

3D CELL-BASED ASSAYS FOR HTS/HCS

FMP™

FULLSCREEN MULTIWELL PLATE

organ in a well.

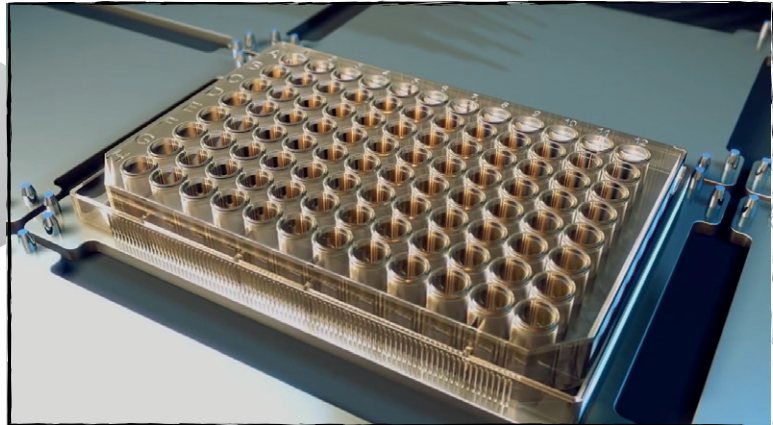
4DCELL FMP™

NEW GENERATION OF MULTIWELL PLATES FOR HTS/HCS

The challenges of understanding biomedicine brings out new questions. Looking at the objectives of pharmaceutical or academic research lead us to consider new and more reliable models, representative of the living organs.

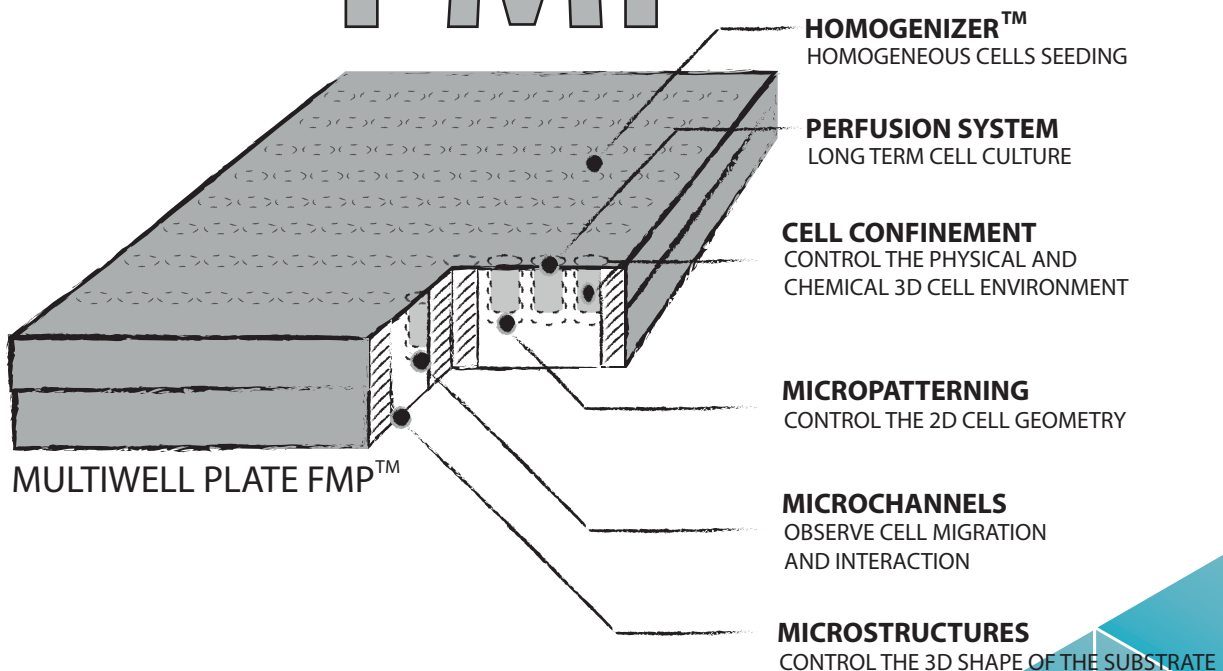
Years of research have led 4Dcell to develop an innovative 3D cell culture technology for complete screening.

Controlling the cell microenvironment, the Fullscreen Multiwell Plate, FMP, allows getting closer to the organs functioning.



YOUR ENVIRONMENT MEANS EVERYTHING TO YOU. SAME FOR CELLS.

FMP™



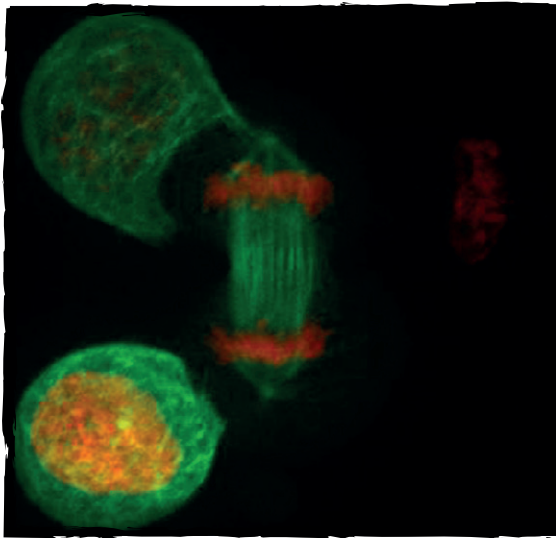
The role of 4Dcell's novel multi-well plates is to provide in HTS/HCS platforms new models that better predict and quantify, *in vitro*, the *in vivo* behavior of cells.

Fully compatible with industrial standards, this new plate model embeds four innovative technologies developed by 4Dcell's team of scientist and industrial experts.

FMP™ APPLICATIONS

NEW BREAKTHROUGH READ-OUTS FOR HTS/HCS

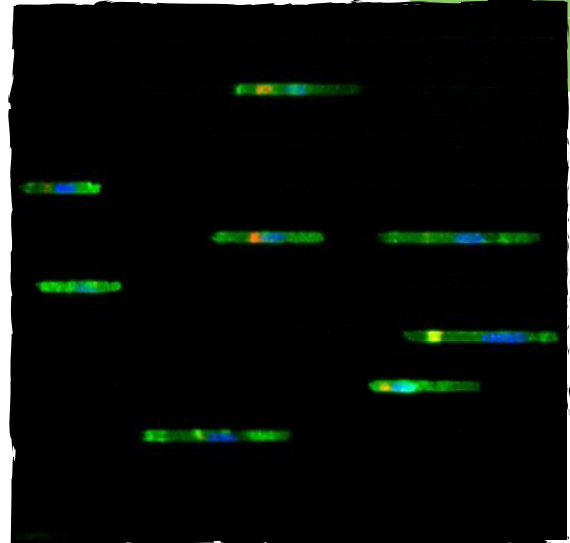
The FMP™ is a versatile solution for cell behaviour modeling with a myriad of applications. Among them, we highlight models for cancer, immune system, organs as heart and guts, circulating cells, wound healing, neuronal network, stem cells and genetic disorders as laminopathy.



HeLa tub-GFB H2B-mCherry cells dividing under 5 µm confinement (4Dcell dynamic confiner)

Cancer

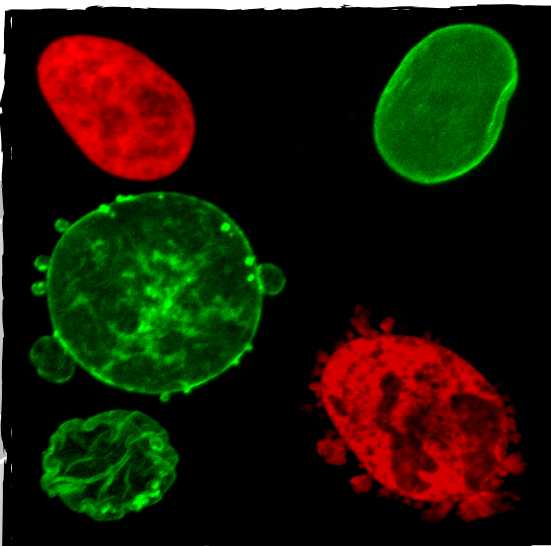
Cell mechanics or cell organization are key parameters for cancer development and metastasis. The FMPs™ enable us to better control these parameters and offer new read-outs to decipher cancer progression and invasiveness. For instance, spindle assembly disorders of cancerous cells are easily assessed via FMPs™ Cell confinement technology.



Dendritic cells migrating in micro-channels of 5 µm width and 4 µm height. Extracted from a time-lapse video taken by 4Dcell partners Lucie Barbier & Dr. Pablo Vargas, Curie Institute/UMR144 (2018)

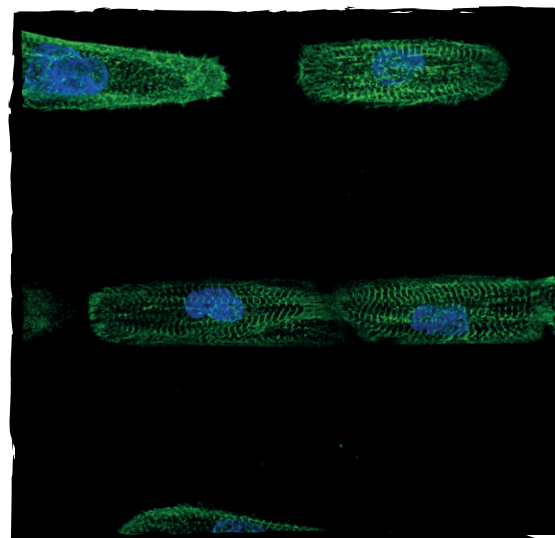
Immune System

Sensing and migration in the tissues is the basis of the immune system functioning. FMPs™ are the best tools to quantify immune activities such as cell migration, cell-cell interaction, nucleus plasticity, among others. For instance, FMPs™ Microchannels can quantify leukocyte extravasation ability, with read-outs such as: cell speed, persistence and ability to pass through constricted spaces.



Rare Diseases

Rare diseases are often linked with cell mechanics or cell organization disorders. The FMPs™ highlight alterations like these and one can measure molecular modifications more easily than with other models. For instance, cell nucleus healing in laminopathy is evaluated using FMPs™ Cell confinement by the observation of lamina reconstruction as a read out.



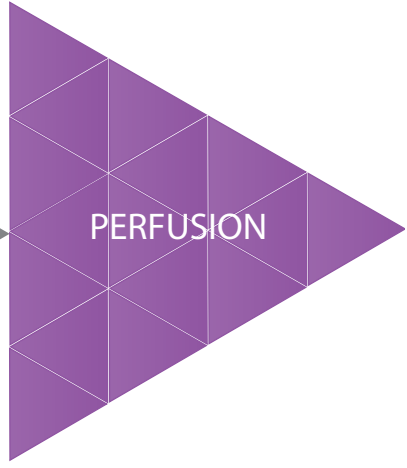
hPSC-CM on 4Dcell line micropatterns imaged by fluorescence microscopy. In collaboration with Dussaud S., Jouve C., Hulot J.S., 2018, INSERM, PARCC

Organ Physiology

The regular physiology of cells in living organs is closely linked with its spatial and mechanical organization. FMPs™ offer simple and representative models highlighting organ specific read-outs. For instance, FMPs™ Micropatterns induce striation of cardiomyocyte leading to standardized beating properties and internal organization.

4D Cell

THE 4 TECHNOLOGIES EMBEDDED IN THE FMPs™



4Dcell FMP™ MICROCHANNELS

CELL-CELL INTERACTION AND MIGRATION SOLUTIONS FOR HTS/HCS

The FMP Microchannels are a new generation of multiwell plates enabling more quantitative cell-cell interaction and cell migration assays than traditional designs.

Cells living in a specifically designed network of microchannels allows the quantification of cell activities such as cell migration, cell-cell interaction or nuclear plasticity.

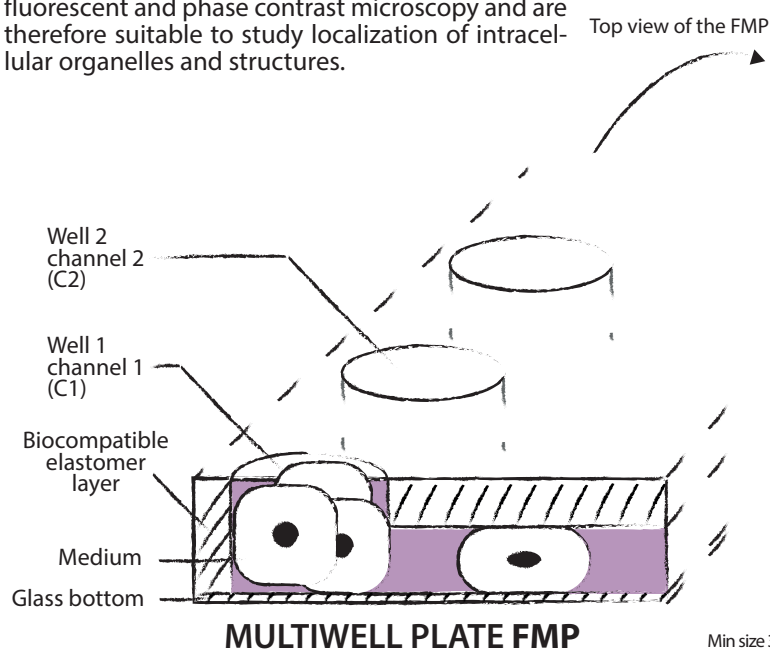
The simplified migration, with restricted directionality, facilitates the automatic tracking of cells and the extraction of quantitative parameters to describe cell movement.

- +** FLEXDYM™ BIOCOMPATIBLE MATERIAL
MORE RELIABLE FOR DRUG SCREENING ASSAYS
- +** FULLY ADAPTED TO
HIGH RESOLUTION IMAGING
- +** HIGH DEFINITION GEOMETRY
DOWN TO 1 MICROMETER
- +** ROBOT PIPETTE READY
SBS 96 WELLPLATES FORMAT

PRINCIPLE

The structures are made of an innovative biocompatible elastomer, which allows gas and nutrients exchange with low absorption effect. Cells are loaded into a central chamber communicating with multiple microchannels. The surface of the channels is functionalized (with adhesive or repulsive coating solution to promote or to prevent cell adhesion) allowing the control of the adhesive properties of the channels.

Microchannels are compatible with high resolution fluorescent and phase contrast microscopy and are therefore suitable to study localization of intracellular organelles and structures.



APPLICATIONS

CANCER

- Migration of metastatic cells
- Nuclear plasticity in metastasis
- DNA DSB repair (mechanically induced)
- Angiogenesis
- Immuno-oncology

IMMUNOLOGY

- Cell-cell interaction
- Migration of immune cells
- Antigen searching
- Extravasation/diapedesis
- Chemotaxis/haptotaxis

ORGAN PHYSIOLOGY

- Migration of cancer cells
- Shear stress
- Angiogenesis
- Epithelium permeability/brain blood barrier
- Neural network

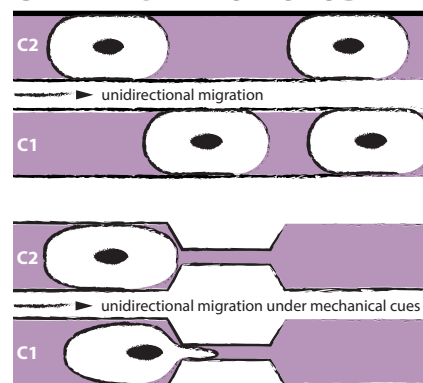
RARE DISEASES

- Cell nucleus integrity
- Nuclear plasticity
- Neural network

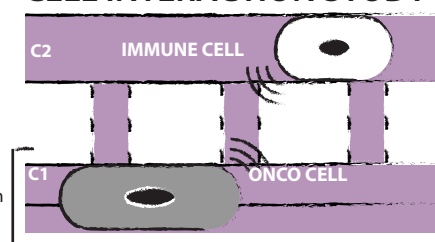
FUNDAMENTAL RESEARCH

- Cell adhesion
- All applications described above

CELL MIGRATION STUDY



CELL INTERACTION STUDY



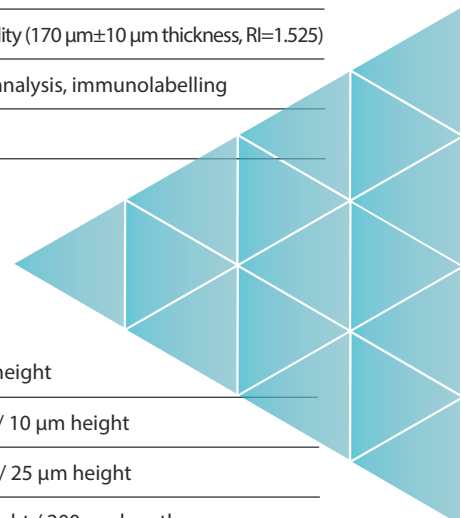
SUPPORTED CELL TYPES

All primary lineages and cell lines showing a migratory behavior: immune cells (dendritic cells, neutrophils, lymphocytes...), IPs, stem cells, tumoral cells, ...

TECHNICAL SPECIFICATIONS

Well dimension (mm)	6,4 mm diameter
Number of channels	Small and medium designs: average of 100 channels/access port / Large designs: from 20 to 2
Volume for microchannels loading	5 to 10 µl per access port
Materials	Flexdym; optical quality glass bottom for better imaging quality (170 µm±10 µm thickness, RI=1.525)
Read-out	Microscopy imaging, cell tracking, migratory behavior analysis, immunolabelling
Shelf life	12 months after date of production (at +4°C)

4DCELL Migration plate	Small size design	3, 4, 5, 6, 7, 8 µm width / 4 µm height
4DCELL Migration plate	Medium size design	10, 12, 14, 16, 18, 20 µm width / 10 µm height
4DCELL Migration plate	Large size design	50, 100, 200, 400 and 1000 µm / 25 µm height
4DCELL Migration plate	Small constrictions size	Channel: 5 µm width / 4µm height / 200 µm length Constriction: from 4 to 1 µm width, 15 µm length
4DCELL Migration plate	Medium constrictions size	Channel: 8 µm width / 4 µm height / 200 µm length Constriction: from 4 to 1 µm width, 15µm length
4DCELL Migration plate	Large constrictions size design	Channel: 12 µm width / 10 µm height / 200 µm length Constriction: from 12 to 1 µm width, 5 µm length



4Dcell FMP™ MICROPATTERNING

STANDARDIZATION SOLUTIONS FOR HTS/HCS

MICROPATTERNING
TECHNOLOGY

4Dcell micropatterned multi-well plates hold a perfectly organized culture substrate aiming for cell normalization. Evenly distributed on adhesive patterns, cells have a controlled geometry allowing a standardization of the assays.

- +** STANDARDIZATION OF CELL SHAPE
- +** FULLY COMPATIBLE WITH HIGH RESOLUTION IMAGING
- +** STABLE MOLECULAR COATING PAcrAm™ TECHNOLOGY
- +** HOMOGENOUS SEEDING 4DCELL HOMOGENIZER™ TECHNOLOGY

PRINCIPLE

The 4Dcell micropatterning technology enables a 2D cell geometry control. A set of patterns is arranged on a glass bottom to receive cells. Using an antiadhesive agent and some ECM proteins such as fibronectin or collagen, cells can adhere to the shape imposed by the micropattern. Cells are going to embrace the geometry of this new environment.

APPLICATIONS

CANCER

- Migration of cancer cells (line patterns)
- Cell shape standardization

ORGAN PHYSIOLOGY

- Migration of somatic and cancer cells
- Cell shape standardization
- Cardiomyocyte beating properties
- Neural network

RARE DISEASES

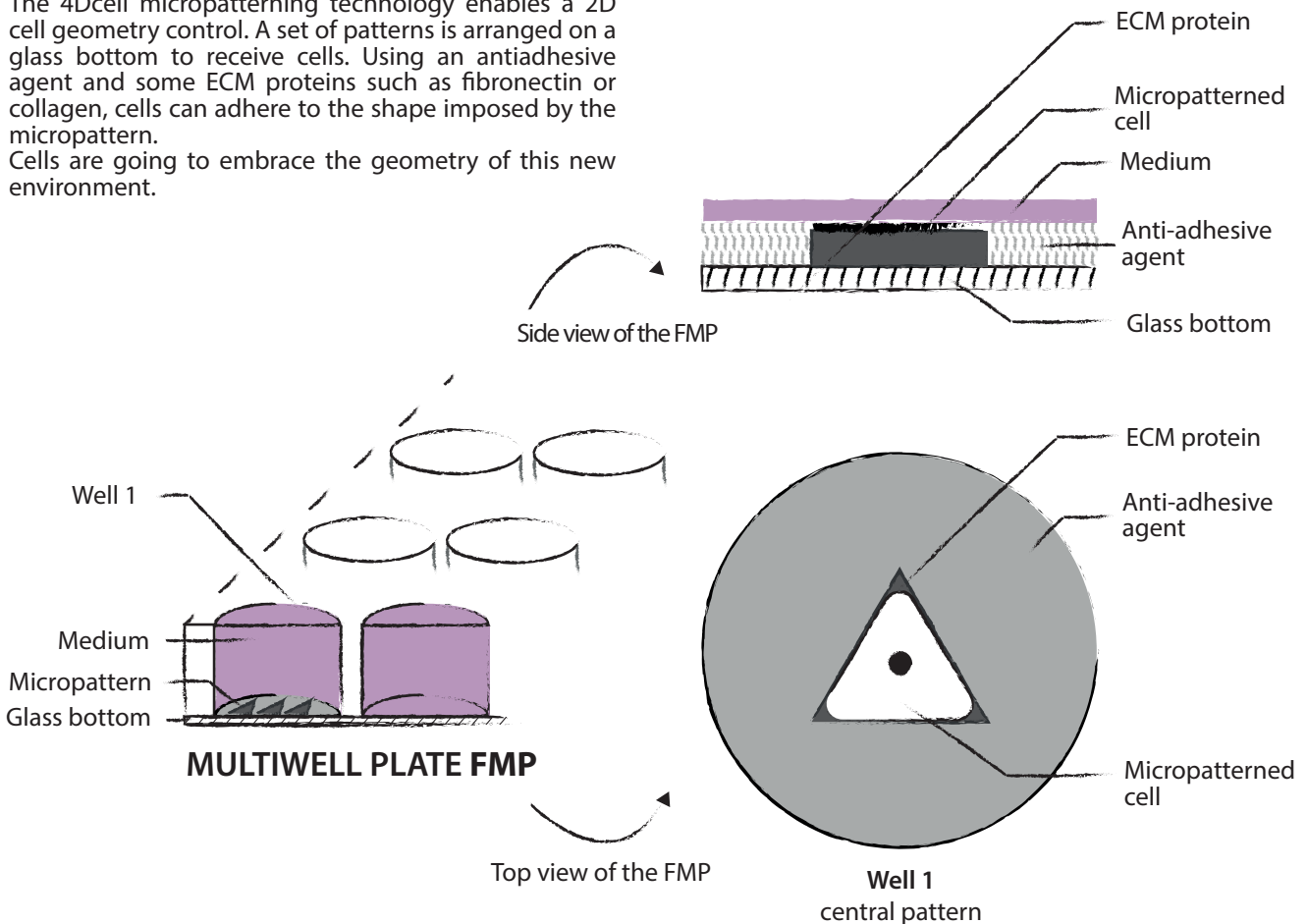
- Cell nucleus integrity
- Nuclear plasticity
- Neural network

FUNDAMENTAL RESEARCH

- Cell shape standardization
- Standardized connectivity between neurons

BIOMOLECULAR IN VITRO MODELS

- Spatial autoorganization of macromolecules (at the microscale)

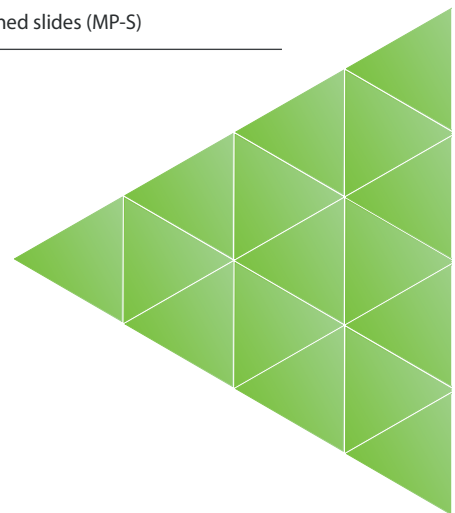


SUPPORTED CELL TYPES

Any adherent cells can be micropatterned in theory. Some cell types might need specific conditions (for instance, insect cell lines).

TECHNICAL SPECIFICATIONS

Plate format	Standard SBS format (127,76 x 85,48 mm)
Number of wells	1, 6, 12, 24, 48 and 96
Standard pattern shapes	Disk, line, rectangle, triangle, square, grid
Sizes of the standard patterns	10, 20, 30, 40, 50, 70 and 100 μm
Anti-adhesive agents	PLL-g-PEG, covalently bonded anti-fouling polymer
Read-out	Cell with a reproducible shape allowing quantification of cell organelles position, etc...
Alternative products	35 mm \varnothing micropatterned dishes (MP-D), 24 mm \varnothing micropatterned slides (MP-S)



4Dcell FMP™ CELL CONFINEMENT

FULL MICROENVIRONMENT CONTROL SOLUTIONS FOR HTS/HCS

The 4Dcell confiner reproduces the natural cell environment. This is possible since we are able to control the mechanical and chemical properties surrounding cells as cell geometry, environment elasticity and surface chemistry.

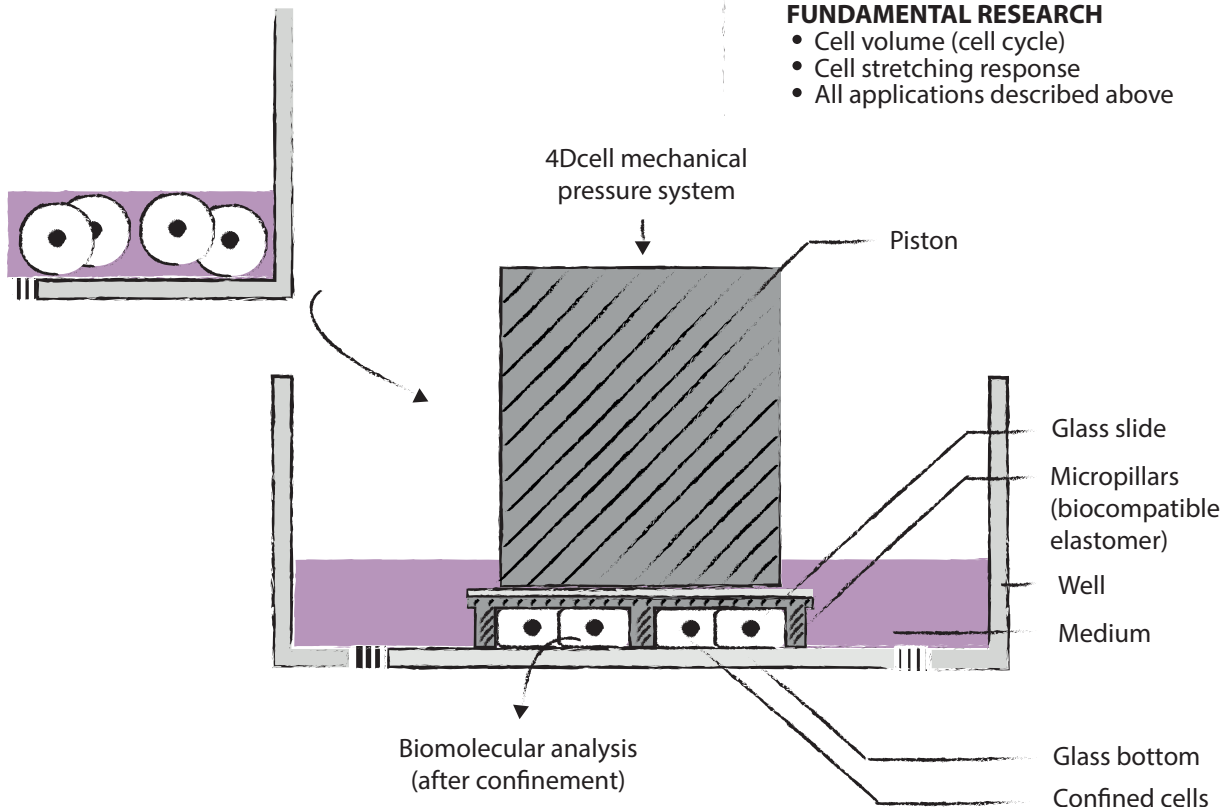
- ⊕ **PRECISE CONTROL OF CELL GEOMETRY**
- ⊕ **CONTROL THE ENVIRONMENT ELASTICITY**
- ⊕ **VERSATILE SURFACE CHEMISTRY**
VARIOUS SURFACE FUNCTIONNALIZATION
- ⊕ **ABERRATION-FREE**
HIGH RESOLUTION IMAGING
- ⊕ **REVERSIBLE PROCESS**
FOR BIOMOLECULAR ANALYSIS

PRINCIPLE

The 4Dcell confiner allows squeezing micrometer-sized cells or other biological samples between two parallel surfaces, with micrometer precision. The method for confinement is based on the application of a confining slide on the cell culture (or tissues, ...).

The patented technology developed at 4Dcell ensures the uniformity of the confinement height.

The confiner was developed to be used with commercially available multi-well plates, enabling confinement of multiple wells simultaneously.



APPLICATIONS

CANCER

- Migration of metastatic cells
- Cell contractility in metastasis
- DNA DSB repair (mechanically induced)
- Genomic instability (cell division)
- Separated co-culture

IMMUNOLOGY

- Migration of immune cells
- Imaging of non-adhesive cells

ORGAN PHYSIOLOGY

- Migration of cancer cells
- Cell differentiation with stiffness control
- Wound healing
- Separated co-culture
- Cell compression response

RARE DISEASES

- Cell nucleus integrity

AGING

- Cell nucleus integrity
- Autophagy related diseases

OBSERVATION OPTIMIZATION

- Imaging of non-adhesive cells
- Planar imaging of organelles

FUNDAMENTAL RESEARCH

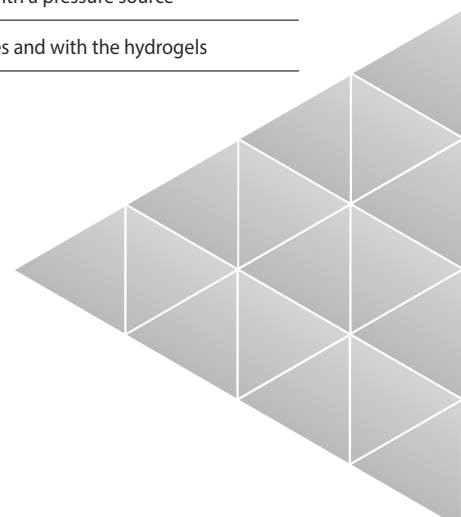
- Cell volume (cell cycle)
- Cell stretching response
- All applications described above

SUPPORTED BIOLOGICAL SAMPLES

- Cells (adherent and non-adherent)
- Uni/pluricellular organisms
- Tissues
- Organoids

TECHNICAL SPECIFICATIONS

Plate dimension (mm)	Standard SBS format (127,76 x 85,48)
Number of wells confined	1, 6, 12, 24, 48 and 96
Confinement height	1, 2, 3, ... 20 μm
Materials	Confinement slides (optically transparent glass and PDMS)
Read-out	Cell imaging of non-adhesive cells, cell contractility, cell volume, nuclear plasticity, etc ...
Alternative product	4DCell dynamic confiner, confinement can be modulated with a pressure source
Integration with other 4Dcell products	The cell confiner can be used with the micropatterned slides and with the hydrogels



4Dcell FMP™ PERFUSION

LONG TERM CELL CULTURE SOLUTIONS FOR HTS/HCS

PERFUSION
TECHNOLOGY

4Dcell perfusion is a novel system embedded in a cell culture plate cover. It enables obtaining a stable flow with a fast change of the reagents at a microscale quantity. The perfusion lid is well for the long term cell culture. It allows removing toxic wastes of the living cells. The high viability and the cell confluency is achieved by changing the flow rate of the medium. The bottom of the lid is made of optically transparent glass enabling the utilisation of high resolution microscopy.

- ⊕ FULLY COMPATIBLE WITH HIGH RESOLUTION IMAGING
- ⊕ FAST REAGENT SWITCH
- ⊕ BIOCOMPATIBILITY
- ⊕ NO BUBBLE FORMATION
- ⊕ LONG TERM LIVE CELL IMAGING

PRINCIPLE

The structure is designed to provide a stable flow around the cells. It deals with a small volume, thus allowing the fast change of the medium, and control the shear stress on cells.

APPLICATIONS

DRUG ASSAY METHODS

- Fast medium switch
- Complex dose response of cells

IMMUNOLOGY

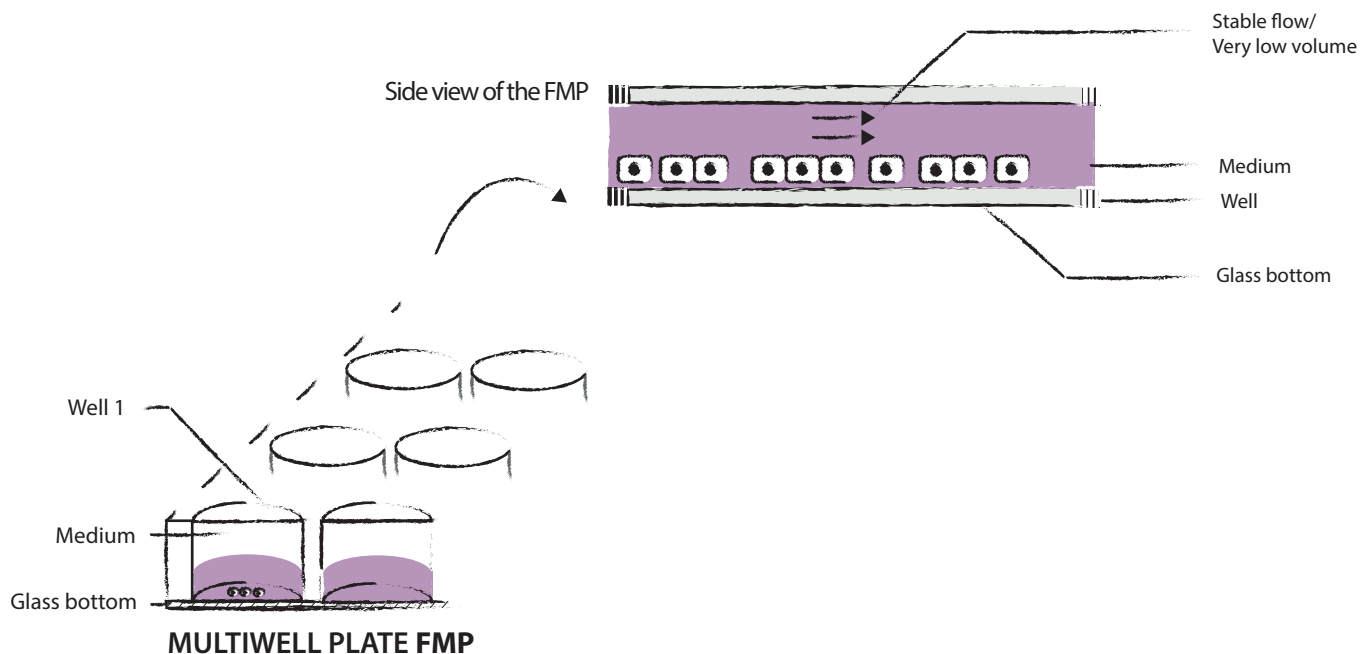
- Fast medium switch

ORGAN PHYSIOLOGY

- Long term cell culture
- Fast medium switch

FUNDAMENTAL RESEARCH

- Cell adhesion in response to a controlled shear stress
- All applications described above

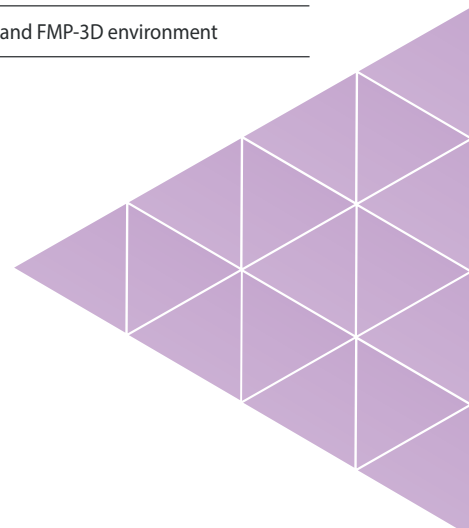


SUPPORTED BIOLOGICAL SAMPLES

- Cells (adherent and non-adherent)
- Tissues
- Organisms

TECHNICAL SPECIFICATIONS

Plate format	Round, rectangle, multi well standard SBS format (127,76 x 85,48)
Perfused chambers	1, 6, 12, 24, 48 and 96
Perfused volume	100-400 μ L
Material	Glass optically transparent
Perfusion rate	10 nL/min - 5 mL/min
Inlet diameter	< 1 mm
Read-out	Long term cell analysis, in time cell response to a medium change
Integration with other 4Dcell products	The perfusion system can be used with FMP-Standardization and FMP-3D environment



4Dcell

EXPLORE BETTER.

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