

Claims

1. A method to be performed with one tissue type, optionally,
in combination with other cells such as stromal cells or
5 immune cells, comprising the steps of:
- a) providing a fully defined hydrogel matrix array with
discrete volumes by crosslinking, onto a substrate or
into discrete volumes of a substrate, preferably a
multi-well plate, different combinations of one or
10 more different hydrogel precursor molecules, optional-
ly in the presence of one or more biologically active
molecules, optionally at least one crosslinking agent
and cells of the tissue type to be tested, so as to
create fully defined three-dimensional extracellular
15 matrix conditions that differ from each other in their
biological, biophysical and/or biochemical character-
istics;
- b) allowing said cells to grow and expand in said dis-
crete volumes of said hydrogel matrix array in the
20 presence of one or more different culture media;
- c) performing an operation with the cells grown in said
discrete volumes of said hydrogel matrix array;
wherein a specific combination of hydrogel features has
been pre-selected for the said one tissue type to be test-
25 ed.
2. The method according to claim 1, wherein the preselection
of at least one of said hydrogel precursor molecules, or of
said hydrogel features, and said culture media is made on
30 the basis of selecting suitable extracellular matrix condi-
tions from a method using random extracellular matrix con-
ditions.

3. The method according to claim 1 or 2, wherein the tissue type is selected from the group consisting of cancer cells and normal/healthy cells.
- 5 4. The method according to any of the preceding claims, wherein freshly isolated or frozen cells from a biopsy or tissue resection of a human or from patient-derived xenograft (PDX) tissue are used.
- 10 5. The method according to any of the preceding claims, wherein in step c) one or more drugs are added to said discrete volumes of said hydrogel matrix.
- 15 6. The method according to any of the preceding claims, wherein the tissue type is lung cancer cells, preferably non-small cell lung cancer cells, overexpressing c-Met, and the hydrogel matrix is preselected as being a non self-degradable PEG hydrogel, wherein the crosslinking agent and said optional bioactive agent do not comprise any RGD motif.
20
7. The method according to claim 6, wherein said culture medium comprises FBS (serum) or Wnt agonist such as R-spondin.
- 25 8. The method according to any of claims 1 to 5, wherein the tissue type is pancreatic ductal adenocarcinoma (PDAC) cells, and the hydrogel matrix is preselected as being a non self-degradable PEG hydrogel having a stiffness in the range of 50 to 3000 Pa, preferably 50 to 2000 Pa and most preferably 50 to 1000 Pa, wherein at least one of the crosslinking agent and/or said optional bioactive agent
30 comprise a RGD motif.

9. The method according to claim 8, wherein said culture medium comprises Wnt agonists such as R-spondin and Wnt 3a.
10. The method according to any of claims 1 to 5, wherein the
5 tissue type is colorectal cancer (CRC) cells, and the hydrogel matrix is preselected as being a PEG hydrogel having at least an initial stiffness in the range of 50 to 2000 Pa, and optionally furthermore comprising one or more biologically active molecules comprising laminin, preferably
10 laminin-111 or laminin-511, and especially preferable natural mouse laminin-111 or recombinant human laminin-511, wherein at least one of the crosslinking agent and/or said optional bioactive agent comprise a RGD motif.
11. The method according to claim 10, wherein said culture medium comprises Wnt agonists such as R-spondin and Wnt 3a.
12. The method according to any of claims 1 to 5, wherein the
20 tissue type is breast cancer cells, and the hydrogel matrix is preselected as being preferably an enzymatic-degradable PEG hydrogel, wherein at least one of the crosslinking agent preferably comprises an enzymatically degradable motif, preferably a MMP-sensitive motif, and said hydrogel optionally furthermore comprises one or more biologically
25 active molecules comprising laminin, preferably laminin-111, and especially preferable natural mouse laminin-111.
13. The method according to claim 12, wherein said culture medium comprises FBS (serum) or Wnt agonist such as R-spondin.
30
14. The method according to any of claims 1 to 5, wherein the tissue type is cancer cells that grow ex vivo more slowly

than their normal counterparts, preferably prostate cancer cells, and the hydrogel matrix is preselected as being a PEG hydrogel, preferably having a stiffness in the range of 50 to 2000 Pa, wherein said crosslinking agent and said optional bioactive agent do not comprise any RGD motif.

15. Kit of parts for performing an operation on or with one or more tissue type, comprising:
- a) components for preparing a fully defined hydrogel matrix array, so as to create fully defined three-dimensional extracellular matrix conditions that differ from each other in their biological, biophysical and/or biochemical characteristics, said components comprising
- one or more different hydrogel precursor molecules,
 - optionally at least one crosslinking agent,
 - optionally one or more biologically active molecules,
- b) one or more different culture media,
- wherein a specific combination of hydrogel features has been pre-selected for the tissue type to be tested.
16. Kit according to claim 15, for testing the influence of drugs on lung cancer cells, preferably non-small cell lung cancer cells, overexpressing c-Met, the hydrogel matrix is preselected as being a non self-degradable PEG hydrogel, wherein the crosslinking agent and said optional bioactive agent do not comprise any RGD motif, and preferably said culture medium comprises FBS (serum) or Wnt agonist such as R-spondin.

17. Kit according to claim 15, for testing the influence of drugs on pancreatic ductal adenocarcinoma (PDAC) cells, the hydrogel matrix is preselected as being a non self-degradable PEG hydrogel having a stiffness in the range of 50 to 3000 Pa, preferably 50 to 2000 Pa and most preferably 50 to 1000 Pa, wherein at least one of the crosslinking agent and/or said optional bioactive agent comprise a RGD motif, and preferably said culture medium comprises Wnt agonists such as R-spondin and Wnt 3a.
18. Kit according to claim 15, for testing the influence of drugs on colorectal cancer (CRC) cells, and the hydrogel matrix is preselected as being a PEG hydrogel having at least an initial stiffness in the range of 50 to 2000 Pa, and optionally furthermore comprising one or more biologically active molecules comprising laminin, preferably laminin-111 or laminin-511, and especially preferable natural mouse laminin-111 or recombinant human laminin-511, wherein at least one of the crosslinking agent and/or said optional bioactive agent comprise a RGD motif, and wherein preferably said culture medium comprises Wnt agonists such as R-spondin and Wnt 3a.
19. Kit according to claim 15, for testing the influence of drugs on breast cancer cells, and the hydrogel matrix is preselected as being preferably an enzymatic-degradable PEG hydrogel, wherein at least one of the crosslinking agent preferably comprises an enzymatically degradable motif, preferably a MMP-sensitive motif, and said hydrogel optionally furthermore comprises one or more biologically active molecules comprising laminin, preferably laminin-111, and especially preferable natural mouse laminin-111, and where-

in preferably said culture medium comprises FBS (serum) or Wnt agonist such as R-spondin.

20. Kit according to claim 15, for testing the influence of
5 drugs on cancer cells that grow ex vivo more slowly than
their normal counterparts, preferably prostate cancer
cells, and the hydrogel matrix is preselected as being a
PEG hydrogel, preferably having a stiffness in the range of
50 to 2000 Pa, wherein said crosslinking agent and said op-
10 tional bioactive agent do not comprise any RGD motif.