specific cells. Specifically, there is a need to construct a system for inducing differentiation.

Furthermore, iPS cells (induced pluripotent stem cells) (see Patent document 1, Patent document 2, Non-patent document 3, and the like) have been reported as adult-derived pluripotent stem cells. However, establishment of iPS cells requires an induction operation using a specific substance, such as introduction of a specific gene into a dermal fibroblast fraction (dermal fibroblast) that is a mesenchymal cell population or introduction of a specific compound into somatic cells.

Patent document 1 JP Patent No. 4183742

Patent document 2 JP Patent Publication (Kokai) No. 2008-307007 A

Non-patent document 1 M. DEZAWA et al., The Journal of Clinical Investigation, 113, 12, pp. 1701-1710, (2004)

Non-patent document 2 M. DEZAWA et al., SCIENCE, 2005 July 8, 309, pp. 314-317, (2005)

Non-patent document 3 Okita K. et al. SCIENCE, 2008 Nov 7, 322 (5903), pp.949-953

SUMMARY ~~OF THE INVENTION~~

An object of the disclosure~~present invention~~ is to provide a method for directly obtaining pluripotent stem cells from body tissue and pluripotent stem cells obtained by the method.

The present inventors have discovered that in the research process concerning bone marrow stromal cell (MSC: bone marrow stromal cell) fractions, characteristic cell clusters are formed at extremely low frequency from untreated (naive) human MSC cells. The appearance of initial cell clusters closely resembles that of ES cells. However, the cell clusters do not undergo infinite growth, unlike ES cells. They stop growth when they reach a size within a certain period and then they form heterogeneous populations containing various cells such as hair cells and pigment cells. Also, immunocytochemistry was performed for such cell clusters, so that different cells

cells can also be isolated from body tissue using SSEA-3 expression as an marker.

The present inventors have also discovered that the above pluripotent stem cells are novel type of pluripotent stem cells that differ from conventionally reported pluripotent stem cells such as ES cells and iPS cells. Specifically, the present inventors have discovered that the pluripotent stem cells can be directly obtained from body tissue without any induction operation. Thus, the present inventors have completed the disclosure~~present invention~~. The present inventors have designated the pluripotent stem cells Muse cells (Multilineage-differentiating Stress Enduring cells).

In a first aspect, the present invention refers to a SSEA-3 (+) pluripotent stem cell, which is negative for CD117 and negative for CD146 and is isolated from body tissue.

In a second aspect, the present invention refers to a cell cluster or a cell fraction, which contains the pluripotent stem cell as defined above.

In a third aspect, the present invention refers to a method for isolating a pluripotent stem cell or a pluripotent cell fraction from body tissue, which uses at least one of the following properties (i) to (vi) as an index: (i) being positive for SSEA-3; (ii) being positive for CD105; (iii) being negative for CD117 and negative for CD146; (iv) being negative for CD117, negative for CD146, negative for NG2, negative for CD34, negative for vWF, and negative for CD271; (v) being negative for CD34, negative for CD117, negative for CD146, negative for CD271, negative for NG2, negative for vWF, negative for Sox10, negative for Snail, negative for Slug, negative for Tyrp1, and negative for Dct; and (vi) having low or no telomerase activity.

In a fourth aspect, the present invention refers to a method for enriching a pluripotent stem cell as defined above, which comprises exposing body tissue-derived cells or mesenchymal culture cells to cellular stress and then collecting surviving cells.

In a fifth aspect, the present invention refers to a pluripotent stem cell, which is a cell derived or induced from the pluripotent stem cell as defined above.

In a sixth aspect, the present invention refers to a differentiated cell, which is a cell derived or induced from the pluripotent stem cell as defined above.

In a seventh aspect, the present invention refers to a pharmaceutical composition, which comprises the pluripotent stem cell as defined above.

In an eighth aspect, the present invention refers to a pharmaceutical composition, which comprises the pluripotent stem cell as defined above.

The ~~present invention is as follows.~~disclosure further describes the following.

[1] A SSEA-3-positive pluripotent stem cell, which can be isolated from body tissue.

The pluripotent stem cells can be isolated from a culture product of body tissue such as cultured fibroblasts and myeloid stem cells and can also be isolated in the form of single cells.

[2] The pluripotent stem cell according to [1], which is positive for CD105.

[3] The pluripotent stem cell according to [1] or [2], which is negative for CD117 (c-Kit) and negative for CD146.

[4] The pluripotent stem cell according to [1] or [2], which is negative for CD117, negative for CD146, negative for NG2, negative for CD34, negative for vWF, and negative for CD271.

[5] The pluripotent stem cell according to [1] or [2], which is negative for CD34, negative for CD117, negative for CD146, negative for CD271, negative for NG2, negative for vWF, negative for Sox10, negative for Snail, negative for Slug, negative for Tyrp1, and negative for Dct.

[6] The pluripotent stem cell according to any one of [1] to [5], which has low or no telomerase activity.

[7] The pluripotent stem cell according to any one of [1] to [6], which is capable of differentiating into the three germ layers.

The pluripotent stem cells of the present invention are capable of differentiating into the three germ layers through *in vitro* adherent culture. Specifically, the

pluripotent stem cells can differentiate into cells representative of the three germ layers, skin, liver, nerve, muscle, bone, fat, and the like through *in vitro* induction culture. Also, the pluripotent stem cells are capable of differentiating into cells characteristic of the three germ layers when transplanted *in vivo* into the testis. Furthermore, the pluripotent stem cells are capable of surviving and differentiating into organs (e.g., skin, spinal cord, liver, and muscle) when transplanted to the damaged organs via intravenous injection into a living body.

[8] The pluripotent stem cell according to any one of [1] to [7], which does not undergo neoplastic proliferation.

The pluripotent stem cells of the disclosure~~present invention~~ have a property such that they grow at a growth rate of about 1.3 days/cell division by suspension culture but stop the growth within about 10 days and also have a property such that when transplanted into the testis, they do not become cancerous for at least a half year.

[9] The pluripotent stem cell according to any one of [1] to [8], which has self-renewal capability.

The pluripotent stem cells of the disclosure~~present invention~~ can be grown through repetition of suspension culture and adherent culture. Also, the pluripotent stem cells disclosed herein~~of the present invention~~ undergo asymmetric division as in the case of other somatic stem cells.

[10] The pluripotent stem cell according to any one of [1] to [9], which is resistant to stress.

[11] The pluripotent stem cell according to any one of [1] to [10], which has high phagocytic ability.

[12] The pluripotent stem cell according to any one of [1] to [11], which is positive for at least one of the 22 following odorant receptors:

olfactory receptor, family 8, subfamily G, member 2 (OR8G2);

olfactory receptor, family 7, subfamily G, member 3 (OR7G3);

olfactory receptor, family 4, subfamily D, member 5 (OR4D5);

olfactory receptor, family 5, subfamily AP, member 2 (OR5AP2);

to any one of [1] to [14].

[16] A method for isolating a pluripotent stem cell or a pluripotent cell fraction from body tissue, which uses at least one of the following properties (i) to (vi) as an index:

(i) being positive for SSEA-3;

(ii) being positive for CD105;

(iii) being negative for CD117 and negative for CD146;

(iv) being negative for CD117, negative for CD146, negative for NG2, negative for CD34, negative for vWF, and negative for CD271;

(v) being negative for CD34, negative for CD117, negative for CD146, negative for CD271, negative for NG2, negative for vWF, negative for Sox10, negative for Snail, negative for Slug, negative for Tyrp1, and negative for Dct; and

(vi) having low or no telomerase activity.

[17] A method for isolating a pluripotent stem cell or a pluripotent cell fraction, which comprises exposing body tissue-derived cells to cellular stress and then collecting surviving cells.

[18] The method for isolating a pluripotent stem cell or a pluripotent cell fraction according to [17], wherein cellular stress is selected from among protease treatment, culture under low-oxygen conditions, culture under low phosphate conditions, culture under serum starvation conditions, culture in a sugar starvation state, culture under exposure to radiation, culture under exposure to heat shock, culture in the presence of a toxic substance, culture in the presence of active oxygen, culture under mechanical stimulation, and culture under pressure treatment.

[19] The method for isolating a pluripotent stem cell or a pluripotent cell fraction according to [18], wherein the cellular stress is trypsin incubation.

[20] A pluripotent stem cell, which is a cell derived or induced from the pluripotent stem cell according to any one of [1] to [14].

Examples of the derived cell or the induced cell include cells induced by gene transfer or addition of a compound. Another example thereof is an iPS cell from the stem cell of the disclosure~~present invention~~.