



dedicated to finding a cure

JDRF



NCI



NIDDK

Trans-Institute Angiogenesis Research Program (TARP)



NEI



NICHD



NINDS



NHLBI

TARP Mission Statement

To encourage and facilitate the study of the underlying mechanisms controlling blood vessel growth and development.

To identify specific targets and to develop therapeutics against pathologic angiogenesis in order to reduce the morbidity due to abnormal blood vessel proliferation in a variety of disease states.

To better understand the process of angiogenesis and vascularization in disease states of decreased vascularization.

To encourage and facilitate the study of the processes of lymphangiogenesis.

To achieve these goals through a multidisciplinary approach, bringing together investigators with varied backgrounds and varied interests.



“The committee is pleased with the progress of angiogenesis research across the institute to involve both intramural and extramural researchers and encourages NCI to continue to pursue efforts to establish greater collaboration between angiogenesis researchers in the field of cancer biology and diabetes. The trans-NIH angiogenesis workshop is an important step toward promoting multidisciplinary research on this

TARP Accomplishments

Organized and sponsored a workshop on opportunities for cross discipline collaboration for vascular developmental biology research.

Established a website for the TARP.

Reviewed collaborative RFAs (NIDDK, JDRF, NINDS, NHLBI, NEI, NICHD).

Organized and co-sponsored a Nature Insight on angiogenesis.

Performed a review of the angiogenesis grant portfolios for 5 member ICs.

Convened a panel to review the current angiogenesis portfolio and to offer opinions on new directions and opportunities.

Opened an Angiogenesis Core Facility at the CCR ATC in March 2006.

- Validate existing angiogenesis assays and reagents.**
- Develop new assays focusing on molecular pathways and systems biology.**
- Develop animal models to study molecular or cellular biology of angiogenesis.**
- Provide clinical trial support to measure changes in angiogenesis in patients on clinical studies.**
- Expand its capabilities over time to provide support services to other investigators.**

Angiogenesis Core Facility the Center for Cancer Research Advanced Technology Center (ATC)



Angiogenesis Core Personnel

Frank Cuttitta, Ph.D. - Director

Igalill Avis, R.N. - Senior Technician

Enrique Zudaire, Ph.D. - Senior Scientist

Sergio Portal, Ph.D. - Research Fellow

Syed Ahmed, B.S. - CRTA

Assays

•Proliferation - MTT, CyQUANT, ACEA

•Migration/Invasion

•Tube Formation

•Ring

•A

Standards

•Anti-VEGF

•2

•Angiomedullin (AM), Anti-AM

•Anti-PAMP

Angio Core

Clinic

- Modified DIVAA
- Isolate Tumor Endothelial Cells

Drugs

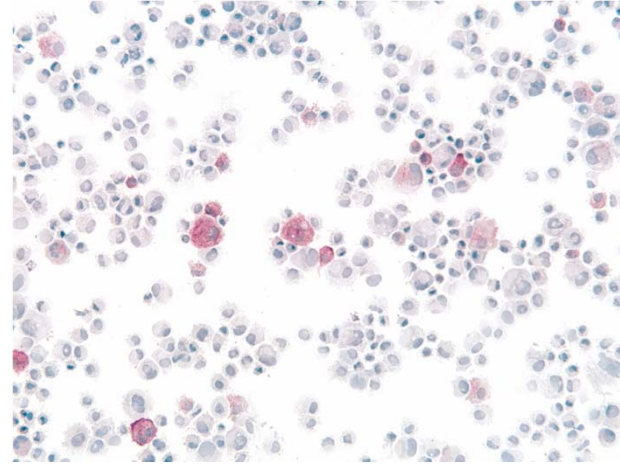
- Neutralizing Monoclonal A
- Peptide Antagonists
- Small Molecule Inhibitors

Cell Line

- Primary Human Derr
Microvascular Endoth
(BEC/LEC)
- Immortalized Human
Endothelial Cells (telc

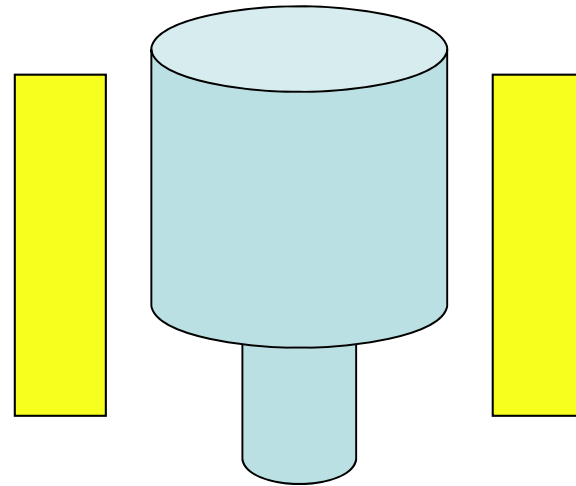
Magnetic Bead Purification of Primary Human Dermal Microvascular Endothelial Cells Using **MACS** System

Starting Material

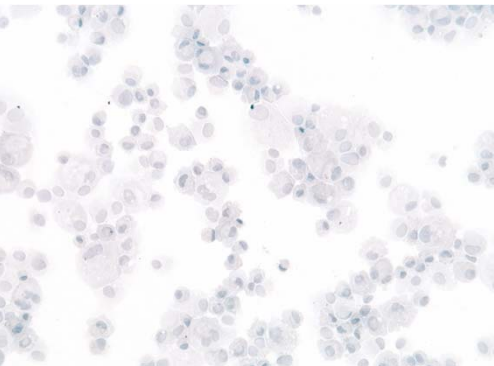


20-30% LYVE-1 Positive

Flow Through



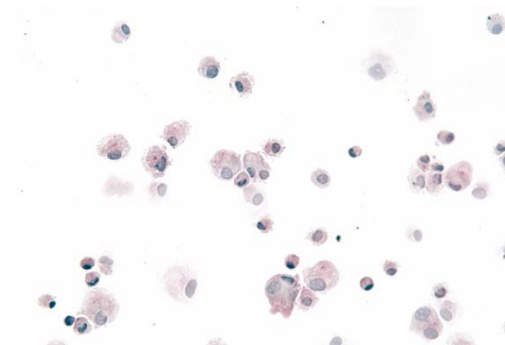
Rabbit Anti-LYVE-1 +
Goat Anti-Rabbit Beads



Zero % LYVE-1
Positive

70 % LYVE-1
Positive

Retained



Angiogenesis Core Facility

-Short Term Goals-

Standardization of Investigative Approaches

- Establish reliable *in vitro/in vivo* angiogenesis assays (CAM, OR, SV, DIVAA)
- Identify commercial source of primary human blood vessel endothelial cells (microvascular) with low lymphatic contamination (<3.0%).
- Identify commercial source of potent angiogenic factors (i.e. VEGF, bFGF, MCP-1 etc) to use as standards and respective suppressor compounds for that activity.

-Long Term Goals-

Bench to Bedside Applications

- Develop new *in vitro/in vivo* angiogenesis or lymphangiogenesis assays which better mimic the clinical setting (i.e. co-cultures studies, DIVLA etc).
- Modify existing DIVAA to assess patient endpoint when treated with anti-angiogenic drugs.
- Identify new anti-angiogenic/lymphangiogenic drugs using established CORE assays (i.e. neutralizing monoclonal antibodies, peptide antagonists or small molecule inhibitors
- Serve as a training center for the intramural/extramural community and organize standardization in the field.

TARP Steering Committee

- **Peter Dudley, Ph.D., *NEI***
- **Stephen Goldman, Ph.D., *NHLBI***
- **Robert A. Goldstein, M.D., Ph.D., *JDRF***
- **Teresa Jones, M.D., *NIDDK***
- **Gabrielle Leblanc, Ph.D., *NINDS***
- **Richard Levine, M.D., *NICHD***
- **Steven K. Libutti, M.D., *NCI***
- **Sheldon Miller, Ph.D., *NEI***
- **Suresh Mohla, Ph.D., *NCI***
- **Kathleen Schlom, *NCI***
- **Eser Tolunay, Ph.D., *NHLBI***