CLAIMS

1. A cell culture medium comprising a CDK1/2/9 inhibitor and a Bcr-Abl/Src kinase inhibitor.

2. A cell culture medium according to Claim 1, in which the CDK1/2/9 inhibitor comprises AZD5438 (4-[2-Methyl-1-(1-methylethyl)-1H-imidazol-5-yl]-N-[4-(methylsulfonyl)phenyl]-2-pyrimidinamine, AZD) or in which the Bcr-Abl/Src kinase inhibitor comprises Dasatinib (*N*-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazole carboxamide monohydrate, DASA).

3. A cell culture medium according to Claim 1 or 2, in which the cell culture medium comprises AZD5438 and Dasatinib, each independently at a concentration of 0.1μM or more, such as 1μM to 0.5μM, preferably 0.1μM.

4. A cell culture medium according to Claim 1, 2 or 3, in which the cell culture medium comprises one or more of: SB590885 ((*NE*)-*N*-[5-[2-[4-[2-(dimethylamino)ethoxy]phenyl]-5-pyridin-4-yl-1*H*-imidazol-4-yl]-2,3-dihydroinden-1-ylidene]hydroxylamine); PD0325901 (*N*-[(2*R*)-2,3-dihydroxypropoxy]-3,4-difluoro-2-(2-fluoro-4-iodoanilino)benzamide); and Y-27632 (4-[(1*R*)-1-aminoethyl]-*N*-pyridin-4-ylcyclohexane-1-carboxamide) such as 0.1 to 2.5μM, preferably 0.5μM of SB590885, 0.2 to 10μM, preferably 1μM of PD0325901 or 5 to 20μM, preferably 10μM of Y-27632.

5. A cell culture medium according to any preceding claim, in which the cell culture medium comprises: 5 to 20μg/ml of recombinant human LIF (UniProtKB - P15018); 0.2 to 10μM, preferably 1μM of PD0325901; 0.1 to 2.5μM, preferably 0.5μM of SB590885; 0.1 to 2.5μM, preferably 1μM of WH4-023; 5 to 20μM, preferably 10μM of Y-27632; and 5 to 20ng/ml, preferably 10ng/ml of Activin A (UniProtKB - P08476).

6. A cell culture medium according to any preceding claim, in which the cell culture medium comprises: DMEM/F12 (Invitrogen; 11320), Neurobasal (Invitrogen; 21103), N2 supplement (Invitrogen; 17502048) (100X dilution), B27 supplement (Invitrogen; 17504044) (50X dilution), 2 mM L-glutamine, 1% non-essential amino acids, 0.1 mM β-mercaptoethanol, 1% penicillin-streptomycin, 50 μg/ml BSA, supplemented with 10 μg/mL recombinant human LIF, 1 μM PD0325901, 0.5 μM SB590885, 1 μM WH4-023, 10 μM Y-27632 and 10 ng/mL Activin A, preferably in which the cell culture medium comprises a 1:1

ratio of F12 DMEM (STEMCELL Technologies) and Neurobasal media (Gibco), 1X N2 supplement (Gibco) and 1X B2 supplement (Gibco), 1X L-Glutamine (Gibco), 1X Non-essential amino acids (Gibco), 0.1mM of B-mercaptoethanol (Sigma) and 62.5ng/ml of bovine serum albumin (BSA, Sigma).

7. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of maintaining or increasing pluripotency in a cell cultured in the cell culture medium in the absence of co-culture such as feeder cells.

8. A cell culture medium according to any preceding claim, in which the pluripotency comprises expression of a naïve pluripotent stem cell marker selected from the group consisting of: *CD130* (Gene ID: 3572), *CD75* (Gene ID: 6480), *DNMT3L* (Gene ID: 29947), *DPPA5* (Gene ID: 340168), *KLF5* (Gene ID: 688), *TFCP2L1* (Gene ID: 29842), *KLF4* (Gene ID: 9314), *DPPA3* (Gene ID: 359787), *NANOG* (Gene ID: 79923), *KLF17* (Gene ID: 128209), *POU5F1* (Gene ID: 5460) and *PRDM14* (Gene ID: 63978).

9. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of maintaining or increasing pluripotency in a cell cultured for 5 or more passages, such as 8 or more passages.

10. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of decreasing the expression of a primed pluripotent stem cell marker such as *ZIC2* (Gene ID: 7546) and *B3GAT1* (Gene ID: 27087) in a cell cultured in the cell culture medium.

11. A method of culturing a cell in a cell culture medium according to any preceding claim.

12. A method according to any preceding claim, in which the method is capable of maintaining or increasing the expression of a naïve pluripotent stem cell marker in the cell.

13. A method according to any preceding claim, in which the method does not include co-culture with feeder cells.

14. A method according to any preceding claim, in which the method comprises culturing the cell for 5 or more passages, such as 8 or more passages.

15. A method according to any preceding claim, in which the cell comprises a naïve pluripotent stem cell, preferably a mammalian naïve pluripotent stem cell, such as a human naïve pluripotent stem cell.

16. A method according to any preceding claim, in which the method is capable of:

(a) maintaining the naïve pluripotent stem cell in a naïve state; and/or

(b) maintaining the survival of a naïve pluripotent stem cell

preferably after at least 5 passages, preferably after at least 8 passages.

17. A method according to any preceding claim, in which the cell comprises a primed pluripotent stem cell, preferably a mammalian primed pluripotent stem cell, such as a human primed pluripotent stem cell, in which the method re-programs the primed pluripotent stem cell into a naïve pluripotent stem cell.

18. A method according to any preceding claim, in which the cell comprises a somatic cell, preferably a mammalian somatic cell, such as a human somatic cell, in which the method re-programs the somatic cell into a naïve pluripotent stem cell, and in which the method preferably further comprises up-regulating the expression of Oct4 (Pou5f1), Sox2, Klf4 and c-Myc in the somatic cell.

19. A method of propagation of a naïve pluripotent stem cell, the method comprising culturing the naïve pluripotent stem cell in a cell culture medium according to any of Claims 1 to 10.

20. A method of re-programming a somatic cell or a primed pluripotent stem cell into a naïve pluripotent stem cell, the method comprising culturing the primed pluripotent stem cell in a cell culture medium according to any of Claims 1 to 10.

21. A cell cultured in a cell culture medium according to any of Claims 1 to 10.

22. A cell produced by a method according to any of Claims 11 to 20.

CLAIMS

1. A cell culture medium comprising a CDK1/2/9 inhibitor and a Bcr-Abl/Src kinase inhibitor, in which the CDK1/2/9 inhibitor comprises AZD5438 (4-[2-Methyl-1-(1-methylethyl)-1H-imidazol-5-yl]-N-[4-(methylsulfonyl)phenyl]-2-pyrimidinamine, AZD) and in which the Bcr-Abl/Src kinase inhibitor comprises Dasatinib (*N*-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazole carboxamide monohydrate, DASA).

2. A cell culture medium according to Claim , in which the cell culture medium comprises AZD5438 and Dasatinib, each independently at a concentration of 0.1μM or more, such as 1μM to 0.5μM, preferably 0.1μM.

3. A cell culture medium according to Claim 1 or 2, in which the cell culture medium comprises one or more of: SB590885 ((*NE*)-*N*-[5-[2-[4-[2-(dimethylamino)ethoxy]phenyl]-5-pyridin-4-yl-1*H*-imidazol-4-yl]-2,3-dihydroinden-1-ylidene]hydroxylamine); PD0325901 (*N*-[(2*R*)-2,3-dihydroxypropoxy]-3,4-difluoro-2-(2-fluoro-4-iodoanilino)benzamide); and Y-27632 (4-[(1*R*)-1-aminoethyl]-*N*-pyridin-4-ylcyclohexane-1-carboxamide) such as 0.1 to 2.5μM, preferably 0.5μM of SB590885, 0.2 to 10μM, preferably 1μM of PD0325901 or 5 to 20μM, preferably 10μM of Y-27632.

4. A cell culture medium according to Claim 1, 2 or 3, in which the cell culture medium comprises: 5 to 20μg/ml of recombinant human LIF (UniProtKB - P15018); 0.2 to 10μM, preferably 1μM of PD0325901; 0.1 to 2.5μM, preferably 0.5μM of SB590885; 0.1 to 2.5μM, preferably 1μM of WH4-023; 5 to 20μM, preferably 10μM of Y-27632; and 5 to 20ng/ml, preferably 10ng/ml of Activin A (UniProtKB - P08476).

5. A cell culture medium according to any preceding claim, in which the cell culture medium comprises: DMEM/F12 (Invitrogen; 11320), Neurobasal (Invitrogen; 21103), N2 supplement (Invitrogen; 17502048) (100X dilution), B27 supplement (Invitrogen; 17504044) (50X dilution), 2 mM L-glutamine, 1% non-essential amino acids, 0.1 mM β-mercaptoethanol, 1% penicillin-streptomycin, 50 μg/ml BSA, supplemented with 10 μg/mL recombinant human LIF, 1 μM PD0325901, 0.5 μM SB590885, 1 μM WH4-023, 10 μM Y-27632 and 10 ng/mL Activin A, preferably in which the cell culture medium comprises a 1:1

ratio of F12 DMEM (STEMCELL Technologies) and Neurobasal media (Gibco), 1X N2 supplement (Gibco) and 1X B2 supplement (Gibco), 1X L-Glutamine (Gibco), 1X Non-essential amino acids (Gibco), 0.1mM of B-mercaptoethanol (Sigma) and 62.5ng/ml of bovine serum albumin (BSA, Sigma).

6. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of maintaining or increasing pluripotency in a cell cultured in the cell culture medium in the absence of co-culture such as feeder cells.

7. A cell culture medium according to Claim 6, in which the pluripotency comprises expression of a naïve pluripotent stem cell marker selected from the group consisting of: *CD130* (Gene ID: 3572), *CD75* (Gene ID: 6480), *DNMT3L* (Gene ID: 29947), *DPPA5* (Gene ID: 340168), *KLF5* (Gene ID: 688), *TFCP2L1* (Gene ID: 29842), *KLF4* (Gene ID: 9314), *DPPA3* (Gene ID: 359787), *NANOG* (Gene ID: 79923), *KLF17* (Gene ID: 128209), *POU5F1* (Gene ID: 5460) and *PRDM14* (Gene ID: 63978).

8. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of maintaining or increasing pluripotency in a cell cultured for 5 or more passages, such as 8 or more passages.

9. A cell culture medium according to any preceding claim, in which the cell culture medium is capable of decreasing the expression of a primed pluripotent stem cell marker such as *ZIC2* (Gene ID: 7546) and *B3GAT1* (Gene ID: 27087) in a cell cultured in the cell culture medium.

10. A method of culturing a cell in a cell culture medium according to any preceding claim.

11. A method according to Claim 10, in which the method is capable of maintaining or increasing the expression of a naïve pluripotent stem cell marker in the cell.

12. A method according to Claim 10 or 11, in which the method does not include co-culture with feeder cells.

13. A method according to Claim 10, 11 or 12, in which the method comprises culturing the cell for 5 or more passages, such as 8 or more passages.

14. A method according to any of Claims 10 to 13, in which the cell comprises a naïve pluripotent stem cell, preferably a mammalian naïve pluripotent stem cell, such as a human naïve pluripotent stem cell.

15. A method according to any of Claims 10 to 14, in which the method is capable of:

(a) maintaining the naïve pluripotent stem cell in a naïve state; and/or

(b) maintaining the survival of a naïve pluripotent stem cell

preferably after at least 5 passages, preferably after at least 8 passages.

16. A method according to any of Claims 10 to 15, in which the cell comprises a primed pluripotent stem cell, preferably a mammalian primed pluripotent stem cell, such as a human primed pluripotent stem cell, in which the method re-programs the primed pluripotent stem cell into a naïve pluripotent stem cell.

17. A method according to any of Claims 10 to 16, in which the cell comprises a somatic cell, preferably a mammalian somatic cell, such as a human somatic cell, in which the method re-programs the somatic cell into a naïve pluripotent stem cell, and in which the method preferably further comprises up-regulating the expression of Oct4 (Pou5f1), Sox2, Klf4 and c-Myc in the somatic cell.

18. A method of propagation of a naïve pluripotent stem cell, the method comprising culturing the naïve pluripotent stem cell in a cell culture medium according to any of Claims 1 to 9.

19. A method of re-programming a somatic cell or a primed pluripotent stem cell into a naïve pluripotent stem cell, the method comprising culturing the primed pluripotent stem cell in a cell culture medium according to any of Claims 1 to 9.