

# Taking iRGD Through the Valley of Death

**3 P01 CA043904-19S1 NIH**

***Antibody Targeting Radiation and  
Immunotherapy for the Treatment of Solid  
Tumors***

***TEAM STRAP***

***Raubitschek, Ruoslahti, Colcher, Jacobs,  
Synold, Liggitt, Chung***

***NCI***

# Erkki Ruoslahti - Inventor of iRGD

## iRGD (CRGDKGPDC)

- Binds to  $\alpha v \beta 3$
- Cleaved to CendR
- Binds to NRP-1
- Increases co-administered drug uptake at tumor
  - Adria, Nabraxane, Herceptin



# Plan to take iRGD into Initial Clinical Trial

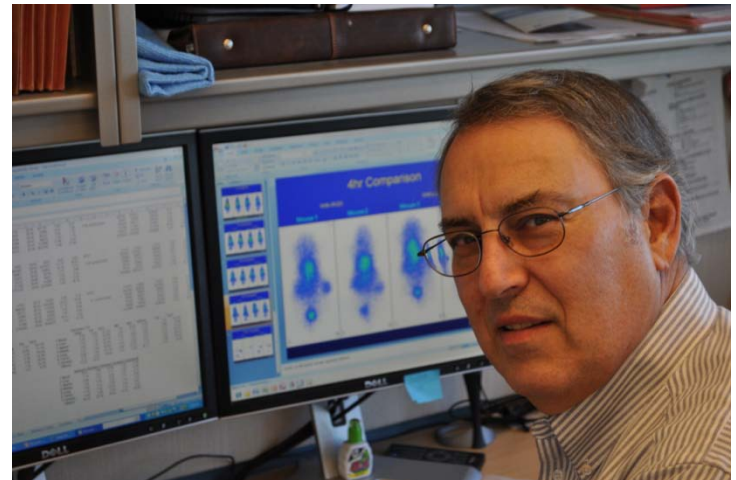
- **Pharmacokinetics**
- **Route of administration**
- **Optimal dose**
- **Optimal schedule – will vary for co-drug**
- **Toxicology**
- **Formulation**
- **preIND meeting**
- **Clinical trial design**
  - iRGD dose and route
  - Clinical imaging
- **IND filing**

# Timothy Synold - Clinical Pharmacologist

- **Establish LC/MS/MS assay**
- **Perform stability studies**
  - dry, aqueous, frozen
- **Perform serum stability studies**
  - mouse and human serum
- **Assay for intravenous and sub cutaneous and multi dosing studies**
- **Assay for NRP-1 levels**

# David Colcher – Animal models, etc

- **Perform pharmacokinetic studies**
  - IV, SQ, multidosing
- **Document biologic activity**
  - Anti-CEA Mab in CEA transgenic mice
  - Herceptin in BT-474
  - Evans blue in BT-474
- **Document therapy**
  - Herceptin in BT-474



# Russell Jacobs – MRI, PET, Optical

- **Explore MRI as correlate for iRGD activity**
  - mouse to man
- **Confirm MRI findings with concomittant PET**
- **Confirm MRI findings with in vivo confocal**
- **Confirm MRI findings with 3D Vibrasym**



# Denny Liggitt – Toxicologist, Vet Pathologist

- **Conduct initial murine toxicology studies**
- **Develop plan for IND toxicology with NCI**
  - Rodent, +/- tumor
  - Dog
  - Limited NHP
- **Participate in preIND meeting with FDA**
- **Conduct GLP murine toxicology in collaboration with David Colcher**





# Vincent Chung - Clinical Trialist

- **Develop initial iRGD clinical trial with Dan Greenwald Andrew Raubitschek MRI scientists NCI**
- **Conduct initial iRGD trial**
- **Conduct first therapy trial with iRGD**
  - Antibody
  - Drug



# NCI STRAP

- **Drug administration**
  - IV
  - SQ
  - Multi-dosing
- **Toxicology**
- **Imaging bioactivity**
- **Clinical trial design**
- **preIND meeting**



# iRGD current status

- **Synthesis of GLP iRGD for animal studies**
- **Confirmation of increased antibody localization in CEA-MC38 and BT-474 by imaging and biodistribution of  $^{111}\text{In}$ -labeled antibodies (Anti-CEA, Herceptin)**
- **Synthesis of cGMP iRGD**
- **Initial stability studies and pK**
- **Initial rodent toxicology**
- **Developing MRI signature of iRGD**
- **Confirmation of iRGD and Herceptin therapy**