Product Selection Guide

Matrigen Softwell®

Hydrogels

Protocol Version 2.1

Contents

Matrigen Softwell® Hydrogels

For a cell, elasticity matters. Softwell® replicates a broad range of physiological tissue softness, from fat to cardiac muscle, so you can routinely venture beyond the rigidity of tissue culture plastic.

Softwell® is available in a variety of stiffness values and available with different coatings as follows:

- **Easy Coat™** hydrogels are chemically activated to bind to your matrix protein of choice.
- **Collagen** pre-coated hydrogels are ready for cell culture.
- **Non-activated** hydrogels form an ultra-low attachment surface.

Scientists have long been growing cells in natural and synthetic matrix environments to elicit phenotypes that are not expressed on conventionally rigid substrates. Unfortunately, growing cells either on or within soft matrices can be an expensive, labor intensive, and impractical undertaking. Softwell® overcomes these challenges. It enables you to study cell behaviors in soft environments with unprecedented efficiency. Not only that, it provides remarkable control over matrix stiffness, a concept that has led to discoveries in a wide range of areas.

Softwell® plates offer uniform flatness over the entire working surface of the plate. They are provided in individual foil packs which keep them in perfect condition for 3 to 6 months at RT or 4°C.

Soft substrates for stem cells tuning the stiffness of the extracellular environment is a relatively new, but powerful approach for stem cell culture that:

1. Promotes self-renewal. Muscle stem cells derived from mice self-renew and sustain their ability to regenerate damaged muscle tissue in-vivo when cultured on substrates replicating the elastic modulus of muscle (E=12 kPa).

2. Maintains pluripotency. On E=0.6 kPa substrates, mouse embryonic stem cells generate homogenous undifferentiated colonies in the absence of exogenous LIF.

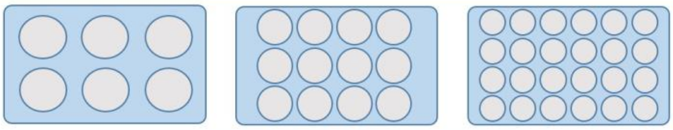
3. Directs lineage specification. Human adult mesenchymal stem cells are directed towards neurogenic, myogenic, and osteogenic lineages on E=1, 11, and 34 kPa substrates, respectively.

Choosing the Matrigen plate that's right for your cells

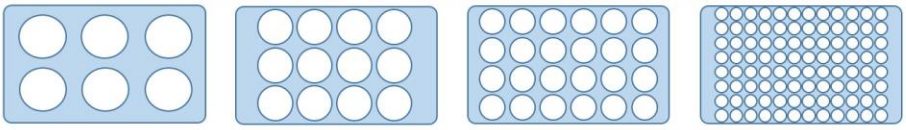
Hint: If you don't know what stiffness is optimal for your cells, you can purchase single plates to test each of 0.2, 0.5, 1, 2, 4, 8, 12, 25, and 50 kPa hydrogels. In addition, there is a 96 well HTS option in which every plate contains a column of 8 wells of each elasticity allowing all elasticities to be tested within a single plate.

FORMAT

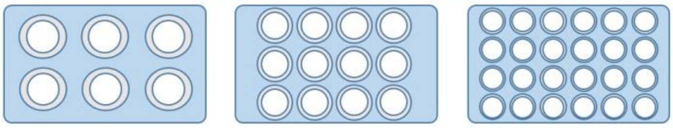
Softwell®
Hydrogels bound to 6, 12, and 24 well polystyrene plates



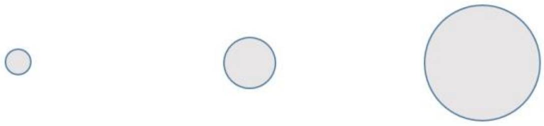
Softwell G™
Hydrogels bound to 6, 12, 24, and 96 well plates with a #1.5 glass bottom



Softslip™
Hydrogels bound to removable glass coverslips in 6, 12, and 24 well plates



Petrisoft™
Hydrogels bound to 35, 100, and 150 mm polystyrene dishes



Softview™
Hydrogels bound to 35 mm dishes with a 10 or 20 mm #1.5 glass bottom

ELASTIC MODULUS (kPa)

0.2	0.5	1	2	4	8	12	25	50
	SOFT			INTERMEDIATE			STIFF	

COATING

Non-activated
hydrogels form an ultra-low attachment surface. Allows the possibility to choose a chemistry method for proteins attachment.

Easy Coat™
hydrogels are chemically activated to bind to your matrix protein of choice, including ECM proteins.

Collagen
pre-coated hydrogels are ready for cell culture. All collagen-coated products use rat tail collagen type I.

SPECIALTY OPTIONS

SoftTrac™
hydrogels with fluorescent microspheres immobilized at the surface, to be used for traction force microscopy.

Adhesion Free™
hydrogels that resist protein adsorption and are 100% non-adherent to cells.

Ultrasoft™
hydrogels as soft as mucus bound to glass substrates. Elastic modulus of 30, 70, and 100 Pa.

Publications

The importance of surface elasticity has been demonstrated in studies utilizing a range of cell types. Example papers are provided below. This list was last updated in March 2014.

Bone, cartilage and skeletal muscle

- Mullen CA et al. (2013). Osteocyte differentiation is regulated by extracellular matrix stiffness and intercellular separation. **Mechanical Behavior of Biomedical Materials** 28:183-94.

- Witkowska-Zimny M et al. (2013). Effect of substrate stiffness on the osteogenic differentiation of bone marrow stem cells and bone-derived cells. **Cell Biology International** 37(6):608-16.

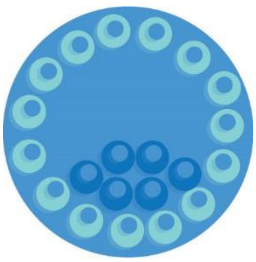
- Sanz-Ramos P et al. (2013). Response of sheep chondrocytes to changes in substrate stiffness from 2 to 20 Pa: effect of cell passaging. **Connective Tissue Research** 54(3):159-66.

- Al-Rekabi Z et al. (2013). Cross talk between matrix elasticity and mechanical force regulates myoblast traction dynamics. **Physical Biology** 10(6):066003.

- Burke DP et al. (2012). Substrate stiffness and oxygen as regulators of stem cell differentiation during skeletal tissue regeneration: a mechanobiological model. **PLoS One** 7(7):e40737.

- Gilbert PM et al. (2010). Substrate elasticity regulates skeletal muscle stem cell self-renewal in culture. **Science** 27;329(5995):1078-81.

Embryonic



- Higuchi S et al. (2014). Culturing of mouse and human cells on soft substrates promote the expression of stem cell markers. **Journal of Bioscience and Bioengineering** 117(6):749-55.

- Lü D et al. (2014). Differential regulation of morphology and stemness of mouse embryonic stem cells by substrate stiffness and topography. **Biomaterials** 35(13):3945-55.

- Wen JH et al. (2014). Interplay of matrix stiffness and protein tethering in stem cell differentiation. **Nature Materials** 13(10):979-87.

- Kolahi KS et al. (2012). Effect of substrate stiffness on early mouse embryo development. **PLoS One** 7(7):e41717.

- Shimizu T et al. (2012). Dual inhibition of Src and GSK3 maintains mouse embryonic stem cells, whose differentiation is mechanically regulated by Src signalling **Stem Cells** 30(7):1394-404.

- Chowdhury F et al. (2010). Soft substrates promote homogeneous self-renewal of embryonic stem cells via downregulating cell-matrix tractions. **PLoS One** 13;5(12):e15655.

- Engler AJ et al. (2006). Matrix elasticity directs stem cell lineage specification. **Cell** 25;126(4):677-89.

Endothelial and blood

- Birukova AA et al. (2013). Endothelial barrier disruption and recovery is controlled by substrate stiffness. **Microvascular Research** 87:50-7.

- Hong Z et al. (2013). Influence of membrane cholesterol and substrate elasticity on endothelial cell spreading behavior. **Journal of Biomedical Materials Research** 101(7):1994-2004.

- Murikipudi S et al. (2013). The effect of substrate modulus on the growth and function of matrix-embedded endothelial cells. **Biomaterials** 34(3):677-84.

- Kumar SS et al. (2013). The combined influence of substrate elasticity and surface-grafted molecules on the ex vivo expansion of hematopoietic stem and progenitor cells. **Biomaterials** 34(31):7632-44.

- Wan Z et al. (2013). B cell activation is regulated by the stiffness properties of the substrate presenting the antigens**. Journal of Immunology** 1;190(9):4661-75.

- Stroka KM et al. (2012). OxLDL and substrate stiffness promote neutrophil transmigration by enhanced endothelial cell contractility and ICAM-1. **Journal of Biomechanics** 26;45(10):1828-34.

- Dickinson LE et al. (2012). Endothelial cell responses to micropillar substrates of varying dimensions and stiffness. **Journal of Biomedical Materials Research** 100(6):1457-66.

- Choi JS et al. (2012). The combined influence of substrate elasticity and ligand density on the viability and biophysical properties of hematopoietic stem and progenitor cells. **Biomaterials** 33(18):4460-8.

- O'Connor RS et al. (2012). Substrate rigidity regulates human T cell activation and proliferation. **Journal of Immunology** 1;189(3):1330-9.

- Brown XQ et al. (2010). Effect of substrate stiffness and PDGF on the behavior of vascular smooth muscle cells: implications for atherosclerosis. **Journal of Cellular Physiology** 225(1):115-22.

- Jannat RA et al. (2010). Neutrophil adhesion and chemotaxis depend on substrate mechanics. **Journal of Physics: Condensed Matter** 19;22(19):194117.

Eye

- Moers K et al. (2013). Substrate elasticity as biomechanical modulator of tissue homeostatic parameters in corneal keratinocytes. **Experimental Cell Research** 15;319(12):1889-901.

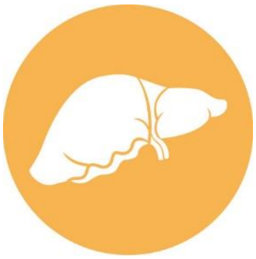
Heart

- Hersch N et al. (2013). The constant beat: cardiomyocytes adapt their forces by equal contraction upon environmental stiffening. **Biology Open** 15;2(3):351-61.

- Forte G et al. (2012). Substrate stiffness modulates gene expression and phenotype in neonatal cardiomyocytes in vitro. **Tissue Engineering Part A** 18(17-18):1837-48.

- Majkut SF et al. (2012). Cardiomyocytes from late embryos and neonates do optimal work and striate best on substrates with tissue-level elasticity: metrics and mathematics. **Biomechanics and Modeling in Mechanobiology** 11(8):1219-25.

Hepatocytes



- Yangben Y et al. (2013). Relative rigidity of cell-substrate effects on hepatic and hepatocellular carcinoma cell migration. **Journal of Biomaterials Science, Polymer Edition** 24(2):148-57.

- Olsen AL et al. (2011). Hepatic stellate cells require a stiff environment for myofibroblastic differentiation. **American Journal of Physiology-Gastrointestinal and Liver Physiology** 301(1):G110-8.

- Li L et al. (2008). Functional modulation of ES-derived hepatocyte lineage cells via substrate compliance alteration. **Annals of Biomedical Engineering** 36(5):865-76.

- Georges PC et al. (2007). Increased stiffness of the rat liver precedes matrix deposition: implications for fibrosis. **American Journal of Physiology-Gastrointestinal and Liver Physiology** 293(6):G1147-54.

- Semler EJ et al. (2005). Engineering hepatocellular morphogenesis and function via ligand-presenting hydrogels with graded mechanical compliance. **Biotechnology and Bioengineering** 5;89(3):296-307.

Mesenchymal

- Li Z et al. (2013). Differential regulation of stiffness, topography, and dimension of substrates in rat mesenchymal stem cells. **Biomaterials** 34(31):7616-25.

- Brown AC et al. (2013). Physical and chemical microenvironmental cues orthogonally control the degree and duration of fibrosis-associated epithelial-to-mesenchymal transitions. **The Journal of Pathology** 229(1):25-35.

- Vincent LG et al. (2013). Mesenchymal stem cell durotaxis depends on substrate stiffness gradient strength. **Biotechnology Journal** 8(4):472-84.

- Park JS et al. (2011). The effect of matrix stiffness on the differentiation of mesenchymal stem cells in response to TGF-β. **Biomaterials** 32(16):3921-30.

Neural

- Mori H et al. (2013). Migration of glial cells differentiated from neurosphere-forming neural stem/progenitor cells depends on the stiffness of the chemically cross-linked collagen gel substrate. **Neuroscience Letters** 25;555:1-6.

- Previtera ML et al. (2013). The effects of substrate elastic modulus on neural precursor cell behavior. **Annals of Biomedical Engineering** 41(6):1193-207.

- Cai L et al. (2012). Photocured biodegradable polymer substrates of varying stiffness and microgroove dimensions for promoting nerve cell guidance and differentiation. **Langmuir** 28;28(34):12557-68.

- Gu Y et al. (2012). The influence of substrate stiffness on the behavior and functions of Schwann cells in culture. **Biomaterials** 33(28):6672-81.

- Previtera ML et al. (2010). Effects of substrate stiffness and cell density on primary hippocampal cultures. **Journal of Bioscience and Bioengineering** 110(4):459-70.

General and mechanistic

- Obbink-Huizer C et al. (2014). Computational model predicts cell orientation in response to a range of mechanical stimuli. **Biomechanics and Modeling in Mechanobiology** 13(1):227-36.

- Ronan W et al. (2014). Cellular contractility and substrate elasticity: a numerical investigation of the actin cytoskeleton and cell adhesion. **Biomechanics and Modeling in Mechanobiology** 13(2):417-35.

- Liu H et al. (2013). Determination of local and global elastic moduli of valve interstitial cells cultured on soft substrates. **Journal of Biomechanics** 26;46(11):1967-71.

- Ziebert F et al. (2013). Effects of adhesion dynamics and substrate compliance on the shape and motility of crawling cells. **PLoS One** 31;8(5):e64511.

- Quinlan AM et al. (2012). Investigating the role of substrate stiffness in the persistence of valvular interstitial cell activation. **Journal of Biomedical Materials Research Part A** 100(9):2474-82.

- Fioretta ES et al. (2012). Influence of substrate stiffness on circulating progenitor cell fate. **Journal of Biomechanics** 15;45(5):736-44.

- Robinson KG et al. (2012). Differential effects of substrate modulus on human vascular endothelial, smooth muscle, and fibroblastic cells. **Journal of Biomedical Materials Research Part A** 100(5):1356-67.

- Trichet L et al. (2012). Evidence of a large-scale mechanosensing mechanism for cellular adaptation to substrate stiffness. **Proceedings of the National Academy of Sciences of the USA** 1;109(18):6933-8.

- Lai T et al. (2011). Mechanochemical model of cell migration on substrates of varying stiffness. **Physical Review E** 84(6 Pt 1):061907.

- Du J et al. (2011). Integrin activation and internalization on soft ECM as a mechanism of induction of stem cell differentiation by ECM elasticity. **Proceedings of the National Academy of Sciences of the USA** 7;108(23):9466-71.

- Tee SY et al. (2011). Cell shape and substrate rigidity both regulate cell stiffness. **Biophysical Journal** 2;100(5):L25-7.
- Dupont S et al. (2011). Role of YAP/TAZ in mechanotransduction. **Nature** 8;474(7350):179-83.

- Liu F et al. (2010). Feedback amplification of fibrosis through matrix stiffening and COX-2 suppression. **Journal of Cell Biology** 23;190(4):693-706.

- Friedland JC et al. (2009). Mechanically activated integrin switch controls alpha5beta1 function. **Science** 30;323(5914):642-4.

- Chan CE et al. (2008). Traction dynamics of filopodia on compliant substrates. **Science** 12;322(5908):1687-91.

Cell Guidance Systems' reagents and services enable control, manipulation and monitoring of the cell, both *in vitro* and *in vivo*

Growth Factors
- Recombinant
- Sustained Release

Exosomes
- Purification
- Detection
- Tracking
- NTA Service

Small Molecules

Cell Counting Reagent

Matrix Proteins

Cell Culture Media
- Pluripotent Stem Cells
- Photostable
- *In Vitro* Blastocyst Culture
- ETS-embryo Culture
- Custom Manufacturing Service

Gene Knock-Up System

Cytogenetics Analysis

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