

APPLICATION REPORT

CELLSTAR® microplates with cell-repellent surface as a platform for BIOMIMESYS®, a new generation of a mimetic hydrogel for 3D cell culture

Research using two-dimensional cell cultures still dominates pharmaceutical and academic research. However, monolayer cultures can only mimic conditions in physiological tissue to a limited extent and so results obtained from them may not fully reflect the situation *in vivo*. The employment of 3D cultures is regarded as a rational approach to more closely mimic the microenvironment in which mammalian cells grow *in vivo*. One option for growing 3D culture is the use of BIOMIMESYS®, a hydrogel scaffold based on hyaluronic acid. Hyaluronic acid is a major component of the cell's extracellular matrix and produces a highly porous scaffold. The porous nature of the scaffold allows for the rapid uptake of nutrients, oxygen, etc. It is also a reproducible study model for subsequent analytical methods. Techniques normally used with 2D cell culture can also be used with 3D cultures produced with BIOMIMESYS® with no changes required to the methodology. The BIOMIMESYS® hydrogel allows the unimpeded passage of antibodies used for labelling and buffers used 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 supplied in a ready-to-use format of 96 / 48 / or 24 hydrogel plugs inserted into the wells of a 96 well Greiner Bio-One CELLSTAR® F-bottom microplate with cell-repellent surface. Due to the surface properties of these microplates cell attachment is effectively prevented from occurring. These cell-repellent properties are applied through an innovative chemical modification of the microplate surface. As with all microplates from Greiner Bio-One, microplates with a cell-repellent surface are manufactured with a footprint that conforms to the

recommendations of the American National Standards Institute (ANSI 1-2004), a standard adopted by all major manufacturers of equipment and consumables associated with microplates. 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). Functionality can be tested in any of the different biological assays compatible with BIOMIMESYS® and Spheroids cultivated in BIOMIMESYS® are suitable for drug screening assays (Fig. 2). Cells can be easily retrieved from the physiological matrix to perform cell cycle analysis (Fig. 3)

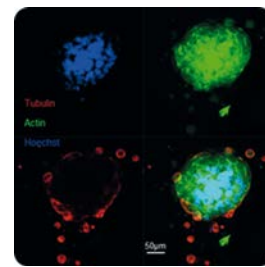


Figure 1: HT29 spheroid after 12 days of culture show a specific, characteristic localisation of α -tubulin at the outer edge of the spheroid.

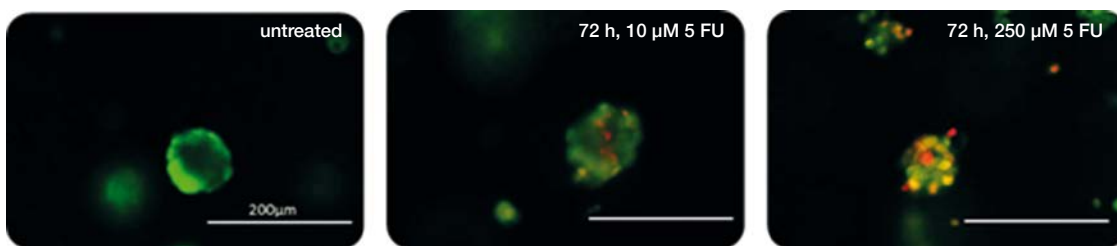
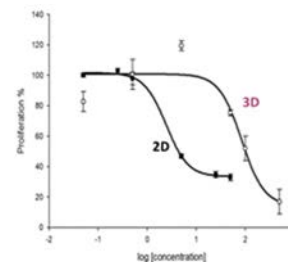


Figure 2: The effect of a cytotoxic agent on DLD-1 spheroids cultivated in BIOMIMESYS® can be measured by quantitative testing (WST1, bottom). Results are in correlation with qualitative analyses (Live/Dead® staining, Life Technologies)



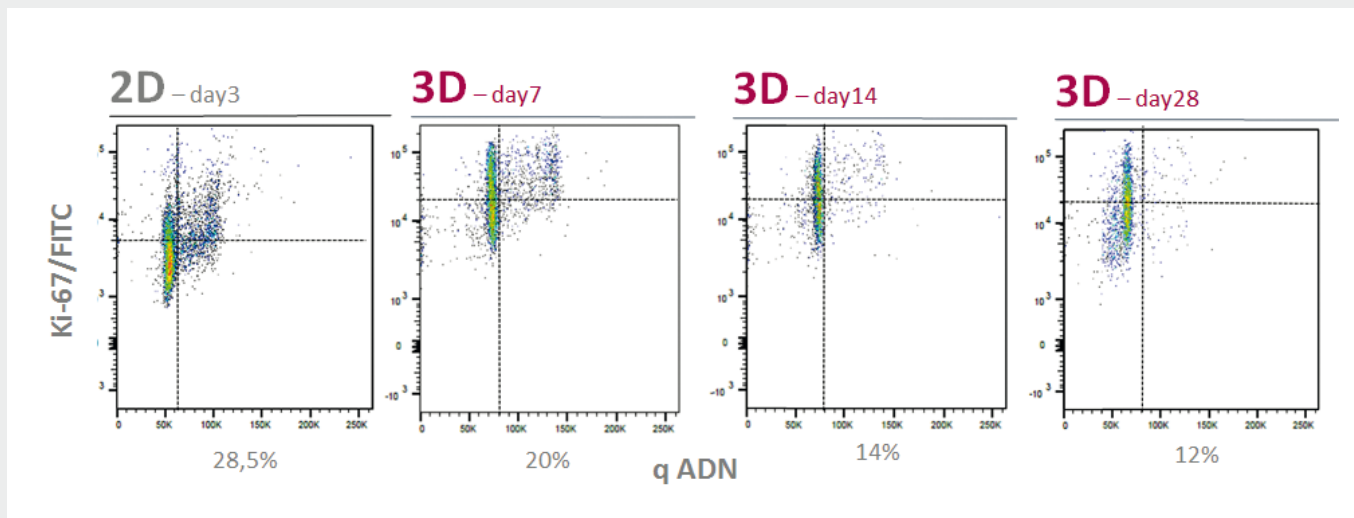


Figure 3: IP= level of cell viability and Ki-67= cell proliferation marker. In 3D, there is less cell proliferation compared with traditional cell culture.

Further fields of applications of BIOMIMESYS® comprise stem cell and adipocyte research. **Table 1** shows cell lines already tested so far successfully with BIOMIMESYS®. For more detailed information please visit www.celenys.com.

Table 1: Tested cell lines

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

Ordering Information Greiner Bio-One GmbH

Cat.-No.	Description	Quantity per bag	Quantity per case
655 970	96 well microplate, PS, F-bottom/chimney well, cell-repellent surface, clear, sterile, with lid	1	6
655 976	96 Well microplate, PS, F-bottom/chimney well, cell-repellent surface, black, µClear®, sterile, with lid	8	32
655 976-SIN	96 Well microplate, PS, F-bottom/chimney well, cell-repellent surface, black, µClear®, sterile, with lid	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



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