CELLSTAR® MICROPLATES WITH CELL-REPELLENT SURFACE AS PLATFORM FOR BIOMIMESYS®, A NEW GENERATION OF A MIMETIC HYDROGEL FOR 3D CELL CULTURE

Research with two-dimensional cell cultures is still predominant in pharmaceutical and basic research. However, monolayer cultures can only mimic conditions in physiological tissue to a limited extend. The employment of 3D cultures is regarded as a rational approach to come closer to the microenvironment, in which mammalian cells grow in vivo. One option for 3D culture is the usage of BIOMIMESYS®, a hydrogel scaffold based on hyaluronic acid, which is a major component of the cell's extracellular matrix. The highly porous nature of the scaffold allows the rapid uptake of nutrients, oxygen, etc. into the cells to create a reproducible study model for all downstream analytical techniques used with 2D cell culture. No changes of technique are needed for 3D cell culture with BIOMIMESYS®. The BIOMIMESYS® hydrogel allows the unimpeded passage of antibodies for labelling and buffers for the extraction of proteins and RNA, with no need for prior cell extraction. Moreover, the Biomimesys® products are compatible with all analytical technologies, e.g. for microscopy, spectroscopic application, histology and flow cytometry.

BIOMIMESYS[®] is a ready-to-use format. 96 / 48 /or 24 hydrogel plugs are contained in the wells of a Greiner Bio-One CELLSTAR[®] 96 well F-bottom microplate with cell-repellent surface. Due to the surface properties of these microplates cell attachment is prevented effectively. Cell-repellent properties are achieved through an innovative chemical modification of the vessel surface. As all microplates from Greiner Bio-One, microplates with cell-repellent surface are manufactured with a footprint conform to the recommendations of the American National Standards Institute (ANSI 1-2004) to guarantee compatibility with all widely-used lab equipment.

A major field of application for BIOMIMESYS® is cancer research. The ability to culture cancer cells effectively *in vitro* is becoming increasingly important as the pace of tumor research accelerates. Tumor development is a complex multistep process involving phenotypic heterogeneity, altered cross-talk and microenvironment which together create the unique characteristics of tumor cells. Cancer cells grown in BIOMIMESYS® have been shown to develop into 3D spheroids with active proliferation and are therefore representative of the tumor microenvironment **(Fig. 1)**.

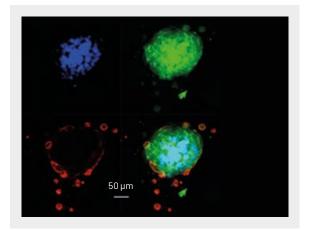
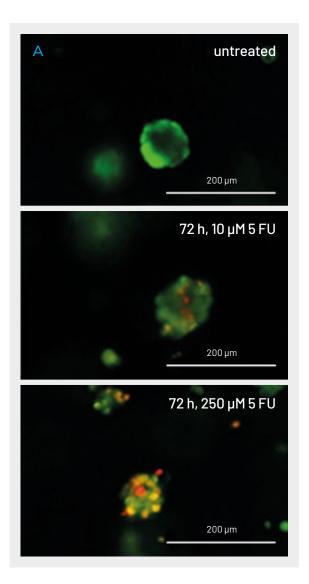
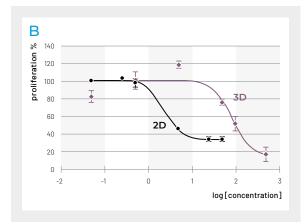


Figure 1: HT29 spheroid after 12 days of culture show a specific, characteristic localisation of α -tubulin at the outer edge of the spheroid.



Functionality can be tested in any of the different biological assays compatible with BIOMIMESYS®. Spheroids cultivated in BIOMI-MESYS® are well applicable for drug screening assays (Fig. 2).

Cells can be easily retrieved from the physiological matrix to perform cell cycle analysis (Fig. 3).



Figures 2A & 2B: The effect of a cytotoxic agent on DLD-1 spheroids cultivated in BIOMIMESYS® can be measured by quantitative testing (WST1, bottom). Results are in correlation with qualitative analyses (Live/Dead® staining, Life Technologies)

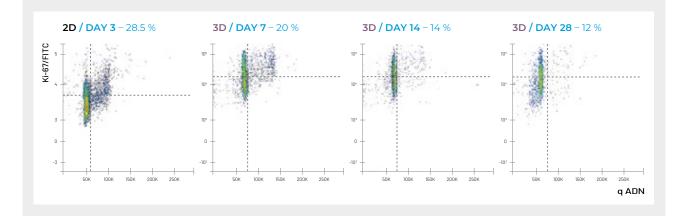


Figure 3: IP= level of cell viability and Ki-67= cell proliferation marker. In 3D, there is less cell proliferation compared with traditional cell culture.

Further fields of applications of BIOMIMESYS[®] comprise stem cell and adipocyte research.

Table 1 shows cell lines already tested so farsuccessfully with BIOMIMESYS®.

CANCER CELL LINES	
Human brain metastasis	SA87
Human breast adenocarcinoma	MCF-7
Human breast carcinoma	CAL-51
Human cervix adenocarcinoma	HeLa
Human colorectal adenocarcinoma	DLD-1, HT29, Caco-2
Human glioblastoma	CB109 / CB74 / CB191
Human liver hepatocellular carcinoma	HepG2
Human liver hepatoma	PLC / PRF-5
Human lung carcinoma	NCI-H460
Human osteosarcoma	SaOs
Human ovarian carcinoma	IGROV-1
Human pancreas carcinoma	PANC-1
Human prostate cancer	PC3
Normal human colon fibroblast	CCD18-co
Normal mouse fibroblast	3T3-L1
STEMCELLS	
Hematopoietic	CD34+
Murine embryonic stem cells	mES
Human induced pluripotent stem cells	hIPSC
PRIMARY CELLS	
Human white pre-adipocyte subcutaneous	HWP cryopreserved
Cryopreserved human hepatocyte	СНН

 Table 1:
 Tested cell lines

Multiwell Plates / Microplates Cell-Repellent Surface

Raw material: PS, Surface treatment: cell-repellent

ltem no.	Well format	Well Pprofile	Bottom	Product colour	Total volume (Well)	Working volume (well)	Lid	Sterile	Qty. inner / outer
655970	96	F-bottom / Chimney Well	solid	⊖ clear	392 µl	25 µl - 340 µl	condensation rings	+	1/6
655976	96	F-bottom / Chimney Well	µClear®	● black	392 µl	25 µl - 340 µl	condensation rings	+	8 / 32
655976-SIN	96	F-bottom / Chimney Well	µClear®	● black	392 µl	25 µl - 340 µl	condensation rings	+	1/32
781970	384	F-bottom	solid	⊖ clear	131 µl	15 µl - 110 µl	yes	+	1/60
781974	384	F-bottom	µClear®	\bigcirc white	131 µl	15 µl - 110 µl	yes	+	8/32
781976	384	F-bottom	µClear®	● black	131 µl	15 µl - 110 µl	yes	+	8/32
781976-SIN	384	F-bottom	µClear®	● black	131 µl	15 µl - 110 µl	yes	+	1/32

/ Further CELLSTAR® cell culture products with cell-repellent surface can be found on our website www.gbo.com.

Product Information BIOMIMESYS®, Celenys

BIOMIMESYS® is available under 96-well plate format containing 96 / 48 /or 24 hydrogel plugs. For further product information and ordering please visit www.celenys.com

