



Cultrex[®]

ANGIOGENESIS • DNA DAMAGE & REPAIR • APOPTOSIS

Directed In Vivo Angiogenesis Assays (DIVAA™)

DIVAA™ was invented to address the short-comings of the plug assay by controlling the site for angiogenesis, increasing reproducibility, conserving test compounds, and supplying more statistical data for quantitative analysis. When injecting plugs subcutaneously, researchers have little control over where the bolus forms, but with DIVAA™, researchers may standardize the placement of angioreactors and create a stable site for angiogenesis. While plugs form amorphous shapes that are synonymous with re-absorption, the angioreactor provides a fixed volume and surface area for reaction, increasing inter- and intra-assay reproducibility, and protects the matrix from incorporation in host tissues, insuring that there will be samples for analysis. Whilst size and volume impose a limit of one plug per mouse, the compactness of the angioreactor conserves precious test compounds and permits implantation of up to four angioreactors per mouse, allowing for multiple data points for quantitative analysis.

During the course of the assay, implant grade silicone cylinders closed at one end, called angioreactors, are filled with basement membrane extract (BME) premixed with or without angiogenic-modulating factors. The angioreactors (positive control, negative control, and experimental angioreactors) are implanted subcutaneously in the dorsal flank of nude mice. Accompanied with the onset of angiogenesis, vascular endothelial cells proceed to grow into the BME and form vessels in the angioreactor. As early as nine days post-implantation, there are enough cells to determine an effective dose response to angiogenic modulating factors. The sleek design of the angioreactor provides a standardized platform for reproducible and quantifiable in vivo angiogenesis assays. These kits include PathClear[®] BME which has been tested and cleared of a battery of 31 pathogens and viruses including LDEV, which provides researchers with assurance that these contaminants are not influencing their experiments. Contact Trevigen for details!

DIVAA™ Starter Kit

The Directed In Vivo Angiogenesis Assay (DIVAA™) Starter Kit was designed to introduce the technology and give the user practical experience assessing angiogenesis. It contains 48 angioreactors, enough growth factor to induce angiogenesis all 48 angioreactors, and an AngioRack™ designed to hold the angioreactors during the course of assay setup.

DIVAA™ Activation Kit

The Directed In Vivo Angiogenesis Assay (DIVAA™) Activation Kit was designed for assessing angiogenesis activation. It contains 48 angioreactors and enough growth factor for eight positive controls. DIVAA™ has been employed in evaluating the enhancement of angiogenesis associated with adrenomedullin and CD97.

DIVAA™ Inhibition Assay

The Directed In Vivo Angiogenesis Assay (DIVAA™) Inhibition Kit was designed for assessing angiogenesis inhibition. It contains 48 angioreactors and enough growth factor to induce angiogenesis in all 48 angioreactors. DIVAA™ has been utilized in demonstrating the inhibition of angiogenesis in matrix metalloprotease (MMP)-2-deficient mice and by TIMP-2.

DIVAA™ AngioRack™

Available as a separate product, the autoclavable, reusable AngioRack™ is precision machined of Teflon[®] to hold 48 sterile silicone angioreactors in the laminar flow hood while filling and preparing for implantation.



Directed In Vivo Angiogenesis Assays (DIVAA™)

Ordering Information:

Description	Size	Catalog #
DIVAA™ Starter Kit	48 Angioreactors	3450-048-SK
DIVAA™ Activation Kit	48 Angioreactors	3450-048-K
DIVAA™ Inhibition Kit	48 Angioreactors	3450-048-IK
AngioRack™	1 Rack	3450-048-09

Related Products:

Description	Size	Catalog #
VasoTACS™ Kit	30 tests	4826-30-K
Cultrex® In Vitro Angiogenesis Assay Kit: Tube Formation	96 tests	3470-096-K
Cultrex® In Vitro Angiogenesis Assay Kit: Endothelial Cell Invasion Kit	96 tests	3471-096-K
Cultrex® 24 Well In Vitro Vascular Permeability Assay	24 tests	3475-024-K
Cultrex® 96 Well In Vitro Vascular Permeability Assay	96 tests	3475-096-K
Cultrex® Mouse Laminin I	1 mg	3400-010-01
Cultrex® Mouse Collagen IV	1 mg	3410-010-01
Cultrex® BME w/ Phenol Red	5 ml	3430-005-01
Cultrex® BME PathClear® w/ Phenol Red	5 ml	3430-005-02
Cultrex® BME RGF w/ Phenol Red	5 ml	3431-005-01
Cultrex® BME PathClear® RGF w/ Phenol Red	5 ml	3431-005-02
Cultrex® BME PathClear®	5 ml	3432-005-01
Cultrex® BME no Phenol red	5 ml	3432-005-02
Cultrex® BME RGF no Phenol red	5 ml	3433-005-01
Cultrex® BME PathClear® RGF no Phenol red	5 ml	3433-005-02
Cultrex® BME PathClear® High Protein Concentration	5 ml	3444-005-02

References

- Martinez A, Vos M, Guedez L, Kaur G, Chen Z, Garayoa M, Pio R, Moody T, Stetler-Stevenson WG, Kleinman HK, Cuttitta F. The effects of adrenomedullin overexpression in breast tumor cells. *J Natl Cancer Inst.* 2002 Aug 21;94(16):1226-37.
- Wang T, Ward Y, Tian L, Lake R, Guedez L, Stetler-Stevenson WG, Kelly K. CD97, an adhesion receptor on inflammatory cells, stimulates angiogenesis through binding integrin counterreceptors on endothelial cells. *Blood* 2005 Apr 1;105(7):2836-44.
- Guedez L, Rivera AM, Salloum R, Miller ML, Diegmüller JJ, Bungay PM, Stetler-Stevenson WG: Quantitative Assessment of Angiogenic Response by the Directed In Vivo Angiogenesis Assay. *AJP* 2003 May; 162(5):1431-1439.
- Seo D, Li H, Guedez L, Wingfield PT, Diaz T, Salloum R, Wei B, Stetler-Stevenson WG: TIMP-2 Mediated Inhibition of Angiogenesis: An MMP-Independent Mechanism. *Cell* 2003 July 25;114:171-180

BME = Basement Membrane Extract, RGF = Reduced Growth Factor.

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