

CLAIMS

1. A process for detecting a chromosome state which represents a subgroup in a population comprising determining whether a chromosome interaction relating to that chromosome state is present or absent
5 within a defined region of the genome; and
- wherein the subgroup relates to prognosis for prostate cancer and wherein the chromosome interaction corresponds to any one of the chromosome interactions represented by any probe shown in Table 6;
or
- wherein the subgroup relates to prognosis for DLBCL and the chromosome interaction corresponds to
10 any one of the chromosome interactions represented by any probe shown in Table 5;
or
- wherein the subgroup relates to prognosis for lymphoma and the chromosome interaction corresponds to any one of the chromosome interactions shown in Table 8.
- 15 2. A process according to claim 1 wherein:
- said prognosis for prostate cancer relates to whether or not the cancer is aggressive or indolent; and/or
- said prognosis for DLBCL relates to survival.
- 20 3. A process according to claim 1 or 2 wherein the subgroup relates to prostate cancer and a specific combination of chromosome interactions are typed:
(i) comprising all of the chromosome interactions represented by the probes in Table 6; and/or
(ii) comprising at least 1, 2, 3 or 4 of the chromosome interactions represented by the probes in Table 6.
- 25 4. A process according to claim 1 or 2 wherein the subgroup relates to DLBCL and a specific combination of chromosome interactions are typed:
(i) comprising all of the chromosome interactions represented by the probes in Table 5; and/or
(ii) comprising at least 10, 20, 30, 50 or 80 of the chromosome interactions represented by the probes in Table 5.
- 30 5. A process according to claim 1 or 2 wherein the subgroup relates to DLBCL and a specific combination of chromosome interactions are typed:
(i) comprising all of the chromosome interactions shown in Table 7; and/or
(ii) comprising at least 1, 2, 5 or 8 of the chromosome interactions shown in Table 7.

6. A process according to any one of the preceding claims wherein the subgroup relates to lymphoma and a specific combination of chromosome interactions are typed:
- (i) comprising all of the chromosome interactions shown in Table 8; and/or
 - 5 (ii) comprising at least 10, 20, 30 or 50 of the chromosome interactions shown in Table 8 or preferably a specific combination of chromosome interactions are typed:
 - (a) comprising all of the chromosome interactions shown in Table 9; and/or
 - (b) comprising at least 5, 10 or 15 of the chromosome interactions shown in Table 9.
- 10 7. A process according to any one of the preceding claims wherein at least 10, 20, 30, 40 or 50, chromosome interactions are typed, and preferably at least 10 chromosome interactions are typed.
8. A process according to any one of the preceding claims in which the chromosome interactions are typed:
- 15 - in a sample from an individual, and/or
 - by detecting the presence or absence of a DNA loop at the site of the chromosome interactions, and/or
 - detecting the presence or absence of distal regions of a chromosome being brought together in a chromosome conformation, and/or
 - by detecting the presence of a ligated nucleic acid which is generated during said typing and whose
 - 20 sequence comprises two regions each corresponding to the regions of the chromosome which come together in the chromosome interaction, wherein detection of the ligated nucleic acid is preferably by:
 - (i) in the case of prognosis of prostate cancer by a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 6, and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 6; or
 - 25 (ii) in the case of prognosis of DLBCL a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 5, and/or (b) by a primer pair which has at least 70% identity to any primer pair in Table 5.
9. A process according to any one of the preceding claims in which the chromosome interactions are typed
- 30 by detecting the presence of a ligated nucleic acid which is generated during said typing and whose sequence comprises two regions each corresponding to the regions of the chromosome which come together in the chromosome interaction, wherein detection of the ligated nucleic acid in the case of prognosis of lymphoma is by:

- a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 5, and/or
- by a primer pair which has at least 70% identity to any primer pair in Table 5, and/or
- by a primer pair which has at least 70% identity to any primer pair in Table 8.

5

10. A process according to any one of the preceding claims, wherein the chromosome interaction is detected by a method comprising the steps of: -

(i) cross-linking of chromosome regions which have come together in a chromosome interaction;

10 (ii) subjecting said cross-linked regions to cleavage, optionally by restriction digestion cleavage with an enzyme;

(iii) ligating said cross-linked cleaved DNA ends to form ligated nucleic acids and.

(iv) detecting the presence or absence of a ligated nucleic acid corresponding to the chromosome interaction.

15 11. A process according to any one of the preceding claims which is carried out to determine whether a prostate cancer is aggressive or indolent which comprises typing at least 5 chromosome interactions as defined in Table 6.

20 12. A process according to any one of the preceding claims which is carried out to determine prognosis of DLBLC which comprises typing at least 5 chromosome interactions as defined in Table 5.

13. A process according to any one of the preceding claims which is carried out to identify or design a therapeutic agent for prostate cancer;

25 - wherein preferably said process is used to detect whether a candidate agent is able to cause a change to a chromosome state which is associated with a different level of prognosis;

- wherein the chromosomal interaction is represented by any probe in Table 6; and/or

- the chromosomal interaction is present in any region or gene listed in Table 6;

and wherein optionally:

30 - the chromosomal interaction has been identified by the method of determining which chromosomal interactions are relevant to a chromosome state as defined in claim 1, and/or

- the change in chromosomal interaction is monitored using (i) a probe that has at least 70% identity to any of the probe sequences mentioned in Table 6, and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 6.

14. A process according to any one of preceding claims 1 to 12 which is carried out to identify or design a therapeutic agent for DLBCL;

- wherein preferably said process is used to detect whether a candidate agent is able to cause a change to a chromosome state which is associated with a different level of prognosis;
- wherein the chromosomal interaction is represented by any probe in Table 5; and/or
- the chromosomal interaction is present in any region or gene listed in Table 5;

and wherein optionally:

- the chromosomal interaction has been identified by the method of determining which chromosomal interactions are relevant to a chromosome state as defined in claim 1, and/or
- the change in chromosomal interaction is monitored using (i) a probe that has at least 70% identity to any of the probe sequences mentioned in Table 5, and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 5.

15. A process according to any one of preceding claims 1 to 12 which is carried out to identify or design a therapeutic agent for lymphoma;

- wherein preferably said process is used to detect whether a candidate agent is able to cause a change to a chromosome state which is associated with a different level of prognosis;

- wherein the chromosomal interaction is represented by any probe in Table 8 or 9; and/or

- the chromosomal interaction is present in any region or gene listed in Table 8 or 9;

and wherein optionally:

- the chromosomal interaction has been identified by the method of determining which chromosomal interactions are relevant to a chromosome state as defined in claim 1, and/or
- the change in chromosomal interaction is monitored using (i) a probe that has at least 70% identity to any of the probe sequences mentioned in Table 5, and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 5 or 8.

16. A process according to any one of claims 13 to 15 which comprises selecting a target based on detection of the chromosome interactions, and preferably screening for a modulator of the target to identify a therapeutic agent for immunotherapy, wherein said target is optionally a protein.

17. A process according to any one of the preceding claims wherein said prognosis is in a human or canine.

18. A process according to any one of the preceding claims, wherein the typing or detecting comprises specific detection of the ligated product by quantitative PCR (qPCR) which uses primers capable of amplifying the ligated product and a probe which binds the ligation site during the PCR reaction, wherein said probe comprises sequence which is complementary to sequence from each of the chromosome regions that have come together in the chromosome interaction, wherein preferably said probe comprises:

an oligonucleotide which specifically binds to said ligated product, and/or
a fluorophore covalently attached to the 5' end of the oligonucleotide, and/or
a quencher covalently attached to the 3' end of the oligonucleotide, and
optionally

said fluorophore is selected from HEX, Texas Red and FAM; and/or

said probe comprises a nucleic acid sequence of length 10 to 40 nucleotide bases, preferably a length of 20 to 30 nucleotide bases.

19. A process according to any one of the preceding claims wherein:

- the result of the process is provided in a report, and/or

- the result of the process is used to select a patient treatment schedule, and preferably to select a specific therapy for the individual.

20. A process according any one of the preceding claims wherein:

- the subgroup relates to prostate cancer and at least one chromosome interaction from Table 25 is typed;
and/or

- the subgroup relates to prostate cancer and at least one of the following combinations of interactions from Table 25 is typed:

(i) ETS1, MAP3K14, SLC22A3 and CASP2, or

(ii) BMP6, ERG, MSR1, MUC1, ACAT1 and DAPK1, or

(iii) HSD3B2, VEGFC, APAF1, MUC1, ACAT1 and DAPK1;

and/or

- the subgroup relates to DLBCL and at least one of the first 10 markers shown in Table 5 is typed, preferably corresponding to one or more of the following genes: STAT3, TNFRSF13B, ANXA11, MAP3K7, MEF2B and IFNAR1; and/or
 - the subgroup relates to lymphoma and at least one of the first 11 markers shown in Figure 6 is typed, preferably corresponding to one or more of the following genes: STAT3, TNFRSF13B, ANXA11, MAP3K7, MEF2B and IFNAR1.
- 5