CLAIMS

1. A method of differentiating an induced pluripotent stem (iPS) cell into a retinal pigment epithelial (RPE) cell, the method comprising culturing a iPS cell derived from a stem cell of the amniotic membrane of the umbilical cord in a differentiation medium under conditions suitable for the differentiation into a RPE cell, thereby differentiating the iPS cell into the RPE cell.

2. The method of claim 1, wherein the differentiation medium comprises

i) a first differentiation medium additionally comprising at least any one of IGF1, DKK1, nicotinamide or LDN-193189, preferably comprising IGF1, DKK1, nicotinamide and LDN-193189;

ii) a second differentiation medium additionally comprising at least any one of IGF1, DKK1, nicotinamide, LDN-193189 or b-FGF, preferably comprising IGF1, DKK1, nicotinamide, LDN-193189 and b-FGF;

iii) a third differentiation medium additionally comprising at least any one of IGF1, DKK1 or Activin A, preferably comprising IGF1, DKK1 and Activin A;

iv) a fourth differentiation medium additionally comprising Activin A and either SU5402 or PD173074, preferably comprising Activin A and PD173074; and/or

v) a fifth differentiation medium additionally comprising at least any one of Activin A, CHIR99021, or either SU5402 or PD173074, preferably comprising Activin A, CHIR99021 and PD173074.

3. The method of claim 2, wherein IGF1 of i), ii) and/or iii) is used in a final concentration of at least 5 ng/ml, preferably wherein IGF1 of i), ii) and/or iii) is used in a final concentration of about 10 ng/ml.

4. The method of claim 2 or 3, wherein DKK1 of claim 2 i), ii) and/or iii) is used in a concentration of at least 5 ng/ml, preferably wherein DKK1 of claim 2 i), ii) and/or iii) is used in a concentration of about 10 ng/ml.

5. The method of any one of claims 2 to 4, wherein nicotinamide of claim 2 i) and/or ii) is used in a concentration of at least 5 mM, preferably wherein nicotinamide of claim 2 i) and/or ii) is used in a concentration of about 10 mM.

6. The method of any one of claims 2 to 5, wherein LDN-193189 of claim 2 i) and/or ii) is used in a concentration of at least 0.1 µM, preferably wherein LDN-193189 of claim 2 i) is used in a concentration of about 1 µM and/or wherein LDN-193189 of claim 2 ii) is used in a concentration of about 0.2 µM.

7. The method of any one of claims 2 to 6, wherein b-FGF of claim 2 ii) is used in a concentration of at least 2.5 ng/ml, preferably wherein b-FGF of claim 2 ii) is used in a concentration of about 5 ng/ml.

8. The method of any one of claims 2 to 7, wherein Activin A of claim 2 iii), iv) and/or v) is used in a concentration of at least 50 ng/ml, preferably wherein Activin A of claim 2 iii), iv) and/or v) is used in a concentration of about 100 ng/ml.

9. The method of any one of claims 2 to 8, wherein SU5402 of claim 2 iv) and/or v) is used in a concentration of at least 5 µM, preferably wherein SU5402 of claim 2 iv) and/or v) is used in a concentration of about 10 µM.

10. The method of any one of claims 2 to 8, wherein PD173074 of claim 2 iv) and/or v) is used in a concentration of at least 0.5 µM, preferably wherein PD173074 of claim 2 iv) and/or v) is used in a concentration of about 1 µM.

11. The method of any one of claims 2 to 10, wherein CHIR99021 of claim 2 v) is used in a concentration of at least 1 µM and less than 3 µM for culturing the cell, preferably culturing the cell for about 3 consecutive culture days.

12. The method of any one of claims 2 to 11, wherein culturing the iPS cell comprises culturing for about 2 days in the first differentiation medium, subsequently culturing for about 2 days in the second differentiation medium, subsequently culturing for about 2 days in the third differentiation medium, subsequently culturing for about 2 days in the fourth differentiation medium, and subsequently culturing for about 8 days in the fifth differentiation medium.

13. The method of any one of claims 2 to 12, wherein LDN-193189 is used for at least 2 culture days.

14. The method of any one of claims 2 to 13, wherein DKK1 is used for at least 2 culture days.

15. The method of any one of claims 2 to 14, wherein SU5402 or PD173074 is used for about 10 culture days.

16. The method of any one of claims 2 to 15, wherein CHIR99021 is used for about 8 culture days.

17. The method of any one of claims 1 to 16, wherein the method further comprises culturing the RPE cell in a retinal pigment epithelial maintenance (RPEM) medium.

18. The method of claim 17, wherein the RPEM medium further comprises about 2 % heat-inactivated fetal bovine serum (FBS), 1x Glutamax, about 0.25 mg/mL taurine, about 0.02

μg/mL hydrocortisone, about 0.013 ng/mL 3,3′,5-Triiodo-L-thyronine, 1x penicillin/streptomycin, about 10 mM nicotinamide and 1x sodium pyruvate.

19. The method of any one of claims 17 to 18, wherein culturing the iPS cell in the differentiation medium and culturing the RPE cell in the RPEM medium comprises 20 to 50 days, preferably 30 to 35 days, most preferably about 35 days.

20. The method of any one of the preceding claims, wherein the iPS cell is generated by expressing exogenous nucleic acids encoding proteins OCT3/4, SOX2, KLF4, LIN28 and L-MYC and p53-shRNA in the stem cell of the amniotic membrane of the umbilical cord under conditions suitable to reprogram the stem cell.

21. A retinal pigment epithelial (RPE) cell culture obtainable by the method as defined in any of claims 1 to 20.

22. A pharmaceutical composition comprising a retinal pigment epithelial (RPE) cell culture obtained by the method as defined in any of claims 1 to 20.

23. Use of a retinal pigment epithelial (RPE) cell differentiated from an induced pluripotent stem (iPS) cell by the method as defined in any of claims 1 to 20 in the preparation of a medicament for the treatment of a retinal degenerative disease in a subject.

24. An *in vivo* method of detecting the survival rate of a retinal pigment epithelial (RPE) cell differentiated from an induced pluripotent stem (iPS) cell by the method as defined in any of claims 1 to 20 in a subject, the method comprising:

a) after a RPE cell has been introduced into a subject, detecting the bioluminescence signal of said RPE cell comprising a bioluminescence label over time using an imaging method, thereby collecting imaging data, wherein the RPE cell is differentiated from an iPS cell by the method as defined in any of claims 1 to 20;

b) comparing the imaging data received in step a) to reference imaging data including bioluminescence signals of RPE cells being differentiated from an ES cell and/or differentiated from a skin iPS,
wherein no difference in the bioluminescence signal in the imaging data from said subject as compared to said reference imaging data indicates survival of said RPE cell in said subject.

25. An *in vitro* method of determining the immunogenicity of a retinal pigment epithelial (RPE) cell differentiated from an induced pluripotent stem (iPS) cell by the method as defined in any of claims 1 to 20 in a subject, to whom said differentiated RPE cell has been pre-delivered, the method comprising:

a) detecting a pro-inflammatory cytokine level using an imaging method in a sample obtained from said subject, the sample comprising said differentiated RPE cell, thereby collecting imaging data;

b) comparing the imaging data received in step a) to reference imaging data including detected pro-inflammatory cytokine level within a sample from a subject to whom RPE cell differentiated from an ES cell and/or differentiated from a skin iPS as reference cell has been pre-delivered,

wherein a decreased cytokine level in the imaging data as compared to said reference imaging data indicates a reduced immunogenicity of said RPE cell in said subject.