







# Organ-on-a-Chip Platforms for Cell Culture Studies

# Microfluidic tools for sophisticated co-culture and cell-cell interaction experiments

The introduction of microfluidic systems in cell culture, tissue culture, and organ-on-a-chip experiments aims to mimic physiological conditions *in vitro*. Miniaturized systems enable to study cells in a controlled environment, leading to significant advancements in various fields of life sciences. The complexity of microfluidic cell cultures can thereby vary greatly.

For advanced cell culture requirements, our **cross-flow membrane chips** and **interaction chips** allow for the co-culture of various cell types.

While the interaction chips feature transmissive pillar barriers to facilitate the exchange of small molecules and migrating cells between compartments, our cross-flow membrane chips are divided by a permeable membrane into two compartments (cross section schematic: see below). Different cell types can be cultivated in either compartment.



#### **Co-Culture of Adherent Cell Types**

- Wide selection of chip designs for different coculture settings
- Different chamber sizes, chamber heights and materials available
- Hydrophilic materials that promote the attachment of cells available

#### **Cross-Flow Membrane Chips**

- Monitor cell-cell interactions between cells cultured in two compartments, divided by a permeable membrane
- Membrane pore sizes from 0.2  $\mu$ m 8  $\mu$ m
- Each compartment with individual fluidic circuit
- Particularly suited for epithelial and endothelial cell culture settings



Cross-flow membrane chip Fluidic 653 with porous membrane embedded between the compartments

## **Chamber & Channel Interaction Chips**

- Transmissive pillar structures on chip serve as physical barriers between co-cultured cells or between cells and a flowing medium
- Monitor cell-cell interactions of cells cultivated in separate compartments
- Various experimental settings possible



Chamber interaction chip Fluidic 782 with transmissive pillar barrier to separate fluidic flow and a cell culture chamber



#### **Experimental Setup - Overview**

Successful cell culture experiments do not require much! Here is what you need for cell culture & organ-on-a-chip experiments:

- 1. Microfluidic chip
- 2. Fluidic accessories such as:
  - a. Fluidic interfaces, e.g., Mini Luer fluid connectors, low volume displacement plugs
  - b. Tubing, e.g., PEEK or PTFE tubing
  - c. Adapter frame for convenient handling
- 3. LOC CCI 1: microfluidic ChipShop's dedicated cell culture incubator in microscope slide formate
- 4. Pump setup

## **Chip Features - Summary**

*microfluidic ChipShop* offers a multitude of cell culture chips in microscope slide format. The chips vary greatly in design and complexity. The following features apply to all of our cell culture chips, serving as the basis for your successful cell culture experiment:



# **Choice of Material**

microfluidic ChipShop's cell culture chips are available in two materials, **Topas** (COC) and **Polystyrene** (PS). PS, the material from which most standard multi-well plates are made, is characterized by its biocompatibility. It shows the best gas exchange properties and is hence recommended for static cell culture experiments with minimal or no flow rates of medium. Topas features a very low autofluorescence and is hence recommended for experiments with fluorescence read-outs.

#### **Surface Modification**

*microfluidic ChipShop's* cell culture chips are made from hydrophobic thermoplastic materials. In their standard configuration, they do not promote cell-attachment, making them well-suited for suspension cell culture experiments.

Want to carry out adherent cell culture experiments? No problem! Each chip can be ordered with an extra **hydrophilization treatment**. Hydrophilic surfaces enhance cell attachment. Please note that all our integrated membranes are always treated to promote cell adhesion, regardless of the chip surface treatment.





#### **Cross-Flow Membrane Chips - Co-Culture in One Chamber**

The cross-flow membrane chips feature two inlet and outlet ports, one above and one below the membrane. While cell culture is a prominent application, the design supports a wide range of experiments, including small molecule transfer measurements and on-chip dialysis.

The cross-flow membrane chip represents a microfluidic chip system for adherent cell culture and thus the generation of diverse cellular co-cultures. Cell cultivation is carried out in two units per chip, with each unit representing a membranedivided two-chamber system in itself. Cell cultivation occurs on the integrated membrane. The cavities are connectable via the ports, allowing for elaborate applications and examinations of the chambers. Cross-flow membrane chips are available with different membranes, each featuring distinct pore sizes. Below is an overview of critical culture vessel characteristics for our cross-flow membrane chips. These will assist to set up defined experimental parameters like cell seeding densities or alike.



Cross-flow membrane chip perfused with colored liquids







Interaction area of a cross-flow membrane chip for cell culture applications

Bottom chamber of cross-flow membrane chip Fluidic 480

Upper chamber of cross-flow membrane chip Fluidic 480

#### **Specifications of the Cross-flow Membrane Chips**

Fluidic Design	Interface Type	Available chip mate- rials	Available membrane pore sizes [µm]	Interaction area [mm <sup>2</sup> ]	U <sub>l</sub> Volume [µl]	oper chan Total Surface [mm <sup>2</sup> ]	nber Ground Surface [mm <sup>2</sup> ]	Botte Volume [µl]	om chaml Total Surface [mm <sup>2</sup> ]	oer Ground Surface [mm <sup>2</sup> ]
480	Mini Luer	Topas, PS	0.2; 0.4; 3; 8	36.0	87.5	440.0	154.0	61.5	271.0	118.0
568	Mini Luer + Luer	Topas, PS	8	40.6	105.8	605.0	151.0	64.0	281.0	120.0
653	Mini Luer	Topas, PS	0.4; 3; 8	71.5	145.0	595.0	223.5	101.8	419.0	185.0
694	Mini Luer	Topas, PS	3; 8	71.5	137.8	573.5	220.0	79.5	340.7	140.0
747	Mini Luer	Topas, PS	0.4; 8	71.5	281.4	1138.0	456.0	101.8	419.0	185.0
846	Mini Luer	Topas, PS	8	395.5	500.0	1795.5	803.0	402.8	1818.7	674.7

#### Did you know? Customization possible!

Upon request microfluidic ChipShop offers integration trials of your customized membrane. Reach out to inquiries@ microfluidic-ChipShop.com to discuss your project!

#### **Available Cross-flow Membrane Designs**

The cross-flow membrane chips are in stock and can be ordered (price on the right) within a few days. Please contact us for the product code corresponding to your preferred product configuration.

Product Code	Chip Material	Membrane pore size [µm]	Surface treatment	Price [€/chip] 1+ 10+ 100+		
Cross-flow membrane chip	Topas or PS	**any available	none	79.50	63.50	42.50
**any design**	Topas or PS	membrane**	hydrophilized	89.50	69.40	47.10







#### **Customization - Open Platform for Membrane Access**

*microfluidic ChipShop's* cross-flow membrane chips can be ordered as an open system for self-assembly. The chips come without a cover lid, to enable the access to the membrane. The chips come with a medical grade double-sided adhesive gasket to ensure proper sealing after handling. Removing the protective liner of the adhesive will enable you to seal the chips with substrate of your choice.

Please reach out to Inquiries@microfluidic-ChipShop.com for feasibility and pricing.





Fluidic 480 with open top and structured adhesive tape (protective liner in white) to integrate e.g. tissues and close off with a substrate of your choice

#### **Real-time Monitoring of Cell Culture Parameters - Integrated Optical Sensors**



Combining the cell culture chips with *microfluidic ChipShop's* dedicated sensor-integration chips enables you to monitor common parameters such as  $CO_2$ ,  $O_2$  or pH, in real-time. These chips feature ports, that are compatible with the PreSens sensor system. The ready-to-use SensorPlug consists of a male Mini Luer interface, an optical fiber for read-out; and a specific sensor at the tip of the fiber. The SensorPlug is mounted directly onto the microfluidic channel network, ensuring that the sensor gets into contact with the fluid pathway. Thereby, changes in the concentration can be monitored in real-time.

The sensor-integration chip can be integrated up- or downstream of the cell culture chip to draw conclusions on factors such as cell viability or metabolic activity. The synergistic approach, combining our expertise in microfluidic designs with PreSens' prevailing sensor-technology, provides you with an advanced solution for dynamic, non-invasive and high-resolution monitoring of crucial cellular parameters in microfluidic environments.



Sensor-integration chip Fluidic 1090 with sensor interface before and after a chamber



Sensor-integration chip Fluidic 1457 with four sequential sensor interfaces along a straight microfluidic channel



Components of the PreSens

Product Code	Fluidic Design	Lid Thickness [µm]	Material	Pri 1 +	ce [€/cł 10+	nip] 100+
10001496	1090	125	PS	42.20	34.30	26.10
10001500	1090	188	Zeonor	42.20	34.30	26.10
10002024	1457	140	Topas	42.20	34.30	26.10



#### Advanced - The Cross-flow Membrane Chip as Multi-organ Platform

*microfluidic ChipShop* is your specialized partner when it comes to the development of complex, integrated microfluidic cartridges.

The **micro-iPS profiler** chip (Fluidic 1356) is a multi-organ chip system in a standardized double-slide format to ensure compatibility with common laboratory equipment.

The chip features in total four organ chambers, each with an incorporated porous cell culture membrane, dividing the chambers into an upper and a lower compartment. The largest chamber is used for the preparation of a liver organoid, while the other three chambers are used to culture different types of kidney cells. The main microfluidic circuit in the upper part connects all four chambers for continuous perfusion. A second circuit in the lower section is exclusively used for the liver chamber. The renal chambers are used for automated media exchange (usually every 24 hours). In addition, each chamber has individual inlet and outlet ports for cell seeding. Additional detection chambers and ports for SensorPlugs, enabling continuous monitoring of pH and  $O_2$  concentration, are integrated into the fluidic circuits.





Product for Fluid	Code lic 1356	Lid Thickness [µm]	Chip Material	Membrane pore size [µm]	Surface treatment	Prio 1 +	ce [€/ch 10+	iip] 100+
100020	52	188	Zeonor	8	none	132.98	88.50	64.70
100020	53	188	Zeonor	8	hydrophilized	135.98	90.50	66.40

# Interaction Chips - Co-culture in Separate Compartments

The interaction chips are a chip family that enables the evaluation of the effects of migrating molecules and cells from one compartment to another. This chip family consists of chamber as well as channel interaction chips. Interconnecting channels or transmissive pillar structures on the chip serve as physical barriers between co-cultured cells or between cells and a fluidic environment.

Cell-cell interactions can be effectively evaluated, such as the metabolic response to varying drug dosages. Various experimental settings can be implemented on the chips, each featuring different pathways and fluidic modules for molecules within the fluidic channel networks.



Channel interaction chip perfused with colored liquids



# The Chamber Interaction Chip Family - Fluidic 688, 737 and 782

The chamber interaction chips enable the co-culture of different cell types in interconnected yet separate chambers. Enabling the co-cultivation of diverse cell types represents a significant advancement in enhancing the physiological accuracy of *in vitro* models related to physiology and disease. Vascular networks connect all organ systems, transporting biomolecules from one location to another, mediating signaling cascades, gene expression and regulation, tissue homeostasis, immune response and disease progression.

There are three different interaction chips, each with slightly different designs enabling the setup of various co-culture scenarios.

# Co-culture different cell types to study:

- Soluble factor effects
- condition medium in the 2<sup>nd</sup> chamber with factors secreted by cells in the 1<sup>st</sup> chamber
- effect of cell "secretome" growth factors, cytokines, che mokines
- molecular gradients for chemotaxis and cell migration assays
- immune response and wound healing

- Multi-organ effects
  - multi organ-on-chip models
  - pharmacokinetic/ pharmacodynamic drug testing (AD MET – drug absorption, distribution, metabolism, excretion, toxicity responses)
- Physiologically relevant length scales
- cell signaling and cell-cell communication over distances









 $Chamber \ interaction \ chip \ Fluidic \ 688 \ with \ two \ subsequent \ cell \ culture \ chambers \ with \ an \ interconnecting \ channel$ 





Chamber interaction chip Fluidic 737 with two subsequent cell culture chambers and an innterconnecting channel, separated from the cultivation chamber by pillar structures Fluidic 782





Chamber interaction chip Fluidic 782 with a large upstream cell culture chamber, followed by two smaller chambers connected to the first chamber by a dividing channel

Product Code	Fluidic	Chamber		Lid Thickness Materi		erial Surface treatment		Price [€/chip]		
	Design	Volume [µl]	Depth [µm]	[µm]			1+	10+	100+	
10001055	688	37.8	400	140	Topas	none	36.20	24.30	16.10	
10001056	688	37.8	400	125	PS	none	36.20	24.30	16.10	
10001057	688	37.8	400	140	Topas	hydrophilized	39.20	26.30	17.80	
10001058	688	37.8	400	125	PS	hydrophilized	39.20	26.30	17.80	
10001059	737	53.1	600	140	Topas	none	36.20	24.30	16.10	
10001061	737	53.1	600	125	PS	none	36.20	24.30	16.10	
10001060	737	53.1	600	140	Topas	hydrophilized	39.20	26.30	17.80	
10001062	737	53.1	600	125	PS	hydrophilized	39.20	26.30	17.80	
10002048	782	59; 27	1100; 430	125	PS	none	36.20	24.30	16.10	
10002049	782	59; 27	1100; 430	125	PS	hydrophilized	39.20	26.30	17.80	



#### **Channel Interaction Chip Fluidic 983**

The channel interaction chip Fluidic 983 has been developed to study cells co-cultured in three adjacent channels, each of which can receive a microfluidic flow. The three channels are separated from each other by transmissive pillar barriers. On each channel interaction chip, five independent co-culture units can be found, which differ in the width of the pillar barriers. One potential culture setting involves using the two outer channels in perfusion mode, while the inner channel can be easily filled with a cell-containing gelatinous extracellular matrix (e.g. Matrigel<sup>®</sup>) for static 3D culture conditions. Both co-culture and migratory cell assays are potential applications.

#### **Chip description:**

Cell cultivation is possible in each of the five units present on one chip. Each unit consists of three adjacent cavities separated from each other by pillars. The central chamber has a size of  $1 \times 0.5 \times 18 \text{ mm}^3$  (w/h/l) and is the largest chamber with 7.8  $\mu$ l. The two adjacent chambers measure  $0.5 \times 0.5 \times 18 \text{ mm}^3$  (w/h/l) each, resulting in a volume of 4.8  $\mu$ l.

The five units differ only in the size of the pillars, which determines the spacing or gap between them.

- Unit V pillar gap of 250 μm
- Unit W pillar gap of 225 μm
- Unit X pillar gap of 200 μm
- Unit Y pillar gap of 175 μm
- Unit Z pillar gap of 150 μm





#### **Microfluidic Use-case Settings of the Channel Interaction Chip Fluidic 983**

Once prepared, the channel interaction chip can be used in different use-case settings. Fluidic operation via syringe- or pressure pumps is enabled by our Mini Luer interfaces and corresponding connectors and tubing.

Furthermore, tanks with different volumes are available, which allow the chip to be powered passively through gravity- or diffusion-driven flow or actively through liquid actuation via mechanical piston or pneumatic pressure. Active operation can be carried out in suction-mode by applying negative pressure at the outlets (connected to tubing) or in push-mode by applying positive pressure to the tanks via interfaces in their lid.





Channel interaction chip with Mini Luer connectors in the in- and outlets of the side channels, connected to  $\ensuremath{\mathsf{PTFE}}$  tubing



Channel interaction chip with 500  $\mu l$  sampling vessels (Fluidic 639) and Mini Luer connectors linked to PTFE tubing



Channel interaction chip Fluidic 983 filled with Matrigel® in the central channel and perfused with colored liquids

Product Code	Material	Lid	Surface	Price [€/	chip]	
for Fluidic 983			Ireatment	1+	10+	100+
10001345	Topas	140	none	36.20	24.30	16.10
10001347	PS	125	none	36.20	24.30	16.10
10001349	Zeonor	188	none	36.20	24.30	16.10
10001346	Topas	140	hydrophilized	39.20	26.30	17.80
10001348	PS	125	hydrophilized	39.20	26.30	17.80
10001350	Zeonor	188	hydrophilized	39.20	26.30	17.80

#### **Ready-To-Use Cell Culture Kits**

*microfluidic ChipShop's* microfluidic toolbox offers the complete set of chip modules and accessories to start directly with cellbased microfluidic experiments. Tubes, accessories for the interconnection, and liquid handling are all included. The kits are designed to gain first experience in both simple (beginners kit) or complex (advanced kit) adherend cell culture.

#### **Cell culture kit - Beginners**

Chips with hydrophilized surfaces and accessories for an immediate start of simple adherent cell culture. The chips are suitable for applications such as immunofluorescence microscopy, screening, apoptosis, and proliferation assays.

#### **Cell culture kit - Advanced**

Chips with hydrophilized surfaces and accessories for an immediate start of complex adherent cell cultures. Similar to the beginner's kit, the applications include immunofluorescence microscopy and screening. However, the more complex chip designs enable more sophisticated culture setups, including the co-culture of various cell types.



Cell culture kit - Beginners

Cell culture kit - Advanced

Product Code	Kit Type	Product Description	Product Code	Price [€/kit]
10001696	Cell culture kit - Beginners	<ul> <li>Male Mini Luer plugs - Low volume displacement (2x)</li> <li>Male Mini Luer fluid connectors, single, opaque (2x)</li> <li>Mini Luer to pipette adapter, opaque, PP (2x)</li> <li>Silicone tube (ID:: 0.76 mm, OD: 1.65 mm), 1m</li> <li>PTFE tube, 1 m (3x)</li> <li>Handling frame with reduced skirt height (1x)</li> <li>Reaction chamber chip Fluidic 842, Zeonor, hydroph. (2x)</li> <li>Cell culture chip w/ pre-heating channel Fluidic 992, Zeonor, hydrophilized (2x)</li> <li>Chamber interaction chip Fluidic 737, PS, hydrophilized (1x)</li> <li>Chamber interaction chip Fluidic 688, PS, hydrophilized (1x)</li> </ul>	10000205 10000116 10000855 10000031 10000032 10000041 10001036 10000559 10001344 10001062 10001058	438.84
10001697	Cell culture kit - Advanced	<ul> <li>Male Mini Luer plugs - Low volume displacement (2x)</li> <li>Male Mini Luer fluid connectors, single, opaque (2x)</li> <li>Mini Luer to pipette adapter, opaque, PP (2x)</li> <li>Silicone tube (ID.: 0.76 mm, OD: 1.65 mm), 1m</li> <li>PTFE tube, 1 m (3x)</li> <li>Handling frame with reduced skirt height (1x)</li> <li>Chamber interaction chip Fluidic 737, PS, hydrophilized (2x)</li> <li>Cross-flow membrane chip Fluidic 653, PS, hydrophilized (2x)</li> <li>Channel interaction chip Fluidic 583, PS, hydrophilized (2x)</li> </ul>	10000205 10000116 10000855 10000031 10000032 10000041 10001062 10001058 10000918 10000918	529.38

#### **Manufacturing Services**

We offer a large variety of off-the-shelf cell culture chips, and our team is happy to advise. Haven't found exactly what you're looking for? No problem - we are specialized in custom manufacturing of microfluidic devices and can tailor custom fabrication exactly according to your experimental needs and design requirements. Contact us with your individual specifications at inquiries@microfluidic-ChipShop.com.



*microfluidic ChipShop GmbH* • Stockholmer Str. 20 • 07747 Jena • Germany Phone: +49 (0) 3641 34705-0 • Fax: +49 (0) 3641 34705-90 • inquiries@microfluidic-ChipShop.com • www.microfluidic-ChipShop.com