

**National Cancer Advisory Board**  
Director's Update

**Dr. John E. Niederhuber**  
February 7, 2005

# FY 2007 President's Budget

|                                   |                    |
|-----------------------------------|--------------------|
| <b>FY 2006 Appropriation</b>      | <b>\$4,793,356</b> |
| <b>FY 2007 President's Budget</b> | <b>\$4,753,609</b> |
| <b>Difference '06 to '07</b>      | <b>- \$39,747</b>  |
| <b>Percent Change '06 to '07</b>  | <b>- 0.8%</b>      |

**(dollars in thousands)**

## FY 2007 NIH Budget Policy

### **Current NIH Working Guidelines:**

- **Average cost of competing Research Project Grants same as FY 06**
- **No inflationary increase for direct recurring costs in non-competing continuation grants**
- **NRSA stipend levels same as FY 06**

## FY 2007 NIH Budget Policy

- **\$1.8M invested in new investigator program called [Pathway to Independence](#)**
- **\$7.8M included within the NCI budget as part of NIH initiative on **Genes, Environment, and Health****

# Budget Mechanisms

|  | <u>FY 2006<br/>Appropriation</u> | <u>FY 2007 PB</u> | <u>Change</u> |
|--|----------------------------------|-------------------|---------------|
| <b><u>Research Projects</u></b>                  |                                  |                   |               |
| <b>Non-Competing</b>                             | \$1,664,664                      | \$1,643,338       | -1.3%         |
| <b>Competing</b>                                 | 444,305                          | 416,945           | -6.2%         |
| <b>Subtotal</b>                                  | 2,108,969                        | 2,060,283         | -2.3%         |
| <b>SBIR/STTR</b>                                 | 95,735                           | 93,735            | -2.1%         |
| <b>Total</b>                                     | 2,204,704                        | 2,154,018         | -2.3%         |
| <b>Centers, SPOREs &amp;<br/>Special Centers</b> | 449,168                          | 446,818           | -0.5%         |
| <b>Other Research Grants</b>                     | 293,892                          | 294,142           | 0.1%          |
| <b>Total Research Grants</b>                     | 2,947,764                        | 2,894,978         | -1.8%         |

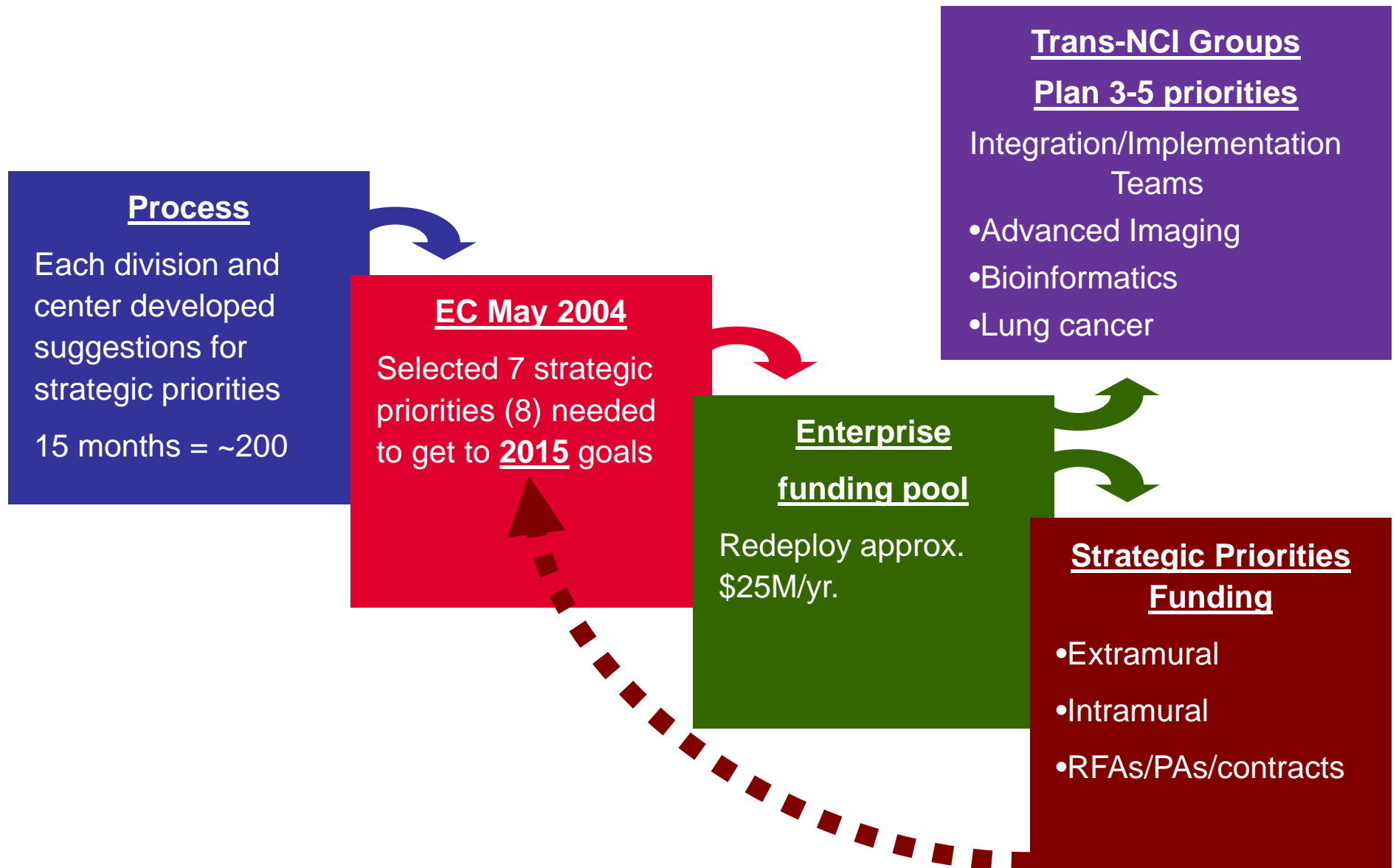
(dollars in thousands)

# Budget Mechanisms

|                                | <u>FY 2006<br/>Appropriation</u> | <u>FY 2007 PB</u> | <u>Change</u> |
|--------------------------------|----------------------------------|-------------------|---------------|
| NRSA                           | \$66,619                         | \$66,279          | -0.5%         |
| R&D Contracts                  | 326,560                          | 330,441           | 1.2%          |
| Intramural Research            | 699,763                          | 696,263           | -0.5%         |
| Rsch. Mgt. & Support           | 182,246                          | 183,246           | 0.5%          |
| Cancer Prev. &<br>Control      | 519,650                          | 517,100           | -0.5%         |
| Construction                   | 0                                | 0                 | 0.0%          |
| Buildings & Facilities         | 7,920                            | 7,920             | 0.0%          |
| <b>Total, NCI</b>              | <b>4,750,522</b>                 | <b>4,696,227</b>  | <b>-1.1%</b>  |
| <b>Total Roadmap</b>           | <b>42,834</b>                    | <b>57,382</b>     | <b>34.0%</b>  |
| <b>Total NCI<br/>w/Roadmap</b> | <b>4,793,356</b>                 | <b>4,753,609</b>  | <b>-0.8%</b>  |

(dollars in thousands)

# Priority-Setting



# EC Mini Retreat – Overview

## Jan. 5, 2006 – Programs and Initiatives

- **Bioinformatics**
- **Nanotechnology**
- **The Cancer Genome Atlas**
- **Clinical Trials Working Group**
- **Proteomics Initiative**
- **Biorepositories and Biospecimens**
- **Translational Research Working Group**



## Joint Board Retreat – Jan. 10, 2006

### **Attended by members of the BSA, BSC and NCAB, and the chairs of the PCP and DCLG**

- Participants offered guidance on how NCI programs can continue their current trajectory, given fiscal limitations
- Modeled alternative budget scenarios for FY 2007
- Advisors agreed to aid an in-depth analysis of strategies, including how to better promote partnerships with industry and other outside groups; support training; and find new mechanisms to measure progress and evaluate programs.

## Joint Board Retreat – Jan. 10, 2006

**Asked to rank their preferences for funding considerations, participants overwhelmingly felt the highest priorities should be:**

- **Fund first-time investigators**
- **Maintain the R01 payline**
- **Maintain the # of grants funded**

**Items given lower priority were:**

- **Limit the # of submissions by an investigator**
- **Limit dollars per grant**
- **Limit the # of grants an investigator may have**

# 2006 Intramural Scientific Retreat

- 11th combined intramural retreat
- CCR and DCEG
- 560 participants



# NCI Director's Intramural Innovations Awards

**Awards for development of highly innovative approaches and technology aimed at significant cancer-related problems**

- **12 Principal Investigator projects**
  - Targeted to tenure-track of newly-tenured PIs (up to \$50,000)
- **22 Career development projects**
  - Targeted to postdoctoral fellows, staff scientists and clinicians, and senior scientists (up to \$10,000)

## 2006 Intramural Scientific Retreat: Award Lectures



- **Rosalind E. Franklin Award  
Lecture for Women in Cancer  
Research**

- Dr. Joan A. Steitz: “More Surprises  
from Studies of snRNP’s”



- **Alfred G. Knudson Award  
Lecture in Cancer Genetics**

- Dr. Elizabeth H. Blackburn:  
“Interventions in Telomerase  
Action in Human Cancer Cells”

## 2006 Intramural Scientific Retreat: Award Lectures

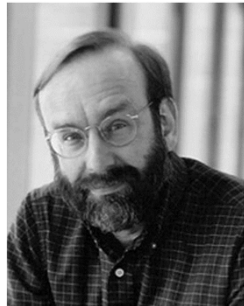


- **Alan S. Rabson Award Lecture  
for Intramural Research**
  - Dr. Steven A. Rosenberg: “The  
Development of Human Cancer  
Immunotherapy”

# Appointments



- **Tom Hooven, M.A.**
  - Deputy Director for Management



- **Lawrence Samelson, M.D.**
  - Deputy Director for CCR



- **Crystal Mackall, M.D.**
  - Acting Chief, Pediatric Oncology Branch

# Interagency Agreement: NCI & FDA

- **Critical Path initiative**
- **Modernize the Drug Development Process**

NATIONAL<sup>®</sup>  
CANCER  
INSTITUTE



FDA



## New Guidance

- **Exploratory IND Studies**
- **INDs – Approaches to complying with CGMP during Phase 1**

# Exploratory IND Studies

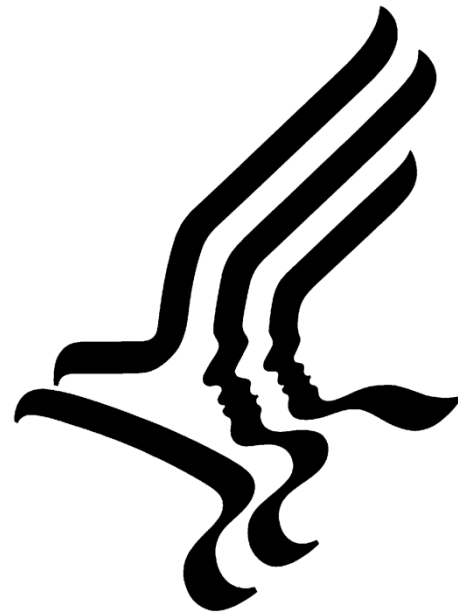
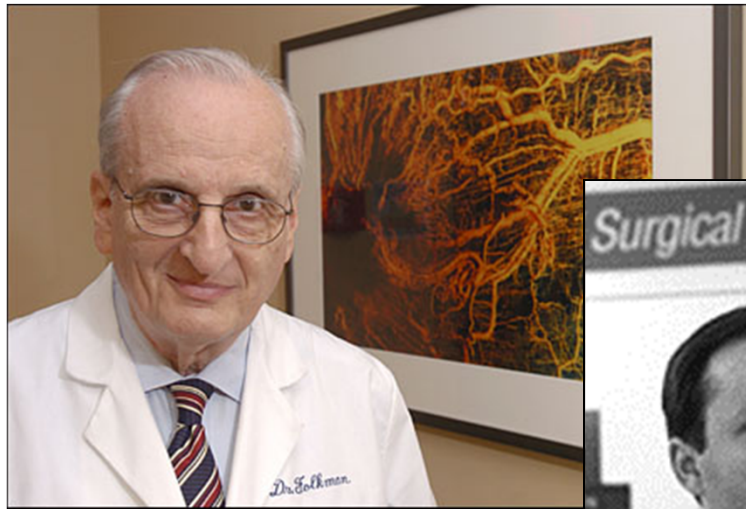
**Trials involving administration of sub-therapeutic doses of candidate product over a limited period of time with no therapeutic intent**

- **Determine mechanism of action**
- **Pharmacokinetic data**
- **Select lead product from a group of candidates**
- **Explore biodistribution using imaging technologies**

## INDs-Approaches to Complying with CGMP during Phase 1

- **Small-scale or laboratory-scale production for exploratory studies**
- **Incremental approach to manufacturing**
- **Manufacturing appropriate for the stage of development**
- **Includes biological/biotechnology products aseptically processed**

# Trans-Institute Angiogenesis Research Program



[www.tarp.nih.gov](http://www.tarp.nih.gov)

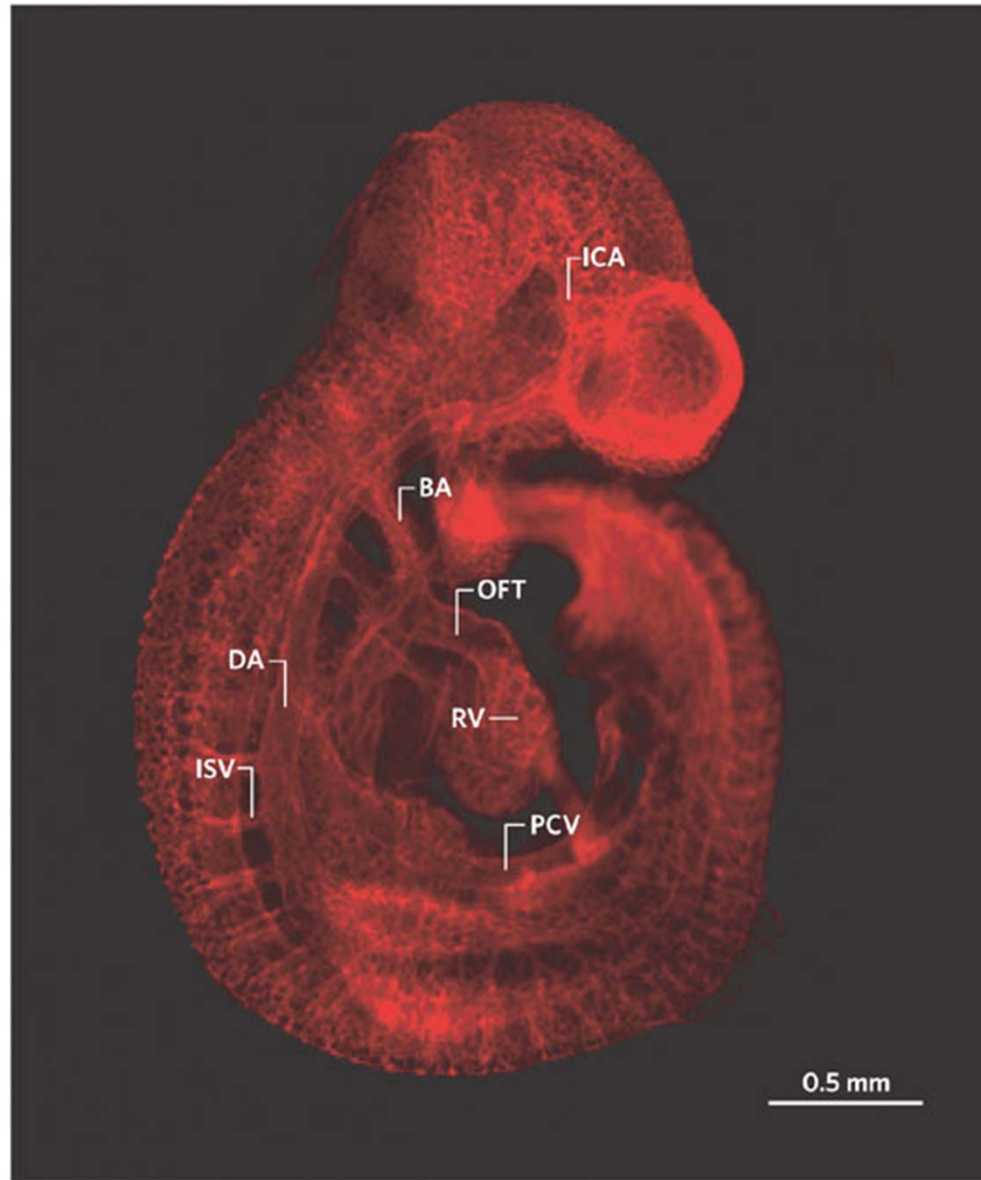
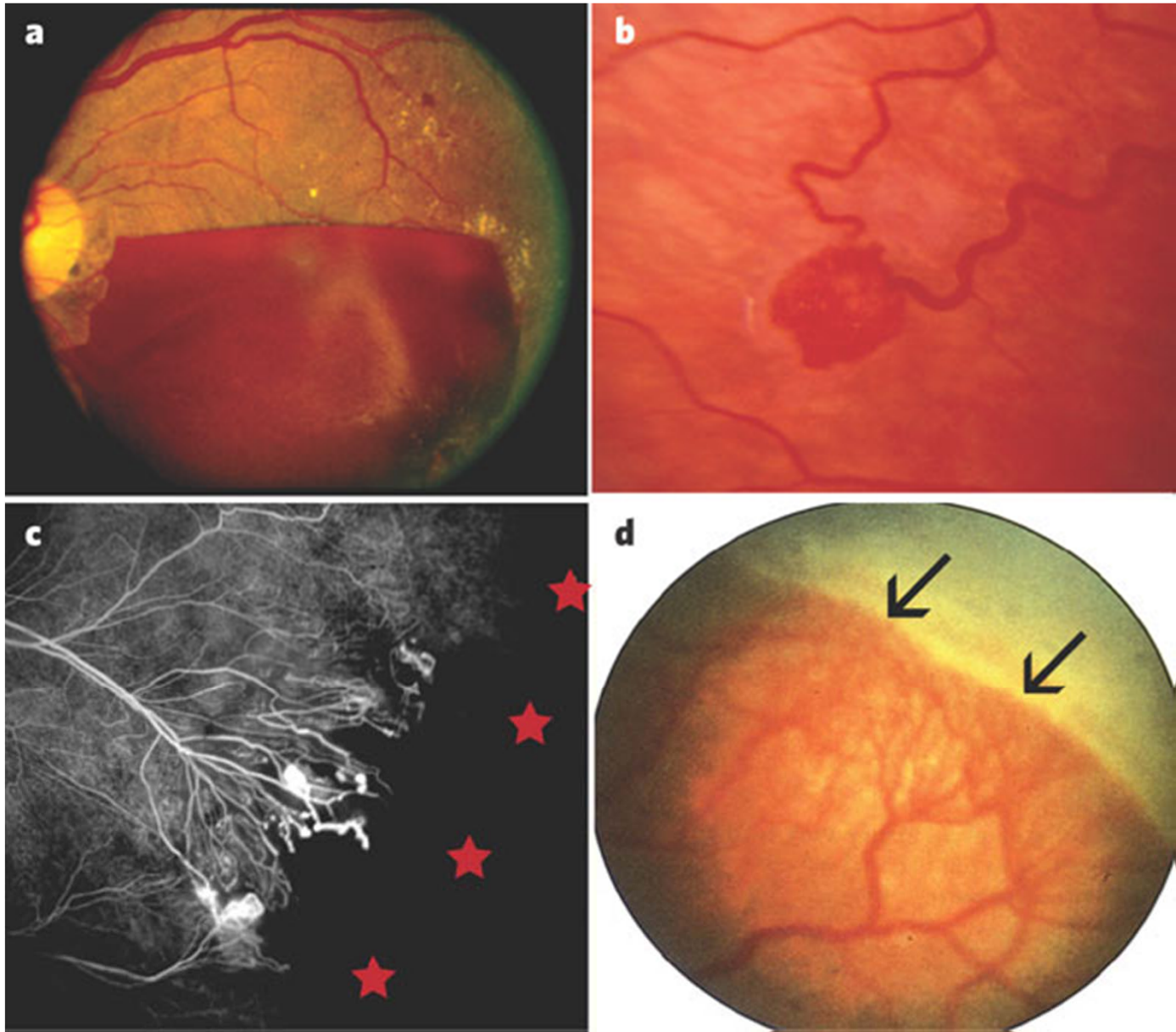


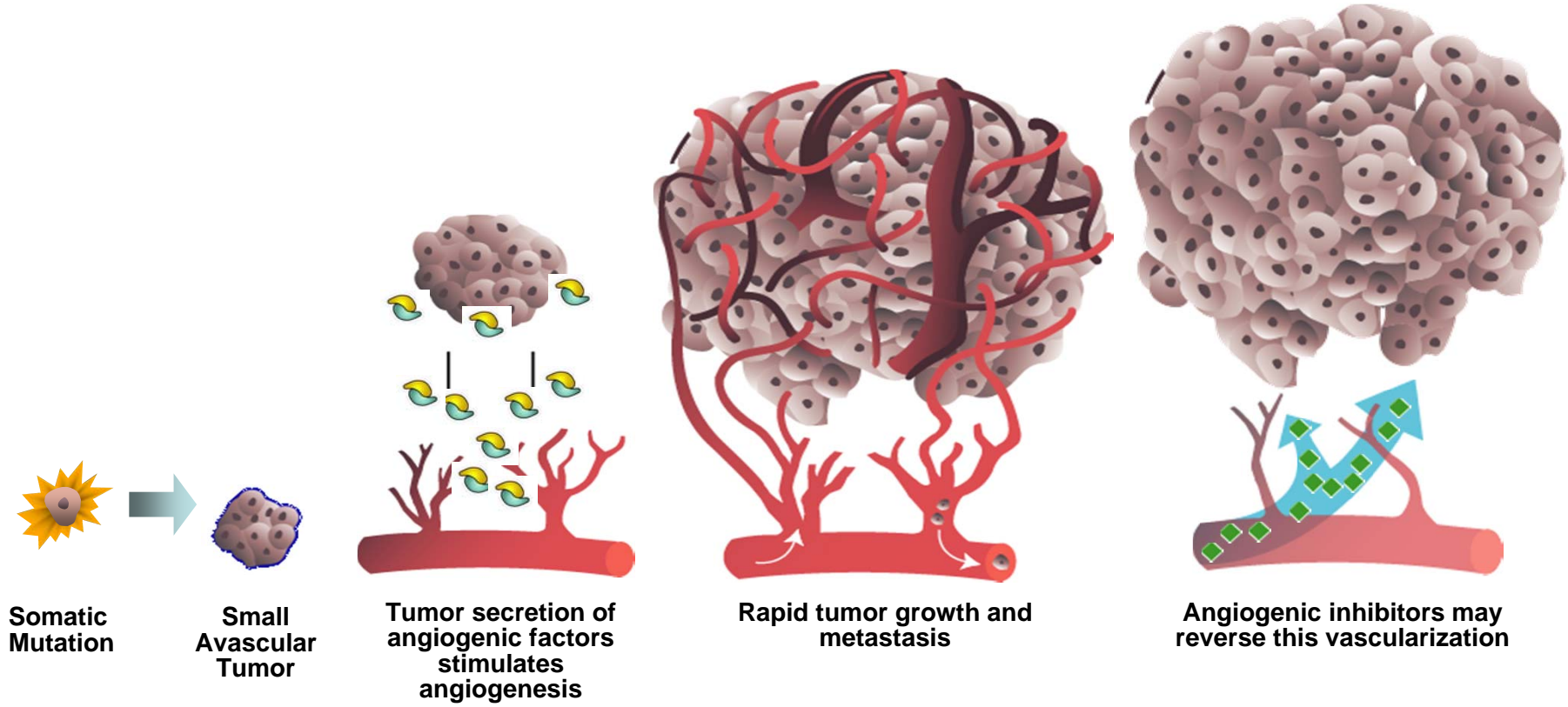
Image courtesy of L. Davidson, Mouse Imaging Centre, Hospital for Sick Children, Toronto, Canada

Nature Insight Angiogenesis 2005



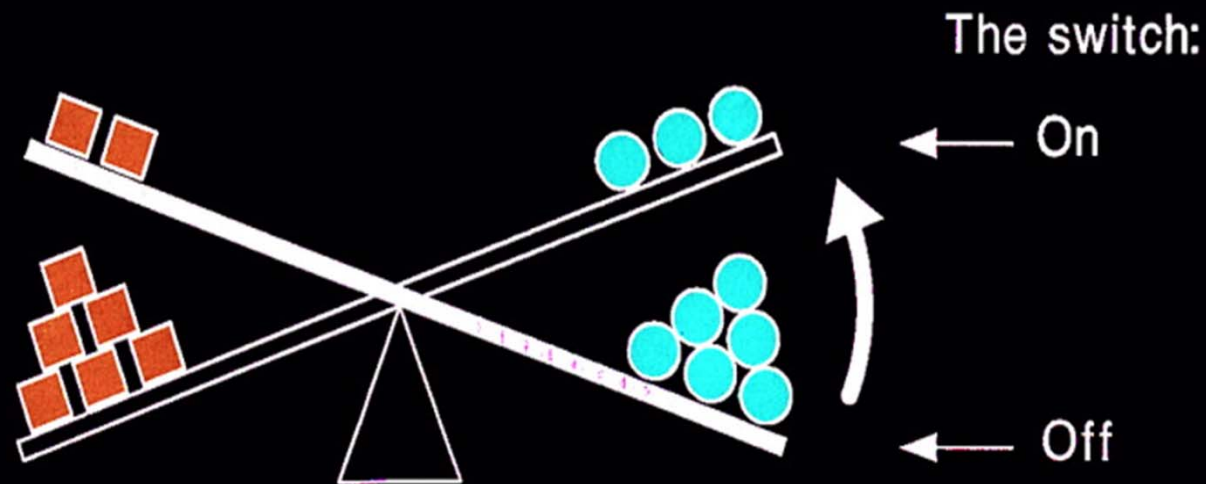
Nature Insight Angiogenesis 2005

# The Angiogenic Switch and Antiangiogenic Therapy



Carmeliet and Jain. *Nature*. 2000;407:249.

# THE BALANCE HYPOTHESIS FOR THE ANGIOGENIC SWITCH



■ Activators

aFGF

bFGF

VEGF

⋮

● Inhibitors

Thrombospondin-1

16 kD Prolactin

Interferon  $\alpha/\beta$

Platelet factor-4

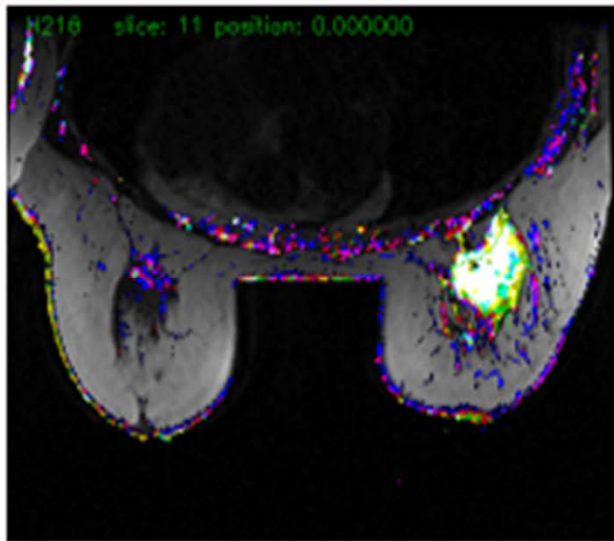
Angiostatin

⋮

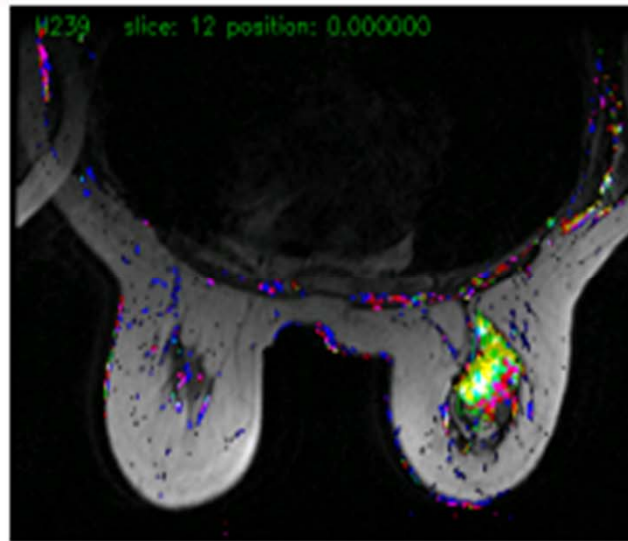
Hanahan D & Folkman J. Cell. 86:353, 1996



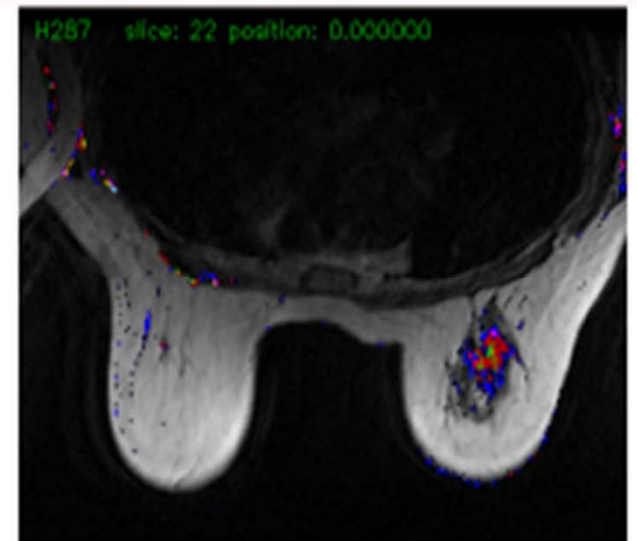
# Dynamic MRI Monitoring of Response to anti-VEGF Antibody Therapy



Pre-treatment



Post Avastin 4 weeks

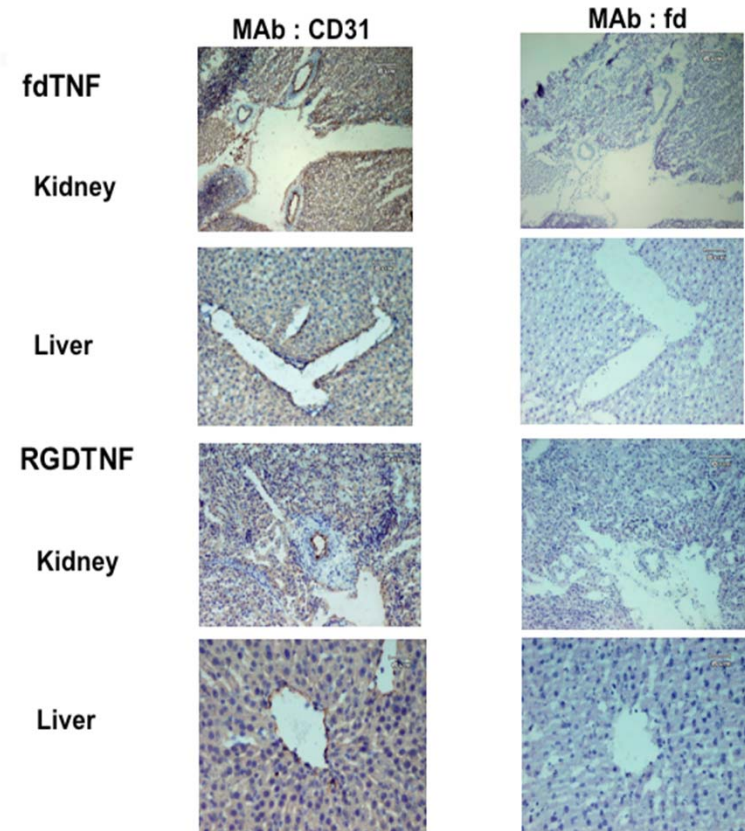
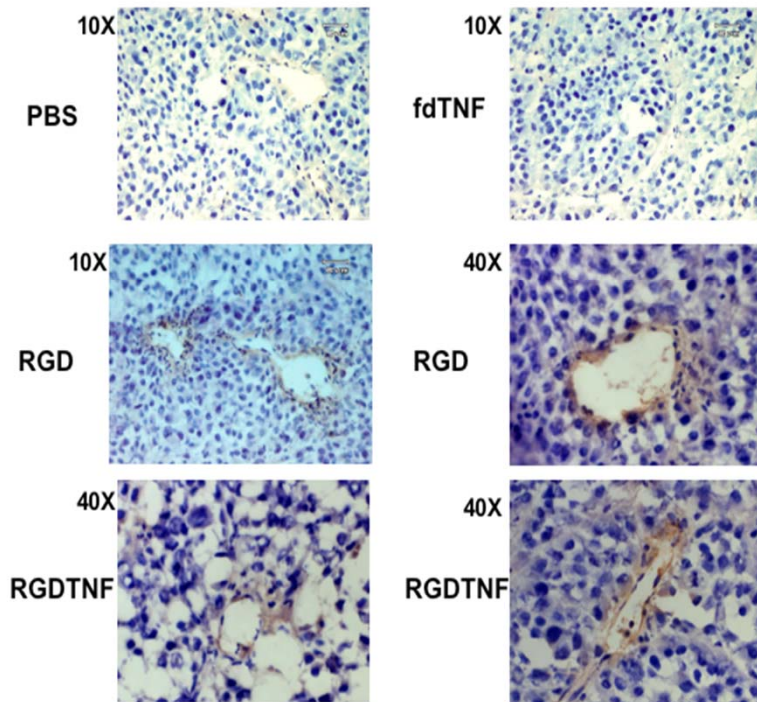


Post Avastin + chemo

Courtesy of Peter Choyke, M.D.

# RGD-Phage Selectively Targets Tumor Vessels

*In-vivo* Tumor Targeting : IHC Mab fd  
5 days I.V.

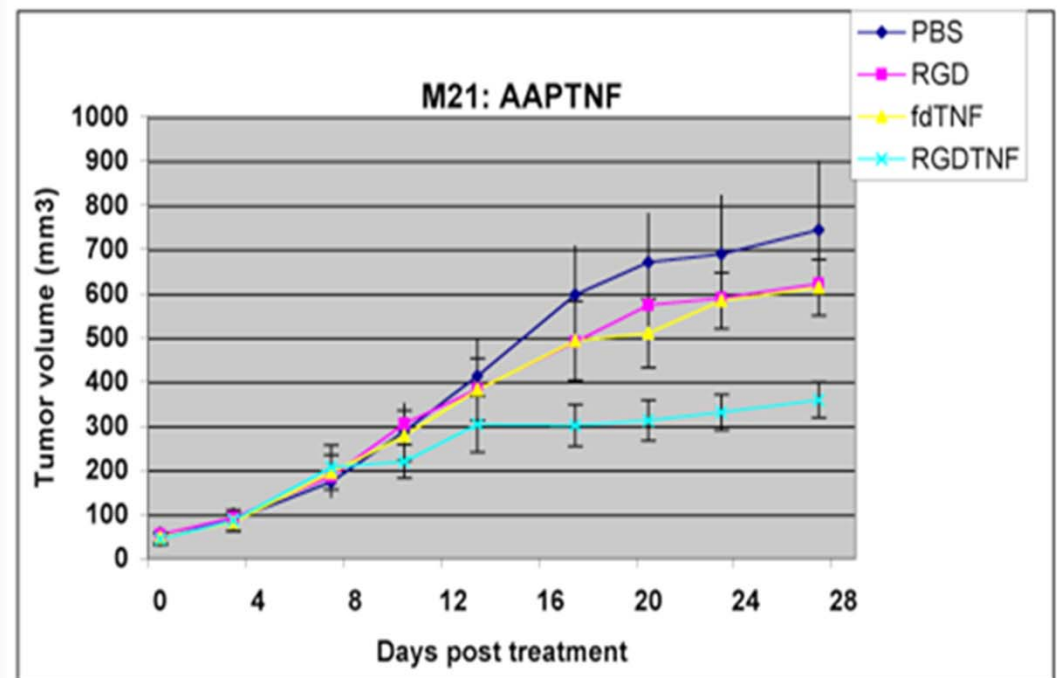
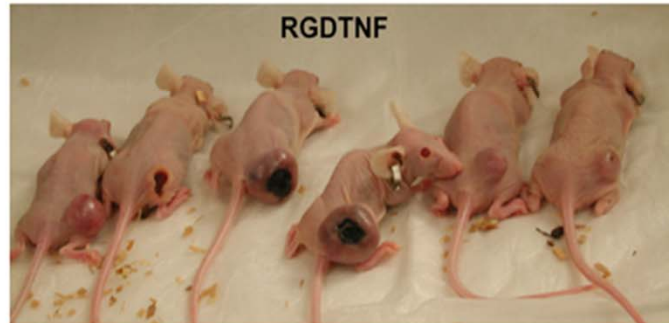
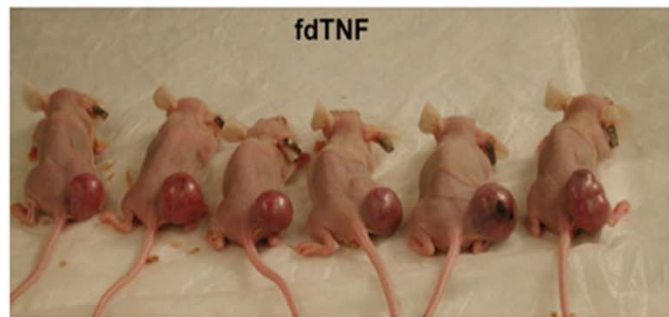


# RGD-Phage Expressing TNF Inhibits Tumor Growth

## Tumor Model

M21 tumors in nude mice  
↓ ~150-200 mm<sup>3</sup>

Systemic injection (tail vein)  $5 \times 10^{10}$  pfu/mouse; d1 and d4





**JDRF**



**NCI**



**NIDDK**

# **Trans-Institute Angiogenesis Research Program (TARP)**



**NEI**



**NINDS**



**NHLBI**

[www.tarp.nih.gov](http://www.tarp.nih.gov)

## TARP Accomplishments

- **Organized and sponsored a workshop on opportunities for cross discipline collaboration for vascular developmental biology research.**
- **Established a website for the TARP.**
- **New collaborative RFAs (NIDDK, JDRF, NINDS, NHLBI, NEI, NCI).**

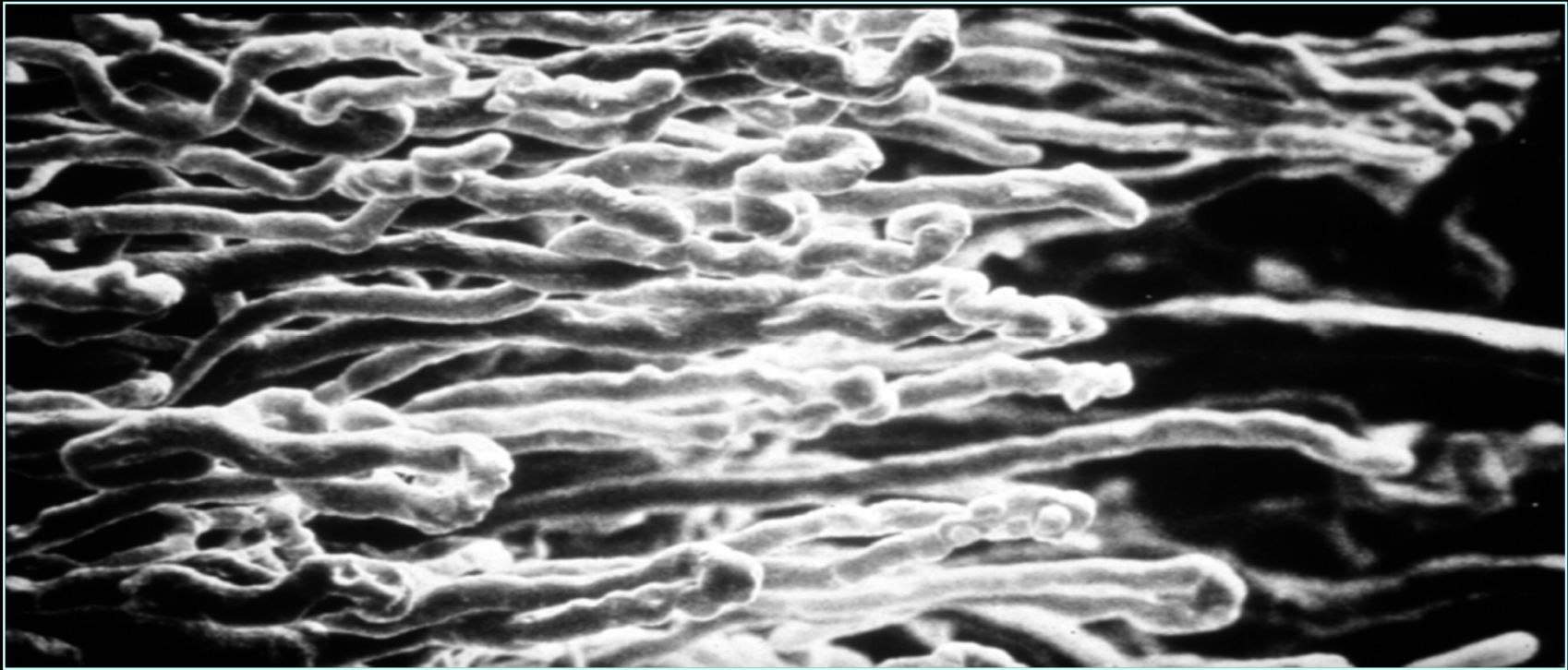
## TARP Accomplishments

- **Organized and co-sponsored a Nature Insight on angiogenesis.**
- **Performed a review of the angiogenesis grant portfolios for the 5 member ICs.**
- **Convened a panel to review the current angiogenesis portfolio and to offer opinions on new directions and opportunities.**



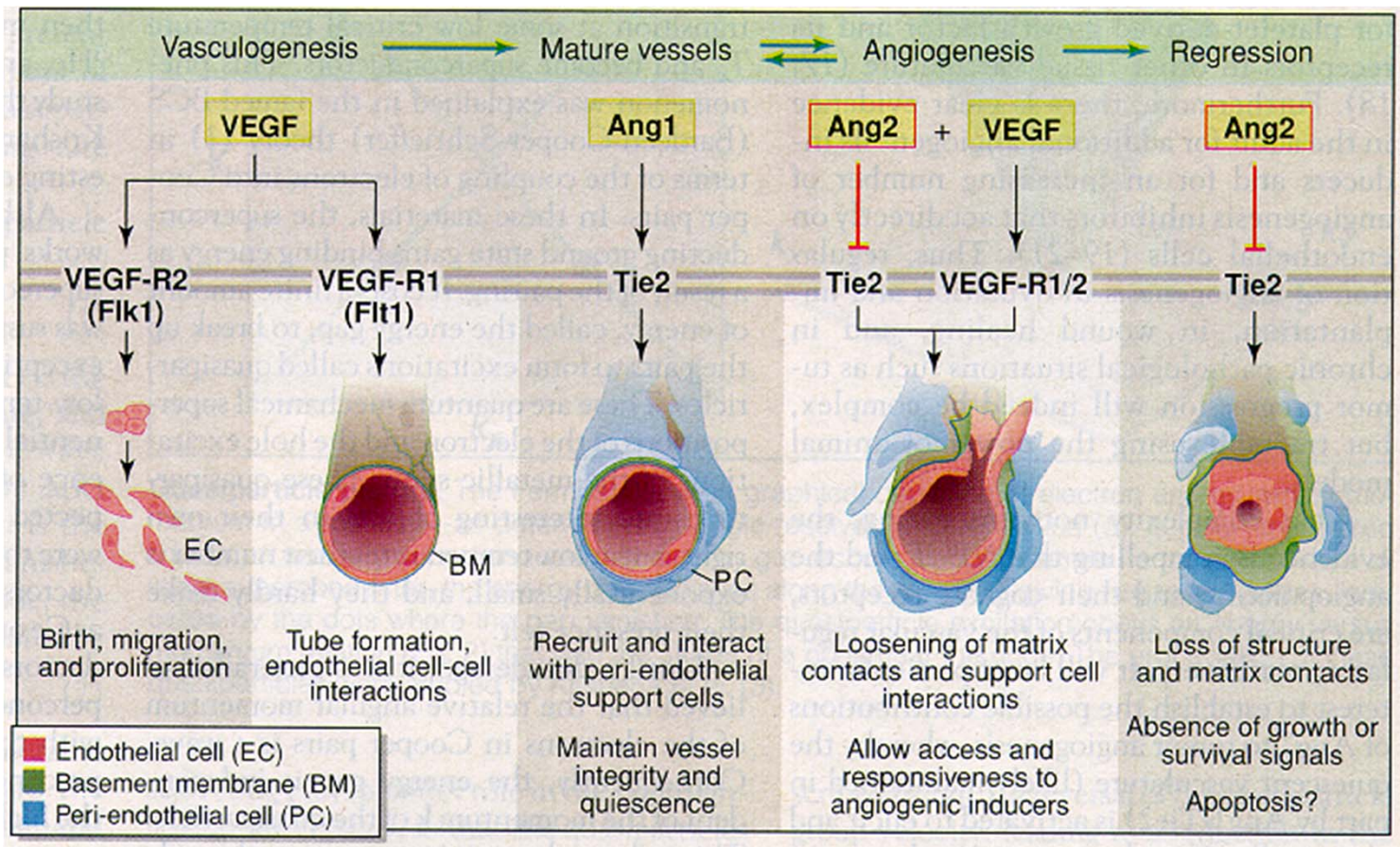


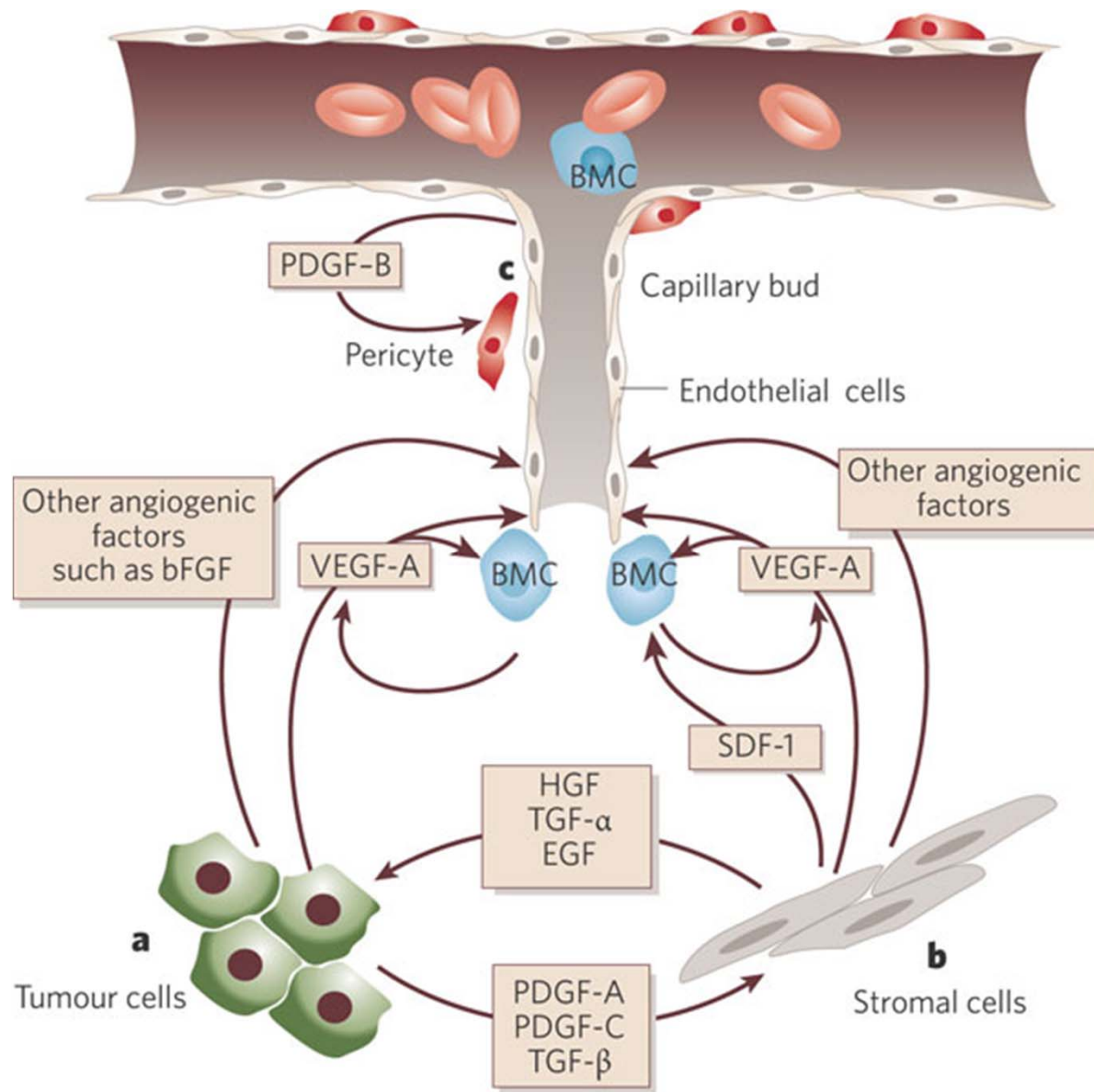




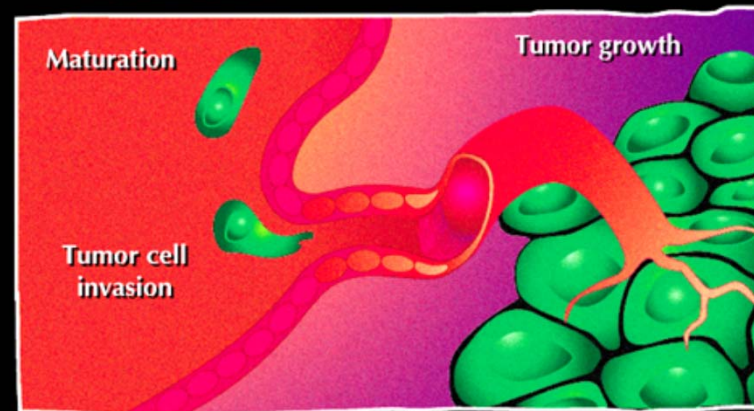
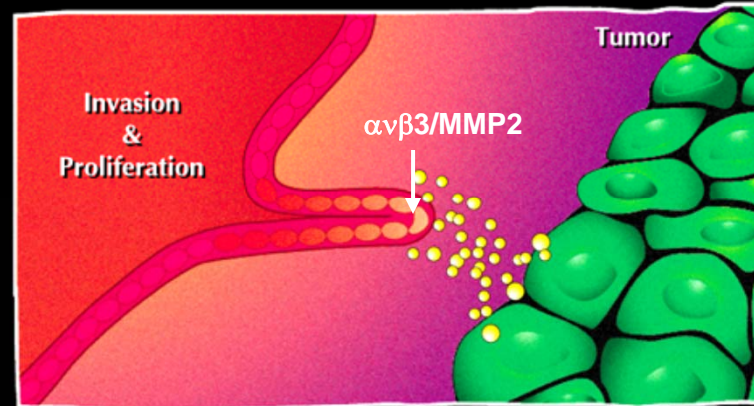
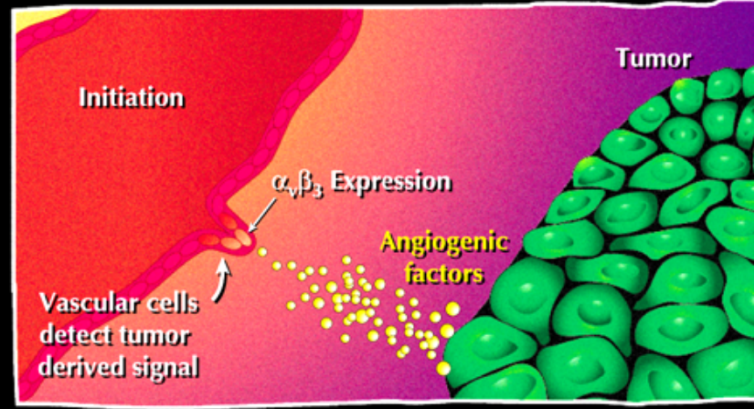
Angiogenesis is a dynamic and complex process that involves new blood vessel formation from established vasculature.

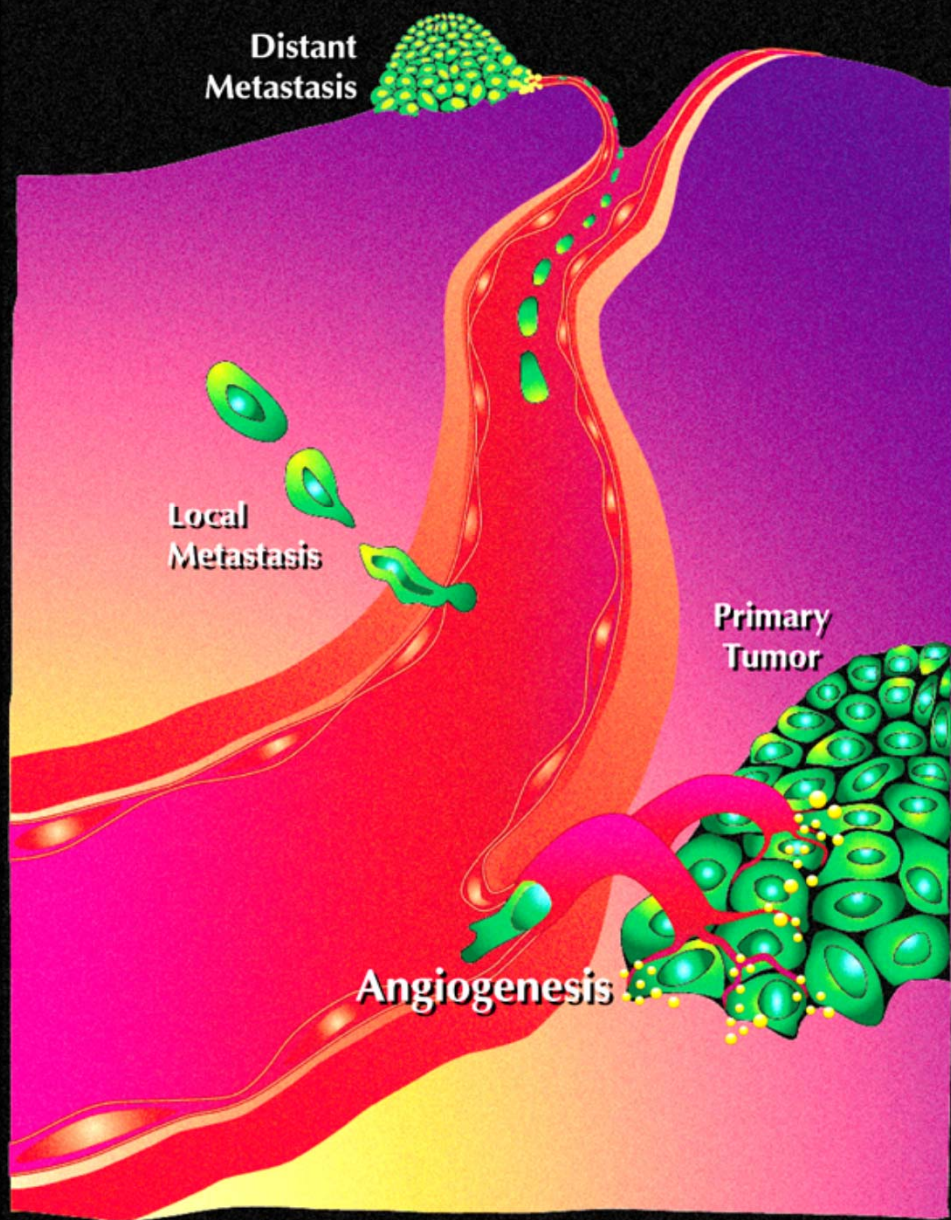
# Vessel Development





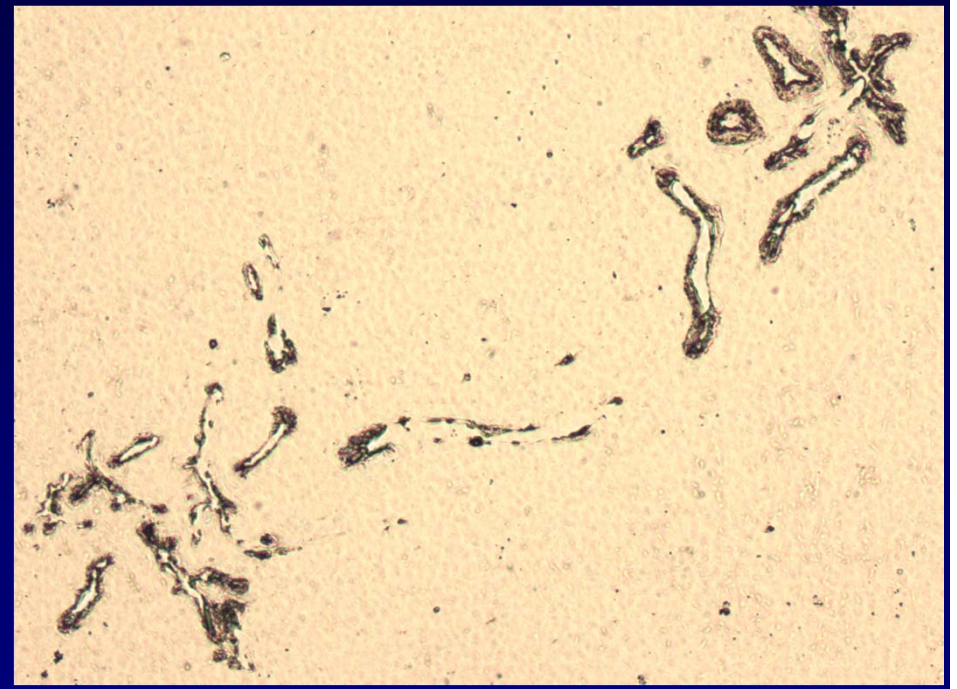
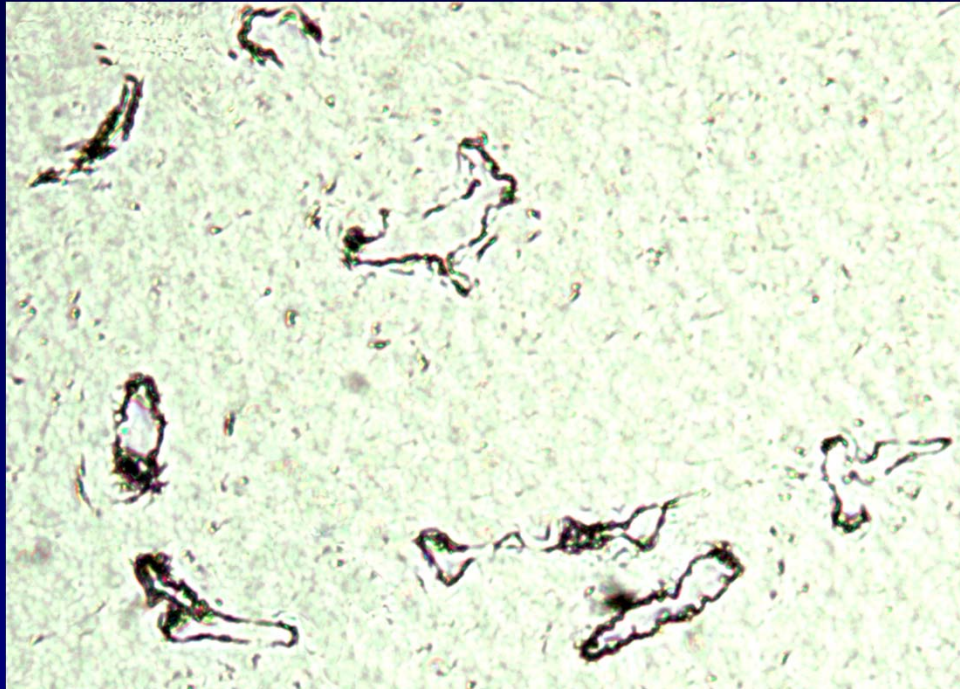
## Steps in Tumor-Induced Angiogenesis





Cheresh

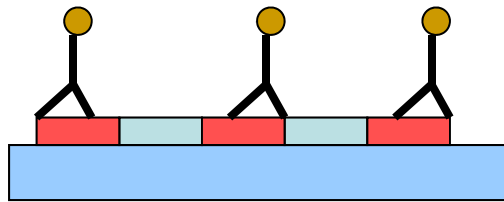
# Procurement of Fine Targets



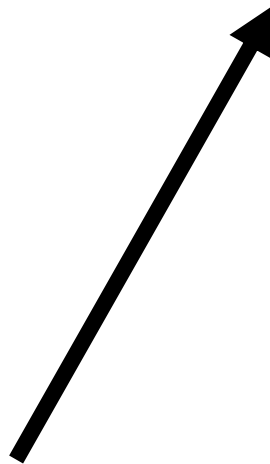
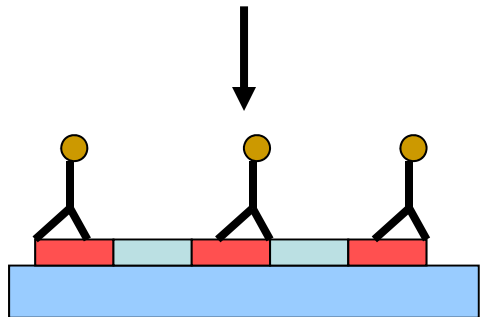
CD31+ Prostate Endothelial Cells

# xMD for Endothelial Cell Dissection

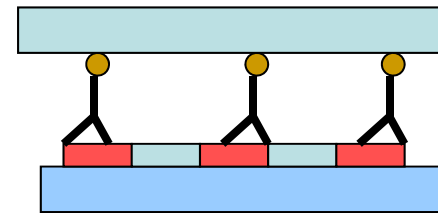
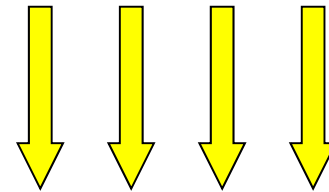
## Immunohistochemistry Staining (IHC)



Apply xMD Film After IHC



## Application of Laser



Procurement

