K14-H2BGFP mice, studies have identified detailed genetic signature of prospectively isolated mouse DP cells [7] and identified Wnt, BMP and FGF singling pathway as a requirement for murine DP maintenance and function [8,9,10]. DP cells play a role in hair growth and cycling [6] and determine hair size and hair type [11,12]. It has been long recognized that DP cells are able to induce hair follicle formation not only in embryogenesis but also postnatal. Vibrissae DP cells induced *de novo* hair formation when transplanted into the footpad of the adult rat, which is normally a non-haired skin area [13]. Human DP cells isolated from scalp skin contribute to hair formation when transplanted into rodents [14,15] and induce keratinocytes morphogenesis in cultures [16].

[0005] DP cells have been proposed as a cell-based treatment for hair loss diseases. However, human DP cells are not suitable for this purpose because they cannot be obtained in necessary amounts and rapidly lose their ability to induce hair follicle formation when cultured [7,8,17,18]. Therefore, there is an unmet need to develop functional DP cells capable of inducing a robust hair growth.

SUMMARY

[0006] Some examples of the methods and compositions provided herein include a method for inducing hair growth in a subject comprising administering a population of induced dermal papillae cells to the subject. Some examples also include obtaining the population of induced dermal papillae cells. In some examples, the population of induced dermal papillae cells comprises a marker selected from the group consisting of P-75, nestin, veriscan, smooth muscle actin, alkaline phosphatase, and vimentin.

[0007] In some examples, the population of induced dermal papillae cells is generated from a population of induced neural crest cells. Some examples also include selecting for adherent cells. In some examples, the population of induced neural crest cells comprises a marker selected from the group consisting of Sox10, Foxd3, integrin alpha 4, cognate receptor for fibronectin, CD47, CD184, CD44, P-75, and nestin. In some examples, the population of induced neural crest cells lacks a marker selected from the group consisting of OCT4, SSEA4, veriscan, smooth muscle actin, and alkaline phosphatase.

[0008] In some examples, the population of induced neural crest cells is generated from a population of stem cells. Some examples also include culturing the population of stem cells under conditions to form clusters of the stem cells. Some examples also include culturing the clusters in suspension to form spheres. Some examples also include plating the spheres on the surface of a substrate, wherein the surface is coated with fibronectin or polyornithine.

[0009] In some examples, the population of stem cells comprises cells selected from the group consisting of embryonic stem cells, and induced pluripotent stem cells. In some examples, the induced pluripotent stem cells are generated from a source selected from the group consisting of fibroblast, renal epithelial cell, and blood cell. In some examples, the population of stem cells comprises cells selected from the group consisting of H9 cells, and human induced pluripotent stem cells generated from human BJ fibroblasts.

[0010] In some examples, the population of induced dermal papillae cells is obtained from a donor subject. In some examples, the donor subject and the subject are the same. In some examples, the donor subject and the subject are different.

[0011] In some examples, the administration comprises subcutaneous transplantation. In some examples, the administration is to a location of the subject's skin comprising hair at the location in a population of subjects. In some examples, the administration is to a location of the subject's skin selected from the group consisting of scalp, face, upper lip, chin, eyebrow, eyelash, arm, leg, back, torso, and abdomen. In some examples, the administration is to a location of the subject's skin comprising scar tissue.

[0012] In some examples, the subject has alopecia.

[0013] In some examples, the subject is mammalian. In some examples, the subject is human.

[0014] Some examples of the methods and compositions provided herein include a method for screening an agent to modulate hair growth comprising contacting a population of induced dermal papillae cells with a test agent; and measuring an effect on hair growth in the population of induced dermal papillae cells.

[0015] In some examples, the effect comprises an increase in the rate of hair growth in the population of induced dermal papillae cells compared to a population of induced dermal papillae cells not contacted with the test agent.

[0016] In some examples, the effect comprises a decrease in the rate of hair growth in the population of induced dermal papillae cells compared to a population of induced dermal papillae cells not contacted with the test agent.

[0017] In some examples, the effect comprises growth of hair characteristic of a specific location of a subject's skin selected from the group consisting of scalp, face, upper lip, chin, eyebrow, eyelash, arm, leg, back, torso, and abdomen.

[0018] In some examples, the subject is mammalian. In some examples, the subject is human.

[0019] In some examples, the population of induced dermal papillae cells is contacted with the test agent *in vivo*. In some examples, the population of induced dermal papillae cells is contacted with the test agent *in vitro*.

[0020] In some examples, the population of induced dermal papillae cells comprises a marker selected from the group consisting of P-75, nestin, veriscan, smooth muscle actin, alkaline phosphatase, and vimentin.

[0021] In some examples, the population of induced dermal papillae cells is generated from a population of induced neural crest cells. Some examples also include selecting for adherent cells. In some examples, the population of induced neural crest cells comprises a marker selected from the group consisting of Sox10, Foxd3, integrin alpha 4, cognate receptor for fibronectin, CD47, CD184, CD44, P-75, and nestin. In some examples, the population of induced neural crest cells lacks a marker selected from the group consisting of OCT4, SSEA4, veriscan, smooth muscle actin, and alkaline phosphatase.

[0022] In some examples, the population of induced neural crest cells is generated from a population of stem cells. Some examples also include culturing the population of stem cells under conditions to form clusters of the stem cells. Some examples also include culturing the clusters in suspension to form spheres. Some examples also include plating the spheres on the surface of a substrate, wherein the surface is coated with fibronectin or polyornithine.

[0023] In some examples, the population of stem cells comprises cells selected from the group consisting of embryonic stem cells, and induced pluripotent stem cells. In some examples, the induced pluripotent stem cells are generated from a source selected from the group consisting of fibroblast, renal epithelial cell, and blood cell. In some examples, the population of stem cells comprises cells selected from the group consisting of H9 cells, and human induced pluripotent stem cells generated from human BJ fibroblasts.

[0024] Some examples of the methods and compositions provided herein include a method for preparing a population of induced dermal papillae cells comprising: generating the population from a population of induced neural crest cells. In one aspect, the present disclosure refers to a method for preparing a population of induced dermal papillae cells comprising: (a) differentiating a population of human induced pluripotent stem cells (hIPSCs) that has been obtained, into a population of human induced pluripotent stem cell-derived neural crest cells (hIPSC-NC), wherein the population of hIPSC-NC lack a marker selected from the group consisting of versican, smooth muscle actin, and alkaline phosphatase; and (b) differentiating the population of hIPSC-NC into a population of human induced pluripotent stem cell-derived dermal papillae-like cells (hIPSC-DP), wherein differentiating the population of hIPSC-NC comprises selecting adherent cells from the population of hIPSC-NC. Some examples also include selecting for adherent cells. In some examples, the population of induced dermal papillae cells comprises a marker selected from the group consisting of P-75, nestin, veriscan, smooth muscle actin, alkaline phosphatase, and vimentin. In some examples, the population of induced neural crest cells comprises a marker selected from the group consisting of Sox10, Foxd3, integrin alpha 4, cognate receptor for fibronectin, CD47, CD184, CD44, P-75, and nestin. In some examples, the population of induced neural crest cells lacks a marker selected from the group consisting of OCT4, SSEA4, veriscan, smooth muscle actin, and alkaline phosphatase.

[0025] In some examples, the population of induced neural crest cells is generated from a population of stem cells. Some examples also include culturing the population of stem cells under conditions to form clusters of the stem cells. Some examples also include culturing the clusters in suspension to form spheres. Some examples also include plating the spheres on the surface of a substrate, wherein the surface is coated with fibronectin or polyornithine.

[0026] In some examples, the population of stem cells comprises cells selected from the group consisting of embryonic stem cells, and induced pluripotent stem cells. In some examples, the induced pluripotent stem cells are generated from a source selected from the group consisting of fibroblast, renal epithelial cell, and blood cell. In some examples, the population of stem cells comprises cells selected from the group consisting of H9 cells, and human induced pluripotent stem cells generated from human BJ fibroblasts.

[0027] Some examples of the methods and compositions provided herein include a population of induced dermal papillae cells prepared by any one of the foregoing methods.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] FIG.s 1A-1E depict differentiation of hESCs into DP-like cells via NC intermediate. FIG. 1A is a schematic representation of the differentiation strategy. FIG. 1B is two photomicrographs depicting expression of migratory NC markers Sox 10 and Foxd3, in hESC-NC cultures. Immunofluorescent staining, DAPI in blue. FIG. 1C is a series of three graphs depicting flow cytometry analysis of NC marker integrin alpha-4 (ITGA4) and hESC markers OCT4 and SSEA4 in hESC-NC cultures. FIG. 1D is a series of photomicrographs depicting expression of p-75, Nestin, Versican, SMA and Alkaline Phosphatase (AP) in hESC-NC, hDP (from normal skin) and hESC-DP cultures. Immunofluorescent staining, DAPI in blue. FIG. 1E is a series of graphs depicting Q-PCR analysis of hDP markers p-75, Nexin-1, Versican, SMA and Vimentin in hESC-DP cultures during DP patterning. Day 0 = hESC-NC cells. Levels of gene expression, shown as log of fold change over hESC-NC levels, were normalized to 18S. For each gene the dashed line represents levels of gene expression in hDP cell cultures. Scale bars 100 μm.

[0029] FIG.s 2A-2C depict effects of subcutaneous cell transplantations into Nude mice. FIG. 2A is a series of photomicrographs showing stereo images of the whole mounts of keratinocytes transplanted alone or in combination with mouse neonatal Dermal Cells (mDC), hDP, hESC-DP, hESC differentiated in serum for 14 days (hESC-serum), human hESC-derived Neural Crest cells (hESC-NC) and hESC-NC differentiated to DP for 7 days (hESC-DP 7 days). FIG. 2B is a graph depicting quantification hairs induced by keratinocytes transplanted alone or in combination with mDC, hDP or hESC-DP. FIG. 2C is a graph depicting dynamics of hair inductive capability of ESC-DP cells with time of differentiation from hESC-NC (day 0) shown as number of hairs formed per transplantation (trend visualized by the red line) or hESC differentiated in presence of serum (blue diamond) in comparison with keratinocytes alone (visualized by the dashed line). All data are represented

WHAT IS CLAIMED IS:

1. A method for preparing a population of induced dermal papillae cells comprising:
    (a) differentiating a population of human induced pluripotent stem cells (hIPSCs) that has been obtained, into a population of human induced pluripotent stem cell-derived neural crest cells (hIPSC-NC), wherein the population of hIPSC-NC lack a marker selected from the group consisting of versican, smooth muscle actin, and alkaline phosphatase; and
    (b) differentiating the population of hIPSC-NC into a population of human induced pluripotent stem cell-derived dermal papillae-like cells (hIPSC-DP), wherein differentiating the population of hIPSC-NC comprises selecting adherent cells from the population of hIPSC-NC.
2. The method of claim 1, wherein the population of human induced pluripotent stem cells are generated from a source selected from the group consisting of fibroblasts, renal epithelial cells, and blood cells.
3. The method of claim 1, wherein the population of human induced pluripotent stem cells are generated from human BJ fibroblasts.
4. The method of claim 1, wherein step (a) further comprises culturing the population of human induced pluripotent stem cells under conditions to form clusters.
5. The method of claim 4, wherein the clusters are in suspension to form spheres.
6. The method of claim 5, wherein the spheres are plated on the surface of a substrate, and wherein the surface is coated with fibronectin or polyornithine.
7. The method of claim 1, wherein step (a) further comprises analyzing the population of hIPSC-NC to confirm the presence of a marker selected from the group consisting of Sox10, Foxd3, integrin alpha 4, cognate receptor for fibronectin, CD47, CD 184, CD44, P-75, and nestin.
8. The method of claim 1, wherein step (a) further comprises analyzing the hIPSC-NC to confirm the absence of a marker selected from the group consisting of OCT4 and SSEA4.
9. The method of claim 1, wherein step (b) further comprises analyzing the hIPSC-DP to confirm the presence of a marker selected from the group consisting of P-75, nestin, versican, smooth muscle actin, alkaline phosphatase, and vimentin.
10. The method of claim 1, wherein the hIPSCs have been obtained from a subject in need of hIPSC-DP.

11. The method of claim 1, wherein the hIPSCs have not been obtained from a subject in need of hIPSC-DP.

12. The method of claim 10 or 11, wherein the subject has alopecia.