

Claims

[Claim 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,

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].

[Claim 2]

The method according to claim 1, wherein the lincRNA or mRNA selected

from Group B is selected from the group consisting of:

(B4) C4orf51,

(B15) HHLA1, and

(B22) ABHD12B.

[Claim 3]

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 or neighborhood thereof 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.

[Claim 4]

A reagent for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing a polynucleotide having at least 15 continuous nucleotides in the nucleotide sequence of at least one mRNA or LincRNA shown in group A or B as defined in claim 1, or a polynucleotide complementary thereto.

[Claim 5]

The reagent according to claim 6, which is a microarray prepared by immobilizing, as a probe, a polynucleotide complementary to a polynucleotide having at least 15 continuous nucleotides in the nucleotide sequence of at least one mRNA or LincRNA shown in group A or B as defined in claim 1.

[Claim 6]

A reagent for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing an antibody that recognizes a protein encoded by at least one mRNA shown in group A or B as defined in claim 1.

[Claim 7]

A kit for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing the reagent according to any one of claims 4 to 6.

Claims

[Claim 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,
- (A15) PITX1,
- (A16) HAND1,
- (A17) CGA,
- (A18) AQP1,
- (A19) DLX6,
- (A20) DLX5,
- (A21) SOX17,
- (A22) FLJ45983,
- (A23) PLCE1,
- (A24) H19,
- (A25) lincRNA:chr11:2016408-2017024 reverse strand,
- (A26) lincRNA:chr11:2017517-2017651 forward strand,
- (A27) IGF2,
- (A28) P2RY6,

(A29) SLN,
(A30) NNMT,
(A31) APOA1,
(A32) ERP27,
(A33) LUM,
(A34) CCDC92,
(A35) CDX2,
(A36) FLJ41170,
(A37) MEG3,
(A38) lincRNA:chr14:101292469-101299626 forward strand,
(A39) lincRNA:chr14:101295637-101302637 forward strand,
(A40) lincRNA:chr14:101296681-101298460 forward strand,
(A41) lincRNA:chr14:101298129-101300147 forward strand,
(A42) lincRNA:chr14:101324825-101327247 forward strand,
(A43) MEG8,
(A44) lincRNA:chr14:101365673-101366049 forward strand,
(A45) lincRNA:chr14:101396955-101397357 forward strand,
(A46) lincRNA:chr14:101430757-101433381 forward strand,
(A47) lincRNA:chr14:101434059-101436282 forward strand,
(A48) lincRNA:chr14:101472355-101473369 forward strand,
(A49) DIO3,
(A50) MEIS2,
(A51) PRTG,
(A52) C17orf51,
(A53) lincRNA:chr17:21434064-21435857 reverse strand,
(A54) lincRNA:chr17:21435180-21454915 reverse strand,
(A55) lincRNA:chr17:21435959-21436405 reverse strand,
(A56) CCR7,
(A57) KRT23,
(A58) GREB1L,
(A59) GATA6,
(A60) TTR,
(A61) UCA1,
(A62) FLRT3,
(A63) lincRNA:chrX:73040495-73047819 reverse strand,
(A64) VGLL1,
(A65) RPS4Y1,
(A66) DDX3Y, and

(A67) RPS4Y2,

Group B consisting of

(B1) DMRTB1,

(B2) lincRNA:chr1:73430887-73446112 reverse strand,

(B3) lincRNA:chr1:73444697-73444997 reverse strand,

(B4) C4orf51,

(B5) PCDHA1,

(B6) lincRNA:chr6:95250854-95263604 reverse strand,

(B7) lincRNA:chr6:14280358-14285376 reverse strand,

(B8) lincRNA:chr6:14283301-14285685 reverse strand,

(B9) C7orf57,

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

(B11) lincRNA:chr8:129599518-129624118 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,

(B18) lincRNA:chr8:138387843-138421643 reverse strand,

(B19) lincRNA:chr8:138418343-138425831 reverse strand,

(B20) NDUFA4L2,

(B21) lincRNA:chr13:54698462-54707001 reverse strand,

(B22) ABHD12B,

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

(B24) ZNF208,

(B25) ZNF257,

(B26) ZNF676,

(B27) ZNF541,

(B28) TBX1,

(B29) CXorf61, and

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

[Claim 2]

The method according to claim 1, 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.
- [Claim 3] The method according to claim 1, 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].
- [Claim 4] The method according to claim 1, wherein the lincRNA or mRNA selected from Group B is selected from the group consisting of;
- (B4) C4orf51,
 - (B15) HHLA1, and
 - (B22) ABHD12B.
- [Claim 5] 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 or neighborhood thereof 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.
- [Claim 6] A reagent for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing a polynucleotide having at least 15 continuous nucleotides in the nucleotide sequence of at least one mRNA or LincRNA shown in the above group A or B, or a polynucleotide complementary thereto.
- [Claim 7] The reagent according to claim 6, which is a microarray prepared by immobilizing, as a probe, a polynucleotide complementary to a polynu-

cleotide having at least 15 continuous nucleotides in the nucleotide sequence of at least one mRNA or LincRNA shown in the above group A or B.

[Claim 8]

A reagent for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing an antibody that recognizes a protein encoded by at least one mRNA shown in the above group A or B.

[Claim 9]

A kit for screening for a human induced pluripotent stem cell line exhibiting no differentiation resistance, containing the reagent according to any one of claims 6 to 8.