

CLAIMS

1. A method of reducing or preventing the agglomeration of spheroids comprising:

- (i) providing one or more individual spheroids;
- (ii) transferring the individual spheroid(s) into a ~~cell culture chamber~~well of a cell culture device, wherein the cell culture device comprises:

~~the cell culture chamber, wherein the cell culture chamber~~ a well comprising
~~comprises~~ a base and side walls extending from the base to enclose a volume of the ~~cell~~
~~culture chamber~~well;

an inlet in the base or side walls of the ~~cell culture chamber~~well adapted for fluid communication into the ~~chamber~~well; and

an outlet in the base or side walls of the ~~cell culture chamber~~well adapted for fluid communication out of the ~~chamber~~well;

wherein the base of the ~~cell culture chamber~~well comprises a discontinuous surface,
the discontinuous surface comprising a plurality of grooves and/or a plurality of holes
capable of trapping one or more individual spheroids to reduce or prevent the agglomeration thereof;

- (iii) contacting the individual spheroid(s) with the discontinuous surface of the base of the ~~cell culture chamber~~well and incubating the individual spheroid(s) therein; and

- (iv) obtaining an individual spheroid(s) on the discontinuous surface of the ~~cell culture device~~well.

2. The method according to claim 1, wherein a known number of individual spheroids are transferred in step (ii) and a known number of individual spheroids are obtained in step (iv).

3. The method according to claim 1 or claim 2, wherein ~~the discontinuous surface comprises a plurality of grooves in which~~ the depth and width of the grooves is between 200 to 1000 μm , suitably, between 200 to 600 μm .

4. The method according to claim 3, wherein the grooves form a plurality of concentric rings on the base of the ~~cell culture chamberwell~~.
5. The method according to any of claims 1 to 4, wherein the ~~discontinuous surface comprises a~~ plurality of holes ~~having have~~ a closed bottom and an open top, the size of the holes corresponding in depth and width to be 10% greater than the largest diameter of a spheroid.
6. The method according to any of the preceding claims, wherein the ~~cell culture chamberwell~~ is manufactured from PEEK.
7. The method according to any of the preceding claims, wherein the ~~cell culture chamberwell~~ is coated, suitably, wherein the coating is a coating of poly(p-xylylene) polymer.
8. The method according to any of the preceding claims, wherein between 40 to 100 spheroids are transferred to the ~~cell culture chamberwell~~ of the cell culture device.
9. The method according to any of the preceding claims, wherein a medium flow is applied to the ~~cell culture chamberwell~~ of the cell culture device, suitably, wherein the flow rate is between 10 to 1000 $\mu\text{L}/\text{min}$.
10. Use of a cell culture device for reducing or preventing the agglomeration of spheroids, said cell culture device comprising:
 - a ~~cell culture chamberwell~~ comprising a base and side walls extending from the base to enclose a volume of the ~~cell culture chamberwell~~,
 - an inlet in the base or side walls of the ~~cell culture chamberwell~~ adapted for fluid communication into the ~~chamberwell~~; and
 - an outlet in the base or side walls of the ~~cell culture chamberwell~~ adapted for fluid communication out of the ~~chamberwell~~;
 - wherein the base of the ~~cell culture chamberwell~~ comprises a discontinuous surface, the discontinuous surface comprising a plurality of grooves and/or a plurality of holes

capable of trapping one or more individual spheroids to reduce or prevent the agglomeration thereof.

11. A multi-well cell culture plate comprising a well comprising a base and side walls extending from the base to enclose a volume of the well,

an inlet in the base or side walls of the well adapted for fluid communication into the well; and

an outlet in the base or side walls of the well adapted for fluid communication out of the well.

wherein the base of at least one of the wells of the multi-well cell culture plate ~~and/or the base of an insert contained in at least one of the wells of the multi-well cell culture plate~~ comprises a discontinuous surface, the discontinuous surface comprising a plurality of grooves and/or a plurality of holes capable of trapping one or more individual spheroids to reduce or prevent the agglomeration thereof.

~~12. An insert for use in a multi-well cell culture plate comprising a discontinuous surface adapted to reduce or prevent the agglomeration of spheroids.~~

~~13.~~12. The multi-well cell culture plate according to claim 11, ~~or the insert according to claim 12,~~ wherein the plate ~~and/or the insert~~ is manufactured from PEEK; or

wherein at least one of the wells ~~or the insert~~ is coated, suitably, wherein the coating is a coating of poly(p-xylylene) polymer.

~~14.~~13. The multi-well cell culture plate ~~or the insert~~ according to ~~any of claims 11 to 13~~claim 11 or 12, wherein the at least one well ~~or the insert~~ comprises an individualised single spheroid.