

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 within a defined region of the genome, wherein said subgroup relates to physical performance in an individual; and~~

~~— wherein said chromosome interaction has optionally been identified by a method of determining which chromosomal interactions are relevant to a chromosome state corresponding to a physical performance subgroup of the population, comprising contacting a first set of nucleic acids from subgroups with different states of the chromosome with a second set of index nucleic acids, and allowing complementary sequences to hybridise, wherein the nucleic acids in the first and second sets of nucleic acids represent a ligated product comprising sequences from both the chromosome regions that have come together in chromosomal interactions, and wherein the pattern of hybridisation between the first and second set of nucleic acids allows a determination of which chromosomal interactions are specific to a physical performance subgroup; and~~

~~— wherein the chromosome interaction either:~~

~~(i) corresponds to any one of the chromosome interactions shown in any of Tables 3, 7, 8, 9, 25 and 30; and/or~~

~~(ii) corresponds to any one of the chromosome interactions shown in any of Tables 13, 14, 18, 22, 23 and 24; and/or~~

~~(iii) corresponds to any one of the chromosome interactions shown in Table 31 or 32; and/or~~

~~(iv) is present in a 4,000 base region which comprises or which flanks (i), (ii) or (iii); and/or~~

~~(v) is present in any one of the regions or genes listed in Table 21, 24, 25, 30, 31 or 32.~~

2. ~~A process according to claim 1 wherein:~~

~~— the individual is a human and the subgroup is a human subgroup~~

~~— the individual is a horse and the subgroup is a horse subgroup, and~~

~~wherein optionally:~~

~~(i) the process is carried out to determine physical performance ability, and/or~~

~~(ii) the process is carried out to detect responsiveness to a stimulus relating to physical performance, which is preferably physical training, and optionally strength or endurance training; and/or~~

~~(iii) the process is carried out to select an individual suitable for a physical activity, which is preferably a sport; and/or~~

~~(iv) the process is carried out to select a stimulus relating to physical performance to give to the individual, wherein said stimulus is a type of physical training.~~

~~3. A process according to claim 1 or 2 wherein a specific combination of chromosome interactions are typed:~~

~~(i) comprising all of the chromosome interactions represented in any of Tables 3, 7, 8, 9, 25 and 30 or any of Tables 13, 14, 18, 22, 23; and/or~~

~~(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in any of Tables 3, 7, 8, 9, 25 and 30 or any of Tables 13, 14, 18, 22, 23; and/or~~

~~(iii) which together are present in at least 10, 50 or 100 of the regions or genes listed in any of Tables 21, 24, 25 or 30; and/or~~

~~(iv) wherein at least 10, 50, 100, 150, 200 or 300 chromosome interactions are typed which are present in a 4,000 base region which comprises or which flanks the chromosome interactions represented in any of Tables 3, 7, 8, 9, 25 and 30 or any of Tables 13, 14, 18, 22, 23.~~

~~4. A process according to any one of the preceding claims wherein a specific combination of chromosome interactions are typed:~~

~~(i) comprising all of the chromosome interactions represented in Table 31 or 32; and/or~~

~~(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in Table 31 or 32; and/or~~

~~(iii) which together are present in at least 5 of the regions or genes listed in Table 31 or 32; and/or~~

~~(iv) wherein at least 5 chromosome interactions are typed which are present in a 4,000 base region which comprises or which flanks the chromosome interactions represented in Table 31 or 32.~~

~~5. A process according to any one of the preceding claims in which the chromosome interactions are typed:~~

~~-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 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 using either:~~

~~(i) a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 24, 25, 30, 31 or 32 and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 24, 25, 30, 31 or 32.~~

~~6. A process according to any one of the preceding claims, wherein:~~

~~—the second set of nucleic acids is from a larger group of individuals than the first set of nucleic acids; and/or~~

~~—the first set of nucleic acids is from at least 8 individuals; and/or~~

~~—the first set of nucleic acids is from at least 4 individuals from a first subgroup and at least 4 individuals from a second subgroup which is preferably non-overlapping with the first subgroup.~~

~~7. A process according to any one of the preceding claims wherein:~~

~~—the second set of nucleic acids represents an unselected group; and/or~~

~~—wherein the second set of nucleic acids is bound to an array at defined locations; and/or~~

~~—wherein the second set of nucleic acids represents chromosome interactions in least 100 different genes; and/or~~

~~—wherein the second set of nucleic acids comprises at least 1,000 different nucleic acids representing at least 1,000 different chromosome interactions; and/or~~

~~—wherein the first set of nucleic acids and the second set of nucleic acids comprise at least 100 nucleic acids with length 10 to 100 nucleotide bases.~~

~~8. A process according to any one of the preceding claims, wherein the first set of nucleic acids is obtainable in a process comprising the steps of:—~~

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

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

~~(iii) ligating said cross-linked cleaved DNA ends to form the first set of nucleic acids (in particular comprising ligated DNA).~~

~~9. A process according to any one of the preceding claims:~~

~~—wherein at least 10 to 50 different chromosome interactions are typed, preferably in 10 to 50 different regions or genes optionally as defined in Table 21, 24, 25, 30, 31 or 32;~~

~~and/or~~

~~—which is:~~

~~(i) carried out on a human or horse athlete; and/or~~

~~(ii) carried out as part of a training regime, preferably after the start of the training regime; and/or~~

~~(iii) carried out on a Thoroughbred horse, preferably a racing horse; or~~

~~(iv) carried out on a human individual of who is less than 20 years old or is carried out on a horse that is less than 18 months old, and/or~~

~~(v) which is carried out at multiple time points to assess physical performance characteristics at specific time points, wherein the process is optionally carried out at at least 3 time points, which are preferably at least 30 days apart from each other.~~

~~10. A process according to any one of the preceding claims wherein said defined region of the genome:~~

~~(i) comprises a single nucleotide polymorphism (SNP); and/or~~

~~(ii) expresses a microRNA (miRNA); and/or~~

~~(iii) expresses a non-coding RNA (ncRNA); and/or~~

~~(iv) expresses a nucleic acid sequence encoding at least 10 contiguous amino acid residues; and/or~~

~~(v) expresses a regulating element; and/or~~

~~(vi) comprises a CTCF binding site.~~

~~11. A process according to any one of the preceding claims:~~

~~—which is carried out to identify an individual that is suited to endurance training, and preferably the identified individual is then subject to endurance training, which optionally occurs on at least 100 days out of the next 365 days after the identification; or~~

~~—which is carried out to identify an individual that is suited to strength training, and preferably the identified individual is then subject to strength training, which optionally occurs on at least 100 days out of the next 365 days after the identification.~~

~~12. A process according to any one of the preceding claims which is carried out to select the individual for racing.~~

~~13. A process according to any one of the preceding claims wherein a specific combination of chromosome interactions are typed:~~

~~(i) comprising all of the chromosome interactions represented in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18; and/or~~

~~(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18; and/or~~

~~(iii) which together are present in at least 10 of the regions or genes listed in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18; and/or~~

~~(iv) wherein at least 10 chromosome interactions are typed which are present in a 4,000 base region which comprises or which flanks the chromosome interactions represented in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18.~~

~~14. A process according to any one of the preceding claims which is carried out to identify or design a an agent that affects physical performance, wherein 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 physical performance state; wherein~~

~~—the chromosomal interaction is any specific interaction or combination of interactions defined in any preceding claim and/or is present in any one of the regions or genes listed in Table 21, 24, 25, 30, 31 or 32; and/or~~

~~—the change in chromosomal interaction is monitored using (i) a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 24, 25, 30, 31 or 32 and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 24, 25, 30, 31 or 32.~~

~~15. A process according to claim 14 which comprises selecting a target based on detection of chromosome interactions, and preferably screening for a modulator of the target to identify an agent which affects physical performance, wherein said target is optionally a protein.~~

16. 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.

17. A process according to any one of the proceeding claims which further comprises:

~~producing a report on the physical performance characteristics of the individual based on the results of the process, or~~

~~inputting the results of the process into a database, or~~

~~assigning a specific fitness or training regime to the individual based on the results of the process, or~~

~~designing a specific fitness or training regime for the individual based on the results of the process.~~

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 within a defined region of the genome, wherein said subgroup relates to endurance or strength in human or horse individual; and wherein the chromosome interaction
5 either:

(i) corresponds to any one of the chromosome interactions shown in Table 25 for a human individual; and/or

(ii) corresponds to any one of the chromosome interactions shown in Table 24 for a horse individual.

2. A process according to claim 1 wherein:

(i) the process is carried out to determine endurance or strength physical performance ability, and/or

(ii) the process is carried out to detect responsiveness to a stimulus relating to endurance or strength physical performance; and/or

(iii) the process is carried out to select an individual suitable for an endurance or strength physical activity, which is preferably a sport; and/or

(iv) the process is carried out to select a stimulus relating to endurance or strength physical performance to give to the individual, wherein said stimulus is a type of physical training.

3. A process according to claim 1 or 2 wherein the individual is a human and a specific combination of chromosome interactions are typed:

(i) comprising all of the chromosome interactions represented in any of Tables 3, 7, 8, 9, 25 and 30; and/or

(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in any of Tables 3, 7, 8, 9, 25 and 30.

4. A process according to claim 1 or 2 wherein the individual is a horse and a specific combination of chromosome interactions are typed:

(i) comprising all of the chromosome interactions represented in any of Tables 13, 14, 18, 22, 23; and/or

(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in any of Tables 13, 14, 18, 22, 23.

5. A process according to any one of the preceding claims wherein the individual is a human and a specific combination of chromosome interactions are typed:

(i) comprising all of the chromosome interactions represented in Table 31 or 32; and/or

(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in Table 31 or 32.

6. A process according to any one of the preceding claims in which the chromosome interactions are typed:

- 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 sequence comprises two regions each corresponding to the regions of the chromosome
which come together in the chromosome interaction.

7. A process according to claim 6 wherein said detecting of the ligated nucleic acid is by using
either:

(i) a probe that has at least 70% identity to any of the specific probe sequences mentioned in
Table 24, 25, 30, 31 or 32; and/or

(ii) by a primer pair which has at least 70% identity to any primer pair in Table 24, 25, 30, 31
or 32.

8. 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;

(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.

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

- wherein at least 10 to 50 different chromosome interactions are typed;
and/or

- which is:

(i) carried out on a human or horse athlete; and/or

(ii) carried out as part of an endurance or strength training regime, preferably after the start
of the training regime; and/or

(iii) carried out on a Thoroughbred horse, preferably a racing horse; or

(iv) carried out on a human individual of who is less than 20 years old or is carried out on a horse that is less than 18 months old, and/or

(v) which is carried out at multiple time points to assess endurance or strength physical performance characteristics at specific time points, wherein the process is optionally carried out at at least 3 time points, which are preferably at least 30 days apart from each other.

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

- which is carried out to identify an individual that is suited to endurance training, and preferably the identified individual is then subject to endurance training, which optionally occurs on at least 100 days out of the next 365 days after the identification; or

- which is carried out to identify an individual that is suited to strength training, and preferably the identified individual is then subject to strength training, which optionally occurs on at least 100 days out of the next 365 days after the identification.

11. A process according to any one of the preceding claims which is carried out to select the individual for racing.

12. A process according to any one of the preceding claims wherein a specific combination of chromosome interactions are typed:

(i) comprising all of the chromosome interactions represented in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18; and/or

(ii) comprising at least 10%, 20%, 50%, or 80% of the chromosome interactions in any of Tables 33, 34, 35, 36, 37, 38, 39, 40 or 41, or in any of Figures 16, 17 or 18.

13. A process according to any one of the preceding claims which is carried out to identify or design an agent that affects endurance or strength physical performance, wherein 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 endurance or strength physical performance state; wherein

- the chromosomal interaction is any specific interaction or combination of interactions defined in any preceding claim; and/or

- the change in chromosomal interaction is monitored using (i) a probe that has at least 70% identity to any of the specific probe sequences mentioned in Table 24, 25, 30, 31 or 32 and/or (ii) by a primer pair which has at least 70% identity to any primer pair in Table 24, 25, 30, 31 or 32.

14. A process according to claim 13 which comprises selecting a target based on detection of chromosome interactions, and preferably screening for a modulator of the target to identify an agent which affects endurance or strength physical performance, wherein said target is optionally a protein.

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15. 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:

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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

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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.

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16. A process according to any one of the preceding claims which further comprises:

- producing a report on the physical performance characteristics of the individual based on the results of the process, or

- inputting the results of the process into a database, or

- assigning a specific fitness or training regime to the individual based on the results of the

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process, or

- designing a specific fitness or training regime for the individual based on the results of the process.