BIODEGRADABLE SCAFFOLD FOR HAIR GROWTH AND METHODS OF USE THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/818,584 filed on March 14, 2019. Priority is claimed pursuant to 35 U.S.C. § 119. The above noted patent application is incorporated by reference as if set forth fully herein.

BACKGROUND

[0002] Folliculogenic-cell related therapies may provide benefit for treatment of hair loss and/or a number of diseases, including alopecias, ectodermal dysplasias, monilethrix, Netherton syndrome, Menkes disease, and hereditary epidermolysis bullosa. Hair loss is associated with diminished self-esteem, emotional distress, secondary morbidity, depressive episodes, and reduced quality of life.

[0003] However, replacement of folliculogenic cells requires control and direction of the cells. Additionally, deriving dermal papilla cells from stem cells such as iPSCs has been challenging. Therefore, there remains a need for effective control of the transplantation and growth of folliculogenic cells. There is also a need for improved approaches for implanting folliculogenic cells.

SUMMARY

[0004] The present disclosure aims to meet one or more of the needs identified herein, provide other benefits, or at least provide the public with a useful choice. Certain examples provide a cellular scaffold that contains one or more folliculogenic cells in a cell reservoir and further comprises a guide comprising one or more first biodegradable polymers, wherein the guide is attached to the reservoir. Following implantation, the scaffold can function to orient the one or more folliculogenic cells and/or facilitate their development into a functioning hair follicle. The combination of the reservoir and the attached guide may provide improved efficacy relative to previous approaches

[0005] In some aspects, disclosed herein are cellular scaffolds comprising a cell reservoir, a guide attached to the cell reservoir comprising one or more first biodegradable polymers; and one or more folliculogenic cells. The cellular scaffolds may be configured to be implantable in a human patient under the skin. In some examples the cellular scaffolds include a cell

reservoir with a guide extending therefrom. The cellular scaffolds may be configured such that when implanted, the cell reservoir is under the skin while the guide extending therefrom extends outside of the skin. In some examples, the cellular scaffolds disclosed herein comprise one or more folliculogenic cells in contact with the cell reservoir. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir that is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped. In some examples, the cell reservoir is configured to enclose or house one or more folliculogenic cells. In this way, such folliculogenic cells may be substantially contained within a location inside of the cell reservoir and under the skin of a patient. In some examples, the cell reservoir includes one or more anchors or barbs extending from a generally spherical center shell. Such anchors or barbs may further house and secure folliculogenic cells in a secure location under the skin of a patient.

[0006] In some examples, the cellular scaffolds disclosed herein comprise one or more first biodegradable polymers comprising poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, the cellular scaffolds disclosed herein comprise one or more biodegradable polymers comprising polycaprolactone (PCL). In some examples, the cellular scaffolds disclosed herein comprise one or more second biodegradable polymers. In some examples, the cellular scaffolds disclosed herein comprise one or more second biodegradable polymers comprising poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, the cellular scaffolds disclosed herein comprise one or more second biodegradable polymers comprising polycaprolactone (PCL). In some examples, the cellular scaffolds disclosed herein comprise one or more first biodegradable polymers and one or more second biodegradable polymers that are the same. In some examples, the cellular scaffolds disclosed herein comprise one or more first biodegradable polymers and one or more second biodegradable polymers that are different. In some examples, the cellular scaffolds disclosed herein comprise one or more first biodegradable polymers with a slower degradation rate than one or more second biodegradable polymers. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir derivatized

with magnetic material. In some examples, the cellular scaffolds disclosed herein comprise a guide derivatized with magnetic material. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir 50 to 500 μm in diameter. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir 250-400 μm in diameter, such as 250-350 μm in diameter or 300-400 μm in diameter. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir about 300 μm in diameter. In some examples, the cellular scaffolds disclosed herein comprise a cell reservoir about 200 μm in diameter. In some examples, the cellular scaffolds disclosed herein comprise a hollow guide. In some examples, the cellular scaffolds disclosed herein comprise a solid guide.

[0007] In some examples, the cellular scaffolds disclosed herein comprise one or more folliculogenic cells and the one or more folliculogenic cells are stem cells. In some examples, the cellular scaffolds disclosed herein comprise stem cells selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs). In some examples, the cellular scaffolds disclosed herein comprise induced pluripotent stem cells (iPSCs) generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells. In some examples, the cellular scaffolds disclosed herein comprise one or more folliculogenic cells and the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

[0008] In some exampleaspects, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue. In some examples, the methods of growing a hair follicle disclosed herein comprise piercing a dermal tissue with a needle prior to implanting the cellular scaffold. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells, wherein each microwell of the microwell plate comprises one or more folliculogenic cells and a cellular scaffold. In some examples, the methods of growing a hair follicle disclosed herein comprise

loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells, and the cellular scaffold is orientated in the microwell such that the cell reservoir is closer to a bottom of the microwell and the guide is closer to an opening of the microwell. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells, and the loading one or more folliculogenic cells into a cellular scaffold is performed manually. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells, and the loading one or more folliculogenic cells into a cellular scaffold is performed robotically. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the cell reservoir, the guide, or both the cell reservoir and the guide are derivatized with magnetic material. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, and the loading comprises applying a magnetic field to the cellular scaffold. In some examples, the methods of growing a hair follicle disclosed herein comprise loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the implanting the cellular scaffold into dermal tissue further comprises applying a magnetic field to the cellular scaffold. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the one or more folliculogenic cells are stem cells at the step of implanting the cellular scaffold into dermal tissue. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the

cellular scaffold into dermal tissue, and further comprising covering the dermal tissue with a bandage after implanting the cellular scaffold into dermal tissue.

[0009] In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the one or more folliculogenic cells are in contact with the cell reservoir. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped. The cell reservoir may have a porous exterior and a hollow or porous interior. In some examples, the cell reservoir is hollow. In some examples, the cell reservoir has a porous interior. For example, a spherical, cylindrical, or ellipsoidal cell reservoir may have a hollow interior or a porous interior. A cell reservoir having a porous interior may have a degree of porosity greater than or equal to 90%, 95%, 97%, 98%, 99%, or 99.5%. The degree of porosity is determined as 100% minus p, where p is the percentage of mass of a non-porous solid object of the same shape, size, and composition as the cell reservoir (thus, a reservoir with 99% porosity would have 1% of the mass of a non-porous solid object of the same shape, size, and composition as the cell reservoir). In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the one or more first biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the one or more first biodegradable polymers comprises

polycaprolactone (PCL). In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir comprises one or more second biodegradable polymers. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the cell reservoir comprises one or more second biodegradable polymers comprising poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir comprises one or more second biodegradable polymers comprising polycaprolactone (PCL). In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir comprises one or more second biodegradable polymers, and wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are the same. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir comprises one or more second biodegradable polymers and wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are different. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic

cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir comprises one or more second biodegradable polymers, and wherein the one or more first biodegradable polymers has a slower degradation rate than the one or more second biodegradable polymers. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the cell reservoir is derivatized with magnetic material. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the guide is derivatized with magnetic material. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the cell reservoir is 50 to 500 μm in diameter. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the cell reservoir is about 200 μm in diameter. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the guide is hollow. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the guide is solid.

[0010] In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the one or more folliculogenic cells are stem cells. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, and wherein the one or more folliculogenic cells are stem cells selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs). In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the one or more folliculogenic cells are stem cells selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs), and wherein the induced pluripotent stem cells (iPSCs) are generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells. In some examples, disclosed herein are methods of growing a hair follicle comprising loading one or more folliculogenic cells into a cellular scaffold, wherein the cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and implanting the cellular scaffold into dermal tissue, wherein the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

[0010a] In some aspects, disclosed herein are methods of growing a hair follicle, comprising implanting the cellular scaffold as described herein into dermal tissue.

[0011] In some aspects, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and distributing one or more folliculogenic cells over the plurality of microwells of the microwell plate; and incubating the microwell plate. In some examples, the microwell plate is subjected to centrifugation after distributing one or more

folliculogenic cells over the plurality of microwells of the microwell plate. Such a step can promote bringing the folliculogenic cells into contact with the cell reservoir and/or promote entry of the folliculogenic cells into the cell reservoir. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and distributing one or more folliculogenic cells over the plurality of microwells of the microwell plate, and wherein the one or more folliculogenic cells are in contact with the cell reservoir. In some examples, the plurality of microwells are conical or U-shaped. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and wherein the cell reservoir is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and wherein the one or more first biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, and wherein the one or more first biodegradable polymers comprises polycaprolactone (PCL). In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more

second biodegradable polymers. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more second biodegradable polymers, wherein the one or more second biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more second biodegradable polymers, wherein the one or more second biodegradable polymers comprises polycaprolactone (PCL). In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more second biodegradable polymers, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are the same. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more second biodegradable polymers, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are different. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers and comprising one or more second biodegradable polymers, wherein the one or

more first biodegradable polymers has a slower degradation rate than the one or more second biodegradable polymers. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the cell reservoir is derivatized with magnetic material. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the guide is derivatized with magnetic material. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the cell reservoir is 50 to 500 μm in diameter. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the cell reservoir is about 200 μm in diameter. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the guide is hollow. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the guide is solid.

[0012] In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein

the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the one or more folliculogenic cells are stem cells. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the one or more folliculogenic cells are stem cells and wherein the stem cells are selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs). In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers, wherein the one or more folliculogenic cells are stem cells and wherein the stem cells are selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs), wherein the induced pluripotent stem cells (iPSCs) are generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells. In some examples, disclosed herein are methods of culturing folliculogenic cells comprising loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises a cell reservoir and a guide attached to the cell

reservoir comprising one or more first biodegradable polymers, wherein the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

[0013] In some aspects, disclosed herein are methods of generating a cellular scaffold comprising utilizing two-photon polymerization to generate a cellular scaffold comprising a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers. In some examples, disclosed herein are methods of generating a cellular scaffold comprising utilizing volumetric techniques such as computed axial lithography to generate a cellular scaffold comprising a cell reservoir and a guide attached to the cell reservoir comprising one or more first biodegradable polymers.

[0014] In some examples, cellular scaffolds disclosed herein are for use in therapy, e.g., in treating hair loss and/or a condition selected from an alopecia, ectodermal dysplasia, monilethrix, Netherton syndrome, Menkes disease, or hereditary epidermolysis bullosa, in a subject in need thereof. Such treatment may comprise the steps of a method of growing a hair follicle described herein.

[0014a] In some aspects, provided herein are uses of the cellular scaffold as described herein, in the manufacture of a medicament for the treatment of hair loss and/or a condition selected from an alopecia, ectodermal dysplasia, monilethrix, Netherton syndrome, Menkes disease, or hereditary epidermolysis bullosa, in a subject in need thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] The patent application contains at least one drawing executed in color. Copies of this patent or patent application with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0016] The novel features of the compositions and methods disclosed herein are set forth with particularity in the appended claims. A better understanding of the features and

CLAIMS

What is claimed is:

1. A cellular scaffold comprising:
    (a) a cell reservoir;
    (b) a guide attached to the cell reservoir comprising one or more first biodegradable polymers; and
    (c) one or more folliculogenic cells.

2. The cellular scaffold of claim 1, wherein the guide is configured such that, when inserted under the skin, at least a portion of the guide extends outside the skin.

3. The cellular scaffold of claim 1, wherein the one or more folliculogenic cells are in contact with the cell reservoir.

4. The cellular scaffold of any of claims 1-3, wherein the cell reservoir is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped.

5. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir has a hollow interior.

6. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir has a porous interior.

7. The cellular scaffold of any one of the preceding claims, wherein the one or more first biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

8. The cellular scaffold of any one of the preceding claims, wherein the one or more first biodegradable polymers comprises polycaprolactone (PCL).

9. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir comprises one or more second biodegradable polymers.

10. The cellular scaffold of claim 9, wherein the one or more second biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

11. The cellular scaffold of claim 9, wherein the one or more second biodegradable polymers comprises polycaprolactone (PCL).

12. The cellular scaffold of any one of claims 9-11, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are the same.

13. The cellular scaffold of any one of claims 9-11, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are different.

14. The cellular scaffold of claim 13, wherein the one or more first biodegradable polymers has a slower degradation rate than the one or more second biodegradable polymers.

15. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir is derivatized with magnetic material.

16. The cellular scaffold of any one of the preceding claims, wherein the guide is derivatized with magnetic material.

17. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir is 50 to 500 μm in diameter.

18. The cellular scaffold of any one of the preceding claims, wherein the cell reservoir is 250 to 400μm in diameter (e.g., 250 to 350 μm in diameter or 300 to 400μm in diameter).

19. The cellular scaffold of claim 17, wherein the cell reservoir is about 200 µm in diameter.

20. The cellular scaffold of claim 17, wherein the cell reservoir is about 300 µm in diameter.

21. The cellular scaffold of any one of the preceding claims, wherein the guide is hollow.

22. The cellular scaffold of any one of the preceding claims, wherein the guide is solid.

23. The cellular scaffold of any one of the preceding claims, wherein the one or more folliculogenic cells are stem cells.

24. The cellular scaffold of claim 23, wherein the stem cells are selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs).

25. The cellular scaffold of claim 24, wherein the induced pluripotent stem cells (iPSCs) are generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells.

26. The cellular scaffold of any one of claims 1-25, wherein the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

27. A method of growing a hair follicle comprising:
    (a) loading one or more folliculogenic cells into a cellular scaffold comprising:
        i. a cell reservoir; and
        ii. a guide attached to the cell reservoir comprising one or more first biodegradable polymers; and
    (b) implanting the cellular scaffold into dermal tissue.

28. The method of claim 27, wherein when implanted in a subject, at least a portion of the guide extends outward and through the skin.

29. The method of claim 27, wherein the loading one or more folliculogenic cells into a cellular scaffold comprises placing the one or more folliculogenic cells and the cellular scaffold into a microwell of a microwell plate comprising multiple microwells.

30. The method of claim 29, wherein the microwell is conical or U-shaped.

31. The method of claim 29 or 30, wherein each microwell of the microwell plate comprises one or more folliculogenic cells and a cellular scaffold.

32. The method of any one of claims 29-31, wherein the cellular scaffold is orientated in the microwell such that the cell reservoir is closer to a bottom of the microwell and the guide is closer to an opening of the microwell.

33. The method of any one of claims 29-32, wherein the step of loading one or more folliculogenic cells into a cellular scaffold further comprises subjecting the microwell plate to centrifugation after placing the one or more folliculogenic cells and the cellular scaffold into the microwell.

34. The method of any one of claims 28-33, wherein the loading one or more folliculogenic cells into a cellular scaffold is performed manually.

35. The method of any one of claims 28-33, wherein the loading one or more folliculogenic cells into a cellular scaffold is performed robotically.

36. A method of growing a hair follicle, comprising implanting the cellular scaffold of any one of claims 1-26 into dermal tissue.

37. The method of any one of claims 27-36, further comprising piercing the dermal tissue with a needle prior to implanting the cellular scaffold.

38. The method of any one of claims 27-37, wherein the cell reservoir, the guide, or both the cell reservoir and the guide are derivatized with magnetic material.

39. The method of claim 38, wherein the loading one or more folliculogenic cells into a cellular scaffold further comprises applying a magnetic field to the cellular scaffold.

40. The method of any one of claims 38 or 39, wherein the implanting the cellular scaffold into dermal tissue further comprises applying a magnetic field to the cellular scaffold.

41. The method of any one of claims 27-40, wherein the one or more folliculogenic cells are stem cells at the step of implanting the cellular scaffold into dermal tissue.

42. The method of any one of claims 27-41, further comprising covering the dermal tissue with a bandage after implanting the cellular scaffold into dermal tissue.

43. The method of any one of claims 27-42, wherein the one or more folliculogenic cells are in contact with the cell reservoir.

44. The method of any one of claims 27-43, wherein the cell reservoir is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped.

45. The method of any one of claims 27-44, wherein the one or more first biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

46. The method of any one of claims 27-44, wherein the one or more first biodegradable polymers comprises polycaprolactone (PCL).

47. The method of any one of claims 27-46, wherein the cell reservoir comprises one or more second biodegradable polymers.

48. The method of claim 47, wherein the one or more second biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA),

poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

49. The method of claim 48, wherein the one or more second biodegradable polymers comprises polycaprolactone (PCL).

50. The method of any one of claims 47-49, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are the same.

51. The method of any one of claims 47-49, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are different.

52. The method of claim 51, wherein the one or more first biodegradable polymers has a slower degradation rate than the one or more second biodegradable polymers.

53. The method of any one of claims 27-52, wherein the cell reservoir is derivatized with magnetic material.

54. The method of any one of claims 27-53, wherein the guide is derivatized with magnetic material.

55. The method of any one of claims 27-54, wherein the cell reservoir is 50 to 500 μm in diameter (e.g., 250 to 400 μm in diameter, 250 to 350 μm in diameter, or 300 to 400 μm in diameter).

56. The method of claim 55, wherein the cell reservoir is about 200 μm in diameter or about 300 μm in diameter.

57. The method of any one of claims 27-56, wherein the guide is hollow.

58. The method of any one of claims 27-56, wherein the guide is solid.

59. The method of any one of claims 27-58, wherein the one or more folliculogenic cells are stem cells.

60. The method of claim 59, wherein the stem cells are selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs).

61. The method of claim 60, wherein the induced pluripotent stem cells (iPSCs) are generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells.

62. The method of any one of claims 27-61, wherein the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

63. A method of culturing folliculogenic cells comprising:

(a) loading one cellular scaffold into each microwell of a microwell plate, wherein the microwell plate comprises a plurality of microwells, and wherein each cellular scaffold comprises:

i. a cell reservoir; and

ii. a guide attached to the cell reservoir comprising one or more first biodegradable polymers;

(b) distributing one or more folliculogenic cells over the plurality of microwells of the microwell plate; and

(c) incubating the microwell plate.

64. The method of claim 63, wherein the one or more folliculogenic cells are in contact with the cell reservoir.

65. The method of claim 63 or 64, wherein the cell reservoir is spherical, ellipsoidal, cylindrical, tubular, or buckyball-shaped.

66. The method of any one of claims 63-65, wherein the cell reservoir has a hollow interior.

67. The method of any one of claims 63-65, wherein the cell reservoir has a porous interior.

68. The method of any one of claims 63-67, wherein the microwells are conical or U-shaped.

69. The method of any one of claims 63-68, further comprising centrifuging the microwell plate after distributing one or more folliculogenic cells over the plurality of microwells of the microwell plate.

70. The method of any one of claims 63-69, wherein the one or more first biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

71. The method of any one of claims 63-70, wherein the one or more first biodegradable polymers comprises polycaprolactone (PCL).

72. The method of any one of claims 63-71, wherein the cell reservoir comprises one or more second biodegradable polymers.

73. The method of claim 72, wherein the one or more second biodegradable polymers comprises poly(glycolic acid) (PGA), poly(lactic-co-glycolic) acid (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), polyethylene glycol, poly(butylene succinate) (PBS), polyphosphazenes, polyanhydrides, polyphosphoesters, polyurethanes, polycarbonates, and combinations thereof.

74. The method of claim 72, wherein the one or more second biodegradable polymers comprises polycaprolactone (PCL).

75. The method of any one of claims 72-74, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are the same.

76. The method of any one of claims 72-74, wherein the one or more first biodegradable polymers and the one or more second biodegradable polymers are different.

77. The method of any one of claims 72-74, wherein the one or more first biodegradable polymers has a slower degradation rate than the one or more second biodegradable polymers.

78. The method of any one of claims 63-77, wherein the cell reservoir is derivatized with magnetic material.

79. The method of any one of claims 63-78, wherein the guide is derivatized with magnetic material.

80. The method of any one of claims 63-79, wherein the cell reservoir is 50 to 500 μm in diameter (e.g., 250 to 400 μm in diameter, 250 to 350 μm in diameter, or 300 to 400 μm in diameter).

81. The method of claim 80, wherein the cell reservoir is about 200 μm in diameter or about 300 μm in diameter.

82. The method of any one of claims 63-81, wherein the guide is hollow.

83. The method of any one of claims 63-81, wherein the guide is solid.

84. The method of any one of claims 63-83, wherein the one or more folliculogenic cells are stem cells.

85. The method of claim 84, wherein the stem cells are selected from the group consisting of embryonic stem cells and induced pluripotent stem cells (iPSCs).

86. The method of claim 85, wherein the induced pluripotent stem cells (iPSCs) are generated from a source selected from the group consisting of fibroblast cells, renal epithelial cells, and blood cells.

87. The method of any one of claims 63-83, wherein the one or more folliculogenic cells are dermal papilla, epithelial stem cells, or a combination thereof.

88. A method of generating a cellular scaffold comprising:

(a) utilizing two-photon polymerization to generate a cellular scaffold comprising:

i. a cell reservoir; and

ii. a guide attached to the cell reservoir comprising one or more first biodegradable polymers.

89. The cellular scaffold of any one of claims 1-26, for use in therapy.

90. Use of the cellular scaffold of any one of claims 1-26, in the manufacture of a medicament for the treatment of hair loss and/or a condition selected from an alopecia, ectodermal dysplasia, monilethrix, Netherton syndrome, Menkes disease, or hereditary epidermolysis bullosa, in a subject in need thereof.

91. The cellular scaffold of claim 89, for use in the method of any one of claims 27-62.