How does it work?

REVIVOCELL



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

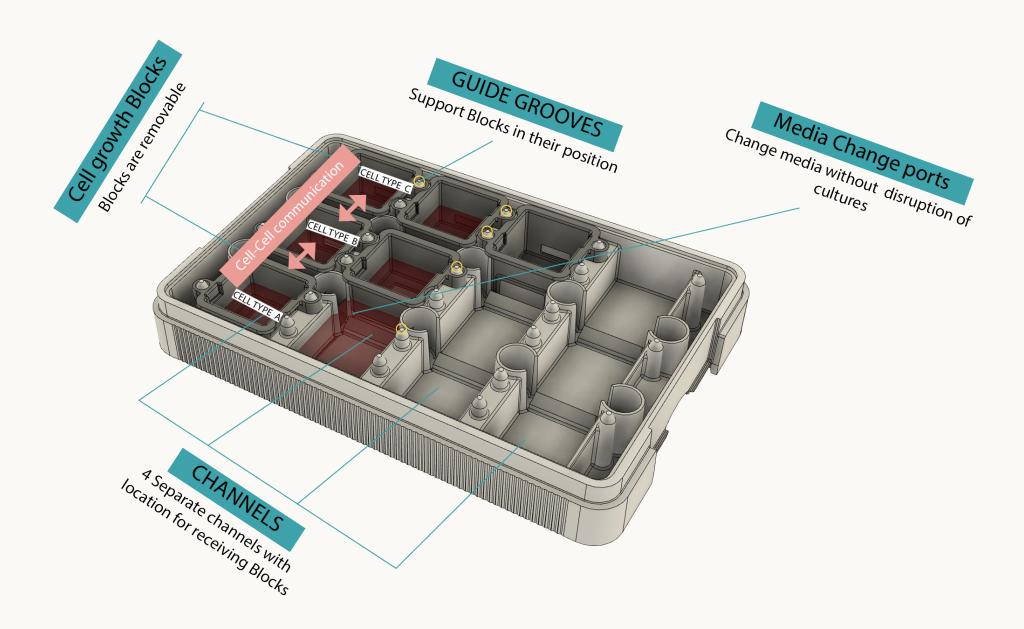
Using **CELL**BLOKS[®] different cell types can be grown on **Barrier Blocks[™]** or **Circulatory Blocks[™]** that emulate barrier organs or those in systematic circulation. Blocks containing organ specific cells can then be connected to each other in variety of ways to simulate complex organ-organ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

In this way you can quickly and easy set up an experiment in the lab to simulate complex body conditions, for example, to test how organs communicate to each other when they are exposed to a test drug

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 the Blocks



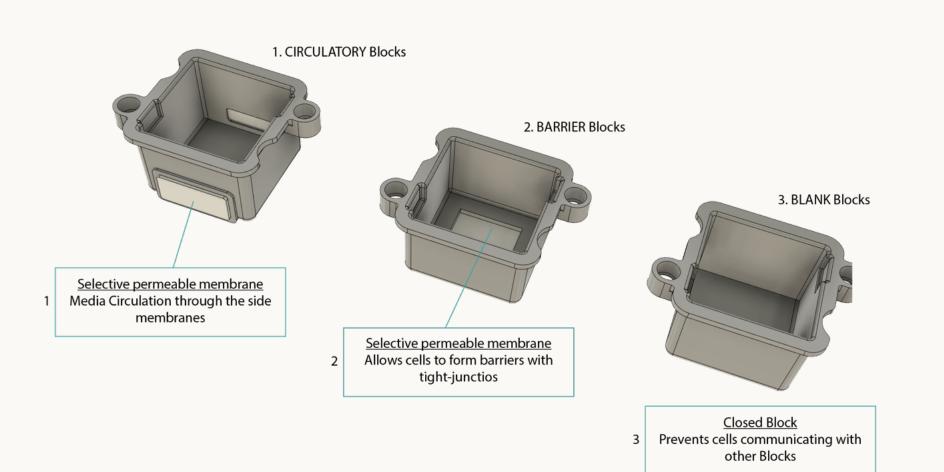
THE CELL GROWTH BLOCKS

Achieve better representation of different Organtype communications

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™ contain a selective permeable membrane on the bottom of the Block, 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 and are often used as controls.



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.

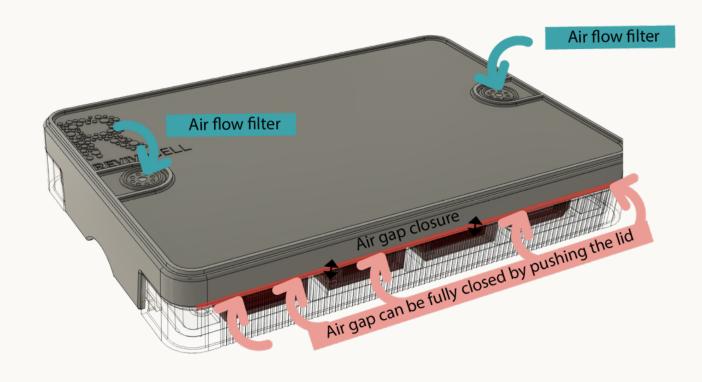
Furthermore, as it provides separate compartments for each cells of a co-culture that crosscommunicate among each other through media without leaving their compartment (unlike the conventional co-culture models), this permits user to study individual biology of each cell (e.g. protein, imaging, DNA).

FILTERED AIR FLOW

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

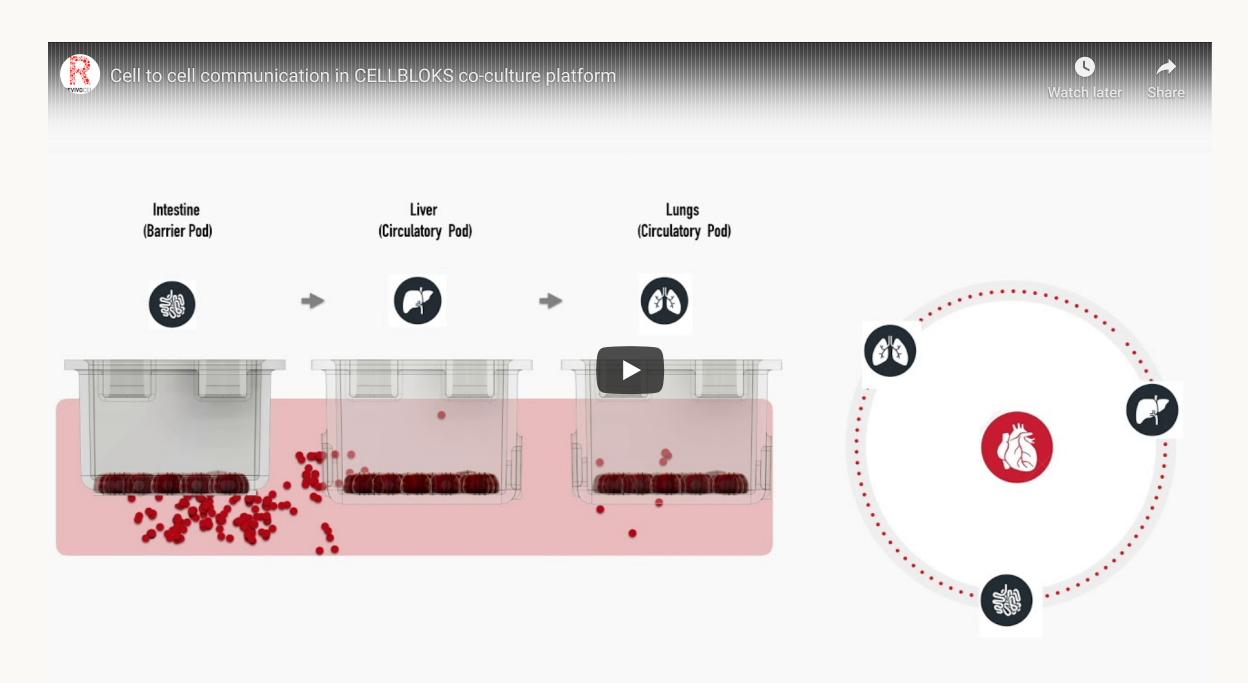
The CELLBLOKS® chamber comes with new design Clip-Closure "Air-Lid" feature with two side clips that make it easy to create 100% hermetic seal around the chamber.

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 culture platforms the Air-Lid technology is first-of-its-kind - enabling more reproducible data acquisitions and handling advantages.



How do the molecules diffuse between the Blocks

Watch the illustrated video



How does it compare to conventional well plate inserts?

<u>Learn more</u>

Applications of **CELL**BLOKS[®].

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 of drugs incorporating GI 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.

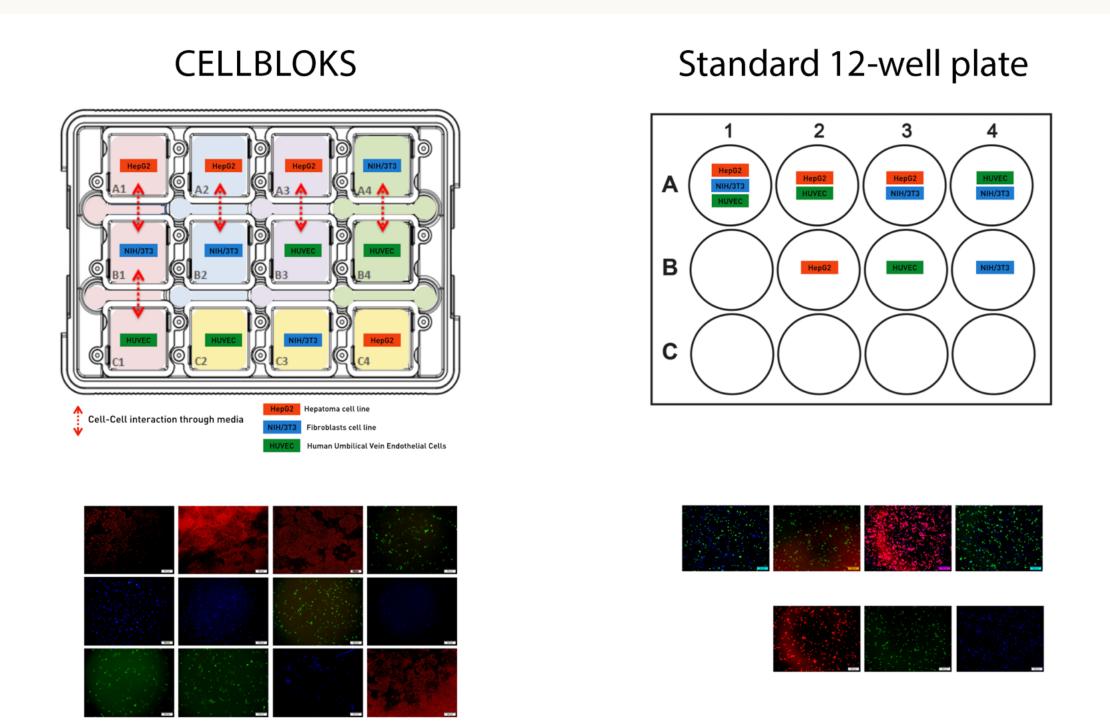


Figure 1. Liver model set up on CELLBLOKS[®] platform in non-contact vs. contact co-culture standard format.

*Circulatory Block Kit was used to model the liver. Cell-cell interactions were tested in a triculture (A1-- B1--C1), set of two combinations (A2--B2), (A3--B3) and (A4--C4) and in isolation to determine which cell-cell combinations producing optimal most hepatic relevance. Each cell type was grown grown in isolation at the same time using in Blank Blocks in (C2), (C3) and (C4) compartments.

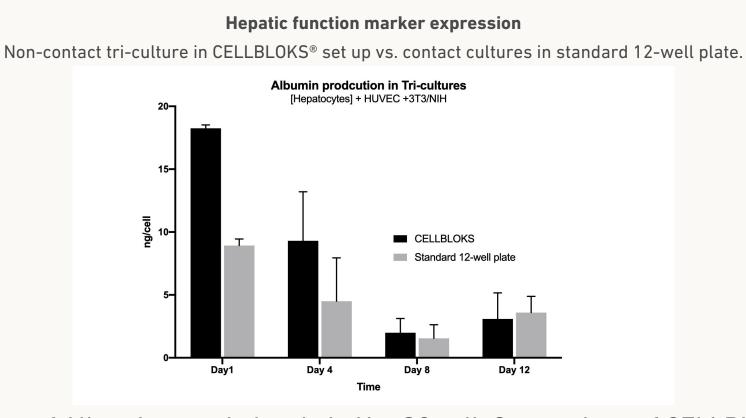


Figure 2. Expression of Albumin protein levels in HepG2 cell. Comparison of CELLBLOKS[®] noncontact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines (HepG2).

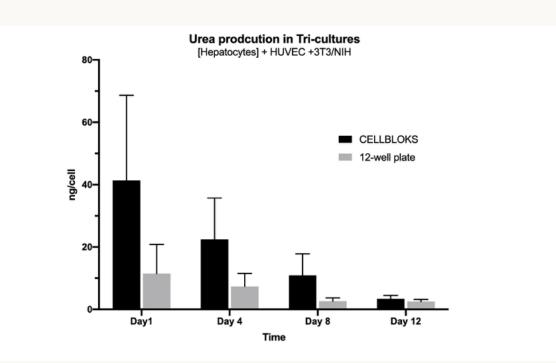


Figure 3. Expression of Urea protein levels in HepG2 cell. Comparison of CELLBLOKS® non-contact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines

(HepG2).

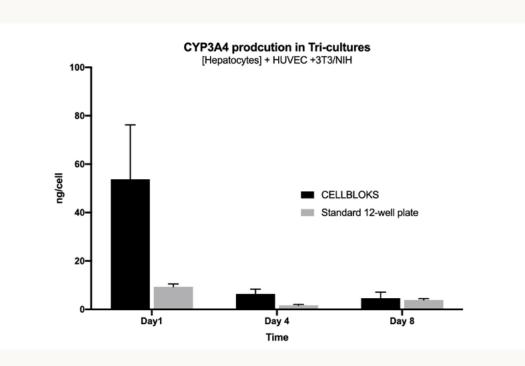
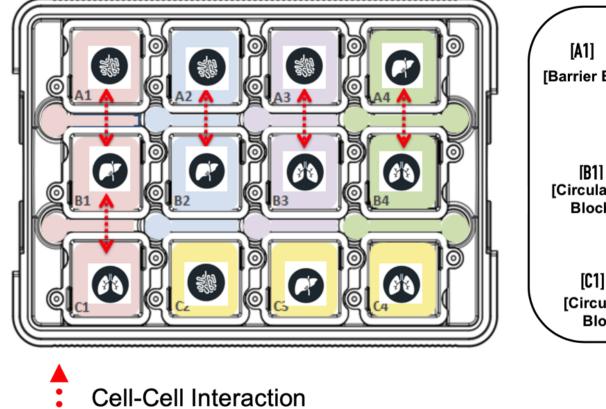


Figure 4. Expression of CYP450 3A4 protein levels in HepG2 cell. Comparison of CELLBLOKS® noncontact vs. standard well plate contact format interaction tri-culture study measured in hepatoma cell lines (HepG2).

TRI-ORGAN CO-CULTURE EXAMPLE

Drug ADME modelling

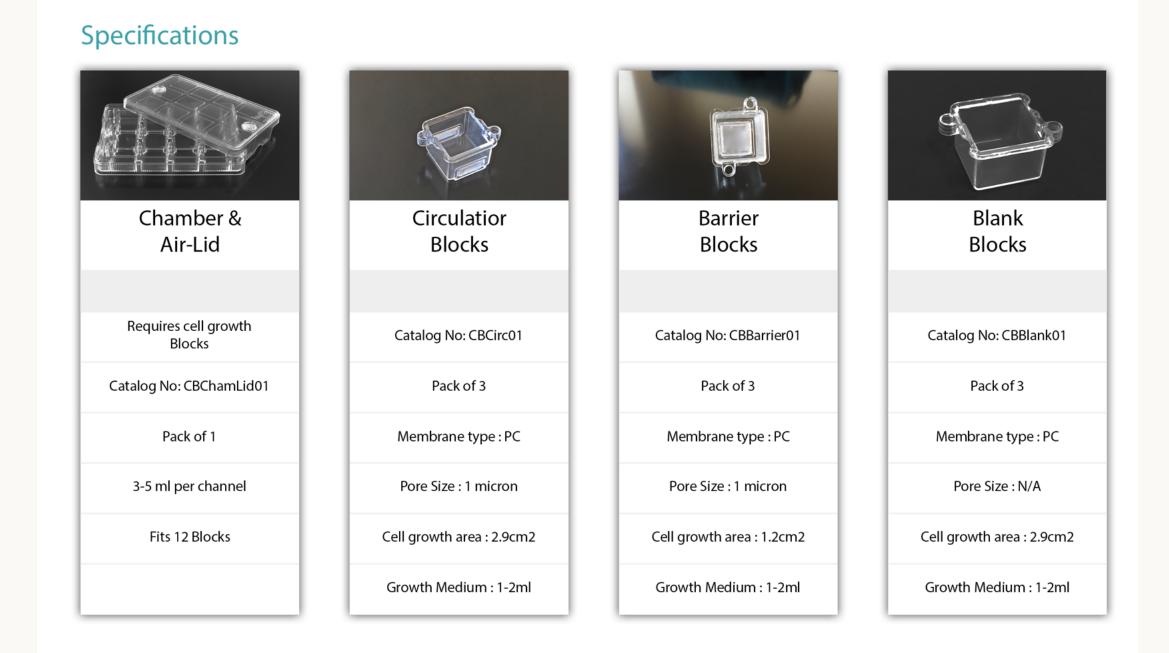
The example below shows how an intestine-hepatic model can be simulated in the **CELL**BLOKS® by using the <u>Customised Kit</u> platform to study the absorption, distribution and metabolism (ADME) of a drug or chemical as well as its effect on a target organ. Briefly, the Intestinal layer is modelled by growing CaCo-2 cells, for example, on Barrier Blocks that allows absorption of the drug. After absorption through the intestinal epithelium, the drug diffuses and is distributed into the channels (containing media) and to latter Blocks containing separate liver and lung compartments. The liver cells in the latter Circulatory Block metabolises the drug and the third compartment (lung) is used as a target organ. **CELL**BLOKS® can be used to set-up a tri-organ co-culture experiment and determine the effect of each compartment on the interaction between them. This is achieved in ONE PLATFOM by using combination of Barrier, Circulatory and Blank Blocks. As illustrated below, 12 Blocks are needed in total and they arranged in combinations of 3s, 2s and isolated blanks.



| [A1] [Barrier Block] | [A2] [Barrier Block] | [A3] [Barrier Block] | [A4] [Circulatory Block] |
|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| [B1] [Circulatory Block] | [B2] [Circulatory Block] | [B3] [Circulatory Block] | [B4] [Circulatory Block] |
| [[1] [Circulatory Block] | [C2] [Blank Block] | [C3] [Blank Block] | [C4] [Blank Block] |

Specifications

through media



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