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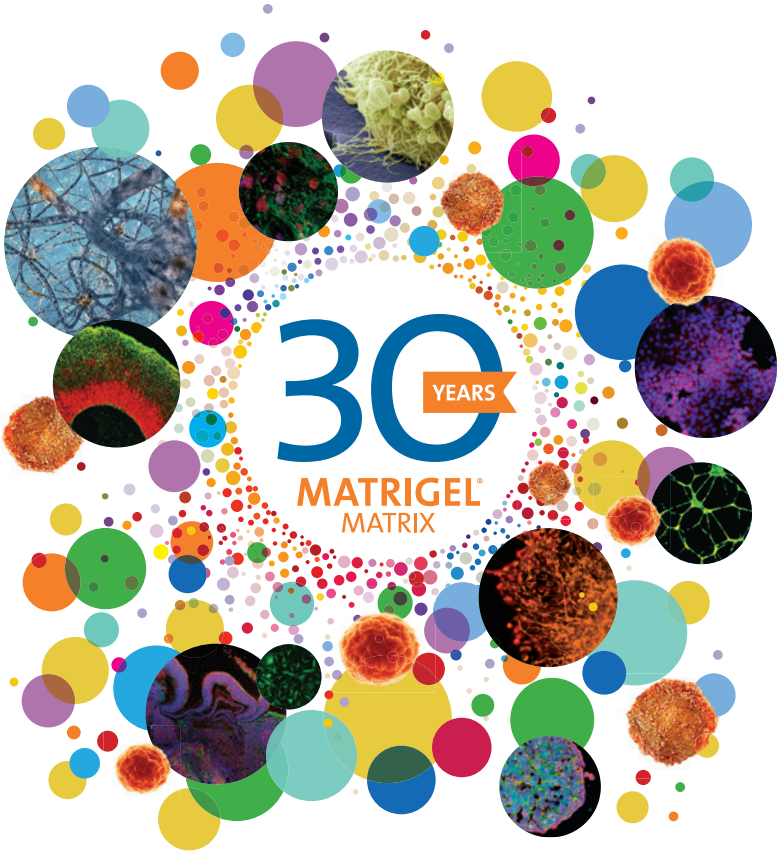


Celebrate the past.
Imagine the future.

10,000 Citations and Counting

For the past 30 years, Corning Matrigel matrix has been used by researchers across the globe in essential applications through to cutting-edge, life-changing research. The number of citations for Matrigel matrix has recently climbed over 10,000 citations. It's an impressive collection from which we have highlighted the top 30 most cited bodies of work. Read on to learn more about the innovative ways scientists have used Corning Matrigel matrix.

1. **Impaired recruitment of bone-marrow-derived endothelial and hematopoietic precursor cells blocks tumor angiogenesis and growth**

   Lyden D, Hattori K, Dias S, et al. Nat Med. 2001;7(11):1194-1201

   Researchers demonstrate that tumor angiogenesis is associated with recruitment of hematopoietic and circulating endothelial bone marrow (BM)-derived precursor cells.

2. **Feeder-free growth of undifferentiated human embryonic stem cells**

   Xu C, Inokuma MS, Denham J, et al. Nat Biotech. 2001;19(10):971-74.

   Contrary to previous research requiring cell culture on mouse embryonic fibroblast (MEF) feeders to maintain undifferentiated human embryonic stem (hES) cells, researchers were able to demonstrate a successful feeder-free hES culture system in which undifferentiated cells can be maintained for at least 130 population doublings.

3. **Morphogenesis and oncogenesis of MCF-10A mammary epithelial acini grown in three-dimensional basement membrane cultures**

   Debnath J, Muthuswamy SK, Brugge JS. Methods. 2003;30(3):256-68.

   Researchers present a collection of protocols demonstrating effective 3D culture of MCF-10A mammary epithelial cells, which has been shown to be an effective model for the biological activity of cancer genes.

4. **Human endothelial progenitor cells from type II diabetics exhibit impaired proliferation, adhesion, and incorporation into vascular structures**

   Tepper OM, Galiano RD, Capla JM, et al. Circulation. 2002;106(22):2881-86.

   Because diabetic complications occur in conditions in which endothelial progenitor cell (EPC) contributions have been demonstrated, EPC dysfunction may be important in their pathophysiology. Through the proliferation of diabetic EPCs, this study demonstrated activity that indicates a correlation between type 2 diabetes and an alteration in EPC biology that is critical for new blood vessel growth.

5. **Vascular channel formation by human melanoma cells *in vivo* and *in vitro*: Vasculogenic mimicry**

   Maniotis AJ, Folberg R, Hess A, et al. Am J Pathol. 1999;155(3):739-52.

   Researchers observed highly invasive primary and metastatic human melanoma cells forming patterned solid and hollow matrix channels in 3D cultures without endothelial cells or fibroblasts, and these cells contracted and remodeled floating hydrated gels, providing a biomechanical explanation for the generation of microvessels *in vitro*. This evidence suggests that aggressive melanoma cells may generate vascular channels that facilitate tumor perfusion independent of tumor angiogenesis.

6. **Multipotent adult progenitor cells from bone marrow differentiate into functional hepatocyte-like cells**

   Schwartz RE, Reyes M, Koodie L, et al. J Clin Invest. 2002;109(10):1291-1302.

   Researchers derived multipotent adult progenitor cells (MAPCs) that can differentiate into most mesodermal cells and neuroectodermal cells *in vitro* and into all embryonic lineages *in vivo* from normal human, mouse, and rat postnatal bone marrow primitive. The MAPCs also acquired functional characteristic of hepatocytes, which may make the cells an ideal cell for liver biotherapies or *in vivo* treatment for disorders.

7. **HMEC-1: Establishment of an immortalized human microvascular endothelial cell line**

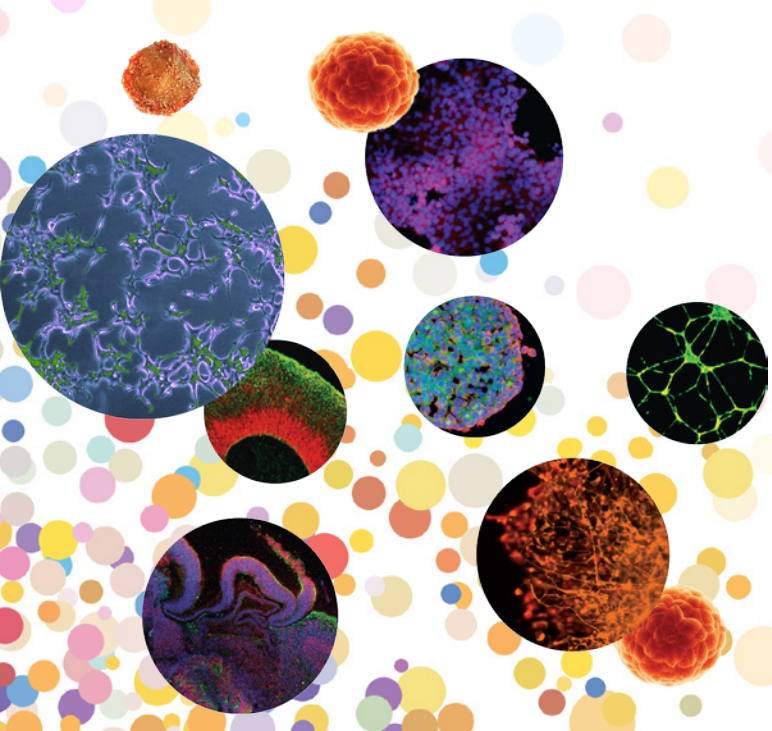
   Ades EW, Candal FJ, Swerlick RA, et al. J Invest Derm. 1992;99(6):683-90.

   Human dermal microvascular endothelia cells (HMECs) were successfully immortalized using a PBR-322-based plasmid containing the coding region for the simian virus 40 A gene product— large T antigen. These cells were the first of their kind to retain the morphologic, phenotypic, and functional characteristics of normal HMECs.

8. **Plasticity of human adipose lineage cells toward endothelial cells: Physiological and therapeutic perspectives**

   Planat-Benard V, Silvestre JS, Cousin B, et al. Circulation. 2004;109(5):656-63.

   This study demonstrates that adipocytes and endothelial cells have a common progenitor. Such adipose lineage cells participate in vascular-like structure formation in Matrigel plug and enhance the neovascularization reaction in ischemic tissue. These results also highlight the concept that adipose lineage cells represent a suitable new cell source for therapeutic angiogenesis in ischemic disease.



9. ***In vitro* cultivation of human islets from expanded ductal tissue**

   Bonner-Weir S, Taneja M, Weir GC, et al. Proceed Nat Acad Sci. 2000;97(14):7999-8004.

   Using digested pancreatic tissue, researchers successfully tested the hypothesis that human adult duct tissue could be expanded and differentiated *in vitro* to form islet cells, providing a potential new source of pancreatic islet cells for transplantation.

10. **Inhibition of VEGF receptors causes lung cell apoptosis and emphysema**

    Kasahara Y, Tuder RM, Taraseviciene-Stewart L, et al. J Clin Invest. 2001;106(11):1311-19.

    Based on the hypothesis that chronic blockade of VEGF receptors could induce alveolar cell apoptosis and emphysema, researchers were able to show cellular activity that indicated that VEGF receptor signaling is required for maintenance of the alveolar structures and, further, that alveolar septal cell apoptosis contributes to the pathogenesis of emphysema.

11. **Constitutive Stat3 activity up-regulates VEGF expression and tumor angiogenesis**

    Niu G, Wright KL, Huang M, et al. Oncogene. 2002;21(13):2000-08.

    Researchers demonstrate that VEGF expression correlates with Stat3 activity in diverse human cancer cell lines, providing evidence that the VEGF gene is regulated directly by Stat3 protein, and indicating that Stat3 represents a common molecular target for blocking angiogenesis induced by multiple signaling pathways in human cancers.

12. **Differing modes for tumour cell invasion have distinct requirements for Rho/ROCK signaling and extracellular proteolysis**

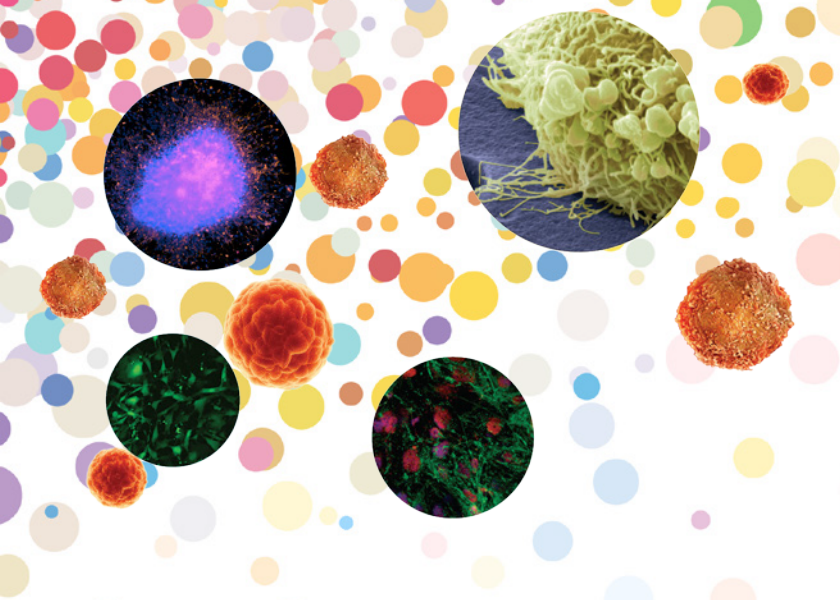
    Sahai E., Marshall C.J. Nat Cell Biol. 2003; 5(8):711-19.

    Researchers identified two modes of tumor-cell motility in 3D matrices that involve different usage of Rho signaling—one which requires ezrin, which is localized in the direction of cello movement, and one which does not require ezrin function. They found that combined blockade of extracellular proteases and ROCK negates the ability of tumor cells to switch between modes of motility and synergizes to prevent tumor cell invasion.

13. **Methods in laboratory investigation: A simple, quantitative method for assessing angiogenesis and antiangiogenic agents using reconstituted basement membrane, heparin, and fibroblast growth factor**

    Passaniti A, Taylor RM, Pili R, et al. Lab Invest. 1992;67(4):519-28.

    A mice study assay showed intense vascular response when basement membrane proteins were supplemented with angiogenic factors, allowing the quantitative assessment of angiogenic and anti-angiogenic factors.



14. Human bone marrow-derived mesenchymal stem cells in the treatment of gliomas

Nakamizo A, Marini F, Amano T, et al. Cancer Res. 2005;65(8):3307-18.

Researchers confirmed a hypothesis that human bone marrow-derived mesenchymal stem cells (hMSCs) integrate into human gliomas after intravascular or local delivery, that this engraftment may be mediated by growth factors, which may have a tropism for brain tumors and thus could be used as delivery vehicles for glioma therapy.

15. Endothelial cells derived from human embryonic stem cells

Levenberg S, Golub JS, Amit M, Itskovitz-Eldor J, Langer R. Proceed Nat Acad Sci. 2002; 99(7):4391-96.

Human embryonic stem cells have the potential to differentiate into various cell types, which may make them useful as a source of cells for transplantation or tissue engineering. In this study, researchers describe the differentiation steps of human embryonic stem cells into endothelial cells forming vascular-like structures.

16. Alveolar epithelial cell mesenchymal transition develops *in vivo* during pulmonary fibrosis and is regulated by the extracellular matrix

Kim KK, Kugler MC, Wolters PJ, et al. Proceed Nat Acad Sci. 2006;103(35):13180-85.

To more definitively test the capacity of alveolar epithelial cells for EMT, mice expressing β-galactosidase (β-gal) exclusively in lung epithelial cells were generated, and their fates were followed in an established model of pulmonary fibrosis, over-expression of active TGF-β1. This research revealed alveolar epithelial cells as progenitors for fibroblasts *in vivo* and implicates the provisional extracellular matrix as a key regulator of epithelial transdifferentiation during fibrogenesis.

17. Side population in human lung cancer cell lines and tumors is enriched with stem-like cancer cells

Ho MM, Ng AV, Lam S, Hung JY. Cancer Res. 2007;67(10):4827-33.

These research findings indicate that side population stem cells are an enriched source of lung tumor-initiating cells with stem cell properties and may be an important target for effective therapy and a useful tool to investigate the tumorigenic process.

18. Exogenous expression of N-cadherin in breast cancer cells induces cell migration, invasion, and metastasis

Hazan RB, Phillips GR, Qiao RF, Norton L, Aaronson SA. J Cell Biol. 2000;148(4):779-90.

This study set out to determine whether N-cadherin promotes invasion and metastasis. When injected into the mammary fat pad of nude mice, N-cadherin-expressing cells, but not control MCF-7 cells, metastasized widely to the liver, pancreas, salivary gland, omentum, lung, lymph nodes, and lumbar spinal muscle, demonstrating that N-cadherin promotes motility, invasion, and metastasis even in the presence of the normally suppressive E-cadherin.

19. Antivascular endothelial growth factor receptor (fetal liver kinase 1) monoclonal antibody inhibits tumor angiogenesis and growth of several mouse and human tumors

Prewett M, Huber J, Li Y, et al. Cancer Res. 1999;59(20):5209-18.

This study reports the effect of anti-Flk-1 mAb [fetal liver kinase 1 (Flk-1)/kinase insert domain-containing receptor] on angiogenesis and tumor growth, demonstrating that anti-Flk-1 mAb treatment inhibits tumor growth by suppression of tumor-induced neovascularization and has the potential for therapeutic application of anti-VEGF receptor antibody in the treatment of angiogenesis-dependent tumors.

20. Fibroblast Growth Factor 10 (FGF10) and branching morphogenesis in the embryonic mouse lung

Bellusci S, Grindley J, Emoto H, Itoh N, Hogan BLM Development. 1997;124(23):4867-78.

Researchers report here that fibroblast growth factor 10 (Fgf10) is expressed dynamically in the mesenchyme adjacent to the distal buds from the earliest stages of lung development and conclude that during early lung development, localized sources of FGF10 in the mesoderm regulate endoderm proliferation and bud outgrowth.

21. Scatter factor induces blood vessel formation *in vivo*

Grant DS, Kleinman HK, Goldberg ID, et al. Proceed Nat Acad Sci. 1993;90(5):1937-41.

Using two different *in vivo* assays, researchers showed that physiologic quantities of purified native mouse scatter factor and recombinant human hepatocyte growth factor induce angiogenesis, which suggests that scatter factor may act as a paracrine mediator in pathologic angiogenesis associated with human inflammatory disease.

22. Human endothelial cells express CCR2 and respond to MCP-1: Direct role of MCP-1 in angiogenesis and tumor progression

Salcedo R, Ponce ML, Young HA, et al. Blood. 2000;96(1):34-40.

This report demonstrates that the CC chemokine, monocyte chemotactic protein 1 (MCP-1), induced chemotaxis of human endothelial cells at nanomolar concentrations. This chemotactic response was inhibited by a monoclonal antibody to MCP-1, which also induced the formation of blood vessels *in vivo* as assessed by the chick chorioallantoic membrane and the Matrigel® plug assays.

23. Migration of tumor cells in 3D matrices is governed by matrix stiffness along with cell-matrix adhesion and proteolysis

Zaman MH, Trapani LM, Siemeski A, et al. Proceed Nat Acad Sci. 2006;103(29):1088-94.

Here researchers demonstrate that, in addition to adhesion and tractile forces, matrix stiffness is a key factor that influences cell movement in 3D. This 3D motility through an extracellular environment of pore size much smaller than cellular dimensions does depend on proteolytic activity, as broad-spectrum matrix metalloproteinase (MMP) inhibitors limit the migration of DU-145 cells and also HT-1080 fibrosarcoma cells.

24. Matrigel: Basement membrane matrix with biological activity

Kleinman HK, Martin GR. Sem Cancer Bio. 2005;15:378-86.

This article demonstrates that Matrigel® matrix promotes cell differentiation and measures the invasive activity of tumor cells. *In vivo*, it can be used for measuring angiogenic inhibitors and stimulators, to improve graft survival, to repair damaged tissues, and to increase tumor growth.

25. The discoidin domain receptor tyrosine kinases are activated by collagen

Vogel W, Gish GD, Alves F, Pawson T. Molec Cell. 1997;1(1):13-23.

Researchers show that mammalian DDR receptors bind and are activated by specific types of collagen. These results suggest that the discoidin-related DDR tyrosine kinases are novel collagen receptors with the potential to control cellular responses to extracellular matrix.

26. Human breast cancer cells generated by oncogenic transformation of primary mammary epithelial cells

Elenbaas B, Spirio L, Koerner F, et al. Genes and Dev. 2001;15(1):50-65.

In this study, mixing epithelial tumor cells with Matrigel or primary human mammary fibroblasts substantially increased the efficiency of tumor formation and decreased the latency of tumor formation, demonstrating a significant influence of the stromal microenvironment on tumorigenicity. These observations establish an experimental system for elucidating both the genetic and cell biological requirements for the development of breast cancer.

27. Human feeders support prolonged undifferentiated growth of human inner cell masses and embryonic stem cells

Richards M, Fong C-Y, Chan W-K, Wong P-C, Bongso A. Nat Biotech. 2002;20(9):933-36.

Researchers show that human fetal and adult fibroblast feeders support prolonged undifferentiated human embryonic stem (HES) cell growth of existing cell lines and are superior to cell-free matrices (collagen I, human extracellular matrix, Matrigel, and laminin) supplemented with human or mouse embryonic fibroblast (MEF) feeder-conditioned medium. Additionally demonstrated is the derivation and establishment of a new HES cell line in completely animal-free conditions.

28. The microtubule-affecting drug paclitaxel has antiangiogenic activity

Belotti D, Vergani V, Drudis T, et al. Clin Cancer Res. 1996;2(11):1843-49.

Paclitaxel (Taxol®), a microtubule-stabilizing antineoplastic cytotoxic drug, inhibits motility and invasiveness of several cell types. The aim of this study was to investigate the effect of paclitaxel on endothelial cell functions and on angiogenesis.

29. An angiogenic role for the human peptide antibiotic LL-37/hCAP-18

Koczulla R, Von Degenfeld G, Kupatt C, et al. J Clin Invest. 2003;111(11):1665-72.

Researchers show that LL-37 induces angiogenesis mediated by formyl peptide receptor-like 1 expressed on endothelial cells. Decreased vascularization during wound repair in mice deficient for CRAMP, the murine homologue of LL-37/hCAP-18, shows that cathelicidin-mediated angiogenesis is important for cutaneous wound neovascularization *in vivo*. These findings demonstrate that LL-37/hCAP-18 is a multifunctional antimicrobial peptide with a central role in innate immunity by linking host defense and inflammation with angiogenesis and arteriogenesis.

30. CD44+/CD24-Breast cancer cells exhibit enhanced invasive properties: An early step necessary for metastasis

Sheridan C, Kishimoto H, Fuchs RK, et al. Breast Cancer Res. 2006;8(5):R59.

Researchers investigated whether CD44+/CD24- breast cancer cells have the unique ability to invade, home, and proliferate at sites of metastasis, and found that they were more invasive than other cell lines. However, only a subset of CD44+/CD24-positive cell lines was able to home and proliferate in lungs.

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