Claims

1. A method of producing a human cell aggregate comprising (i) adenohypophysis or
(ii) a precursor tissue comprising hypophysial precode and/or Rathke's pouch,
which comprises culturing an aggregate of human pluripotent stem cells in suspension in a medium containing a bone morphogenetic protein signal transduction pathway activating substance and a substance activating or enhancing the Shh signal pathway.

2. The production method according to claim 1, comprising culturing an aggregate of human pluripotent stem cells in suspension in a medium containing a bone morphogenetic protein signal transduction pathway activating substance and a substance activating or enhancing the Shh signal pathway to obtain a human cell aggregate comprising a hypothalamus neuroepithelial tissue and a surface ectoderm, and further culturing the obtained human cell aggregate comprising the hypothalamus neuroepithelial tissue and the surface ectoderm in suspension in a medium containing a bone morphogenetic protein signal transduction pathway activating substance and a substance activating or enhancing the Shh signal pathway to induce formation of hypophysial placode and/or Rathke's pouch in the surface ectoderm, thereby obtaining a human cell aggregate comprising 1) hypothalamus neuroepithelial tissue, and 2) hypophysial placode and/or Rathke's pouch.

3. The production method according to claim 2, wherein the medium used for the further culturing in suspension further comprises FGF2.

4. The production method according to claim 2 or 3, which comprises further culturing the human cell aggregate comprising

1) hypothalamus neuroepithelial tissue, and 2) hypophysial placode and/or Rathke's pouch in suspension in a medium comprising a substance activating or enhancing the Shh signal pathway to induce differentiation of hypophysial placode and/or Rathke's pouch into pituitary hormone-producing cells, thereby obtaining a human cell aggregate comprising adenohypophysis.

5. The production method according to claim 4, wherein the medium used for the further culturing in suspension further comprises FGF2.

6. The production method according to claim 4 or 5, wherein the medium used for the further culturing in suspension further comprises a Notch signal inhibitor.

7. The production method according to claim 6, wherein the Notch signal inhibitor is DAPT.

8. The production method according to any one of claims 4 to 7, wherein the pituitary hormone-producing cell is at least one selected from the group consisting of growth hormone (GH)-producing cell, prolactin (PRL)-producing cell, and adrenocorticotropic hormone (ACTH)-producing cell.

9. The production method according to any one of claims 1 to 8, wherein the bone morphogenetic protein signal transduction pathway activating substance is BMP4.

10. The production method according to any one of claims 1 to 9, wherein the substance activating or enhancing the Shh signal pathway is SAG.

11. The production method according to any one of claims 1 to 10, wherein the hypothalamus neuroepithelial tissue is a ventral hypothalamus neuroepithelial tissue.

12. The production method according to any one of claims 1 to 11, wherein the pluripotent stem cells are embryonic stem cells or induced pluripotent stem cells.

13. The production method according to any one of claims 1 to 12, wherein the culturing in suspension is performed in the absence of feeder cells.

14. A cell aggregate obtainable by the production method according to any one of claims 1 to 13.