NON-PATENT DOCUMENTS

[0011]

Non-patent Document 1: Homepage for research groups on rare intractable skin diseases (http://kinan.info/)

Non-patent Document 2: Tamai K. J Natl Inst Public Health 2011; 60: 118-124.

Non-patent Document 3: Chino T et al. Am J Pathol 2008; 173: 803-814.

Non-patent Document 4: Tamai K et al. Proc Natl Acad Sci USA 2011; 108: 6609-6614.

Non-patent Document 5: Wagner JE et al. N Engl J Med 2010; 363: 629-639.

Non-patent Document 6: Conget P et al. Cytotherapy 2010; 12: 429-431.

Non-patent Document 7: Petrof G et al. J Invest Dermatol 2015; 135: 2319-2321.

Non-patent Document 8: El-Darouti M et al. Dermatol Ther 2016; 29: 96-100.

Non-patent Document 9: Kuroda Y et al. Proc Natl Acad Sci USA 2010; 107: 8639-8643.

Non-patent Document 10: Wakao S et al. Proc Natl Acad Sci USA 2011; 108: 9875-9880.

Non-patent Document 11: Kuroda Y et al. Nat Protc 2013; 8: 1391-1415.

SUMMARY

[0012]

An object of the present disclosure is to provide a cell product for treatment of skin diseases such as epidermolysis bullosa.

[0013]

The present inventors found that administration of human Muse cells to a mouse having experimentally injured skin via its blood vessel leads to expression of human collagen at the wound site, which facilitates wound repair. The present inventors also found that after blister formation in the epidermis of a collagen type XVII (COL17) gene-deficient mouse model of epidermolysis bullosa, administration of human Muse cells via its blood vessel or the like can provide human collagen type XVII to the epidermis, meaning that Muse cells can be used in treatment of epidermolysis bullosa. The present inventors further found that skin cells that are effective in treatment of skin diseases, such as keratinocytes and fibroblasts, can be obtained from Muse cells, thereby completed the present disclosure.

[0014]

Accordingly, the present disclosure provides the following [1] to [11]:

[1] A cell product for treatment of epidermolysis bullosa, comprising a SSEA-3-positive pluripotent stem cell derived from a mesenchymal tissue in a living body or a cultured mesenchymal cell;

[2] The cell product of item [1], wherein said epidermolysis bullosa is epidermolysis bullosa simplex;

[3] The cell product of item [1], wherein said epidermolysis bullosa is junctional epidermolysis bullosa;

[4] The cell product of item [1], wherein said epidermolysis bullosa is dystrophic epidermolysis bullosa;

[5] The cell product of item [4], wherein said dystrophic epidermolysis bullosa is dominant dystrophic epidermolysis bullosa or recessive dystrophic epidermolysis bullosa;

[6] The cell product of any one of items [1] to [5], wherein said pluripotent stem cell is one having all of the following characteristics:

(i) having low or no telomerase activity;

(ii) capable of differentiating into any of tridermic cells;

(iii) showing no neoplastic proliferation; and

(iv) having self-renewal capacities;

[7] The cell product of any one of items [1] to [5], wherein said pluripotent stem cell is one having all of the following characteristics:

(i) SSEA-3 positive;

(ii) CD105 positive;

(iii) having low or no telomerase activity;

(iv) capable of differentiating into any of tridermic cells;

(v) showing no neoplastic proliferation; and

(vi) having self-renewal capacities;

[8] A skin cell differentiated from a SSEA-3-positive pluripotent stem cell derived from a mesenchymal tissue in a living body or a cultured mesenchymal cell;

[9] The skin cell of item [8], wherein said skin cell is a keratinocyte and/or a fibroblast;

[10] A cell product for treatment of a skin disease, comprising the skin cell of item [8] or [9];

[11] The cell product of item [10], wherein said skin disease is epidermolysis bullosa;

[12] A method for treating epidermolysis bullosa, comprising a step of administering an effective dose of the cell product of any one of items [1] to [6] to a patient in need thereof.

[0014a]

In one aspect, the present invention provides a use of a SSEA-3-positive pluripotent stem cell derived from a mesenchymal tissue in a living body or a cultured mesenchymal cell in the manufacture of a cell product for treatment of epidermolysis bullosa.

[0014b]

In one aspect, the present invention provides a skin cell as described herein for use in therapy.

[0014c]

In another aspect, the present invention provides a use of the skin cell as described herein in the manufacture of a cell product for treatment of a skin disease.

[0015]

According to the present disclosure, Muse cells can be administered to a patient with epidermolysis bullosa via a blood vessel or the like, or directly to its skin site forming a blister or erosion and its periphery, to reconstruct and repair the damaged skin, thereby ameliorating or healing the skin symptoms. Thus, the cell product comprising Muse cells of the present disclosure can be used for treatment of epidermolysis bullosa.

[0016]

Since Muse cells can efficiently migrate and engraft to a skin site forming a blister or erosion, and then spontaneously differentiate into epidermal cells at the engraftment site, they do not require differentiation induction into cells to be treated prior to transplantation. In addition, Muse cells are non-tumorigenic and excellent in safety. Furthermore, since Muse cells does not induce any immune rejection, treatment with allogenic preparations produced from donors is also possible. Therefore, Muse cells having the excellent characteristics as described above can provide easy and viable means for treatment of patients with epidermolysis bullosa.

[0017]

According to the present disclosure, skin cells differentiated from Muse cells, such as keratinocytes or fibroblasts, can be administered to a site affected by a skin disease and its periphery of a patient with the skin disease such as epidermolysis bullosa to reconstruct and repair the damaged skin, thereby ameliorating or healing the skin symptoms. Thus, the cell product comprising skin cells differentiated from Muse cells of the present disclosure can be used for treatment of skin diseases such as epidermolysis bullosa.

CLAIMS

1. Use of a SSEA-3-positive pluripotent stem cell derived from a mesenchymal tissue in a living body or a cultured mesenchymal cell in the manufacture of a cell product for treatment of epidermolysis bullosa.

2. The use of claim 1, wherein said epidermolysis bullosa is epidermolysis bullosa simplex.

3. The use of claim 1, wherein said epidermolysis bullosa is junctional epidermolysis bullosa.

4. The use of claim 1, wherein said epidermolysis bullosa is dystrophic epidermolysis bullosa.

5. The use of claim 4, wherein said dystrophic epidermolysis bullosa is dominant dystrophic epidermolysis bullosa or recessive dystrophic epidermolysis bullosa.

6. The use of any one of claims 1 to 5, wherein said pluripotent stem cell has all of the following characteristics:

(i) having low or no telomerase activity;

(ii) capable of differentiating into any of tridermic cells;

(iii) showing no neoplastic proliferation; and

(iv) having self-renewal capacities.

7. The use of any one of claims 1 to 5, wherein said pluripotent stem cell has all of the following characteristics:

(i) SSEA-3 positive;

(ii) CD105 positive;

(iii) having low or no telomerase activity;

(iv) capable of differentiating into any of tridermic cells;

(v) showing no neoplastic proliferation; and

(vi) having self-renewal capacities.

8. A skin cell differentiated from a SSEA-3-positive pluripotent stem cell derived from a mesenchymal tissue in a living body or a cultured mesenchymal cell.

9. The skin cell of claim 8, wherein said skin cell is a keratinocyte and/or a fibroblast.

10. The skin cell of claim 8 or 9 for use in therapy.

11. Use of the skin cell of claim 8 or 9 in the manufacture of a cell product for treatment of a skin disease.

12. The use of claim 11, wherein said skin disease is epidermolysis bullosa.