~claim 1, wherein the nucleic acid sequence:

(a) results in any one or more of the following effects selected from the group consisting of cell death, abrogation of addiction, activation of any one or more p53 target genes, relief of a dominant negative effect, increased sensitivity to one or more anti-cancer agents, and retardation or halting of tumour growth; and/or

(b) is capable of substantially silencing mutant p53 tumour suppressor gene alleles.

~~4~~3. The nucleic acid sequence of any one of the preceding claims, wherein the shRNA sequence comprises stems with the length of between 15 to 30 base pairs.

~~5~~4. A nucleic acid sequence which is:

(a) an siRNA sequence selected from SEQ ID NOs 17, 13, 16 and 21; or

(b) an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 17, 13, 16 and 21.

~~6~~5. A nucleic acid sequence which encodes an shRNA sequence according to any one of the preceding claims.

~~7~~6. The nucleic acid sequence of claim ~~6~~ 5 comprising:

(a) SEQ ID NOs 24, 40 and 41;

(b) SEQ ID NOs 25, 42 and 43; or

(c) SEQ ID NO: 28, 29, 30, 31, 32 or 33.

7. A double stranded siRNA molecule in which the sense strand consists of the sequence in SEQ ID NO 17, 13, 16 or 21.

8. A nucleic acid sequence according to any one of claims 1 to 5 or a double stranded siRNA molecule according to claim 7 for use in therapy.

9. One or more nucleic acid sequence according to any one of claims 1 to 5 or one or more double stranded siRNA molecule according to claim 7 for use in a method of treating cancer in a subject~~, wherein the one or more nucleic acid sequences target~~ having one or more single point mutations ~~sites~~ within the p53 tumour suppressor gene at one more sites, wherein:

(a) the subject has a single point mutation in the p53 tumour suppressor gene at R249(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence selected from SEQ ID NOs 16 and 17, an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 16 and 17 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 16 or 17; and/or

(b) the subject has a single point mutation in the p53 tumour suppressor gene at R248(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 13, an

shRNA sequence having an siRNA sequence which is SEQ ID NO: 13 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 13; and/or

(c) the subject has a single point mutation in the p53 tumour suppressor gene at R273(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 21, an shRNA sequence having an siRNA sequence which is SEQ ID NO: 21 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 21.

~~the point mutation site is selected from the group consisting of R249 (p53), R248 (p53) and R273 (p53) and combinations thereof.~~

10. One or more nucleic acid sequence or one or more double stranded siRNA molecule for use according to claim 9, wherein the cancer is:

(a) selected from the group consisting of oesophagus, upper respiratory tract, skin, epithelial, central nervous system, ovarian, breast, gastro-intestinal, large intestines, small intestines, colorectal, liver, adenocarcinoma, adrenal adenocarcinoma, thyroid, lung, pancreas, kidney, endometrial, hematopoietic, muscles, connective tissue (such as tendon or cartilage), bone, soft tissue, lymphoid tissue, lymph and the immune system;

(b) selected from the group consisting of melanomas, myelomas, carcinomas, sarcomas, lymphomas, blastomas and germ cell tumours;

(c) selected from the group consisting of lung carcinoma, malignant melanoma, colon carcinoma, breast carcinoma, endometrial adenocarcinoma, rhabdomyosarcoma, kidney adenocarcinoma, colon adenocarcinoma, hepatocellular carcinoma, bronchial squamous cancer, ovarian carcinoma and pancreatic adenocarcinoma; and/or

(d) dependent on the p53 tumour suppressor gene.

11. One or more nucleic acid sequence or one or more double stranded siRNA molecule for use according to claim 9 or 10, wherein the one or more point mutations ~~is~~ are selected from the group consisting of R249S (p53), R249G (p53), R249M (p53), R248W (p53), R248Q (p53), R273H (p53) and R273L (p53), and combinations thereof.

12. One or more nucleic acid sequence or one or more double stranded siRNA molecule for use according to any one of claims 9 to 11, wherein administration of the one or more of the nucleic acid sequences or one or more double stranded siRNA molecules

results in one or more of the following effects selected from the group consisting of cell death, abrogation of addiction, activation of any one or more p53 target genes, relief of a dominant negative effect, increased sensitivity to one or more anti-cancer agents, and retardation or halting of tumour growth.

13. One or more nucleic acid sequence or one or more double stranded siRNA molecule for use according to any one of claims 9 to 12, wherein the nucleic acid sequence is for use with a therapeutic agent.

14. One or more nucleic acid sequence or one or more double stranded siRNA molecule for use according to claim 13, wherein the therapeutic agent is an anti-cancer agent.

15. Use of one or more nucleic acid sequence according to any one of claims 1 to 5 or one or more double stranded siRNA molecule according to claim 7 for the manufacture of a medicament for treating cancer in a subject~~, wherein the medicament is to be administered to the subject, wherein the one or more nucleic acid sequences target~~ having one or more single point mutations ~~sites~~ within the p53 tumour suppressor gene at one or more sites, wherein:

(a) the subject has a single point mutation in the p53 tumour suppressor gene at R249(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence selected from SEQ ID NOs 16 and 17, an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 16 and 17 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 16 or 17; and/or

(b) the subject has a single point mutation in the p53 tumour suppressor gene at R248(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 13, an shRNA sequence having an siRNA sequence which is SEQ ID NO: 13 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 13; and/or

(c) the subject has a single point mutation in the p53 tumour suppressor gene at R273(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 21, an shRNA sequence having an siRNA sequence which is SEQ ID NO: 21 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 21.

~~the point mutation site is selected from the group consisting of R249 (p53), R248 (p53) and R273 (p53) and combinations thereof.~~

16. Use of one or more nucleic acid sequence or one or more double stranded siRNA molecule for the manufacture of a medicament according to claim 15 wherein the cancer is:

(a) selected from the group consisting of oesophagus, upper respiratory tract, skin, epithelial, central nervous system, ovarian, breast, gastro-intestinal, large intestines, small intestines, colorectal, liver, adenocarcinoma, adrenal adenocarcinoma, thyroid, lung, pancreas, kidney, endometrial, hematopoietic, muscles, connective tissue (such as tendon or cartilage), bone, soft tissue, lymphoid tissue, lymph and the immune system;

(b) selected from the group consisting of melanomas, myelomas, carcinomas, sarcomas, lymphomas, blastomas and germ cell tumours;

(c) selected from the group consisting of lung carcinoma, malignant melanoma, colon carcinoma, breast carcinoma, endometrial adenocarcinoma, rhabdomyosarcoma, kidney adenocarcinoma, colon adenocarcinoma, hepatocellular carcinoma, bronchial squamous cancer, ovarian carcinoma and pancreatic adenocarcinoma; and/or

(d) dependent on the p53 tumour suppressor gene.

17. Use of one or more nucleic acid sequence or one or more double stranded siRNA molecule for the manufacture of a medicament according to claim 15 or 16 wherein the one or more point mutations ~~is~~ are selected from the group consisting of R249S (p53), R249G (p53), R249M (p53), R248W (p53), R248Q (p53), R273H (p53) and R273L (p53), and combinations thereof.

18. Use of one or more nucleic acid sequence or one or more double stranded siRNA molecule for the manufacture of a medicament according to any one of claims 15 to 17 wherein administration of the one or more of the nucleic acid sequences or one or more double stranded siRNA molecules results in one or more of the following effects selected from the group consisting of cell death, abrogation of addiction, activation of any one or more p53 target genes, relief of a dominant negative effect, increased sensitivity to one or more anti-cancer agents, and retardation or halting of tumour growth.

19. Use of one or more nucleic acid sequence or one or more double stranded siRNA molecule for the manufacture of a medicament according to any one of claims 15 to 18 wherein the medicament is to be administered with a therapeutic agent, optionally wherein the therapeutic agent is an anti-cancer agent.

20. Use of one or more nucleic acid sequence according to any of claims 1 to 5 or one or more double stranded siRNA molecule according to claim 7 for the manufacture of a medicament for treating a subject susceptible to treatment, said susceptible subject being identified as having one or more single point mutations within the p53 tumour suppressor gene at one or more sites, wherein:

(a) the subject is identified as having a single point mutation in the p53 tumour suppressor gene at R249(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence selected from SEQ ID NOs 16 and 17, an shRNA sequence having an siRNA sequence selected from SEQ ID NOs 16 and 17 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 16 or 17; and/or

(b) the subject is identified as having a single point mutation in the p53 tumour suppressor gene at R248(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 13, an shRNA sequence having an siRNA sequence which is SEQ ID NO: 13 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 13; and/or

(c) the subject is identified as having a single point mutation in the p53 tumour suppressor gene at R273(p53) and the one or more nucleic acid sequence or one or more double stranded siRNA molecule is selected from an siRNA sequence which is SEQ ID NO: 21, an shRNA sequence having an siRNA sequence which is SEQ ID NO: 21 and a double stranded siRNA molecule in which the sense sequence consists of the sequence in SEQ ID NO 21.

~~the site of the one or more point mutations is selected from the group consisting of R249 (p53), R248 (p53) and R273 (p53), wherein the medicament is to be administered to the subject and wherein the one or more nucleic acid sequences target the one or more point mutations sites within the p53 gene.~~

21. Use of one or more nucleic acid sequence or one or more double stranded siRNA molecule for the manufacture of a medicament according to claim 20 wherein the one or more point mutations ~~is~~ are selected from the group consisting of R249S (p53), R249G (p53), R249M (p53), R248W (p53), R248Q (p53), R273H (p53) and R273L.