Solution to Problem

[0020] The present inventors have obtained a surprising finding where when a lipid (in particular, a phospholipid) is added to a liquid culture medium and cells are cultured in suspension in the medium, a large amount of population of cell aggregates with an appropriate size can be produced. Based on this finding, the present inventors have completed the present invention. The present invention does not rely on mechanical/physical means, i.e., modifying culturing conditions, such as the viscosity of a culture medium, shear stress due to stirring, or the shape of cultureware such as a microwell plate. The present invention uses biochemical/chemical means, i.e., modifying the composition of a culture medium by using a substance present *in vivo*. In one aspect, the present invention refers to a method for producing cell aggregates, comprising a step of culturing cells while suspended in a liquid culture medium comprising a lysophospholipid. In another aspect, the present invention refers to the use of a lysophospholipid for inhibition of cell aggregation. In still another aspect, the present invention refers to a composition comprising a lysophospholipid, wherein the composition is a liquid culture medium or a composition added to a liquid culture medium. Also disclosed herein are the following examples.

(1) A method for producing cell aggregates, comprising a step of culturing cells while suspended in a liquid culture medium comprising a lysophospholipid. The step involves culturing cells while suspended in a liquid culture medium containing a lysophospholipid, so that an increase in the size of the cell aggregates in the culture is controlled. (2) The method according to item (1), wherein the liquid culture medium comprises the lysophospholipid in an amount of more than 0.0064 μg/mL and 100 μg/mL or less. (3) The method according to item (1) or (2), further comprising at least one of a step of adding the lysophospholipid to prepare the liquid culture medium and a step of generating the lysophospholipid through an enzymatic reaction to prepare the liquid culture medium. (4) The method according to any one of items (1) to (3), wherein the cells are cells isolated after undergoing adherent or suspension culture. (5) The method according to any one of items (1) to (4), wherein the lysophospholipid is at least one of lysophosphatidic acid and sphingosine-1-phosphoric acid.

(6) The method according to any one of items (1) to (5), wherein the liquid culture medium comprises at least one selected from the group consisting of L-ascorbic acid, insulin, transferrin, selenium, and sodium bicarbonate.

CLAIMS

[Claim 1]

A method for producing cell aggregates, comprising a step of culturing cells while suspended in a liquid culture medium comprising a lysophospholipid.

[Claim 2]

The method according to claim 1, wherein the liquid culture medium comprises the lysophospholipid in an amount of more than 0.0064 μg/mL and 100 μg/mL or less.

[Claim 3]

The method according to claim 1 or 2, further comprising at least one of a step of adding the lysophospholipid to prepare the liquid culture medium and a step of generating the lysophospholipid through an enzymatic reaction to prepare the liquid culture medium.

[Claim 4]

The method according to any one of claims 1 o 3, wherein the cells are cells isolated after undergoing adherent or suspension culture.

[Claim 5]

The method according to any one of claims 1 to 4, wherein the lysophospholipid is at least one of lysophosphatidic acid and sphingosine-1-phosphoric acid.

[Claim 6]

The method according to any one of claims 1 to 5, wherein the liquid culture medium comprises at least one selected from the group consisting of L-ascorbic acid, insulin, transferrin, selenium, and sodium bicarbonate.

[Claim 7]

The method according to any one of claims 1 to 6, wherein the liquid culture medium comprises a growth factor.

[Claim 8]

The method according to claim 7, wherein the growth factor is at least one of FGF2 and TGF-β1.

[Claim 9]

The method according to any one of claims 1 to 8, wherein the liquid culture medium comprises a ROCK inhibitor.

[Claim 10]

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

[Claim 11]

Use of a lysophospholipid for inhibition of cell aggregation.

[Claim 12]

The use according to claim 11, wherein the lysophospholipid is present in a concentration of more than 0.0064 μg/mL and 100 μg/mL or less.

[Claim 13]

The use according to claim 11 or 12, wherein the lysophospholipid is used in combination with a growth factor.

[Claim 14]

The use according to claim 13, wherein the growth factor is at least one of FGF2 and TGF-β1.

[Claim 15]

The use according to any one of claims 11 to 14, wherein the lysophospholipid is used in combination with a ROCK inhibitor.

[Claim 16]

The use according to any one of claims 11 to 15, wherein the lysophospholipid is at least one of lysophosphatidic acid and sphingosine-1-phosphoric acid.

[Claim 17]

A composition comprising a lysophospholipid, wherein the composition is a liquid culture medium or a composition added to a liquid culture medium.