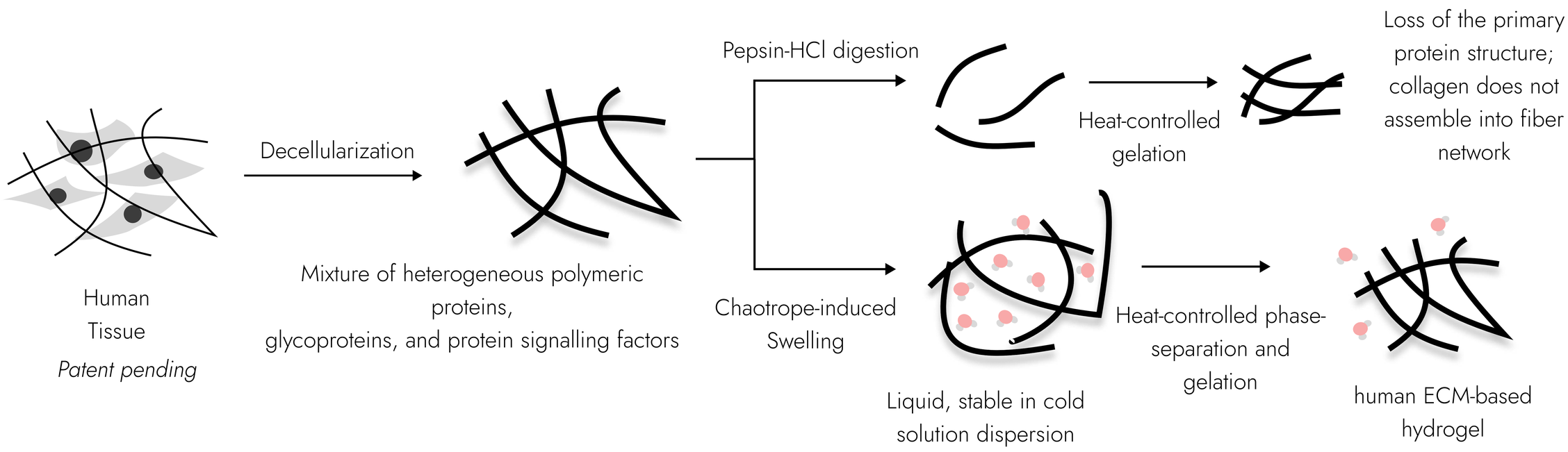
Human-Derived Extracellular Matrix - from the concept to applications

Native ECM microenvironment representativity

	Synthetic scaffolds	EHS-derived BME extract	Recombinant Collagens, Fibronectin, Vitronectin	Pepsin-digested human ECM extracts	Chaotrope-swelled ECM dispersion
	Peptigel *HyStem*	*Corning Matrigel* *BME* *Cultrex*		*HuGentra* *TissueSpec*	**ExViGel**
	Synthetic polymer-based scaffolds, modified wirh peptides	Laminin 111-based Scaffolds, EHS mouse-derived	Native ECM proteins, without natural heterogeniety	Pepsin-cleaved ECM proteins. Heterogeneous, however, without representative primary structure	ECM extract, obtained via disruption of the tertiary protein structure. No synthetic modification or alteration

Extracellular Matrix (ECM) research traditionally involves the separate exploration of individual protein components through proteomic analysis and in vitro cellular studies using generic scaffolds. At Preci, our research objective was to bridge these two domains by developing a human-derived native ECM matrix. Previous methods attempted to achieve this by relying on pepsin digestion of ECM proteins, which unfortunately resulted in the complete breakdown of both structural and signaling proteins within the ECM. This limitation was a significant hurdle, as it was the only available method to generate sol-gel systems from ECM proteins.
Preci has redefined the state-of-the-art in ECM research with the introduction of ExViGel, an innovative ECM dispersion created through the gentle swelling of ECM proteins. ExViGel represents a significant advancement, preserving the native structure and functionality of ECM components. This breakthrough product is now accessible to the research community, offering a reliable and scalable solution with multi-liter production capability and validated continuous production processes.
Our advanced technique allows for the isolation of ECM from a diverse range of organs, including tumor, liver, heart, and lung tissues. The resulting ECM-derived products, such as ExViGel, are now available for various experimental applications.



ExViGel's sol-gel mixture exhibits temperature-controlled gelation properties, making it an ideal choice for a broad spectrum of research applications. Whether your work involves 2D and 3D culture systems or in vivo tumor engraftment studies, ExViGel integrates seamlessly into your workflows.
In addition to providing the scaffold itself, Preci offers a comprehensive package of support and information. This includes guidance on optimizing your experiments, protein quantification, mechanoelastic property analysis, and detailed structural analysis of the formed gels. With ExViGel, you can enhance your research outcomes with confidence, knowing that you are using the most advanced ECM product available.

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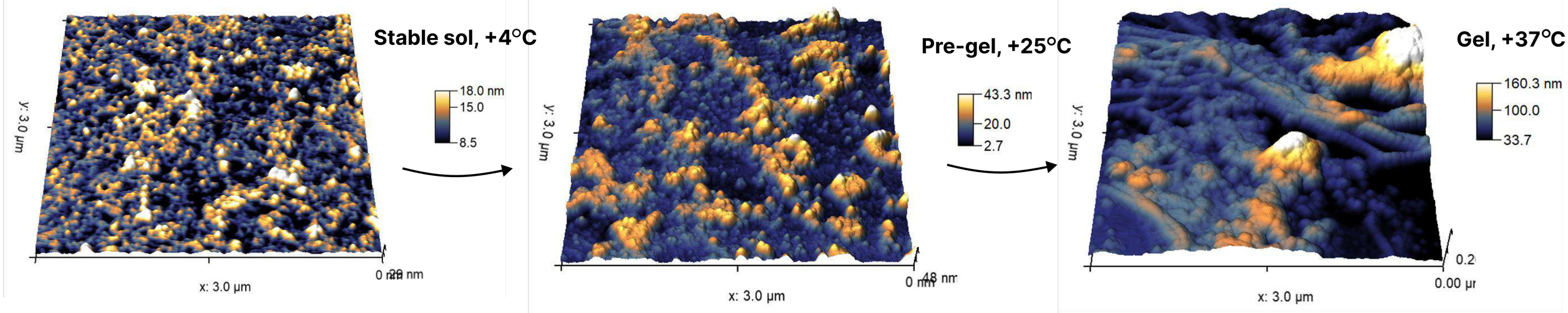
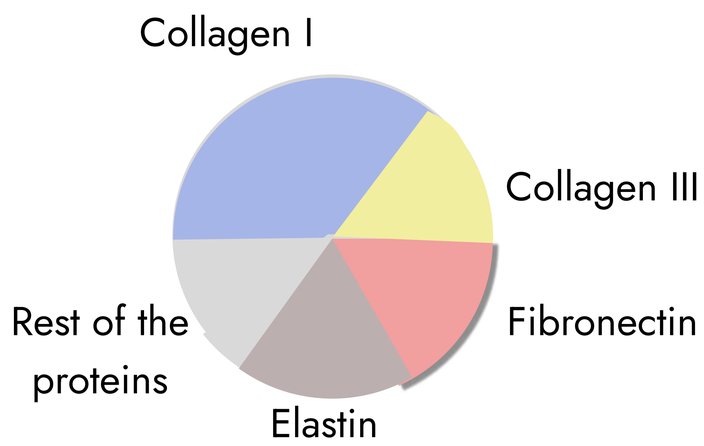
Both ligand-specific and ligand-independent effects have a profound impact on cellular physiology. To address these complexities, we meticulously control both colloidal properties and protein content within our extracellular matrix (ECM) products. In the sol state, the system exists as a uniform colloid. However, upon phase transition, a fibrillar network forms, resulting in a gel with distinctive D-bands in its quaternary structure. The polymerization of this gel induces network contraction and triggers the release of excess water that had accumulated during the sol state. Advanced microscopy techniques, such as atomic force microscopy (AFM), allow us to visualize the stepwise polymerization process and the intricate structural changes occurring within the network.



The colloidal behavior of this system leads to the contraction of the polymer network, resulting in slight phase separation when the sol is left standing at its native concentration of 12-15 mg/mL. This system is well-suited for 2D culture plasticware coating. The process involves centrifugation of the well-plate followed by polymerization of the network over several hours in a cell culture incubator. By varying the centrifugation force and concentration, the degree of gel compression and surface elasticity can be precisely controlled. Additionally, introducing cells to ExViGel may further promote network contraction. The concentration and method of surface treatment can be tailored to support a wide range of experimental settings.

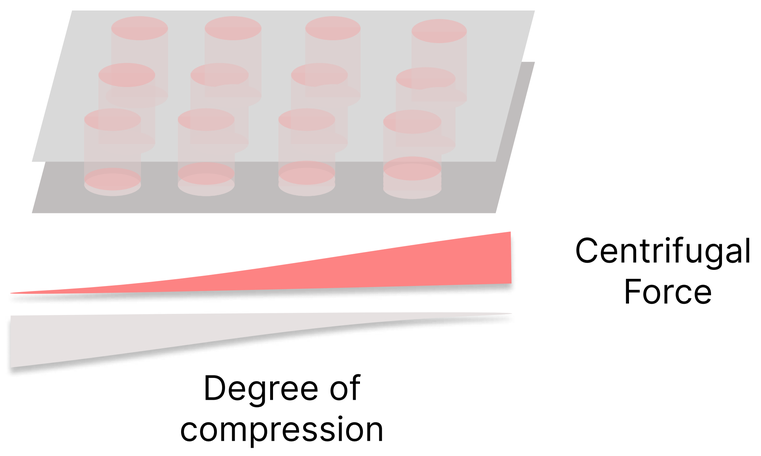
For 3D cultures, cells can be grown within the polymerized network of a thick-layer gel. Standard gel concentrations can be used, with dilutions down to 5 mg/mL of protein. It's important to note that the network is temperature-sensitive, so cold solutions should not be applied.

Modern cell-culture hydrogels typically contain undefined protein content or are limited to one or two proteins. In contrast, human-derived matrices are heterogeneous, with significant variation in the concentrations of major structural and minor signaling components across different organs. Our products are characterized for 14 different proteins, including Collagens I-VI, Fibronectin, Laminin, Elastin, and signaling proteins, using ELISA protocols. You can also request batch-specific characterization for specific markers of interest. The product Certificate of Analysis provides detailed data, including these protein measurements and the rheological properties of the gels under various conditions. It also includes information on precise gelation time, critical gelation concentration, and more, allowing you to select the batches that best fit your experimental needs.



Characterized for 14 structural and signaling proteins

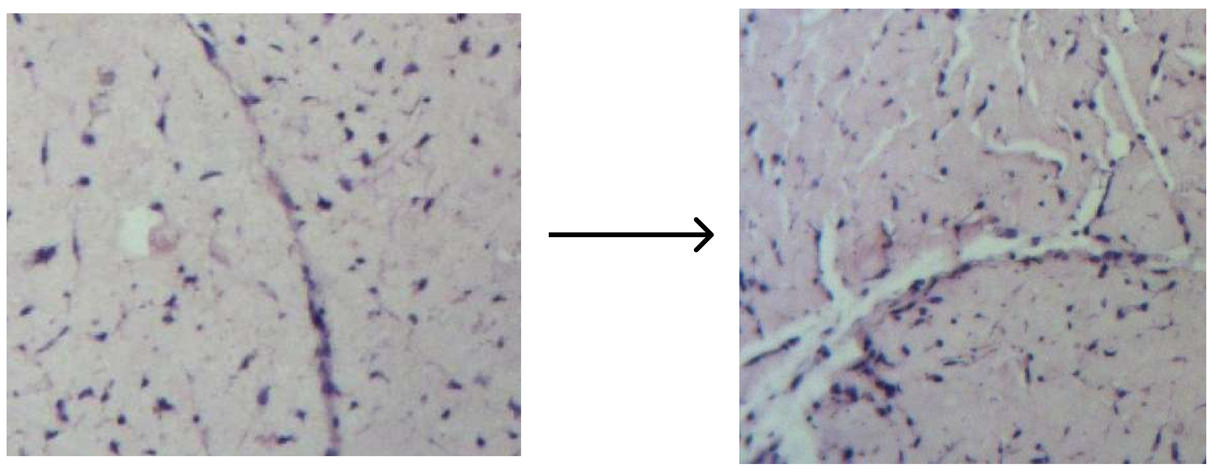
Controlled and defined stiffness for the range of culture conditions



In terms of biological properties of the obtained hydrogels, our system offers an unmatched insights into cellular behaviour using scaffold as a support for 2D cell cultures, 3D cell culture assays, in vivo injection etc.
Following table represents the conditions for application of ExViGel, compared to other products on the market.

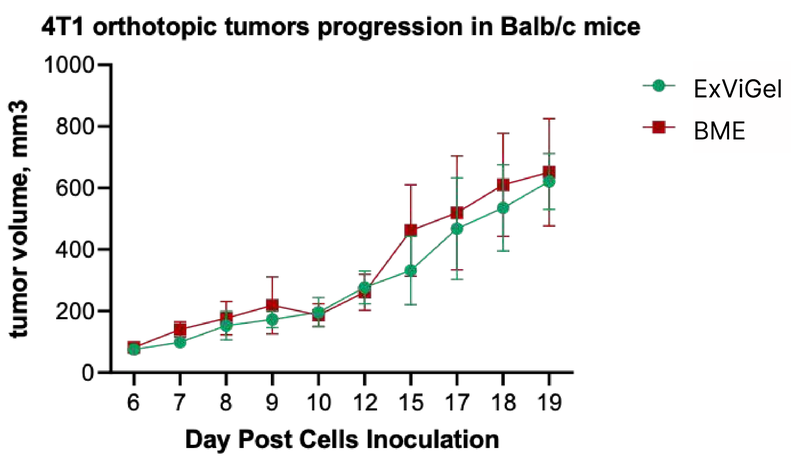
Property	ExViGel	Matrigel	Synthetic hydrogels
Degree of the cell-matrix interactions	High, very adhesive	Non-adhesive	Moderate, no native integrin interactions
Protein content data	Freely available, for every batch	Not available for every batch	No native ECM proteins
In vivo engraphment	Yes, with vascularisation	Yes, without vascularisation	Yes, in some cases. No vascularisation
Stiffness modulation within laboratory setting	Yes, via concentration and centrifugation force	No	Yes, in some embodiments
Contractibility by cellular remodelling	Yes, highly contractible	No	No
Integrin binding	Native	Weak, partial	No

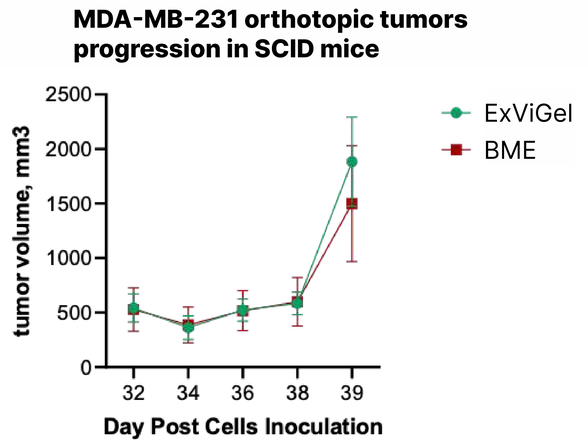
Native tissue ECM systems plays not only supporting role for the structural integrity of the tissue, it is also essential component of the signal transduction. Integrin-dependent pathways drive a lot of cellular physiology reactions via impacting signalling. Examples of such signalling routes include EGFR-pathway, MAPK/ERK-pathway, PI3K-pathway, and apoptotic pathways. Apart from that, many cells-matrix interactions frequently navigate tissue behaviour via the local contraction or release of the ECM proteins. Cell-matrix interactions are crucial in modelling of cellular adhesion, cell-cell interactions, cellular invasion, migration, vascularisation and much more.

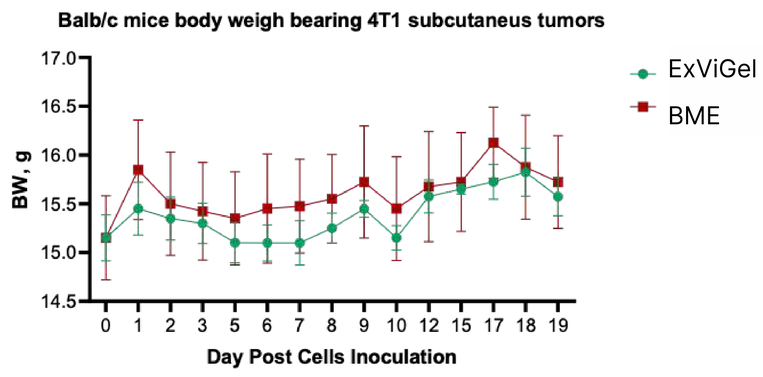


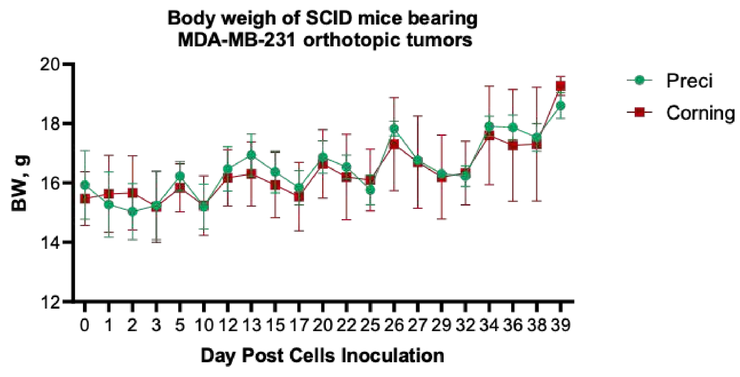
Our in vivo studies showed the maturation of the vascular structure after the injection of ECM mixture to mice. High-content of fibronectin in ExViGel, probably, promotes such effects.
We have positively validated vascularised tumor growth using the immortalised cell lines subcutaneous implantation into nude mice, with no significant adverse effects.

Reliable tumor engraphment and no mouse weight loss after hECM injection.





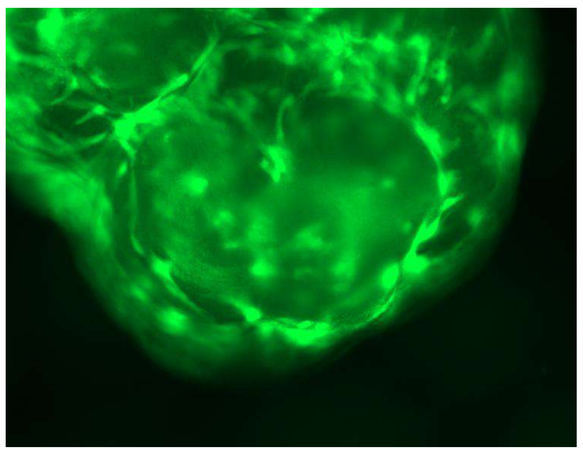


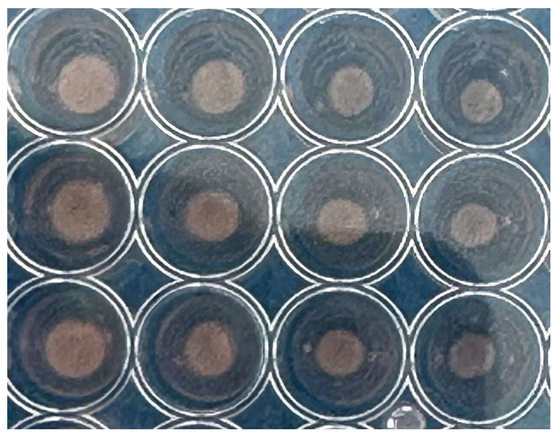


Human-Derived Extracellular Matrix - from the concept to applications

Cell-matrix interactions play a crucial role in the development of fibrosis by influencing the behavior of fibroblasts and other cellular components involved in tissue repair. These interactions regulate the deposition of extracellular matrix proteins, leading to an imbalance that promotes the stiffening of tissue, which is a hallmark of fibrotic disease. The altered extracellular matrix (ECM) not only provides structural support but also sends biochemical and mechanical signals to cells, further exacerbating the fibrotic response. Understanding these processes is essential for developing therapeutic strategies to prevent or reverse fibrosis by targeting specific pathways that mediate cell-matrix dynamics.
Our cellular and ECM products are devoted to improve the understanding and modelling capacity of the human fibrotic diseases.

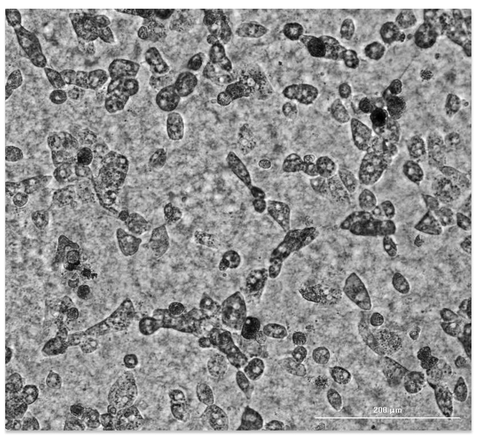
Collagen Contraction Assays with Hepatic Stellate Cells using hECM matrix

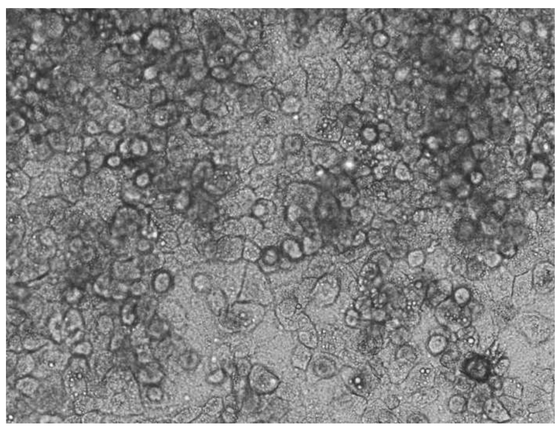




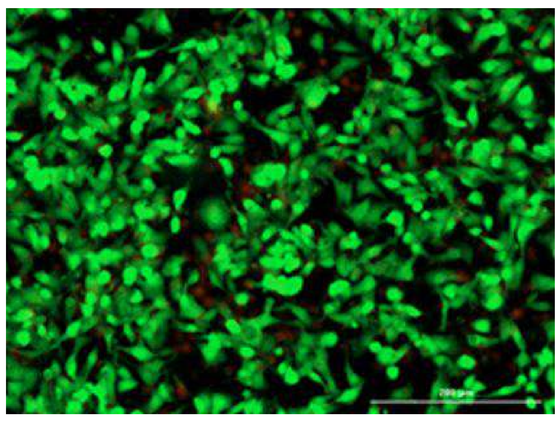
hECM concentration

Preci can supply fibroblasts along with ECM scaffold, even derived from the single patient to improve primary cell-based cellular assays. Collagen contraction assays, along with migration assays have been used to model the process in vitro. Additionally, we can provide information about specific protein content in our ECM hydrogels along with its rheological properties in the particular assay settings.

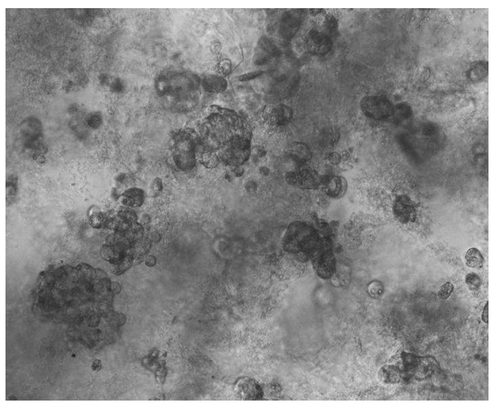




Human Hepatocytes Adhesion to the ExViGel-coated Surface



HepG2 on the ECM-coated surface



Scaffold-Embedded HepG2 spheroids

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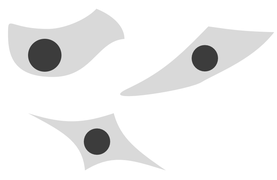
Our ECM products can significantly enhance advanced 2D and 3D modelling of tumor and healthy tissues by providing a highly realistic and tuneable extracellular matrix that closely mimics the in vivo environment. These products offer a more accurate representation of the native tissue architecture, allowing researchers to study cell behaviour, drug response, and disease progression with greater precision. Our system can integrate into the liquid handling and imaging setups, and thus allow high-throughput or high-content experimentation, using the native ECM morphology.

- Sarcoma-derived
- Liver-derived
- Heart-derived
- Lung-derived

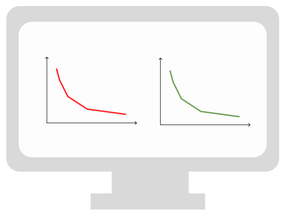
Custom origin

ECM dispersion



Isogenic fibroblasts and other cell types

- Cancer-associated fibroblasts
- IPF-derived fibroblasts
- Hepatic Stellate Cells
- Tissue-specific cells



Batch-specific data

- Defined ECM protein content
- Elasticity at specific culture conditions
- Compatibility with various cellular systems