

interface culture after some maturation period (e.g. ranging without limitation from 1 hour to 7 days, or from 1 day to 14 days).

A particular advantage of the various open-top embodiments of the present disclosure is that aerosol may be delivered to the lung cells in the open region, such as open region 404. In one exemplary embodiment, while operating the device without the optional cover (or by removing the cover), aerosol can be delivered directly into the open region 404 from above (or substantially above). The aerosol may be generated using any of a variety of aerosol-generation techniques known in the art. Alternatively, an aerosol generation means may be included in a cover that can be placed on top of the open region 404. A cover may be optionally removed or exchanged during use; for example, an aerosol-generating cover may be applied when aerosol is desired and replaced with a fluidic cover 410 when fluidic perfusion is desired. In some embodiments, non-aerosol materials or samples can be applied to cells present in an open region, such as open region 404. This may include, but are not limited to, materials or samples that are difficult to apply fluidically due to their properties, such as slurries, pastes, solids, or viscous fluids.

Referring now to FIGS. 5A-5F, multiple perspective views, including additional cross-sectional details through an exemplary open-top microfluidic device, are illustrated. The microfluidic device 500 includes a membrane 540 disposed between a bottom structure 525 and a top structure 520. The bottom structure defines a bottom chamber 506, and the top structure 520 includes a top chamber 506 that defines an open region 504, of the microfluidic device 500. In some embodiments, it is desirable that the open region 504, includes a gel layer 550, comprising a porous volume, or another material for testing (e.g., an extracellular matrix or cells embedded in an extracellular matrix). For example, a gel layer 550 can include gels used in an organ-on-chip model of the skin to house fibroblasts and to support a layer or keratinocytes. In FIG. 5B, a gel layer 550 is introduced into the open region 504 (see FIG. 5A) where the gel layer 550 is bounded on the bottom by membrane 540.

In some embodiments, a gel layer 550, or porous volume, is formed by injecting one or more suitable precursors through one or more fluidic channels included in the top structure 520 (such optional channels are depicted in FIGS. 5A-5C). The one or more precursors can then be treated as desired to form the gel or porous volume (e.g. UV light, chemical treatment,

CLAIMS

1. A microfluidic device comprising (i) a chamber comprising a lumen and a fluidic cover comprising a microfluidic channel, the lumen comprising (ii) a gel matrix, the gel matrix positioned above (iii) a porous membrane, and the membrane positioned under the chamber,
5 in which the fluidic cover is configured to removably cover and close the chamber.
2. A microfluidic device according to Claim 1, in which fibroblasts are within the gel matrix and keratinocytes are on top of the gel matrix.
3. A microfluidic device according to Claim 2, in which the keratinocytes comprise more than one layer on top of the gel matrix.
- 10 4. A microfluidic device according to Claim 1, in which a layer of endothelial cells is positioned on the bottom of the membrane so as to be in contact with the microfluidic channels.
5. A microfluidic device according to Claim 1, in which the lumen is circular.
6. A microfluidic device according to Claim 1, in which the gel matrix comprises at least
15 one of neurons and astrocytes and the membrane comprises brain microvascular endothelial cells in contact with the microfluidic channels.
7. A microfluidic device according to Claim 6, in which neurons are on, in or under the gel matrix.
8. A microfluidic device according to Claim 6, in which astrocytes are on, in or under the
20 gel matrix.
9. A microfluidic device according to Claim 1, in which the gel matrix comprises cells.
10. A microfluidic device according to Claim 9, in which the cells comprise lung cells.
11. A microfluidic device according to Claim 1, in which the chamber is configured for fluid flow.
- 25 12. A method, comprising:
 - (a) providing a microfluidic device comprising (i) a chamber comprising a lumen and a fluidic cover comprising a microfluidic channel, the lumen comprising (ii) a gel

matrix, the gel matrix comprising cells and positioned above (iii) a porous membrane, the membrane positioned under the chamber, in which the fluidic cover is configured to removably cover and close the chamber;

(b) extracting the gel matrix in whole or in part from the lumen; and

5 (c) staining the cells from the extracted gel matrix.

13. A method according to Claim 12, further comprising, prior to step (b), removing the cover and treating the cells with an aerosol.

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A particular advantage of the various open-top embodiments of the present disclosure is that aerosol may be delivered to the lung cells in the open region, such as open region 404. In one exemplary embodiment, while operating the device without the optional cover (or by removing the cover), aerosol can be delivered directly into the open region 404 from above (or substantially above). The aerosol may be generated using any of a variety of aerosol-generation techniques known in the art. Alternatively, an aerosol generation means may be included in a cover that can be placed on top of the open region 404. A cover may be optionally removed or exchanged during use; for example, an aerosol-generating cover may be applied when aerosol is desired and replaced with a fluidic cover 410 when fluidic perfusion is desired. In some embodiments, non-aerosol materials or samples can be applied to cells present in an open region, such as open region 404. This may include, but are not limited to, materials or samples that are difficult to apply fluidically due to their properties, such as slurries, pastes, solids, or viscous fluids.

Referring now to FIGS. 5A-5F, multiple perspective views, including additional cross-sectional details through an exemplary open-top microfluidic device, are illustrated. The microfluidic device 500 includes a membrane 540 disposed between a bottom structure 525 and a top structure 520. The bottom structure defines a bottom chamber 506, and the top structure 520 includes a top chamber 507 that defines an open region 504, of the microfluidic device 500. In some embodiments, it is desirable that the open region 504, includes a gel layer 550, comprising a porous volume, or another material for testing (e.g., an extracellular matrix or cells embedded in an extracellular matrix). For example, a gel layer 550 can include gels used in an organ-on-chip model of the skin to house fibroblasts and to support a layer or keratinocytes. In FIG. 5B, a gel layer 550 is introduced into the open region 504 (see FIG. 5A) where the gel layer 550 is bounded on the bottom by membrane 540.

In some embodiments, a gel layer 550, or porous volume, is formed by injecting one or more suitable precursors through one or more fluidic channels included in the top structure 520 (such optional channels are depicted in FIGS. 5A-5C). The one or more precursors can then be treated as desired to form the gel or porous volume (e.g. UV light, chemical treatment,

CLAIMS

1. A microfluidic device comprising (i) a chamber comprising a lumen and (ii) a fluidic cover comprising a microfluidic channel, the lumen comprising (iii) a gel matrix, the gel matrix positioned above (iv) a porous membrane, and the membrane positioned under the chamber, in which the chamber is in fluidic communication with the microfluidic channel, and in which the fluidic cover is configured to removably cover and close the chamber.
2. A microfluidic device according to Claim 1, in which fibroblasts are within the gel matrix and keratinocytes are on top of the gel matrix.
3. A microfluidic device according to Claim 2, in which the keratinocytes comprise more than one layer on top of the gel matrix.
4. A microfluidic device according to Claim 1, in which a layer of endothelial cells is positioned on the bottom of the membrane so as to be in contact with the microfluidic channel.
5. A microfluidic device according to Claim 1, in which the lumen is circular.
6. A microfluidic device according to Claim 1, in which the gel matrix comprises at least one of neurons and astrocytes and the membrane comprises brain microvascular endothelial cells in contact with the microfluidic channel.
7. A microfluidic device according to Claim 6, in which neurons are on, in or under the gel matrix.
8. A microfluidic device according to Claim 6, in which astrocytes are on, in or under the gel matrix.
9. A microfluidic device according to Claim 1, in which the gel matrix comprises cells.
10. A microfluidic device according to Claim 9, in which the cells comprise lung cells.
11. A microfluidic device according to Claim 1, in which the chamber is configured for fluid flow.
12. A method, comprising:
 - (a) providing a microfluidic device comprising (i) a chamber comprising a lumen and (ii) a fluidic cover comprising a microfluidic channel, the lumen comprising (iii) a gel

matrix, the gel matrix comprising cells and positioned above (iv) a porous membrane, the membrane positioned under the chamber, and in which the chamber is in fluidic communication with the microfluidic channel, in which the fluidic cover is configured to removably cover and close the chamber;

- 5 (b) extracting the gel matrix in whole or in part from the lumen; and
- (c) staining the cells from the extracted gel matrix.

13. A method according to Claim 12, further comprising, prior to step (b), removing the cover and treating the cells with an aerosol.