

to provide a means for screening for a cell line exhibiting no differentiation resistance.

Solution to Problem

[0005] To achieve the above objects, the present inventors have examined RNA that is specifically expressed in iPS cell lines exhibiting differentiation resistance or RNA that is specifically expressed in iPS cell lines exhibiting no differentiation resistance using iPS cell lines exhibiting differentiation resistance and iPS cell lines exhibiting no differentiation resistance. It was thus confirmed that large intergenic non-coding RNA (lincRNA) or mRNA encoded by a specific genomic region is specifically expressed in iPS cell lines exhibiting differentiation resistance or iPS cell lines exhibiting no differentiation resistance.

[0006] Based on the above results, the present inventors have discovered that iPS cells exhibiting differentiation resistance can be screened for through the use of large intergenic non-coding RNA (lincRNA) or mRNA encoded by a specific genomic region as an indicator (marker), and thus have completed the present invention.

Thus, in one aspect, the present invention refers to a method for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, comprising the steps of:

- (i) measuring expression of at least one large intergenic non-coding RNA (lincRNA) or mRNA selected from group A and/or group B,
- (ii) selecting a human induced pluripotent stem cell line in which the lincRNA or mRNA selected from group A expresses or the lincRNA or mRNA selected from group B does not express,

wherein the lincRNA or mRNA selected from group A is selected from the group consisting of

(A20) DLX5,

(A50) MEIS2,

(A53) lincRNA:chr17:21434064-21435857 reverse strand, and

(A58) GREB1L,

wherein the lincRNA or mRNA selected from Group B is selected from the group consisting of

(B4) C4orf51,

(B9) C7orf57,

(B10) lincRNA:chr7:124873114-124899839 reverse strand,

(B12) OC90.

(B13) lincRNA:chr8:133071643-133092468 reverse strand.

(B14) lincRNA:chr8:133073732-133075753 reverse strand.

(B15) HHLA1.

(B16) lincRNA:chr8:133076031-133093351 reverse strand.

(B17) lincRNA:chr8:133090096-133097869 reverse strand.

(B22) ABHD12B.

(B23) lincRNA:chr18:54721302-54731677 reverse strand.

(B27) ZNF541.

(B28) TBX1.

(B29) CXorf61. and

(B30) DB090170 TESTI4 Homo sapiens cDNA clone TESTI4038997 5' mRNA sequence [DB090170].

In another aspect, the present invention refers to a method for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, comprising the following steps:

(i) measuring DNA-methylated state of LTR region located in at least one gene selected from group of (B4) C4orf51, (B15) HHLA1, and (B22) ABHD12B, and

(ii) selecting a human induced pluripotent stem cell line in which the LTR7 region is in a DNA-methylated state.

Also disclosed herein is~~Specifically, the present invention includes~~ the following [1] to [9].

[1] A method for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, comprising the steps of:

(i) measuring expression of at least one large intergenic non-coding RNA (lincRNA) or mRNA selected from group A and/or group B,

(ii) selecting a human induced pluripotent stem cell line in which the lincRNA or mRNA selected from group A expresses or the lincRNA or mRNA selected from group B does not express;

Group A consisting of

(A1) lincRNA:chr1:852245-854050 reverse strand,

(A2) GPR177,

(A3) VTCN1,

(A4) lincRNA:chr1:142803013-142804254 reverse strand,

- (A5) APOA2,
- (A6) WNT6,
- (A7) EPAS1,
- (A8) COL3A1,
- (A9) SLC40A1,
- (A10) S100P,
- (A11) HOPX,
- (A12) GUCY1A3,
- (A13) CDH10,
- (A14) HAPLN1,

SEQUENCE LISTING

<110> Kyoto University

<120> METHOD FOR SCREENING INDUCED PLURIPOTENT STEM CELLS

<130> PH-4896-PCT

<150> 61/511,156

<151> 2011-07-25

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<170> PatentIn version 3.5

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SEQUENCE LISTING

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<120> METHOD FOR SCREENING INDUCED PLURIPOTENT STEM CELLS

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actgatgaca ttccaccaca aaacaagtgt aaatggcggg tcttgccctt aactgatgac	180
attaccttgt gaaagtcctt tttctggctc atcctggctc aaaagcacc ccaactgagca	240
ccttgcgacc cccactcctg ccgcccagag aacaaacccc ctttgactgt aattttcctt	300
tacctacca aatcctataa aacggcccca cccttaactc ccttcaactga ctctcttttc	360
ggactcagcc cacctgtacc caggtgatta aaagctttat tgcacacaca aaacctgttt	420
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 <220>
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 <400> 9
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 <220>
 <223> sequencing primer

 <400> 10
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agcccgcctg caccaggtg aaataaacag ctttattgct cacacaaagc ctgtttggtg	240
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 ctgcccagat ggctg 196

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ctgcacaggg ttgttgtgaa gactgaatta agtaagataa tgtatgtaaa gtaccagct 180
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<210> 38
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gaggacttcc acacaagtct ttgcactcg ttattctttt aaatcctcac agcaactctc 180
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<210> 39
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ctctgagccc aagccaagcc atcgcatccc ctgtgacttg cacatatacg cccagatggc 180
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<212> DNA

<213> Homo sapiens

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tataaaacgg ccccacctt aactcecttc actgactctc tttteggact cageccacct 180

gtaccaggt gattaaaagc ttattgctc acacaaaacc tgtttggtgg tctcttcaca 240

cggacgcgca tgaaactcct tatctgagat atggtttgc 279