

CLAIMS

1. A tissue structure obtained by co-culturing a hepatic endoderm cell derived from a fetal stem cell and a hepatic endoderm cell derived from an induced pluripotent stem cell with a vascular cell and a mesenchymal cell,

wherein a value obtained by assay of a plurality of functions using a Pearson product-moment correlation coefficient is closer to a value of a cell or biological tissue sampled from an adult than a value of a cell or biological tissue sampled from a fetus,

the tissue structure has a spheroid shape and a diameter of the spheroid is in a range from 50 μm to 2 mm,

the plurality of functions are a gene expression level of a gene selected from 61 genes in which the Variation Factors in Table 2-1 and Table 2-2 disclosed in the specification are x2, and

the 61 genes contains 49 genes in which the Variation Factors in Table 2-1 and Table 2-2 disclosed in the specification are x10.

2. The tissue structure according to Claim 1, wherein

the gene expression level is a value obtained by an analysis using a DNA chip on which all gene segments are immobilized.

3. The tissue structure according to Claim 1 or 2, wherein the plurality of functions are functions specific to a liver.

4. A method of preparing a tissue structure, comprising:

preparing a cultured form by co-culturing a hepatic endoderm cell derived from a fetal stem cell and a hepatic endoderm cell derived from an induced pluripotent stem cell with a vascular cell and a mesenchymal cell;

performing an assay of a plurality of functions of the cultured form by using a Pearson product-moment correlation coefficient; and

picking, as a tissue structure, a cultured form in which a value obtained by the assay is closer to a value of a cell or biological tissue sampled from an adult than a value of a cell or biological tissue sampled from a fetus, wherein

the co-culturing is performed using a microchamber having an equivalent diameter in a range from 20 μm to 2.5 mm and a depth in a range from 20 μm to 1000 μm ,

the microchamber is formed of a bottom portion and an opening,

the opening is defined by a wall that surrounds an area from a boundary between the opening and the bottom portion to an end of the opening, the wall having a taper angle in a range from 1 to 20 degrees,

the bottom portion has one of a hemispherical shape and a truncated cone shape,

the plurality of functions are a gene expression level of a gene selected from 61 genes in which the Variation Factors in Table 2-1 and Table 2-2 disclosed in the specification are x2, and the 61 genes contains 49 genes in which the Variation Factors in Table 2-1 and Table 2-2 disclosed in the specification are x10.

5. The method of preparing a tissue structure according to Claim 4, wherein the gene expression levels are analyzed using a DNA chip on which all gene segments are immobilized.

6. The method of preparing a tissue structure according to Claim 4 or 5, wherein the co-culture step comprises the steps of: forming an aggregate; forming an organ bud; and further culturing the organ bud for maturation.

7. The method of preparing a tissue structure according to Claim 6, wherein in the steps of forming an aggregate, forming an organ bud, and further culturing the organ bud for maturation, cells are combined to form an aggregate.

8. The method of preparing a tissue structure according to Claim 6 or 7, wherein in the steps of forming an aggregate, forming an organ bud, and further culturing the organ bud for maturation, cells are combined to form a cluster having a spheroid shape.

9. The method of preparing a tissue structure according to Claim 8, wherein a spheroid formed by the cells has a diameter in a range from 50 μm to 2 mm.

10. The method of preparing a tissue structure according to any one of Claims 4 to 9, wherein the hepatic endoderm cell is a cell derived from an induced pluripotent stem cell.

11. The method of preparing a tissue structure according to any one of Claims 4 to 10, wherein the plurality of functions are functions specific to a liver.

12. The method of preparing a tissue structure according to any one of Claims 4 to 11, wherein the tissue structure is cultured using a culture chamber having a culture surface which is a cell non-adhesive surface.

5 13. The method of preparing a tissue structure according to Claim 12, wherein the culture surface of the culture chamber is coated with a polymer selected from the group consisting of a phospholipid, a phospholipid-polymer complex, poly(2-hydroxyethyl methacrylate) (PHEMA), polyvinyl alcohol, agarose, chitosan, polyethyleneglycol, and albumin, or a combination thereof, the culture surface being a surface in contact with cells.

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14. The method of preparing a tissue structure according to any one of Claims 4 to 13, wherein a vascular cell: a hepatic endoderm cell : and a mesenchymal cell are co-cultured at a ratio of 10:7-10:1-2, and the cells are seeded at a density of 20 to 2000 cells per microchamber.

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