

# TRANSLATIONAL NANOMEDICINE



***C-TRAIN @ Washington University  
Consortium For Translational Research in Advanced  
Imaging and Nanomedicine***

***Disclosures: Kereos, Inc. (equity), PixelEXX Systems, Inc. (equity),  
Philips Medical Systems (research grants)***

# NANOMEDICINE: A *NEW* ARENA FOR DRUG AND DIAGNOSTIC DEVICE DEVELOPMENT

- New *complex* assemblages (drugs and devices) operating at the atomic and molecular level that interact with cellular and subcellular structures and processes to detect and manage diseases
- New pharmacokinetics, pharmacodynamics, and efficacy
- Improved safety
- New opportunities to rescue existing potent but toxic agents
- “Synthetic biology”



# NEW NANOSYSTEMS FROM C-TRAIN

Nanoplatforms	Modality	Size (nm)	Drug Delivery	In vitro	In vivo	Selected Reference	Disdosure/patents
Octane thiol coated gold nanophere	Precursor	2	-	-	-	-	-
Oleate coated iron oxide nanoparticle	Precursor	10	-	-	-	-	-
Oleate coated manganese oxide nanophere	Precursor	12	-	-	-	-	-
Polymer coated Gold nanorods	Precursor	30	-	-	-	-	-
Nanobialys	MR (1H)	120	Yes	Yes	Yes	JACS, 2008, 130(29), 9186	PCT filed
Colloidal Iron Oxide Nanoparticles (Oil-based)	MR (1H)	160	Yes	Yes	Yes	Circulation. 2008;118:5_691.	PCT filed
(Sorbitan-based)	MR (1H)	120	Yes	Yes	Yes		
Colloidal Manganese Oleate (OL) Nanoparticles	MR (1H)	160	Yes	Yes	Yes	Chem Comm, 2009, 22, 3234	PCT filed
Colloidal Manganese Oxide Nanoparticles	MR (1H)	160	Yes	Yes	Yes	-do-	
Colloidal Radio-opaque Metal Entrapped Polymeric NP Bismuth and Iodine	CT/SCT	160	No	Yes	Yes	JACS, 2009, 131 (in press)	PCT filed
Photoacoustic Gold Nanobeacons	PAT	80	Yes	Yes	Yes	Angew Chem Int Ed 2009;48(23):4170-3.	PCT filed
Photoacoustic Gold Nanobeacons (Sphere)	PAT	160	Yes	Yes	Yes		
(Rod)	PAT	160	Yes	Yes	Yes		
Spectral CT(SCT) Nanocolloids (Bismuth)	CT/Dual Energy/SCT	200	Yes	Yes	Yes	Circulation. 2008;118:5_777	PCT filed
(Gold)	CT/Dual Energy/SCT	200	Yes	Yes	Yes		
PFC nanoparticles	US/MR 19F	180-250	Yes	Yes	Yes	Circulation. 1996;94:3334-3340.	>15 Issued US
Gd PFC nanoparticles	MR (1H)	180-250	Yes	Yes	Yes	Circulation. 2003;107:1092.	10 Applications
99mTc or 111In PFC nanoparticle	Nuclear (SPECT/CT)	180-250	Yes	Yes	Yes	FASEB J, 2008; 22:2758-2767.	
Gd/99mTc nanoparticles	MR: 1H/Nuclear	180-250	Yes	Yes	Yes	Int J Cancer 2007, 120, 1951-1957.	
Eu Paracest PFC Nanoparticle	MR Paracest (1H)	180-250	Yes	Yes	Yes	Mag. Res. Med 2006, 56, 1384.	
Fluorescent PFC Nanoparticles	Optical	180-250	Yes	Yes	Yes	Unpublished	
NIR PFC nanoparticles	NIR	180-250	Yes	Yes	Yes	Unpublished	
Streptokinase PFC Nanoparticles	MR (19F)/US	300	Yes	Yes	Yes	Nanomedicine, 2007, 2:533-543.	
PFC Nanoparticle-Melittin peptide construct	MR/US/Nuclear	180-259	Yes	Yes	Yes	J. Clin. Invest. 2009;119(9):2830-42.	
PPACK antithrombin nanoparticles	MRI (H and F)/US	180-250	Yes	Yes	Yes	Nanomedicine, 2007, 2:533-543.	



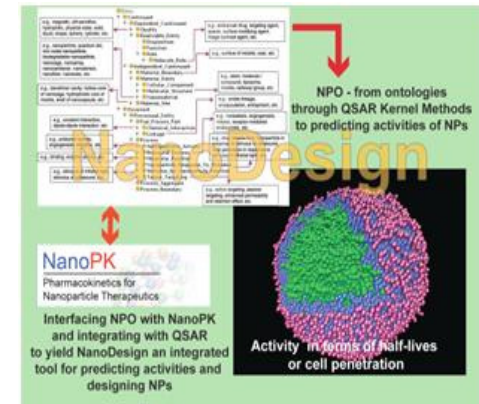
# OTHER TOPICS

## Multispectral (color) CT



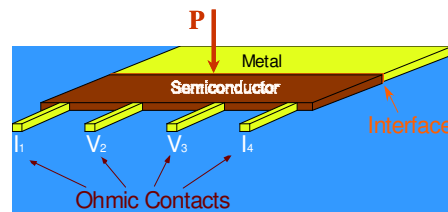
“k-edge” imaging:  $\lambda$  dependence

## NanoDesign Toolkit

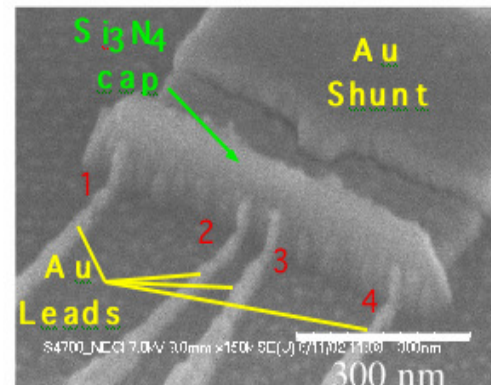


NanoOntology/NanoPK

## PixelEXX Systems, Inc.



Perturbation	EXX	Application
Magnetic Field	EMR	High Density Hard Drive Read head
Strain	EPC	High Precision Strain Gauge
Photons	EOC	Photon Sensor
Electric Field	EEC	Surface Charge Sensing & Imaging
Temperature	ETC	High Precision Thermometer



“EXX” (extraordinarily sensitive) nanoarrays for high-throughput, high-content, high-resolution screening/microscopy

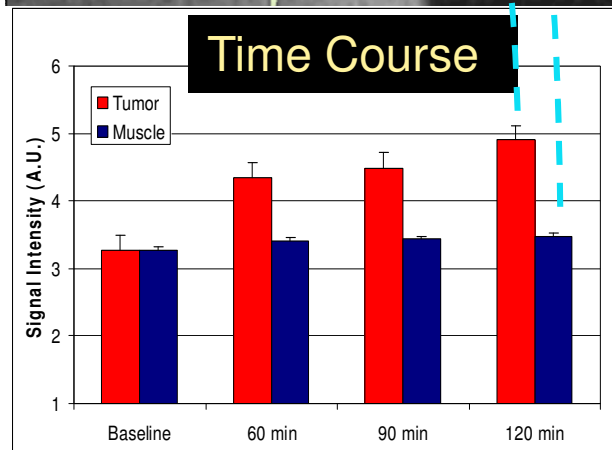
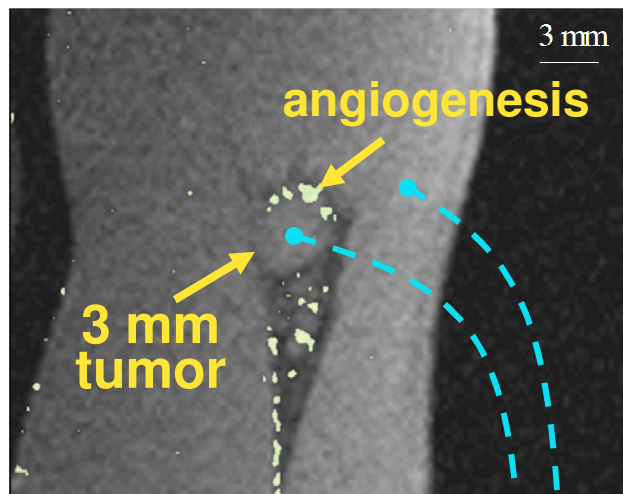


# Detecting Very Small Tumors With MRI:

Angiogenesis Targeted Paramagnetic Nanoparticles

(Winter et al. *Cancer Research* 2004)

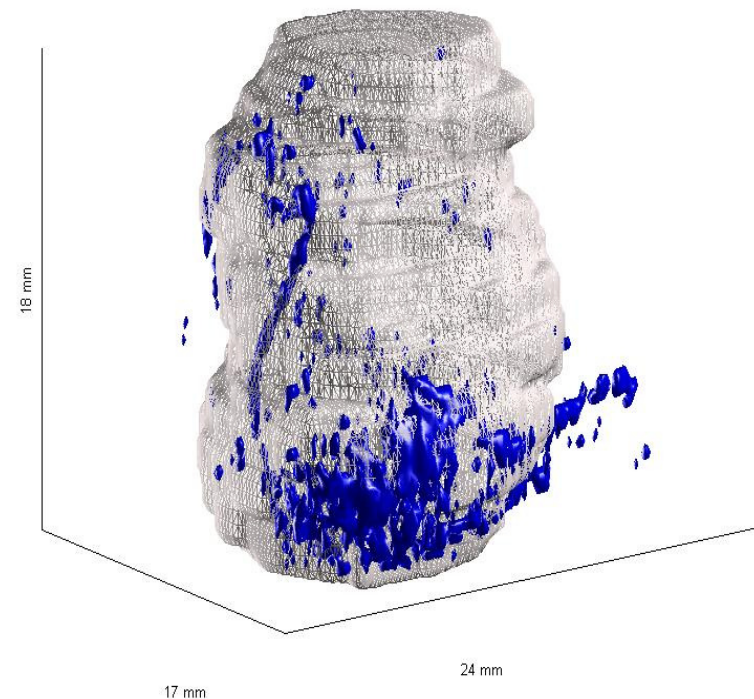
Rabbit: angiogenesis  
around small VX2 tumor



0 min

120 min

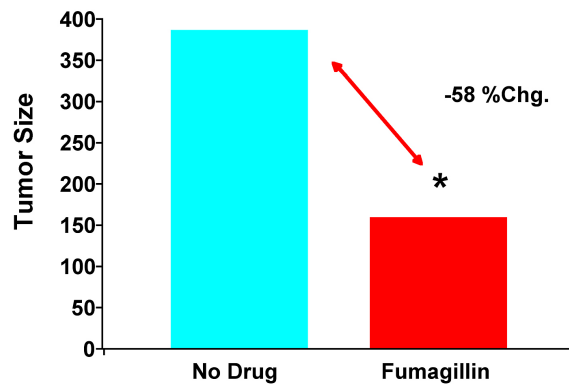
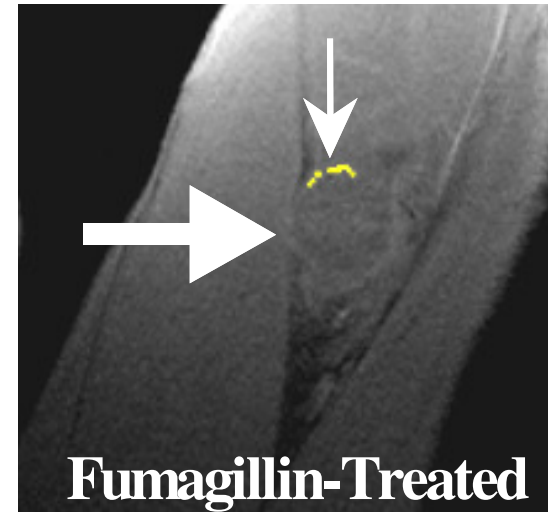
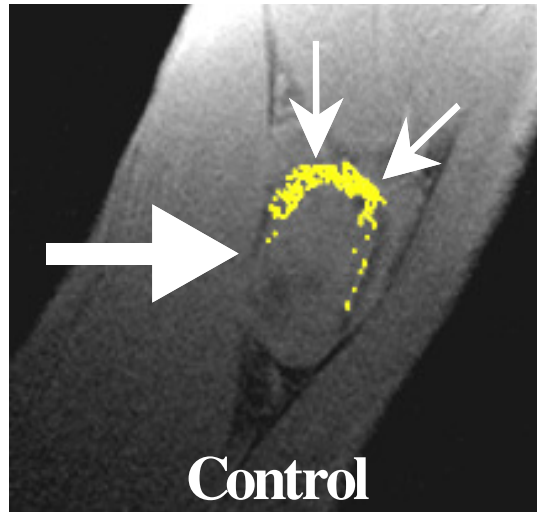
Heterogeneous display  
of  $\alpha_v\beta_3$  epitopes



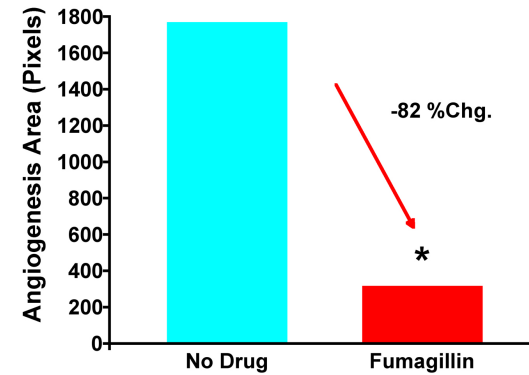
Nanoparticles bound to VX2 tumor

# VX2 TUMOR THERAPY IN RABBITS WITH $\alpha_v\beta_3$ -INTEGRIN TARGETED FUMAGILLAN NANOPARTICLES

MRI of  $\alpha_v\beta_3$  integrin binding in angiogenesis



**Decreased Tumor Size**



**Decreased Angiogenesis**

*3 doses over ~3 weeks in rabbit VX2 tumor*



# NEW REGIONAL BUSINESS OPPORTUNITIES

- “National Nanotechnology Initiative”
  - Regional “nodes”
- Nano “hotspots”: US investments of \$10’s to \$100’s millions in state dollars for infrastructure
  - Houston, Boston, LA, Chicago, U-C, etc.
  - MO: Columbia
- \$Trillion business in next few years
- Missouri startups: a handful at present

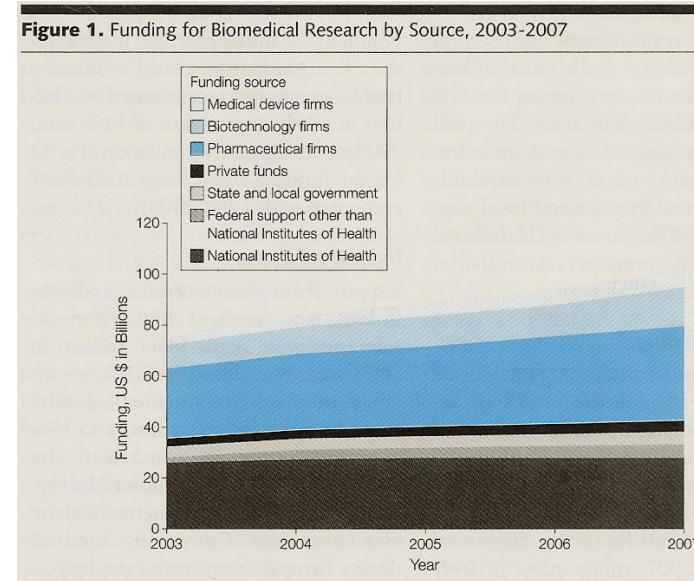


# “FUNDING OF US BIOMEDICAL RESEARCH 2003-2008.”

## DORSEY ET AL. JAMA. JAN 13, 2010



- ~ \$100 billion/yr
  - Industry: >1/2
  - NIH: ~1/4



### FUNDING OF US BIOMEDICAL RESEARCH, 2003-2008

**Table 2. New Drug and Device Approvals by US Food and Drug Administration, 2003-2008**

Category	2003	2004	2005	2006	2007	2008
New molecular entities	21	31	18	18	16	17
Biologic license applications <sup>a</sup>		5	2	4	2	3
Device premarket application approvals <sup>b</sup>	33	46	32	38	25	25

<sup>a</sup>The Food and Drug Administration reported biologic license approvals beginning in 2004.

<sup>b</sup>Numbers include instruments, implantables, patient monitoring, diagnostic devices, and in vitro tests.







St. Louis Institute of Nanomedicine

**A JOINT VENTURE SPONSORED BY LEADING LOCAL ACADEMIC INSTITUTIONS (WASHINGTON UNIVERSITY, SAINT LOUIS UNIVERSITY, SAINT LOUIS COMMUNITY COLLEGE, AND THE UNIVERSITY OF MISSOURI-SAINT LOUIS) WITH THE GOAL OF ADVANCING THE SAFE AND EFFECTIVE USE OF NANOTECHNOLOGIES TO REDUCE DEATH AND SUFFERING FROM HUMAN DISEASE.**

**THE INSTITUTE WILL ASSEMBLE A BROAD BASE OF REGIONAL EXPERTISE IN THE AREAS OF NANOTECHNOLOGY, MEDICINE, TECHNOLOGY TRANSFER, AND EDUCATION TO CREATE NOVEL SOLUTIONS TO COMPLEX HEALTH CARE PROBLEMS**

# SLIN GOALS

**Russ Carnahan**  
3RD DISTRICT, MISSOURI

SENATOR WHOOP

FOREIGN AFFAIRS COMMITTEE  
VICE CHAIRMAN  
INTERNATIONAL ORGANIZATIONS, HUMAN RIGHTS AND OVERSIGHT SUBCOMMITTEE  
MIDDLE EAST & SOUTH ASIA SUBCOMMITTEE  
TRANSPORTATION AND INFRASTRUCTURE COMMITTEE  
AVIATION SUBCOMMITTEE  
WATER RESOURCES & ENVIRONMENT SUBCOMMITTEE  
SCIENCE AND TECHNOLOGY COMMITTEE  
RESEARCH AND SCIENCE EDUCATION SUBCOMMITTEE



Congress of the United States  
House of Representatives  
Washington, DC

February 13, 2010

St. Louis Institute of Nanomedicine  
Washington University, Farrell Learning and Teaching Center  
520 South Euclid Avenue  
St. Louis, MO 63110

Dear Participants:

As a member of the U.S. House of Representatives' Committee on Science and Technology, I understand the importance of keeping the United States at the forefront of nanotechnology research, development and deployment. The National Nanotechnology Initiative (NNI) was established in 2001 in order to foster exactly this kind of coordinated nanotechnology research and development effort. The St. Louis Institute of Nanomedicine is just the kind of collaborative vision from which the NNI was founded. By taking advantage of the St. Louis region's strengths in nanotechnology and leveraging local business, education and community resources, we will be able to position St. Louis at the forefront of discovery, innovation and commercialization.

I firmly believe that the role of government is to help create the right conditions for business and innovation to thrive. To this point, in February 2009 the U.S. House of Representatives passed H.R. 554, the National Nanotechnology Initiative Amendments Act of 2009 with broad bipartisan support. This bill will provide transparency in federal research efforts to understand the potential environmental, health, and safety risks of nanotechnology.

We must ensure that we are capturing the economic benefits of nanotechnology. In 2007, \$60 billion in nano-enabled products were sold; and it is predicted that the number will rise to \$2.6 trillion by 2014. To encourage commercialization in the U.S., the bill strengthens public-private partnerships by encouraging the creation of industry liaison groups to foster technology transfer and to help guide the NNI research agenda. The bill also promotes the use of nanotechnology research facilities to assist companies in the development of prototypes. The legislation is currently awaiting action from the Senate and I am hopeful that they will act soon.

As we search for new and innovative ways to establish the necessary regional business development infrastructure to improve nanotechnology ventures in St. Louis, I hope that you will share your findings with me. I look forward to working with you in the future.

Sincerely,

Russ Carnahan, Member of Congress

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- Translational nexus for moving ideas out of academe into the commercial sector
- Facilitator of preclinical development and clinical trials
- Seed funding for piloting new ideas that can grow into bigger projects
- Biotech development driver locally and nationally

