



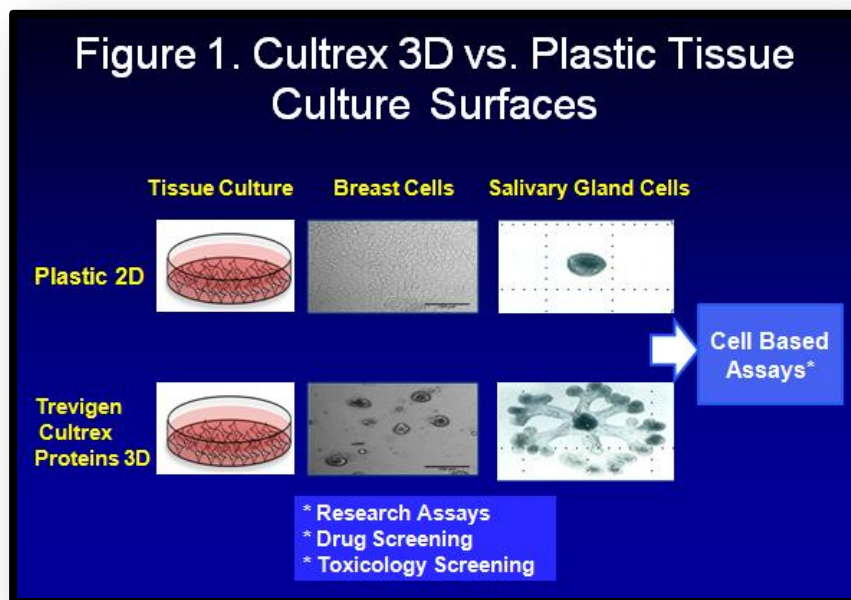
# Trevigen®

Better Products. Better Results.

## Innovative Matrices for Multiple Uses

### Why Choose Cultrex Basement Membrane Extract?

**Demonstrated Expertise of Trevigen Scientists:** A major part of Trevigen's effort is dedicated to the Basement Membrane Extract (BME), its components, and related technologies such as cell adhesion, cell invasion, and angiogenesis. Dr. Hynda Kleinman, a scientific advisor for Trevigen and inventor of BME and Matrigel has published over 400 papers related to basement membrane matrices. She has co-published with Trevigen scientists in high impact journal methods describing 3D culture, tumor growth and metastasis, wound healing, and basement membrane matrices. Other Trevigen collaborations with Hynda have included methods detailing angiogenesis assays and approaches for the development and propagation of xenograft models in murine hosts. We also discovered and have published that gene expression patterns in endothelial cells grown on traditional tissue plastic culture surfaces are significantly different compared to being cultured on ECM proteins. We have demonstrated that the organized structures observed in 3D culture assays compared to those on plastic surfaces are a result of the over expression of DNA methyltransferase 1 in traditionally cultured cells. The cells grown on Trevigen's BME clearly retained many of the phenotypic properties of the tissue from which they were isolated as shown in Figure 1. Undoubtedly the BME facilitated an optimal environment for the endothelial cells.



**Bench Experienced Technical Support:** When you call in with a technical question you will speak with a bench experienced scientist. Offering more than just technical support, you will have the opportunity to discuss your research challenges with the same Trevigen scientists that are publishing in peer reviewed journals. In addition, Dr. Kleinman takes great pleasure in providing advice to customers.

**Innovative Response to Customer Needs:** We have always tried to provide innovative solutions to meet our customers' needs. Our scientists do more than provide advice and answer technical questions; they listen to you,

address your immediate issue, and discuss options that might be available to you within the broader context of your project.

Through several discussions with our customers we have come to the realization that the heterogeneous nature of the microenvironment needs to be addressed. The microenvironment is both tissue and organ specific and its' specificity not only comes from organ specific stromal cells, growth factors, proteoglycans, and protein composition but also from the stiffness or tensile strength of the BME. Many studies have concluded that there is a relationship between abnormal tensile strength and both cancer progression and fibrotic tissues. When we use the term microenvironment we are really talking about many microenvironments. It is both the chemical and physical properties of the BME that are responsible for the mechanical and biological properties of tissues and organs. It is interesting in light of this heterogeneity, that for the past 25 years the scientific community has been forced to use one commercial ECM matrix formulation.

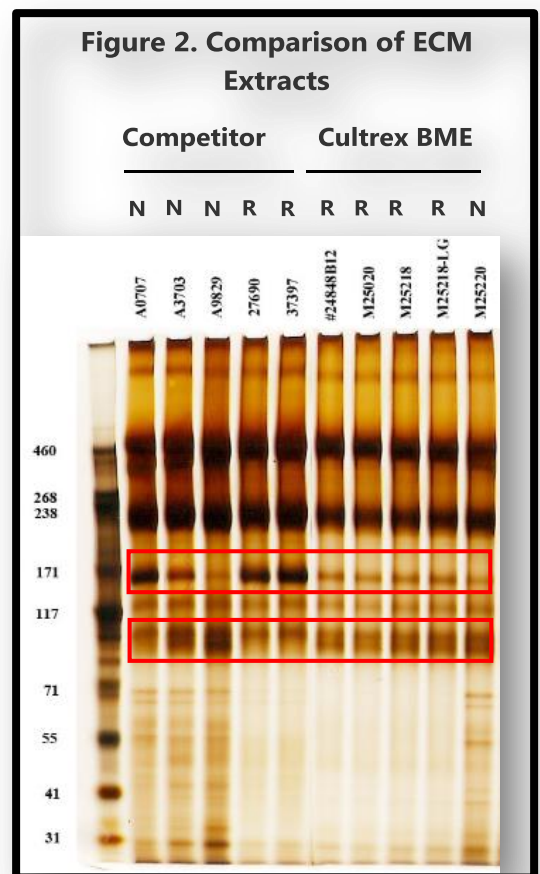
As a result we have developed two additional formulations of Cultrex BME known as Cultrex BME 2 and Cultrex BME 3. BME 2 provides a proprietary formulation that is higher in tensile strength when compared to our original BME, while BME 3 is physiologically aligned with the in vivo tumor environment and is recommended for xenografts and other in vivo applications. It is difficult to know which matrix formulation is best suited for any specific cell type or application. However in competitive beta tests utilizing either in vitro or in vivo model systems, Cultrex BME, BME 2 or BME 3 consistently outperforms competitor products.

### **Lot to Lot Performance Consistency Compared to Competitive**

**Products:** We know from listening to our customers that they observe lot to lot performance inconsistencies in our competitor's products. Before they start a large experiment they routinely evaluate several lots of material prior to making a purchase similarly to serum evaluation for cell culture operations. However we know that some of the lot to lot inconsistency originates from an inconsistent distribution of ECM proteins observed in different lots as shown in Figure 2.

Figure 2 shows a silver stained gel of multiple lots of Normal (N) and Growth Factor Reduced (R) ECM extracts from Trevigen (Cultrex BME) and a competitor. In all lots of growth factor reduced material (R) lower molecular weight bands have been removed as a result of the growth factor reduction process. However, the lot to lot inconsistency of the protein bands identified within the red boxes for the competitive products may contribute to their observed performance irregularities between lots.

**Summary:** In summary, we have listened to our customers' needs relating to varying microenvironment requirements. Trevigen has worked with our in house team of experts and with Dr. Hynda Kleinman to develop and manufacture Cultrex BME to the highest standards in the industry. Lot-to-lot product consistency is second to none. Performance and contamination testing is thorough and comprehensive. Now, in our continuing effort to develop the best product for evolving researcher's needs, we offer choices in BME formulations, Cultrex BME, Cultrex BME Type 2, and Cultrex BME Type 3, in order to



cater to your cell's preferred microenvironment. Find out which Cultrex BME formulation is optimal for your cells. Contact Trevigen today to order your samples.

Catalog Number	Name	Size
3432-001-01	Cultrex® Basement Membrane Extract, PathClear®	1 ml
3432-005-01	Cultrex® Basement Membrane Extract, PathClear®	5 ml
3432-010-01	Cultrex® Basement Membrane Extract, PathClear®	2 x 5 ml
3433-001-01	Cultrex® Reduced Growth Factor Basement Membrane Extract, PathClear®	1 ml
3433-005-01	Cultrex® Reduced Growth Factor Basement Membrane Extract, PathClear®	5 ml
3433-010-01	Cultrex® Reduced Growth Factor Basement Membrane Extract, PathClear®	2 x 5 ml
3532-001-02	Cultrex® Basement Membrane Extract, Type 2, PathClear®	1 ml
3532-005-02	Cultrex® Basement Membrane Extract, Type 2, PathClear®	5 ml
3532-010-02	Cultrex® Basement Membrane Extract, Type 2, PathClear®	2 x 5 ml
3533-001-02	Cultrex® Reduced Growth Factor Basement Membrane Extract, Type 2, PathClear®	1 ml
3533-005-02	Cultrex® Reduced Growth Factor Basement Membrane Extract, Type 2, PathClear®	5 ml
3533-010-02	Cultrex® Reduced Growth Factor Basement Membrane Extract, Type 2, PathClear®	2 x 5 ml
3632-001-02	Cultrex® Basement Membrane Extract, Type 3, PathClear®	1 ml
3632-005-02	Cultrex® Basement Membrane Extract, Type 3, PathClear®	5 ml
3632-010-02	Cultrex® Basement Membrane Extract, Type 3, PathClear®	2 x 5 ml

Cultrex® BME Selection Chart				
NAME	BUFFER	TENSILE STRENGTH	CONCENTRATION	APPLICATIONS
<b>Cultrex® BME, PathClear®</b>	DMEM	MEDIUM	14-17 mg	xenograft/tumorgraft 2D cell culture 3D spheroids/organoids stem cell
<b>Cultrex® BME Type 2, PathClear®</b>	DMEM	HIGH	14-17 mg	xenograft/tumorgraft 2D cell culture 3D spheroids/organoids stem cell
<b>Cultrex® BME Type 3, PathClear®</b>	RPMI1640	HIGH	14-17 mg	xenograft/tumorgraft

#### How to Order:

Contact Trevigen at (301) 216-2800, [info@trevigen.com](mailto:info@trevigen.com), or [www.trevigen.com](http://www.trevigen.com) for full ordering and sampling options.

## References citing Cultrex Basement Membrane Extract:

1. Solange Landreville, Olga A. Agapova, Katie A. Matatall, Zachary T. Kneass, Michael D. Onken, Ryan S. Lee, Anne M. Bowcock, and J. William Harbour. 2012. Histone Deacetylase Inhibitors Induce Growth Arrest and Differentiation in Uveal Melanoma. *Clin. Cancer Res.* 18:408-416.
2. Ryan A. Virden, Carol J. Thiele and Zihui Liu. 2012. Characterization of Critical Domains within the Tumor Suppressor CASZ1 Required for Transcriptional Regulation and Growth Suppression. *Mol. Cell. Biol.* 32:1518 - 1528.
3. Jennifer M. Munson, Levi Fried, Sydney A. Rowson, Michael Y. Bonner, Lohitash Karumbaiah, Begoña Diaz, Sara A. Courtneidge, Ulla G. Knaus, Daniel J. Brat, Jack L. Arbiser, and Ravi V. Bellamkonda. 2012. Anti-Invasive Adjuvant Therapy with Imipramine Blue Enhances Chemotherapeutic Efficacy Against Glioma. *Science Translational Medicine.* 4:127ra36.
4. Nimali P. Withana, Galia Blum, Mansoureh Sameni, Clare Slaney, Arulselvi Anbalagan, Mary B. Olive, Bradley N. Bidwell, Laura Edgington, Ling Wang, Kamiar Moin, Bonnie F. Sloane, Robin L. Anderson, Matthew S. Bogyo, and Belinda S. Parker. 2012. Cathepsin B Inhibition Limits Bone Metastasis in Breast Cancer. *Cancer Res.* 72:1199-1209.
5. Alessandro Antonelli, Guido Bocci, Concettina La Motta, Silvia Martina Ferrari, Poupak Fallahi, Ilaria Ruffilli, Andrea Di Domenicantonio, Anna Fioravanti, Stefania Sartini, Michele Minuto, Simona Piaggi, Alessandro Corti, Greta Ali, Teresa Di Desidero, Piero Berti, Gabriella Fontanini, Romano Danesi, Federico Da Settimo, and Paolo Miccoli. 2012. CLM94, a Novel Cyclic Amide with Anti-VEGFR-2 and Antiangiogenic Properties, Is Active against Primary Anaplastic Thyroid Cancer in Vitro and in Vivo. *J. Clin. Endocrinol. Metab.* 97:E528-E536.
6. Benjamin Cieply, Philip Riley IV, Phillip M. Pifer, Joseph Widmeyer, Joseph B. Addison, Alexey V. Ivanov, James Denvir, and Steven M. Frisch. 2012. Suppression of the Epithelial–Mesenchymal Transition by Grainyhead-like-2. *Cancer Res.* 72:2440-2453.
7. Patricia M. Day, Yuk-Ying S. Pang, Rhonda C. Kines, Cynthia D. Thompson, Douglas R. Lowy, and John T. Schiller. 2012. A Human Papillomavirus (HPV) In Vitro Neutralization Assay That Recapitulates the In Vitro Process of Infection Provides a Sensitive Measure of HPV L2 Infection-Inhibiting Antibodies. *Clin. Vaccine Immunol.* 19:1075-1082.
8. Zhijie Li, Shuang Yan, Navid Attayan, Sridevi Ramalingam, and Carol J. Thiele. 2012. Combination of an Allosteric Akt Inhibitor MK-2206 with Etoposide or Rapamycin Enhances the Antitumor Growth Effect in Neuroblastoma. *Clin. Cancer Res.* 18:3603-3615.
9. Eberhard Krausz, Ronald de Hoogt, Emmanuel Gustin, Frans Cornelissen, Thierry Grand-Perret, Lut Janssen, Nele Vloemans, Dirk Wuyts, Sandy Frans, Amy Axel, Pieter Johan Peeters, Brett Hall, and Miroslav Cik. 2012. Translation of a Tumor Microenvironment Mimicking 3D Tumor Growth Co-culture Assay Platform to High-Content Screening. *J Biomol Screen.* 10.1177/1087057112456874
10. Francesca Caccuri, Cinzia Giagulli, Antonella Bugatti, Anna Benetti, Giulio Alessandri, Domenico Ribatti, Stefania Marsico, Paola Apostoli, Mark A. Slevin, Marco Rusnati, Carlos A. Guzman, Simona Fiorentini, and Arnaldo Caruso. 2012. HIV-1 matrix protein p17 promotes angiogenesis via chemokine receptors CXCR1 and CXCR2. *PNAS.* 10.1073/pnas.1206605109.
11. Tim Eiseler, Conny Köhler, Subbaiah Chary Nimmagadda, Arsia Jamali, Nancy Funk, Golsa Joodi, Peter Storz, and Thomas Seufferlein. 2012. Protein Kinase D1 Mediates Anchorage-dependent and -independent Growth of Tumor Cells via the Zinc Finger Transcription Factor Snail1. *J. Biol. Chem.* 287:32367-32380.

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