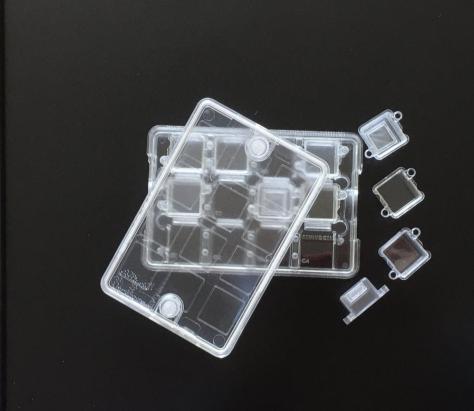


A single platform enabling the study of different cell-cell interactions in real time

www.revivocell.com







Revivocell is a UK spin-out from Lancaster University based at Sci-Tech Daresbury Science Incubator Hub, Warrington. We develop cell culture technology to improve life sciences research and enhance drug discovery success. We want to enable scientists to be more creative in their research by proving next dimension cell culture technology, which is easy to use and interactive, whilst closely mimicking body-like conditions and reducing animal testing.

Create your own unique experiments using this versatile and straightforward platform

CELLBLOKS® is unique because like no other plate platform allows you to study complex in-vivo like cell-cell interaction studies with ease. The interactive "plug and play" nature of the device makes it versatile allowing you to perform a wide range of cell-cell combination studies. Using **CELL**BLOKS® you can build complex models by simply putting together different cell growth Pods in one platform that are designed to mimic both barrier organs and those in systematic circulation.

The platform is designed in standard SBS plate format that makes it compatible with standard readout equipment and minimizes any workflow disruption.

Save time

Easy to set up "Plug and Play" POD design also facilitates modification of experiments in real time

This unique platform design allows you to **remove and substitute** individual cell growth Pods from the base chamber at any time during the study without disturbing other cells in culture. This gives you more time to generate data that you need and spend less time in re-setting the experiments from the beginning. Since the platform is compatible with standard equipment no major investment is required and no special training is needed for conducting your research.

Multiple cell type co-culture

Configure combinations matrix to determine the interaction of each cell type being studied

CELLBLOKS® system allows you to set-up of three-way combination possibilities which means that each cell type in a system can be tested individually, in sets of two and in a tri-culture all within one plate. In fact, **CELL**BLOKS®, is the only platform that enables researchers this three-way expansion.

CELLBLOKS® matrix enables you to identify and select correct cell type combinations for further study at early stage, helping you save time and money.

Quick and simple analysis

Visualise and monitor in real-time

The open top access allows you to monitor the experiments in real-time. Whilst cells can also be imaged live by a standard confocal microscopy without being disrupted. In addition, using media collection ports diffused molecules can be collected for further analysis while the cells are interacting permitting long term effect to be studied.



More productive

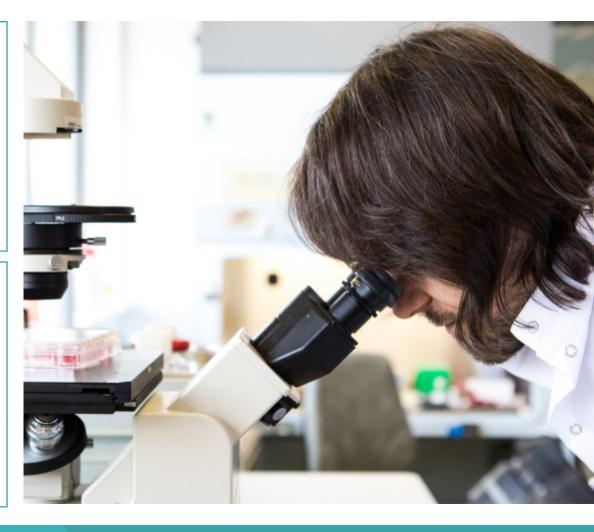
Perform multiple experiments simultaneously in one platform

Each platform has four individual channels that permits you to perform separate cell-cell interaction experiments all at the same time within one device, enabling more productivity in less time.

Improved reproducability

Produce reliable data by maintaining similar environments across experiments

The **CELL**BLOKS® is designed in a standard SBS plate format to work with regular CO₂ incubator and readout equipment. This enables you to minimize environmental differences across standard culture vessels and read-out equipment giving you more reliable and reproducible data.



How does it work?

The technology

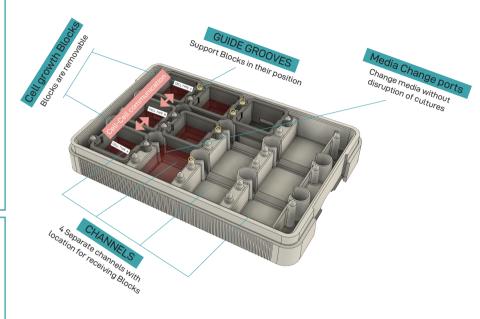
CELLBLOKS®, is a multi-organ/cell type modular "plug and play" co-culture technology. It serves the purpose of emulating the organ microenvironment in a standard in-vitro setting. It provides the feasibility of studying the assays in 2-D, 3-D cell growth condition, and in static or flow system, by using a standard perfusion rocker

Using **CELL**BLOKS® different cell types can be grown on Barrier Pod ™ or Circulatory Blocks™ that emulate barrier organs or those in systematic circulation. Blocks containing organ specific cells can then be connected to each other in variety of ways to simulate complex organ-organ interactions. For instance, Intestinal cell are grown on Barrier Blocks, whereas Liver and lung cells in Circulatory Blocks

The Platform

Cell-cell communication studies made easy

CELLBLOKS® platform has dimensions of a SBS standard Tissue Culture well plate. It has four sperate elongated channels with location for three separate Blocks. Each channel is filled with media (3-5 ml) to allow the cell-cell communication between Blocks.



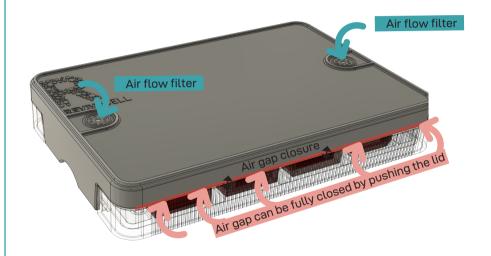


The Air-Lid

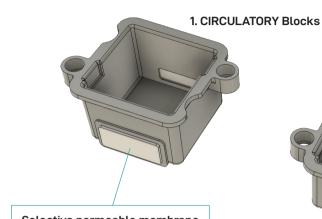
Better ways to reduce contamination, media evaporation and avoid pH drifts

The **CELL**BLOKS® chamber comes with new design Clip-Closure "Air-Lid" feature with two side clips that make it easy to create 100% hermetic seal around the chamber.

PTFE air filters and an o-ring seal have been incorporated in the lid in order to filter the air reaching cell cultures. Gas is in cultures is only exchanged through selectively permeable air filters (0.2 micorn) which reduce potential contamination of cells, evaporation of media, and fluctuations of pH during experimentation. In contrast to other cell culure platforms the Air-Lid technology is first-of-its-kind - enabling more reproducible data acqusitions and handling advantages.



THE CELL GROWTH Blocks



Selective permeable membrane

Media Circulation through the side
membranes



Selective permeable membrane
Allows cells to form barriers with
tight-junctios



<u>Closed Block</u>
Prevents cells communicating
with other Blocks



Achieve better representation of different Organtype communications

CELLBLOKS® Blocks are of three different types.

- 1. Circulatory Blocks[™] provide a flat plastic surface for cells to grow with side circulatory windows on the walls allowing selective media diffusion (both inlet and outlet, simulating organs in systematic circulation e.g. liver, brain, heart, lung).
 - **2. Barrier Blocks** $^{\text{TM}}$ contain a selective permeable membrane on the bottom of the Pod, allowing cell to proliferative on basolateral membrane (simulating epithelial cells and tissues).



3. Blank Blocks[™] have the same flat surface as the Circulatory Blocks for cell growth but no inlet or outlet for media diffusion. Blank Blocks are used to isolate cell cultures from other compartments.

In addition, the modular nature of the device allows the removal of one or more cell growth Blocks from the chamber to perform separate analysis without disturbing others cell compartments in culture.

Furthermore, as it provides separate compartments for each cells of a co-culture that cross-communicate among each other through media without leaving their compartment (unlike the conventional co-culture models), this permits user to study individual biology of each cell (e.g. protein, imaging, DNA).

Application of CELLBLOKS ®

CELLBLOKS[™] facilitates a unique customisable platform for multi-organ or cell type co-culture physiological experiments not provided by any other product. The platform covers number of applications including:

- » Study the absorption, distribution and metabolism (ADME) for drug discovery
- » Liver Modelling for pre-clinical Drug induced liver injury (DILI) screening (case study below)
- » First pass metabolism incorporating GI tract and Liver compartments
- » Modelling of Skin layers
- » Tissue engineering
- » Stem cell interaction with cancer and immune compartments



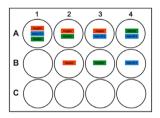


Case Study: Modelling multiple cell type liver architype for drug induced liver injury (DILI) screening using CELLBLOKS®

A liver architype was built by creating three-way co-culture interaction study involving three cell types, Hepatoma cell line (HepG2), Fibroblast cell line (NIH/3T3) and endothelial cells (HUVEC). The performance of CELLBLOKS® non-contact co-culture model was compared to that of cell mixture contact culture model in standard well plate format. Hepatic function markers including Albumin, Urea and Cytochrome P450 enzymes were measured and compared in both models.

CELLBLOKS Total Coll interaction through models The coll coll interaction through models The coll interaction through m

Standard 12-well plate



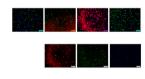
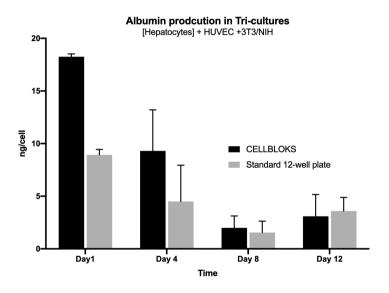


Figure 1. Liver model set up on CELLBLOKS® platform in non-contact vs. contact co-culture standard format.

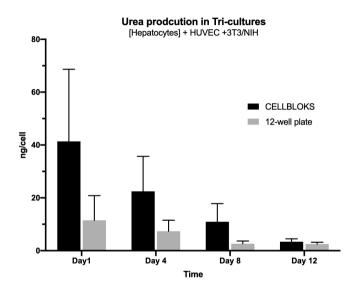
Hepatic function marker expression

Non-contact tri-culture in CELLBLOKS® set up vs. contact cultures in standard 12-well plate.

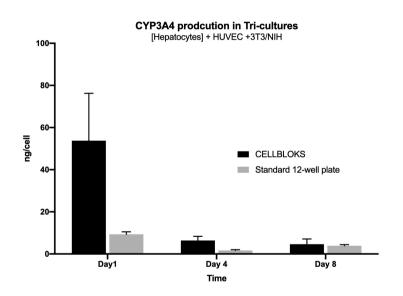


Expression of Albumin protein levels in HepG2 cell. Comparison of CELLBLOKS® non-contact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines (HepG2).





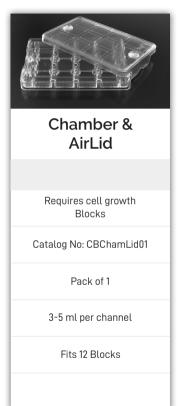
Expression of Urea protein levels in HepG2 cell. Comparison of CELLBLOKS® non-contact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines (HepG2).

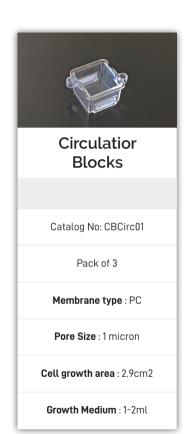


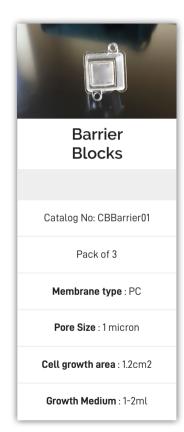
Expression of CYP450 3A4 protein levels in HepG2 cell. Comparison of CELLBLOKS® non-contact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines (HepG2).

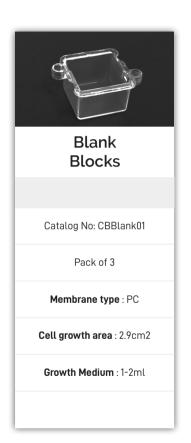


Specifications











A single platform enabling the study of different cell-cell interactions in real time



Improving research in drug discovery

Revivocell Limited, Sci-Tech Daresbury, Keckwick Lane Daresbury, Warrington, WA4 4AD, United Kingdom

Phone: +44(0)7588015987 Website: www.revivocell.com Email: info@revivocell.com