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(54) Title: TEMPLATED ISLET CELLS AND SMALL ISLET CELL CLUSTERS FOR DIABETES TREATMENT

(57) Abstract: Substrates and devices for culturing cells are disclosed, along with methods of using the same. The substrates and devices include top surfaces with one or more divots disposed therein. Each divot is defined by an opening in the top surface, a rounded bottom surface spaced from the opening, and an interior side-wall surface extending between the rounded bottom surface and the opening. The top surface of the substrates and devices are optionally walled to form wells containing one or more divots. The substrates and devices may be used for reaggregating cells, for example, to form small islet cell clusters and for high throughput testing methodologies.

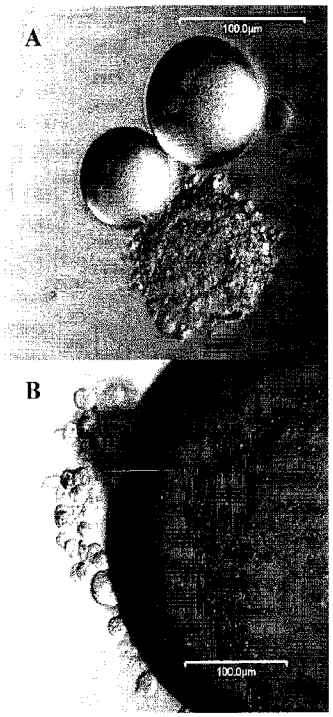

FIG. 1

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1-8. (Canceled)

9. A device for culturing cells, comprising:

a substrate comprising

a substantially planar top surface,

a plurality of divots disposed within the top surface, each divot defined by an opening in the top surface, a rounded bottom surface spaced from the opening, and an interior side-wall surface extending between the rounded bottom surface and the opening, wherein each divot has a depth of between 50 - 300 μηι (± 20%) and a diameter of between 100 - 1000 μm (± 20%); and

at least one well disposed on the top surface, the well comprising a peripheral side-wall extending upwardly from the top surface in a direction generally perpendicular to a plane defined by the top surface and forming an interior space within the well,

wherein the peripheral side-wall circumscribes the opening of at least one divot to prevent liquid communication between the at least one divot within the well periphery and an adjacent divot outside of the well.

10. The device of claim 9 further comprising a plurality of wells.

11. The device of claim 10, wherein each well comprises 1-14 divots.

12. The device of claim 9 further comprising islet cells.

13. The device of claim 12, wherein the islet cells form small islet cell clusters with a diameter of less than 125 μη.

14. The device of claim 9 further comprising reaggregated 3-dimensional cell clusters.

15. A device for culturing cells, comprising:

a substrate having a substantially planar top surface;

a side-wall extending upwardly from the surface in a direction generally perpendicular to a plane defined by the top surface and circumscribing a portion of the surface, said side-wall and top surface cooperatively forming a liquid impermeable well, wherein the well has a bottom surface corresponding to the portion of the top surface circumscribed by the side-wall; and

a divot disposed in the bottom surface of the well,

wherein the divot is defined by an opening in the bottom surface of the well, a rounded bottom surface spaced from the opening, and an interior side-wall surface extending between the rounded bottom surface and the opening.

16. The device of claim 15, wherein the divot has a depth of less than 300 μη (± 20%) and a diameter of 50 - 300 μηι (±20%).

17. The device of claim 15 further comprising a plurality of wells, wherein each well comprises 1-14 divots.

18. The device of claim 17, wherein each divot comprises a 3-dimensional cell spheroid.

19. A method of evaluating a xenobiotic for biological activity, said method comprising:

providing a device according to claim 15, said device comprising a plurality of wells, each well comprising 1 or more divots;

culturing cells in said divots to form a 3-dimensional cell cluster in each divot;

adding a first xenobiotic to at least a first well, wherein said first xenobiotic comes into contact with at least a first cell cluster in said first well; and

evaluating the effects of said first xenobiotic on said first cell cluster.

20. The method of claim 19, wherein said first well comprises a plurality of divots, said first xenobiotic coming into contact with a first plurality cell clusters, each cell cluster being in respective divots in said first well, said method further comprising determining the average effect of said first xenobiotic on said first plurality of cell clusters.

21. The method of claim 19, further comprising:

adding a second xenobiotic to at least a second well, wherein said second xenobiotic comes into contact with at least a second cell cluster in said second well; and

evaluating the effects of said second xenobiotic on said second cell cluster.

22. The method of claim 21, wherein said second well comprises a plurality of divots, said second xenobiotic coming into contact with a second plurality cell clusters, each cell cluster being in respective divots in said second well, said method further comprising determining the average effect of said second xenobiotic on said second plurality of cell clusters.

23. The method of claim 21, wherein said first and second xenobiotics are added to said device substantially simultaneously.

24. The method of claim 19, wherein each divot comprises a single 3-dimensional cell cluster.

25. The method of claim 19, wherein said 3-dimensional cell clusters are islets.