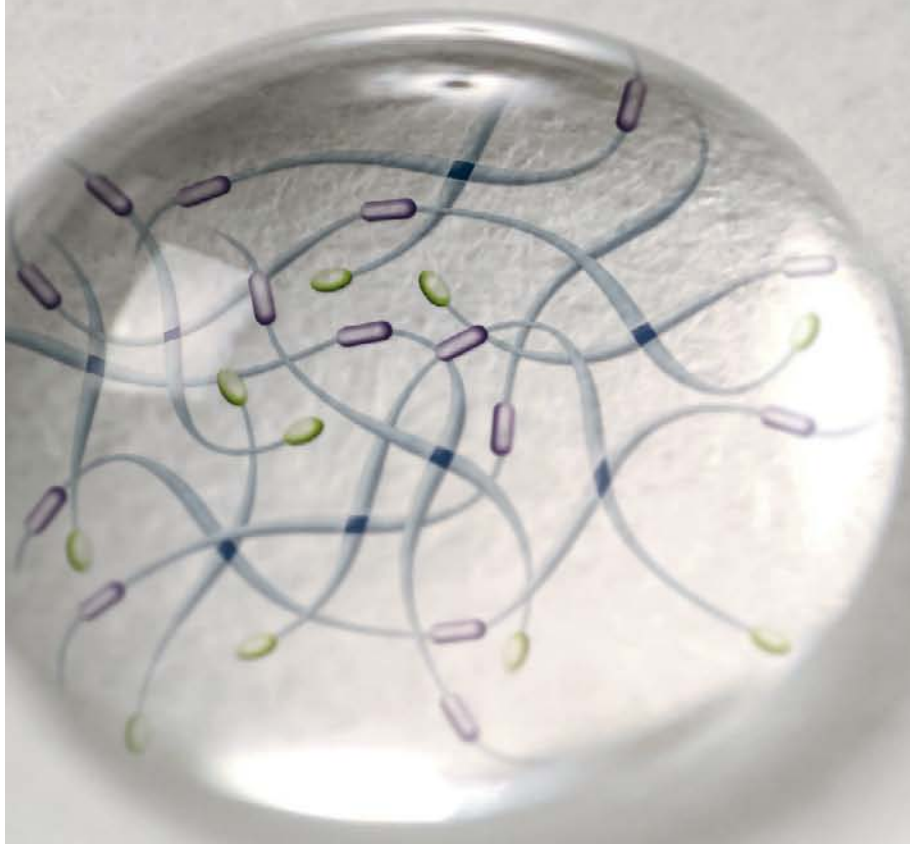
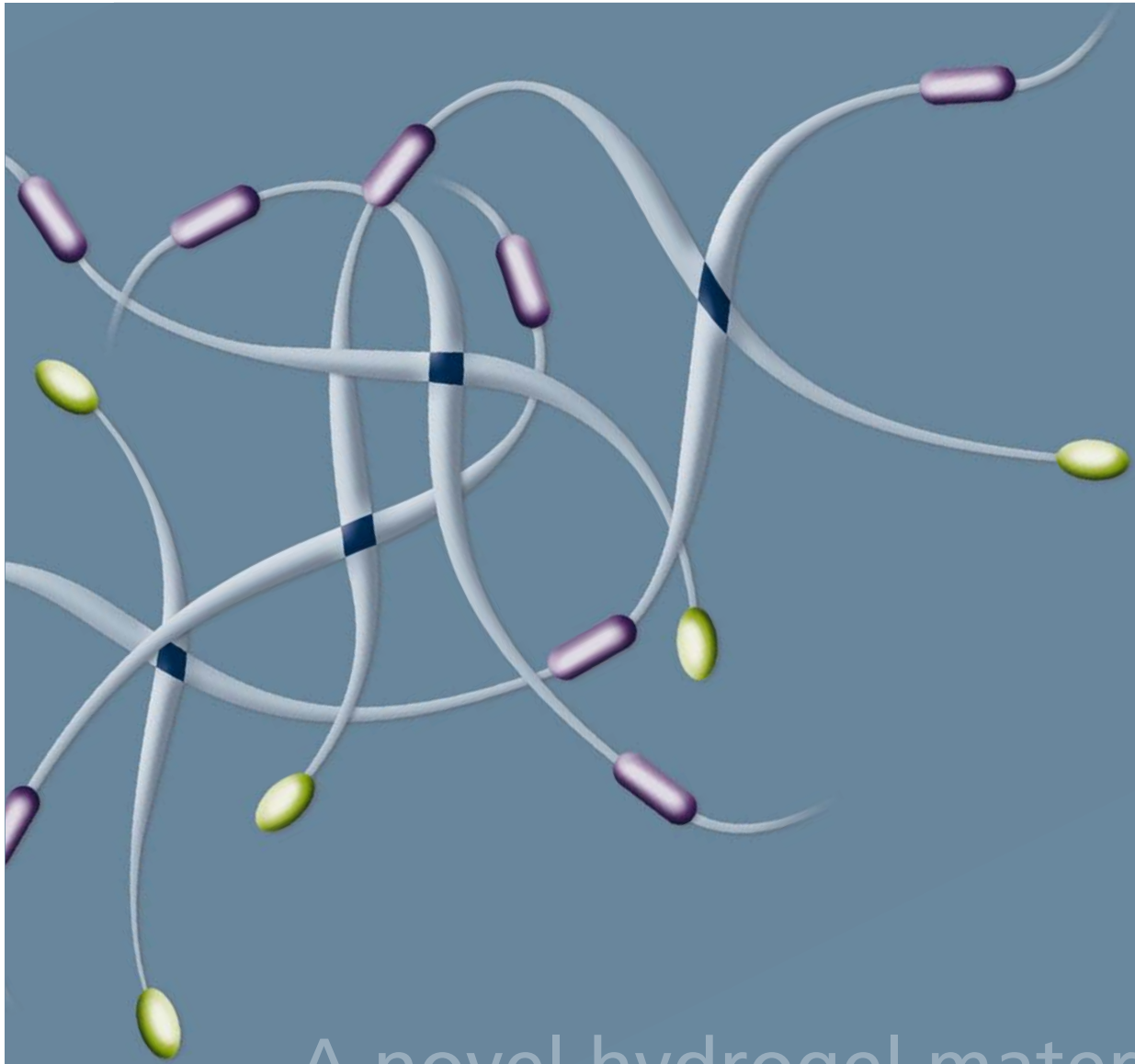


the 3D matrix for life science

3D Cell Culture and
QGel™ Technology



QGel



A novel hydrogel material
to culture cells in 3D
and grow tissue.

A fully synthetic matrix
with controllable stiffness,
adhesion and enzymatic
degradation properties.

About QGel™ technology



QGel™ products are particularly interesting for specialists in:

- Stem cell bioengineering
- Regenerative medicine
- Cancer research

FEATURES

FULLY SYNTHETIC

QGel™ provides a novel synthetic hydrogel to grow cells in a three-dimensional (3D) way that mimics key features of the natural cell environment.

BIOACTIVE

QGel™ can incorporate active components in order to interact biologically with cells.

3D CELL MIGRATION & PROLIFERATION

QGel™ MT 3D matrix allows cells to fully proliferate in vitro and organize themselves in 3D structures within the gel. Cells degrade the gel upon protease secretion and activation.

EASY HANDLING

Just add QGel™ Buffer and your cell solution to QGel™ powder. The hydrogel forms within minutes under physiological pH and temperature.

BENEFITS

CONTROLLABLE ADHESION PROPERTIES

Depending on your experiment and the cell type used, the incorporation of adhesion-promoting peptide, such as RGD, is possible.

CONTROLLABLE DEGRADABILITY

For more flexibility with your experiment, QGel™ offers gels with different degradation sensitivity to proteases (e.g. proteolytically and non-proteolytically degradable).

CONTROLLABLE STIFFNESS

Soft, medium and hard gels are available and you can choose the stiffness according to the experiment planned and the type of cells used.

What is 3D cell culture?

Only 3D cell culture allow scientists to closely recreate actual in vivo conditions, and research is already benefiting from this new 3D perspective.





Research in tissue engineering, cancer research, stem cells and molecular biology often involves cultures of cells on flat plastic dishes. It has recently become clear that considering biology in just **two dimensions (2D)** has serious limitations.

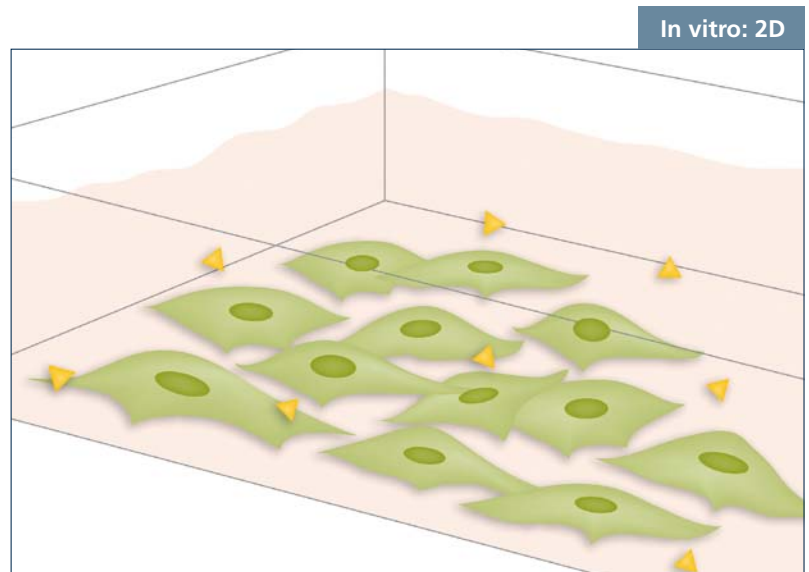
Researchers are therefore turning to **three-dimensional (3D) cell culture models, that more closely mimic what happens in living organisms.**

Using 3D culture, they are discovering patterns of gene expression and other cellular activities or responses that are much more similar to the results from in vivo studies.

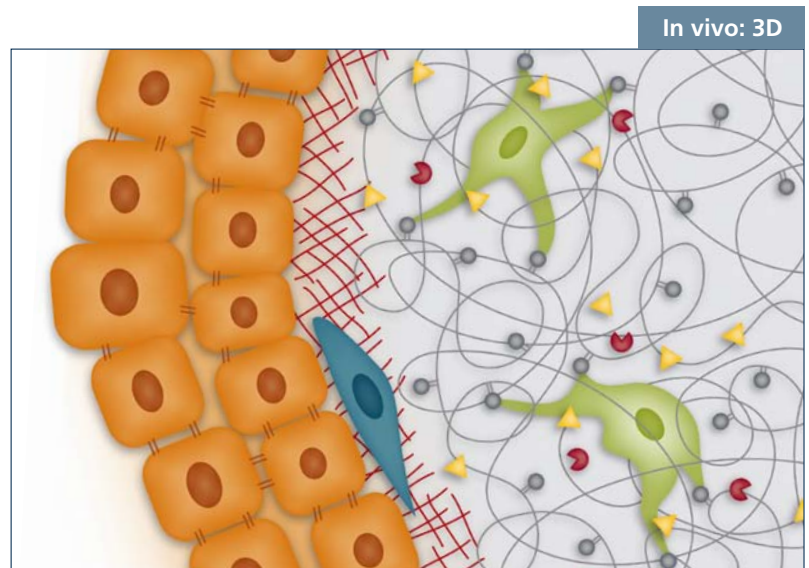
There are **important differences in the behavior of cells grown in 2D and 3D** culture. The essential cell interactions and organization levels occurring within a 3D context demonstrate the severe drawbacks of 2D studies.

LEGEND

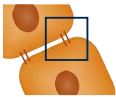


	Physical signaling molecules (e.g. adhesion ligand)
	Soluble signaling molecules (e.g. growth factor)
	Extracellular matrices (consist of proteoglycans, collagen, elastin fibers, fibronectin, laminin, etc.)
	



Cells cultured in vitro on a traditional plastic flask surface. They present a non natural morphology (flat shaped).

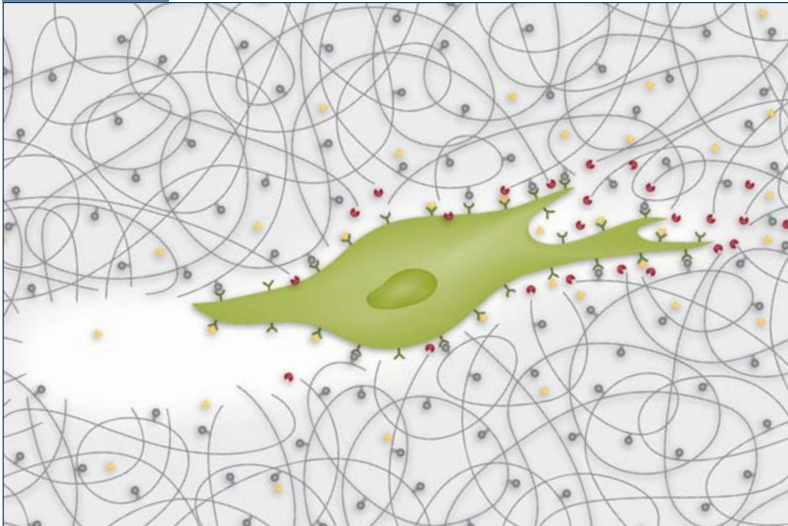


Cells in their natural in vivo environment assume very different morphologies than 2D culture. They are organized spatially with other types of cells within different matrices.

	Cell-cell interaction		Cell receptors
			Cell-secreted proteases (e.g. MMPs)

The essential role of extracellular matrices

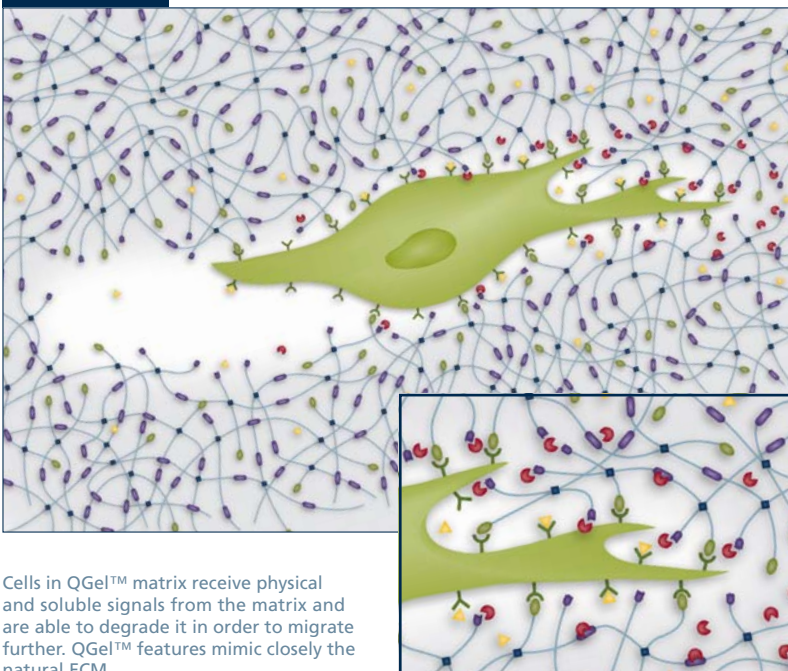
ECM in vivo



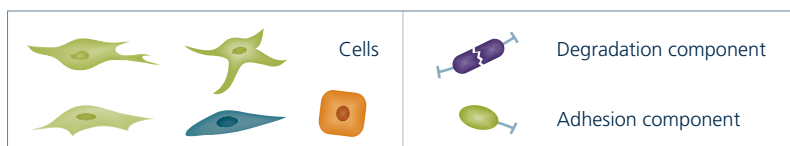
Cells in vivo receive physical and soluble signals from their environment. If needed, they secrete proteases to degrade the surrounding matrix and migrate further.



QGel™



Cells in QGel™ matrix receive physical and soluble signals from the matrix and are able to degrade it in order to migrate further. QGel™ features mimic closely the natural ECM.



In mammalian tissues, cells connect not only to each other, but also to a **support structure called the extracellular matrix (ECM)**. Cells are receiving continuous information from their particular surrounding environment. These **temporal and spatial signals** are integrated by intracellular signaling pathways and **regulate gene expression**, leading to cell fate processes such as replication, migration, differentiation or apoptosis.

ECM has an essential role in tissue dynamics. ECM provides adhesion ligands and soluble factors which guide development and maintain cell function. Furthermore, the matrix provides mechanical support and controls how external forces are transmitted to cells.

Cell migration through extracellular matrices is fundamental in a variety of physiological situations such as tissue development, homeostasis and regeneration. Cell migration in 3D is entirely different than what happens in a 2D context primarily because **in 3D, cells need to overcome the physical barrier posed by the matrix.** In most cases, cells remodel their extracellular environment in order to migrate in 3D. This is often triggered by cell-secreted enzymes that degrade the ECM locally and allow cells to migrate further.

What is the most appropriate ECM for your studies?

3D cell culture models that use matrices are structures capable of supporting physiological activities of cells and three-dimensional tissue formation.

Cells are encapsulated and cultured within these scaffolds which usually serve at least one of the following purposes:

- Allow cell attachment, migration and proliferation
- Retain or deliver cells
- Retain or deliver biochemical factors
- Exert certain mechanical and biological signaling to control cell behavior

In the field of regenerative medicine, the goal of growing cells within a biomaterial scaffold is that over time cells replace the temporary biomaterial by secreting their own natural extracellular matrix.

	NATURAL ECM derived from animals or plants	CONVENTIONAL SYNTHETIC ECM
ADVANTAGES +	The closest to physiological in vivo conditions in terms of degradability, bioactivity and biointeractions with encapsulated cells	<ul style="list-style-type: none"> • No risk of pathogen transmission • controllable degradation rate, porosity as well as chemical and mechanical properties • high reproducibility
DISADVANTAGES	<ul style="list-style-type: none"> • Biological variability in results and large degrees of experimental error • Risk for an immunogenic response or pathogen transmission • Generally weak mechanical strength • Properties are hard to control and modify independently 	<ul style="list-style-type: none"> • For most synthetic materials: poor inherent bioactivity
EXAMPLES	<ul style="list-style-type: none"> • Collagen • Basement membrane extracted from mouse tumor • Alginate • Fibrin • Chitosan • ... 	<ul style="list-style-type: none"> • Hyaluronic acid (HA) modified forms • Poly-ethylen glycol (PEG) modified forms • Self-assembling protein hydrogels • Poly(lactic-co-glycolic acid) (PLGA) • Polycaprolactone (PCL) • ...

Why is QGel™ a state-of-the-art material?

QGEL™ MT* 3D MATRIX



BIOLOGICALLY AND CHEMICALLY TAILORED

QGel™ MT 3D Matrix is a synthetic ECM that does not present disadvantages often associated with other synthetic materials: **QGel™ matrix can be engineered with biological and biochemical entities such as adhesion ligands, protease sensitive sites and/or soluble growth factors** in order to include capabilities of native tissues.

CELL-MEDIATED DEGRADATION

Contrary to typical synthetic matrices, QGel™ **degradation is exclusively mediated by the cells themselves via protease secretion and activation** according to how they migrate. There is no bulk hydrolysis process taking place.

EASY HANDLING

QGel™ is **easy to handle: just add QGel™ Buffer and your cell solution to the QGel™ MT 3D Matrix powder**. The hydrogel forms within 5-10 minutes under physiological conditions. No temperature precaution are required and cells are not exposed to unphysiological pH during the encapsulation process.

HIGH REPRODUCIBILITY

QGel™ guarantees **high gel property reproducibility between batches and vials** and QGel™ MT 3D matrix is manufactured following strict pharmaceutical standards.

HIGH LEVEL OF EVIDENCE

QGel™ technology is **based on over 10 years of research** that have demonstrated its efficacy in 3D cell culture and tissue engineering. QGel™ MT 3D matrix chemistry and several applications are **published in among the best biotechnology journals**.

*MT stands for Michael-Type referring to the crosslinking reaction.

QGel™ matrix applications

QGel™ material properties have been well characterized and present unique design flexibility*, stability in long-term cell culture experiments and cell-invasion characteristics**.

QGel™ MT 3D matrix has been shown to promote growth and proliferation of a variety of cell types. More specific applications include analysis of stem cell proliferation, tumor cell migration and invasion, study of the angiogenesis process, and in vivo wound repair. The table below outlines some of the key studies that have been done with QGel™ MT 3D matrix.

APPLICATION 1

3D CELL CULTURE

suitable for multiple cell types, including :

- stem cells, cancer stem cells and tumor cells
- fibroblasts, chondrocytes, endothelial cells, ...

for screening of anti-cancer drugs and other therapeutics factors

APPLICATION 2

REGENERATIVE MEDICINE

in vitro and in vivo :

- toxicology models (e.g. grow metabolically competent liver-like or skin-equivalent tissues)
- bioactive molecule delivery (e.g. BMP release for bone formation)
- study of complex physiological and pathological processes in vitro

APPLICATION 3

IN VIVO CELL DELIVERY

- tumor induction and growth in vivo
- tissue regeneration

EXAMPLES OF APPLICATIONS with QGel™ MT 3D Matrix

PUBLICATION References

Study of 3D cell invasion characteristics	Lutolf M et al., Synthetic matrix metalloproteinase-sensitive hydrogels for the conduction of tissue regeneration: engineered cell invasion characteristics, <i>PNAS</i> , 2003.
Model to investigate 3D cell migration mechanisms	Raeber G, et al., Molecularly engineered PEG-hydrogels: a novel model system for proteolytically mediated cell migration, <i>Biophysical Journal</i> , 2005.
Temporary matrix to sustain repair of bone defects via rhBMP-2 delivery	Lutolf M et al., Repair of bone defects using synthetic mimetics of collagenous extracellular matrices, <i>Nature Biotechnology</i> , 2003.
Versatile incorporation of integrin signaling molecules to guide embryonic stem cells (ESCs) behavior	Lee S et al., Engineering integrin signaling for promoting embryonic stem cell self-renewal in a precisely defined niche, <i>Biomaterials</i> , 2009.
Differentiation of human mesenchymal stem cells (MSCs) into smooth muscle cell (SMC)-like cells	Adelöw C et al., The effect of enzymatically degradable poly(ethylene glycol) hydrogels on smooth muscle cell phenotype, <i>Biomaterials</i> , 2008.
Embryonic carcinoma cells differentiation into cardioprogenitors	Kraehenbuehl T et al., Three-dimensional extracellular matrix-directed cardioprogenitor differentiation: systematic modulation of a synthetic cell-responsive PEG-hydrogel, <i>Biomaterials</i> , 2008.
Vascularized tissue growth via cell-demanded release of genetically engineered VEGF	Zisch A et al., Cell demanded release of VEGF from synthetic, biointeractive cell-ingrowth matrices for vascularized tissue growth, <i>The FASEB Journal</i> , 2003.
Chondrocytes 3D cell culture	Park Y et al., Bovine primary chondrocyte culture in synthetic matrix metalloproteinase-sensitive poly(ethylene glycol)-based hydrogels as a scaffold for cartilage repair, <i>Tissue Engineering</i> , 2004.

*Lutolf M, Hubbell J, Synthesis and physicochemical characterizing of end-linked poly(ethylene glycol)-co-peptide hydrogels formed by Michael-type addition, *American Chemical Society, Biomacromolecules*, 2003.

**Lutolf M et al., Synthetic matrix metalloproteinase-sensitive hydrogels for the conduction of tissue regeneration: engineered cell invasion characteristics, *PNAS*, 2003.

Further experiments and analysis

MICROSCOPIC OBSERVATION OF THE CELLS

QGel™ matrix is fully transparent and encapsulated cells can be observed clearly after weeks, even months, of culture. Both conventional light microscope and confocal laser microscope (fluorescence staining) can be used.

CELL VIABILITY AND PROLIFERATION ASSAYS

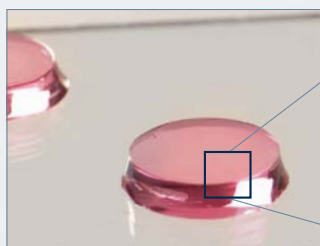
Traditional assays, such as live/dead stainings and other qualitative/quantitative tests that involve spectroscopic measurements, can be used to assess cell viability and proliferation in QGel™ matrix.

IMMUNOCYTOCHEMISTRY AND HISTOCHEMISTRY

QGel™ matrix allows for conventional immunofluorescence labelling of cells in gels and high-quality imaging using confocal laser microscopy. Histology can also be performed on QGel™ matrix. Frozen section methods of gels are preferable.

CELL RECOVERY VIA QGEL™ MATRIX DISSOLUTION

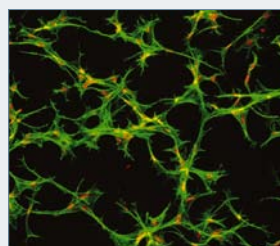
For sub-culture, cells can be recovered from QGel™ matrix by proteolytic digestion of the gels with trypsin. For DNA and RNA extraction, other proteases (e.g. proteinase K or collagenase) can also be used to digest QGel™ matrix.



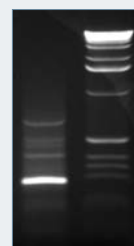
QGel™ MT 3D Matrix disc



Cells observed with conventional light microscope



Cells observed with immunostaining techniques



RNA analysis

Product portfolio and ordering information

Please find below the list of QGel products.

QGel™ MT 3D matrix is delivered in vials as a lyophilized powder: one vial allows you to cast up to 500 µl gel.

QGel™ Buffer is recommended. Please make sure you include QGel™ Buffer with your order.

www.qgelbio.com/shop

ITEM DESCRIPTION	STIFFNESS	DEGRADABLE	ADHESION PROPERTIES	CATALOG NUMBER
QGel™ MT 3D Matrix for 500 µl gel	Soft	Yes	with RGD	1001
QGel™ MT 3D Matrix for 500 µl gel	Soft	Yes	none	1004
QGel™ MT 3D Matrix for 500 µl gel	Soft	No	with RGD	1007
QGel™ MT 3D Matrix for 500 µl gel	Soft	No	none	*
QGel™ MT 3D Matrix for 500 µl gel	Hard	Yes	with RGD	*
QGel™ MT 3D Matrix for 500 µl gel	Hard	Yes	none	*
QGel™ MT 3D Matrix for 500 µl gel	Hard	No	with RGD	*
QGel™ MT 3D Matrix for 500 µl gel	Hard	No	none	*
QGel™ Buffer A (4ml)				2001
QGel 3D Disc Caster				4001

* Part of the QGel products are currently under development and will be available soon. Please check QGel website www.qgelbio.com for current product availability.

All QGel™ products are manufactured according to strict pharmaceutical standards. Each vial is sealed in a sterile nitrogen gas environment.

More detailed information about products and availability on: www.qgelbio.com

Contact: info@qgelbio.com

**NOT FOR
HUMAN USE.
FOR RESEARCH
USE ONLY.**

For more details on the subjects below, please refer to the following publications :

3D CELL CULTURE AND ITS RELEVANCE

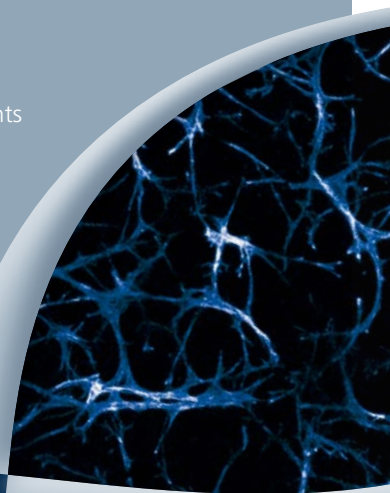
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- Yamada K and Cukierman E, Modeling tissue morphogenesis and cancer in 3D, *Cell*, 2007.
- Blow N, Cell culture : building a better matrix, *Nature Methods*, 2009.

MATRIX REMODELLING AND 3D CELL MIGRATION

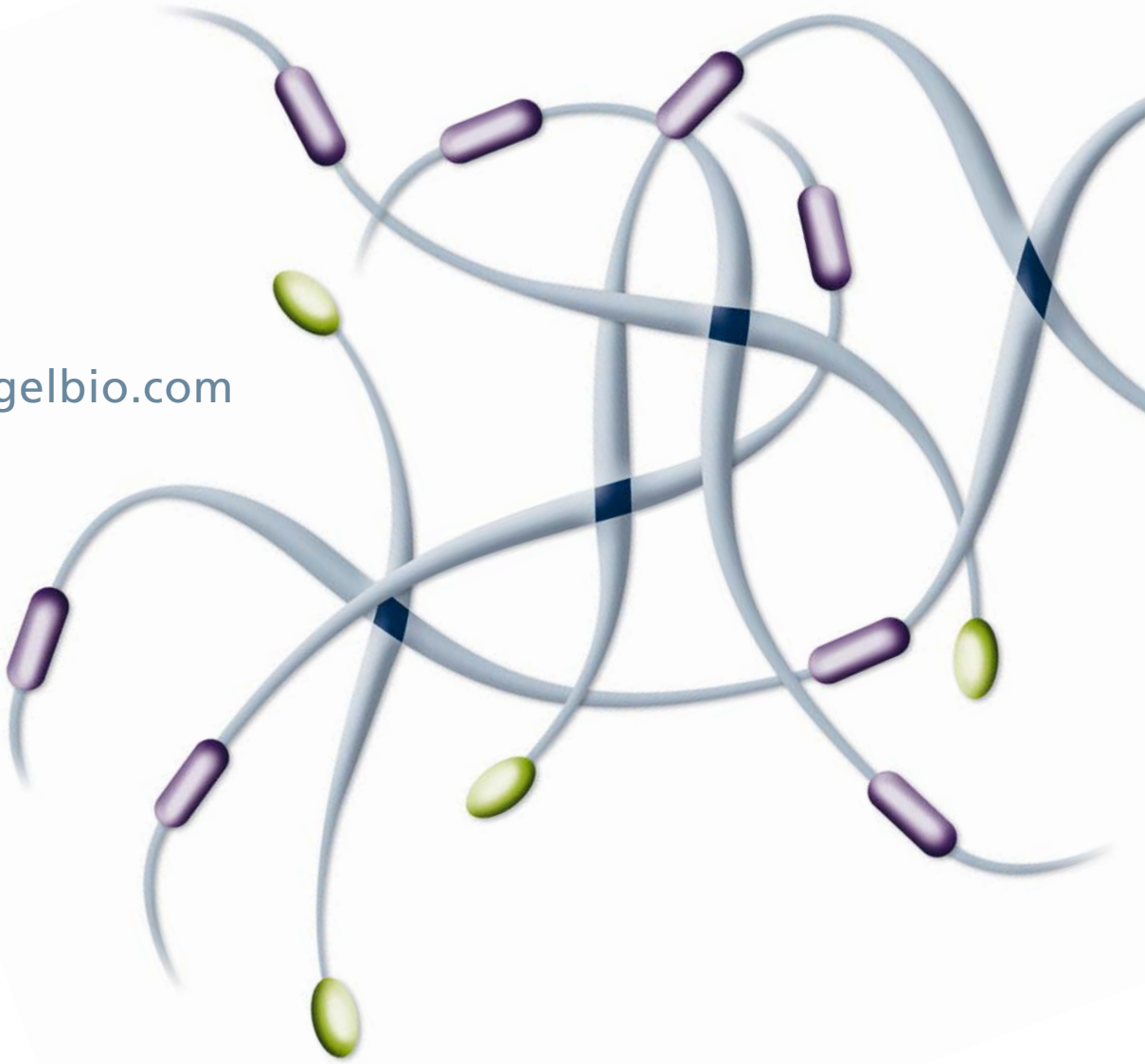
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- Friedl P and Gilmour D, Collective cell migration in morphogenesis, regeneration and cancer, *Nature Reviews Molecular Cell Biology*, 2009.
- Rowe R and Weiss S, Navigating ECM barriers at the invasive front: the cancer cell-stroma interface, *Annual Review of Cell and Developmental Biology*, 2009.

NATURAL AND SYNTHETIC EXTRACELLULAR MATRICES AS 3D CELL CULTURE MODELS

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- Lutolf M and Hubbell J, Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering, *Nature Biotechnology*, 2005
- Chan G and Mooney D, New materials for tissue engineering: towards greater control over the biological response, *Trends in Biotechnology*, 2008.
- Tibbitt M and Anseth K, Hydrogels as extracellular matrix mimics for 3D cell culture, *Biotechnology and Bioengineering*, 2009.



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