Claims

1. A method for producing a retinal pigment epithelial cell, comprising
(1) a first step of subjecting pluripotent stem cells to floating culture in a serum-free medium to form an aggregate of pluripotent stem cells,
(2) a second step of subjecting the aggregate formed in step (1) to floating culture in a serum-free medium or serum-containing medium each being free of a substance that can enhance signal transduction mediated by Sonic hedgehog signal transduction pathway and containing a substance that can enhance signal transduction pathway mediated by BMP, thereby obtaining an aggregate containing retinal progenitor cells, and
(3) a third step of subjecting the aggregate obtained in step (2) to floating culture in a serum-free medium or serum-containing medium each being free of a substance that can enhance signal transduction pathway mediated by Sonic hedgehog and a substance that can enhance signal transduction pathway mediated by BMP and containing a substance that can enhance signal transduction mediated by Wnt, thereby obtaining an aggregate containing retinal pigment epithelial cell.

2. A method for producing a retinal pigment epithelial cell sheet, comprising
(1) a first step of subjecting pluripotent stem cells to floating culture in a serum-free medium to form an aggregate of pluripotent stem cells,
(2) a second step of subjecting the aggregate formed in step (1) to floating culture in a serum-free medium or serum-containing medium each being free of a substance that can enhance signal transduction pathway mediated by Sonic hedgehog and containing a substance that can enhance signal transduction pathway mediated by BMP, thereby obtaining an aggregate containing retinal progenitor cells,

(3) a third step of subjecting the aggregate obtained in step (2) to floating culture in a serum-free medium or serum-containing medium each being free of a substance that can enhance signal transduction pathway mediated by Sonic hedgehog and a substance that can enhance signal transduction pathway mediated by BMP and containing a substance that can enhance signal transduction mediated by Wnt, thereby obtaining an aggregate containing retinal pigment epithelial cell, and
(4) a fourth step of dispersing the aggregate obtained in step (3) and subjecting the resulting cells to adhesion culture.

3. The production method according to claim 2, wherein the adhesion culture is performed in the presence of a serum replacement in said step (4).

4. The production method according to claim 2 or 3, wherein the adhesion culture is performed in the presence of a ROCK inhibitory substance, in said step (4).

5. The production method according to any one of claims 2 to 4, wherein the adhesion culture is performed in a serum-free medium or serum-containing medium further comprising one or more substances selected from the group consisting of a substance that can enhance signal transduction mediated by Wnt, a substance inhibiting the FGF signal pathway, a substance capable of enhancing a signal mediated by Activin and a substance that can enhance signal transduction pathway mediated by BMP, in said step (4).

6. The production method according to any one of claims 2 to 5, wherein the adhesion culture is performed on a culture vessel material having a surface treated with a culture substrate, in said step (4).

7. The production method according to claim 6, wherein said culture substrate is a synthetic culture substrate.

8. The production method according to claim 6, wherein said culture substrate is laminin.

9. The production method according to any one of claims 1 to 8, wherein the pluripotent stem cells are primate pluripotent stem cells.

10. The production method according to any one of claims 1 to 9, wherein the pluripotent stem cells are human pluripotent stem cells.

11. The method according to any one of claims 1 to 10, wherein the step (1) and step (2) are performed in the presence of a serum replacement.

12. The method according to any one of claims 1 to 11, wherein the floating culture is performed in the absence of a basement membrane preparation.

13. The method according to any one of claims 1 to 12, wherein the substance that can enhance signal transduction pathway mediated by BMP is one or more proteins selected from the group consisting of BMP2, BMP4, BMP7 and GDF7.

14. The method according to any one of claims 1 to 13, wherein the serum-free medium or serum-containing medium each being free of a substance that can enhance signal transduction pathway mediated by Sonic hedgehog and a substance that can enhance signal transduction pathway mediated by BMP and containing a substance that can enhance signal transduction mediated by Wnt in step (2) further comprises a substance inhibiting the FGF signal pathway.

15. A method of evaluating toxicity or drug efficacy of a test substance, comprising producing a retinal pigment epithelial cell or retinal pigment epithelial cell sheet by the method according to any one of claims 1 to 14, and bringing the retinal pigment epithelial cell or the retinal pigment epithelial cell sheet into contact with the test substance, and examining the influence of the substance on the cell or cell sheet.

16. Use of a retinal pigment epithelial cell or retinal pigment epithelial cell sheet produced by the method according to any one of claims 1 to 14 in the manufacture of a medicament for treating a disease due to a disorder of a retinal tissue, wherein an effective amount of the retinal pigment epithelial cell or retinal pigment epithelial cell sheet is to be transplanted to a subject in need of the transplantation, wherein the disease due to a disorder of a retinal tissue is organic mercury poisoning, chloroquine retinopathy, retinitis pigmentosa, age-related macular degeneration, glaucoma, diabetic retinopathy or neonatal retinopathy.

17. A retinal pigment epithelial cell or a retinal pigment epithelial cell sheet produced by the method according to any one of claims 1 to 14, for use in the treatment of a disease due to a disorder of a retinal tissue, wherein the disease due to a disorder of a retinal tissue is organic mercury poisoning, chloroquine retinopathy, retinitis pigmentosa, age-related macular degeneration, glaucoma, diabetic retinopathy or neonatal retinopathy.