

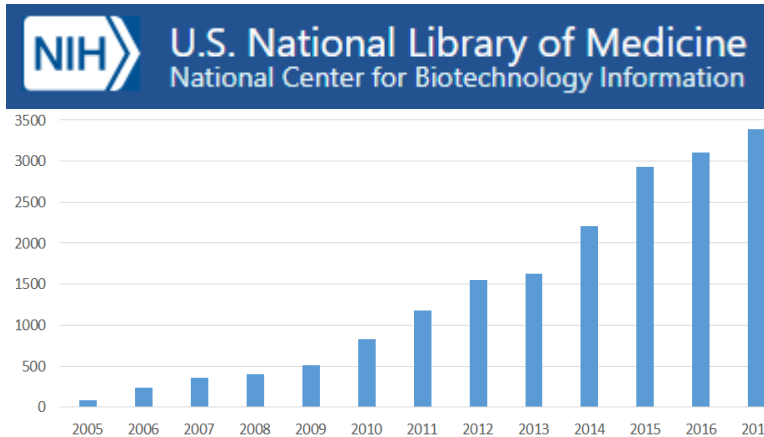
# *in vivo* Imaging Using Nanoparticles

**Keon Wook Kang, MD, PhD**



**Department of Nuclear Medicine  
& Cancer Research Institute  
Seoul National University College of Medicine**

# Failure of Nanomedicine



**nature**

**Bankruptcy of nanomedicine firm worries drug developers**

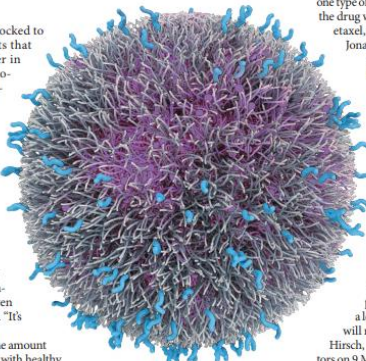
*Financial troubles of leading biotech firm highlight challenges of making innovative drugs.*

**BY HEIDI LEFORD**

Not long ago, investors flocked to a firm in Massachusetts that was hailed as the leader in a wave of next-generation nanotechnology companies developing ways to ferry cancer drugs to tumours. But on 2 May, the company — BIND Therapeutics — declared bankruptcy.

Researchers in the field of nanomedicine are waiting anxiously to see whether the Cambridge-based firm will pull through its financial crisis — and whether its troubles will taint the swiftly evolving field of nanoparticle drug delivery. "It's been a rapid rise and fall," says Eric Schmidt, a biotechnology analyst at the investment bank Cowen and Company in New York City. "It's all unravelled pretty quickly."

Because nanoparticles lessen the amount of contact that cancer drugs have with healthy tissue, they offer a chance to deliver higher doses with fewer side effects. In 1995, the US



BIND Therapeutics' nanoparticle is coated in molecules that target it to tumours.

one type of lung cancer, it was not clear whether the drug worked any better than regular docetaxel, says BIND's chief scientific officer Jonathan Yingling.

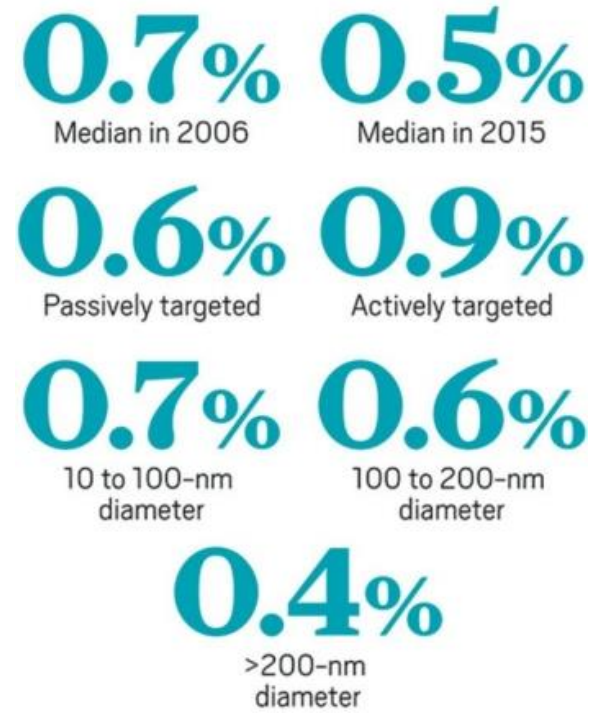
In April, the company announced that it would cut back on its work with BIND-014, and Yingling says that the firm will now explore new targets. It cut the number of employees by 38% and aims to trim its expenses to \$6 million per quarter — a dramatic decrease for a company that spent \$11 million on research and development alone in the first quarter of 2016.

After one of its creditors demanded that BIND repay a loan ahead of schedule, the company filed for bankruptcy (see "Troubled times"). It plans to dispute the need for early repayment at a legal hearing on 18 May. "BIND is and will remain open for business," Andrew Hirsch, president of the company, told investors on 9 May.

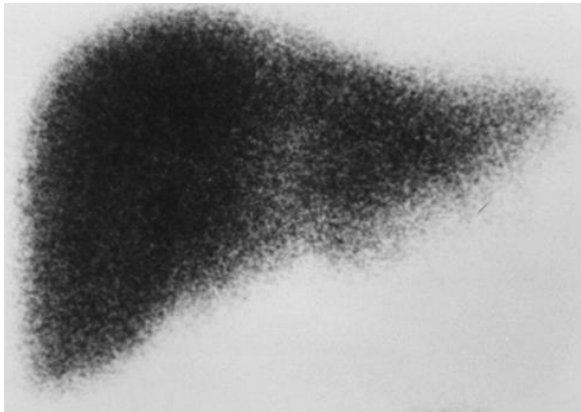
Schmidt says that BIND remains at the technological forefront of nanoparticle drug

**nature**  
**REVIEWS** **MATERIALS** **2016**

## Analysis of nanoparticle delivery to tumours



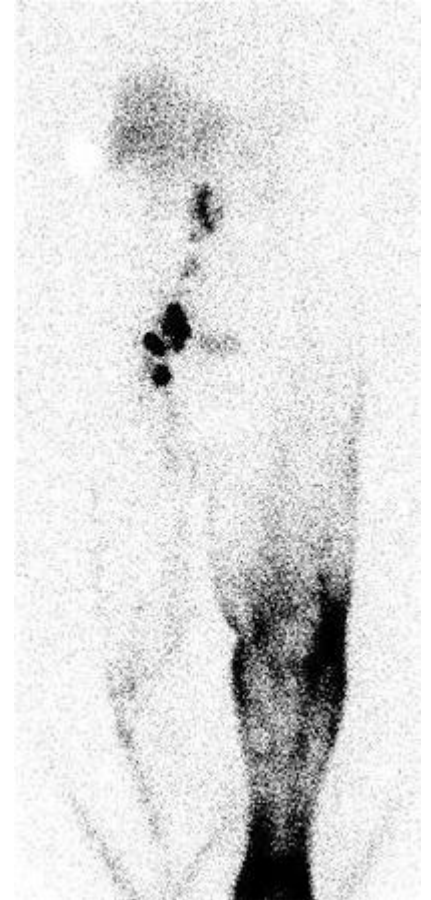
# Nanoparticle Imaging in Nuclear Medicine



Liver scan

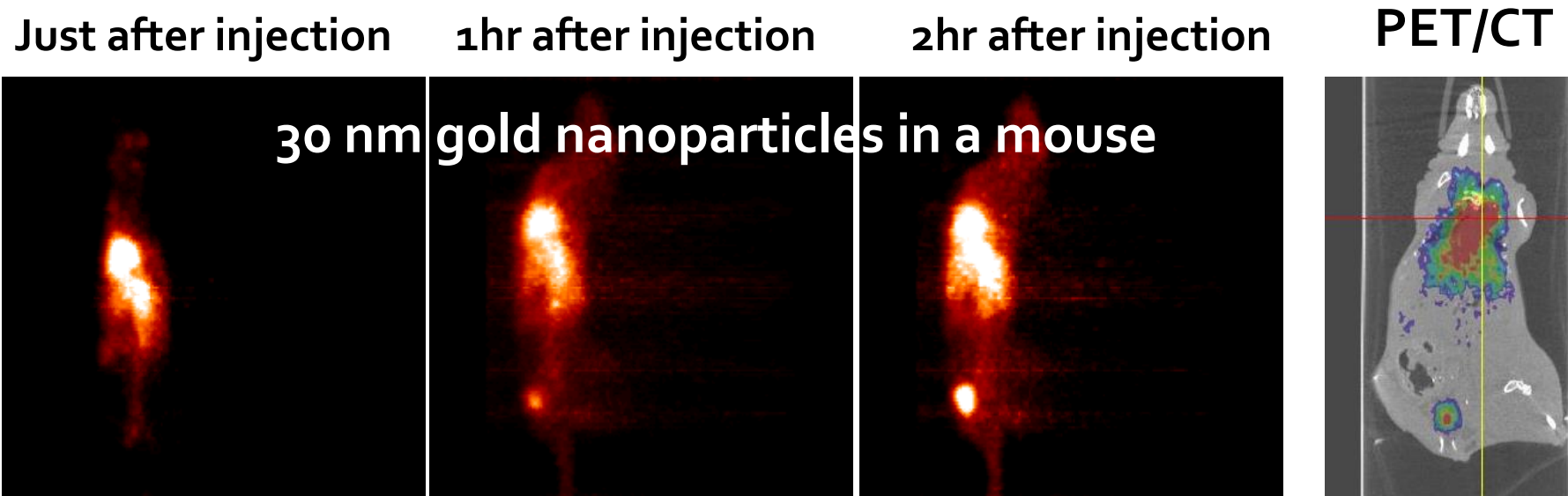
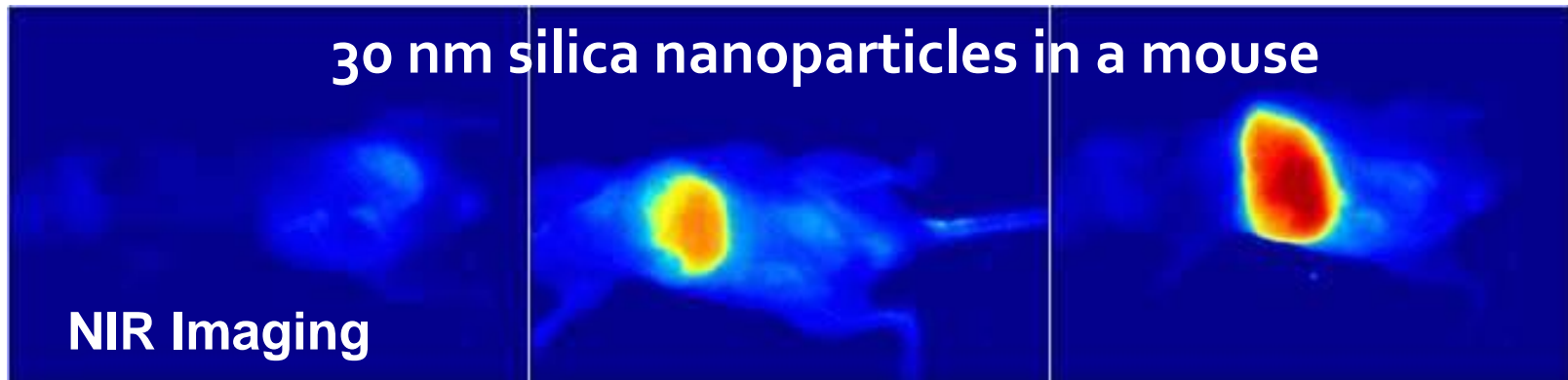


Bone marrow scan



Lymphoscintigraphy

# Biodistribution of nanoparticles

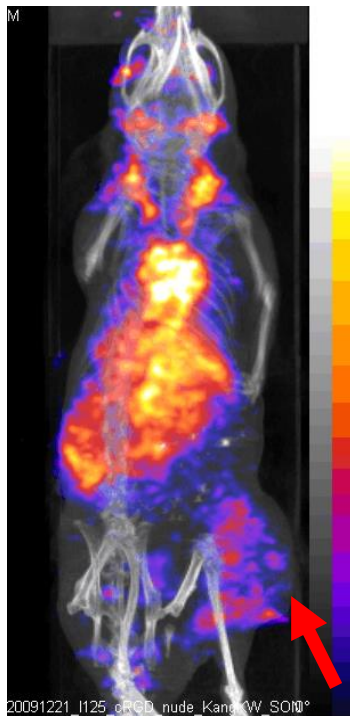




# $^{125}\text{I}$ -labeled cyclic RGD peptide-gold nanoparticle

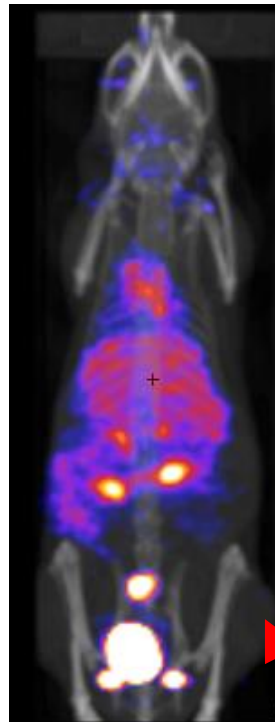
In vivo SPECT/CT imaging of in a U87MG tumor bearing mouse

$^{125}\text{I}$ -cRGD-gold nanoparticles



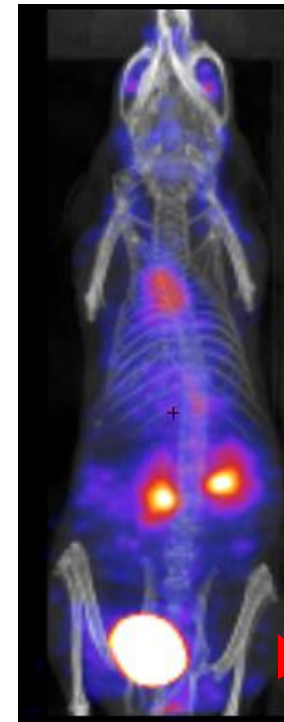
tumor

Cold blocking test



tumor

$^{125}\text{I}$ -gold nanoparticles



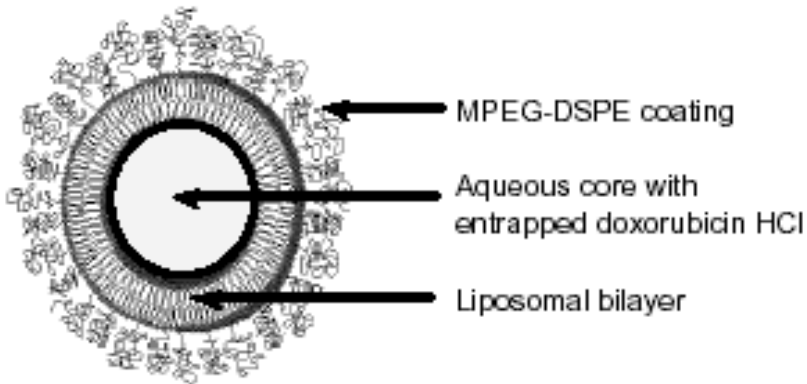
tumor

*Small 2011*

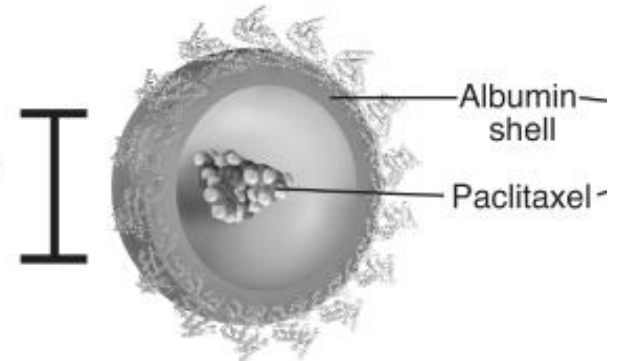
# FDA approved nano-drugs



Abraxane<sup>®</sup>  
for Injectable Suspension  
(paclitaxel protein-bound particles for injectable suspension)  
(albumin-bound)



$Z_{ave}$  = 120-150 nm  
Negative charge

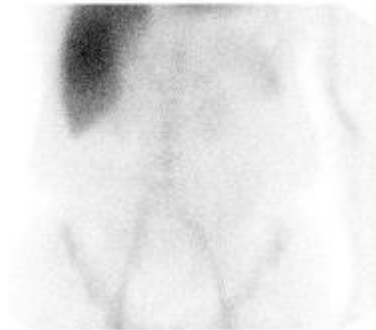


# $^{99m}\text{Tc}$ -albumin scan in human

5 min



10 min



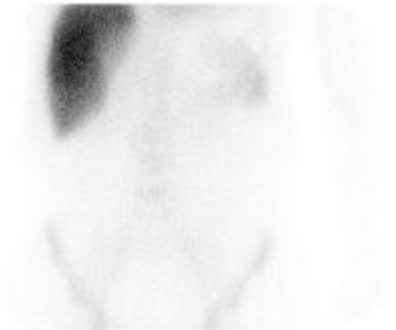
15 min



30 min



60 min



2 h



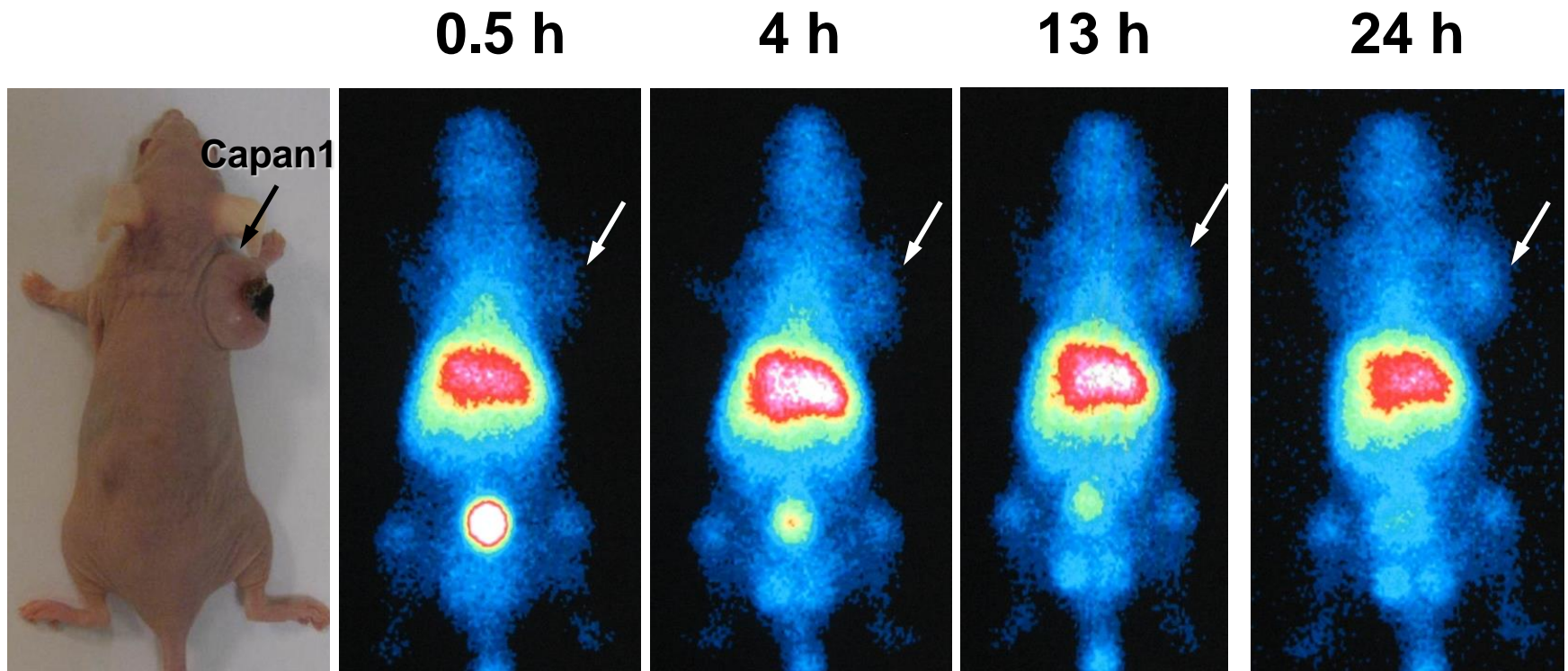
4 h



24 h



# $^{99m}\text{Tc}$ -albumin scan in mouse





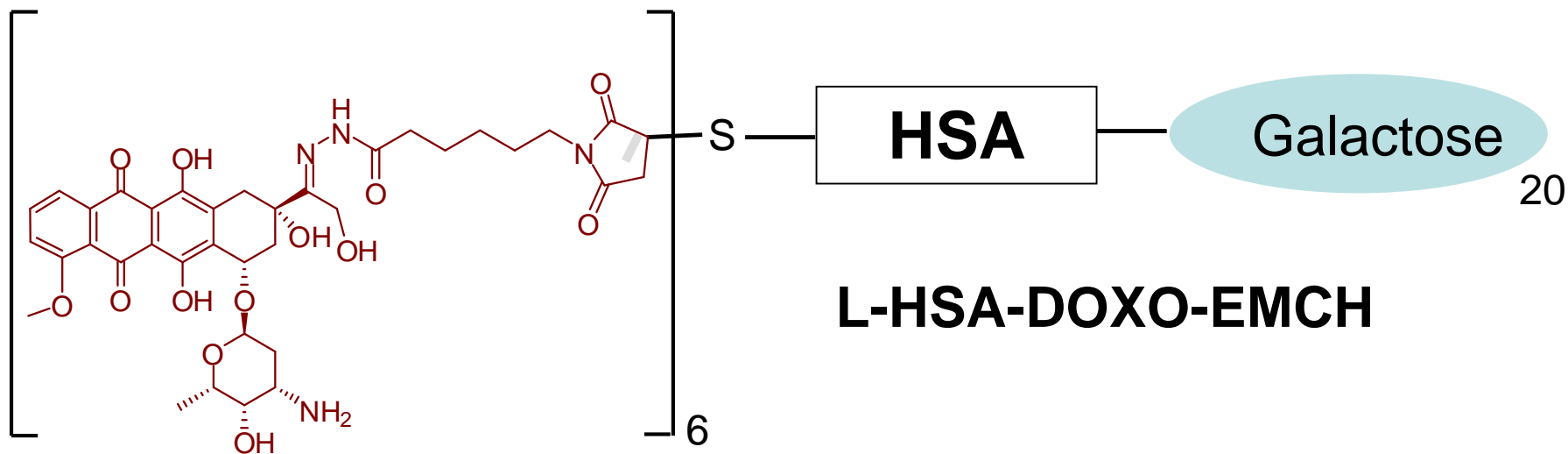


# Liver targeting: Exploiting the asialoglycoprotein receptor for drug delivery to hepatocellular carcinomas

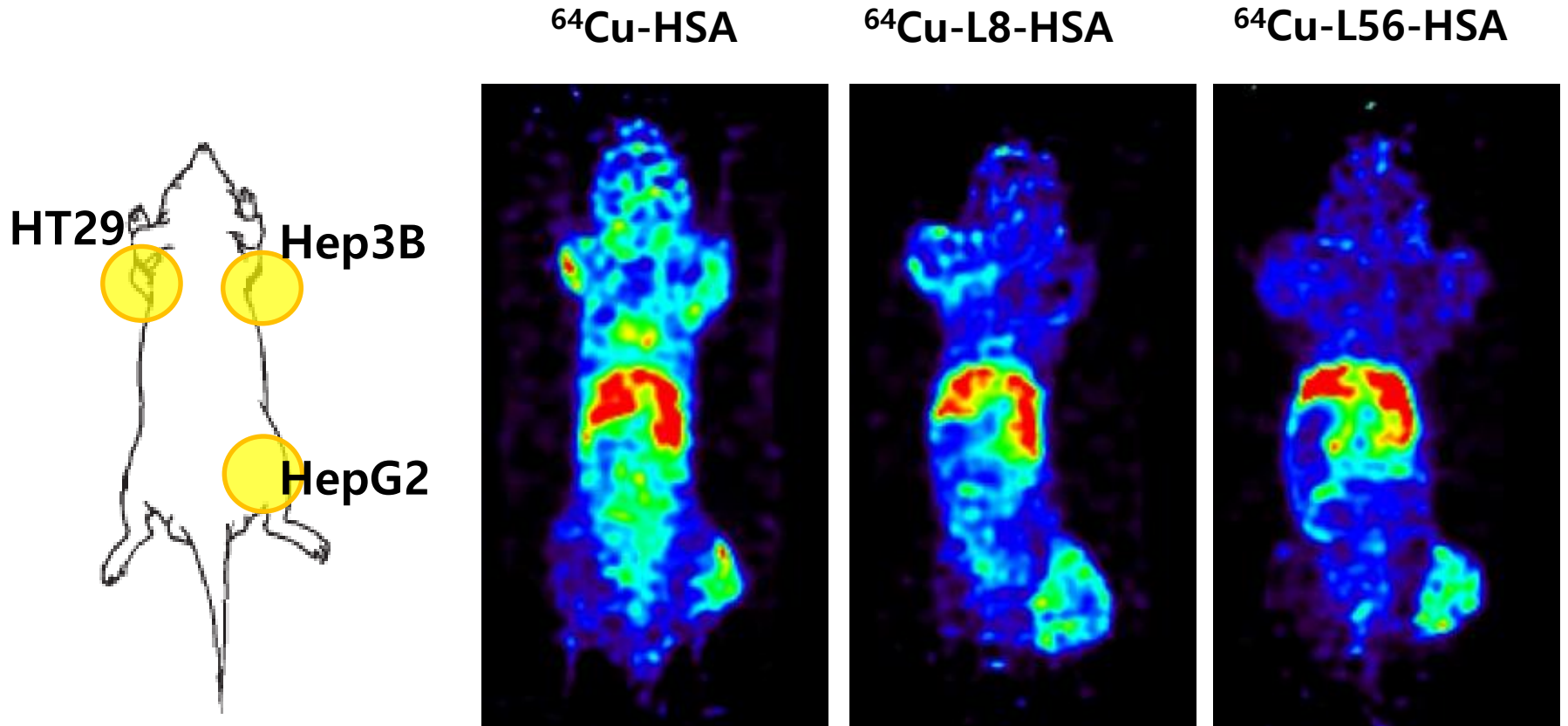


- The asialoglycoprotein receptor is expressed in ~ 80 % of hepatocellular carcinomas.
- Felix Kratz in cooperation with Prof. Luigi Fiume and Dr. G. Di Stefano

Fiume et al.: *J. Hepatology* 43, 645-652, 2005; Di Stefano et al., *Europ.J. Pharm. Sciences* 23,393-397, 2004; Di Stefano et al., *Liver Int.* 24, 246-252, 2004; Di Stefano et al., *Digestive and Liver Disease* 35, 428-33, 2003.

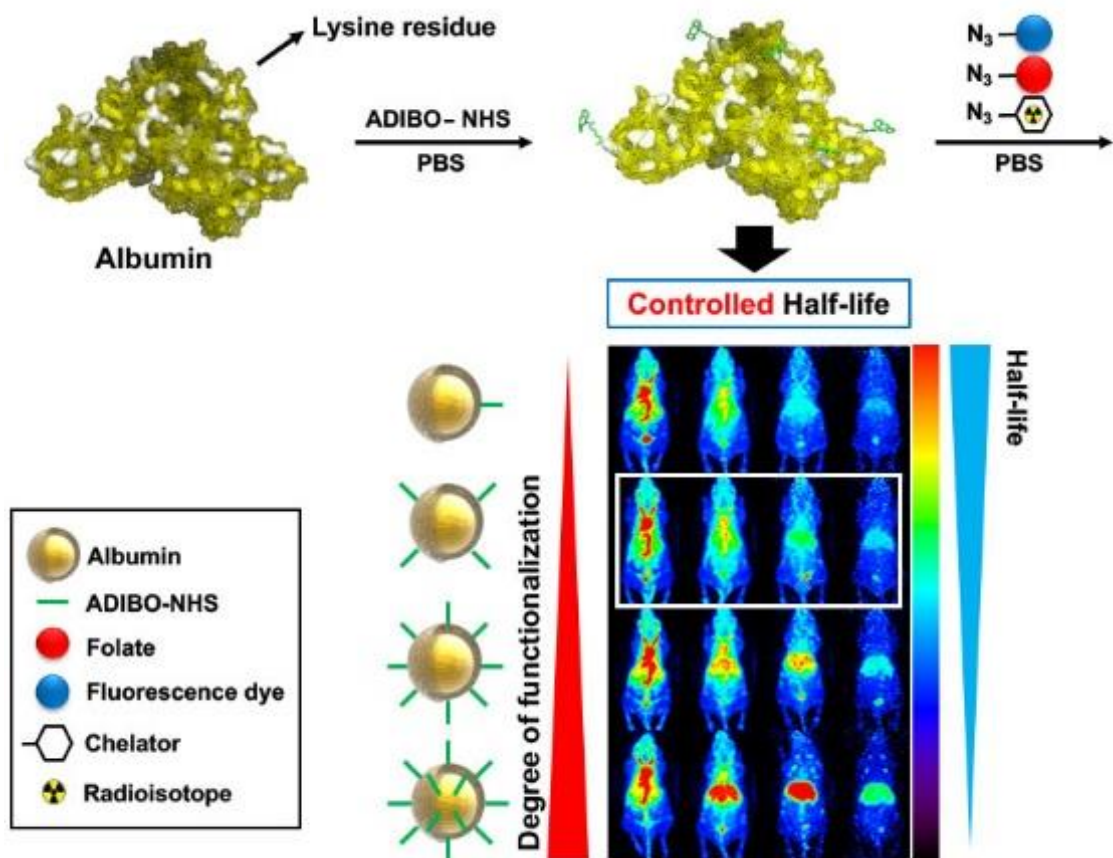


# $^{64}\text{Cu}$ -lactoamine-albumin PET



46 h after injection

# Versatile and Finely Tuned Albumin Nanoplatfrom based on Click Chemistry



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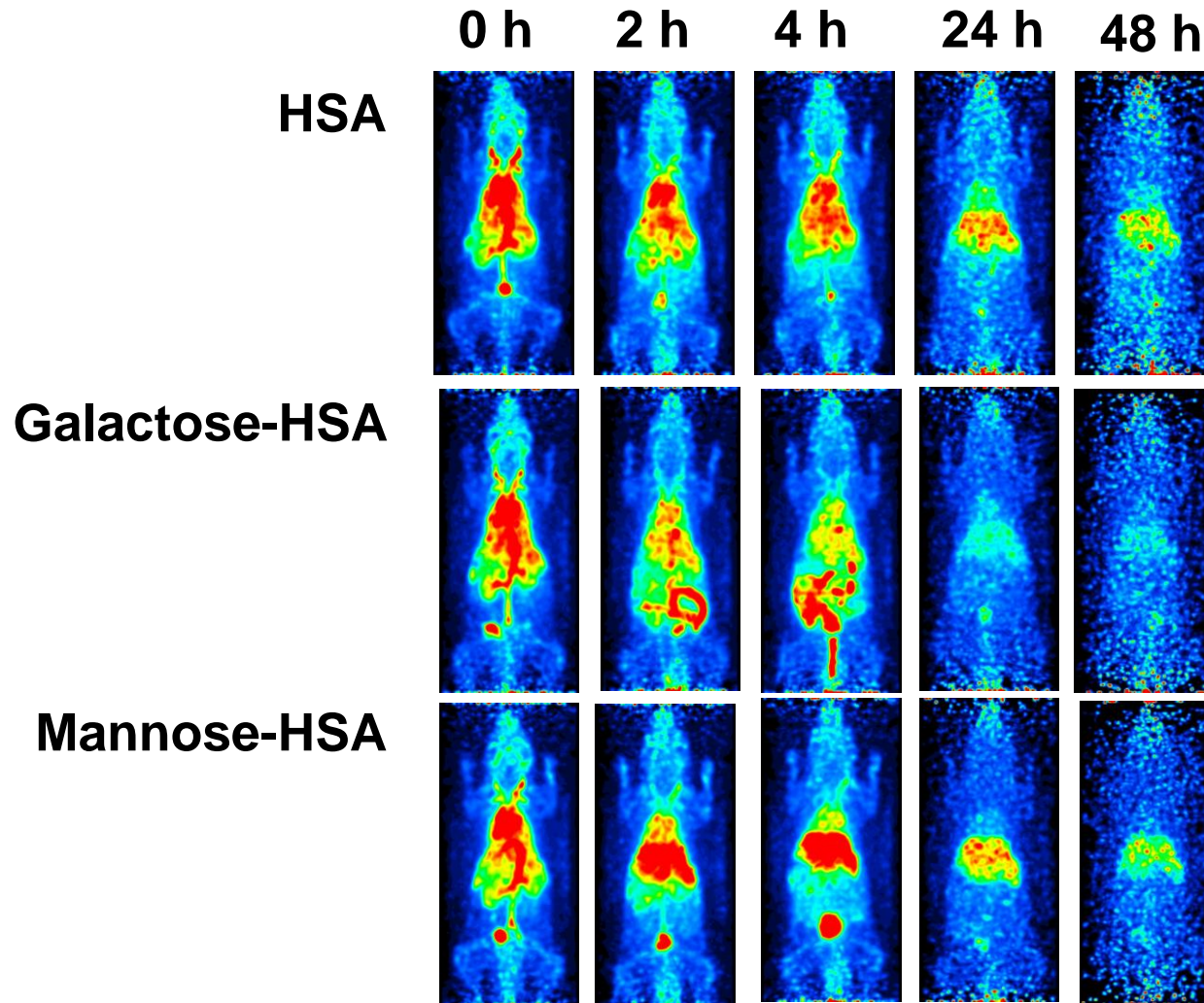
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## Theranostics

The Forum for Diagnostics, Imaging, and Therapy Research

**Back Cover:**  
**Versatile and Finely Tuned Albumin Nanoplatfrom based on Click Chemistry**  
*J.Y. Park et al. pp.3398*

# $^{64}\text{Cu}$ labeled Albumin Platform PET imaging



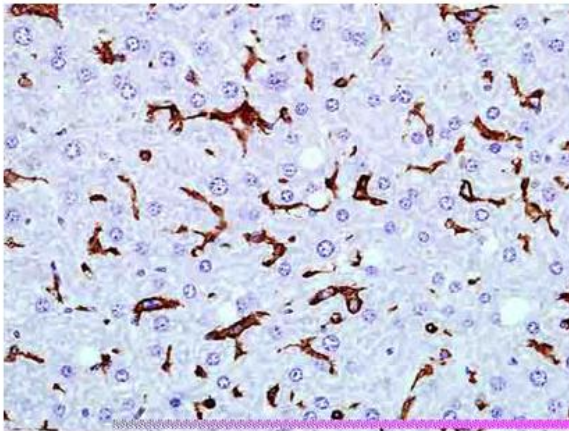
# Hepatocyte vs Kupffer cell

GSA - Cy3

MSA - FNR-648

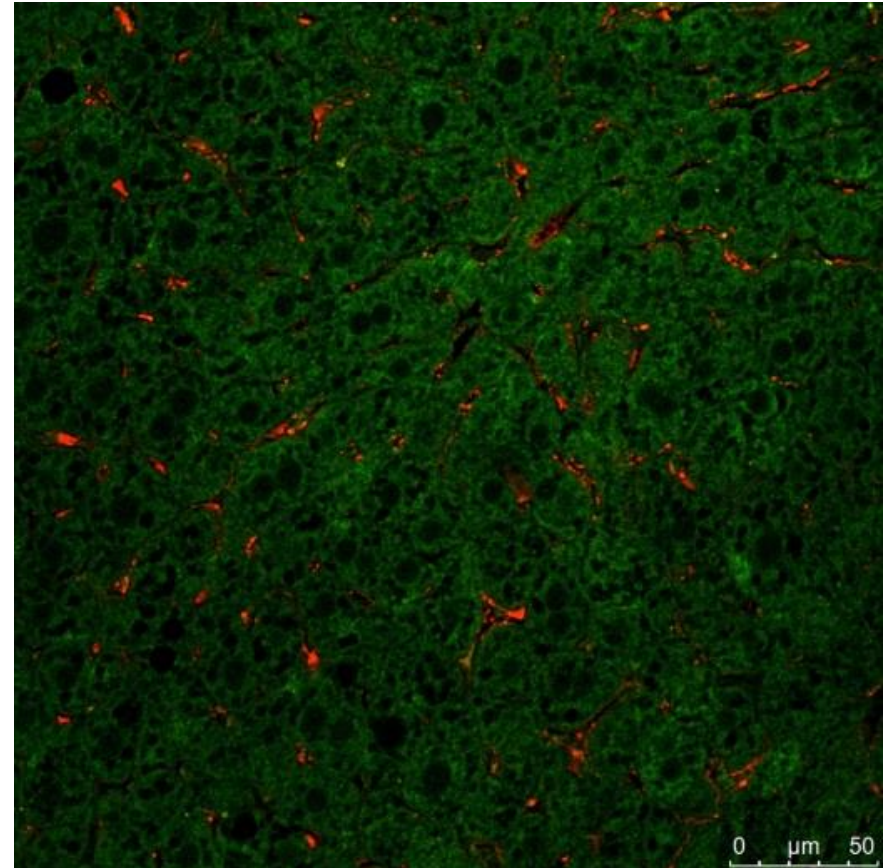
## Pathology: Kupffer cells

Posted on [July 19, 2012](#)



The resident hepatic macrophage, the Kupffer cell, has many important roles in health maintenance and injury. In the the histologic specimen above, the Kupffer cells are stained dark brown. They line the hepatic sinusoids.

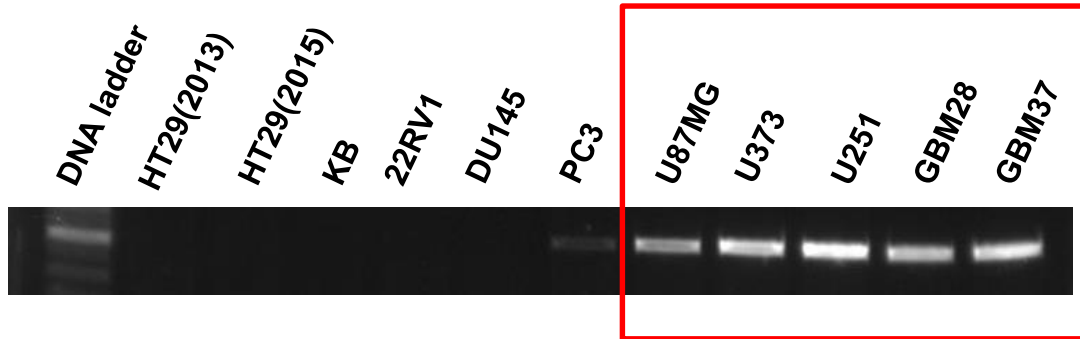
Historically, this macrophage's role lied in phagocytic clearance of infections, tissue development and wound repair. However, it is *far* more functionally complex. In addition, they regulate hematopoiesis, vasoregulation, apoptosis, cancer metastasis and lipid metabolism. They also stimulate lymphocyte production of interleukins and TNF (inflammation).



# SPARC in cell lines

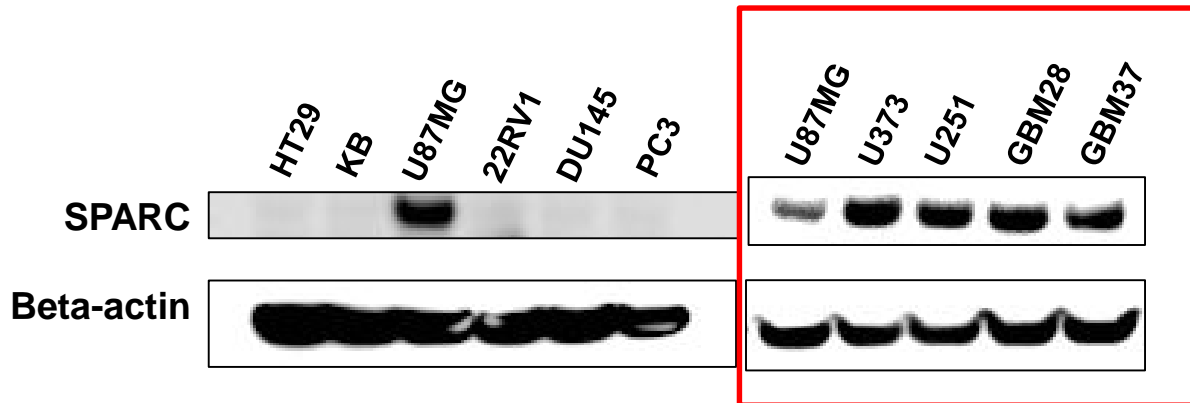
## RT-PCR

Glioma cells

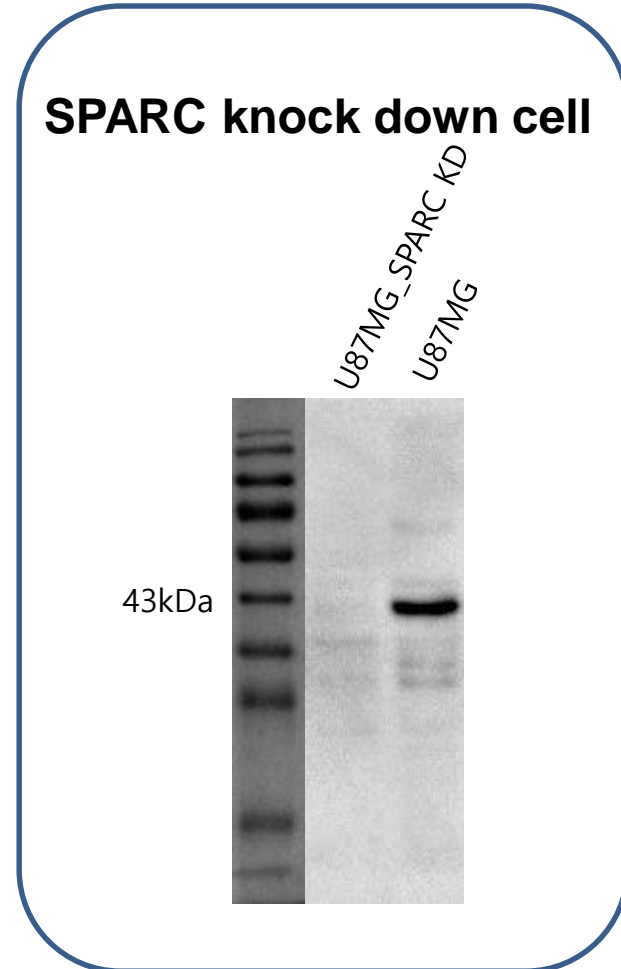


## western blot

Glioma cells



## SPARC knock down cell



# *in vivo* fluorescent imaging

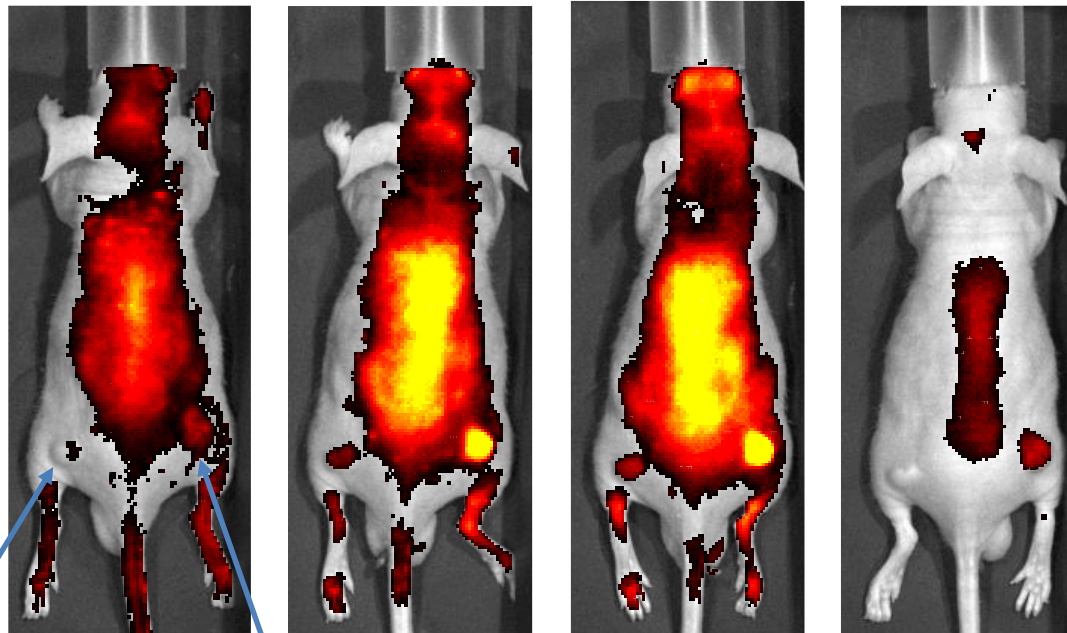
HSA-FNR648 injection via tail vein

0 h

4 h

8 h

24 h

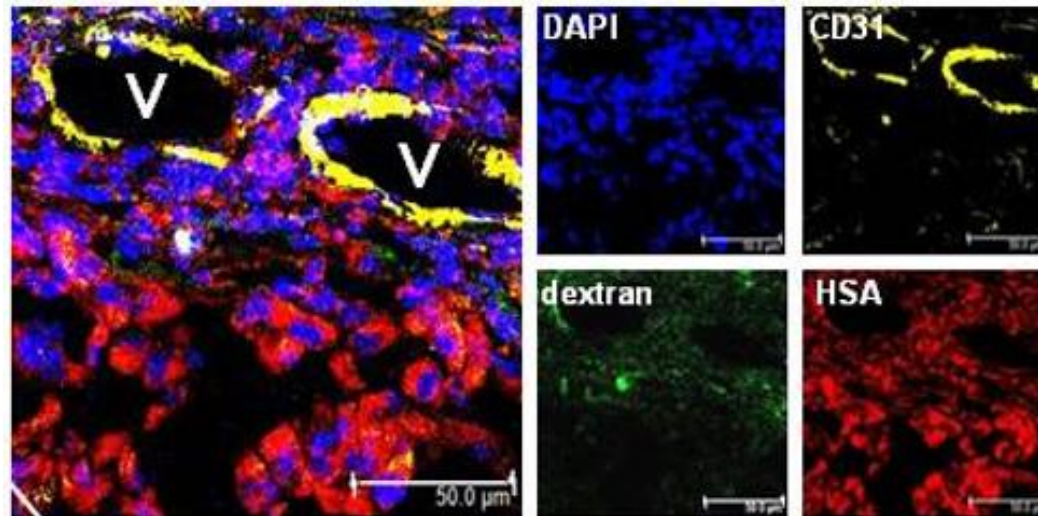


U87MG SPARC KD  
6.0 x 5.9 mm<sup>2</sup>

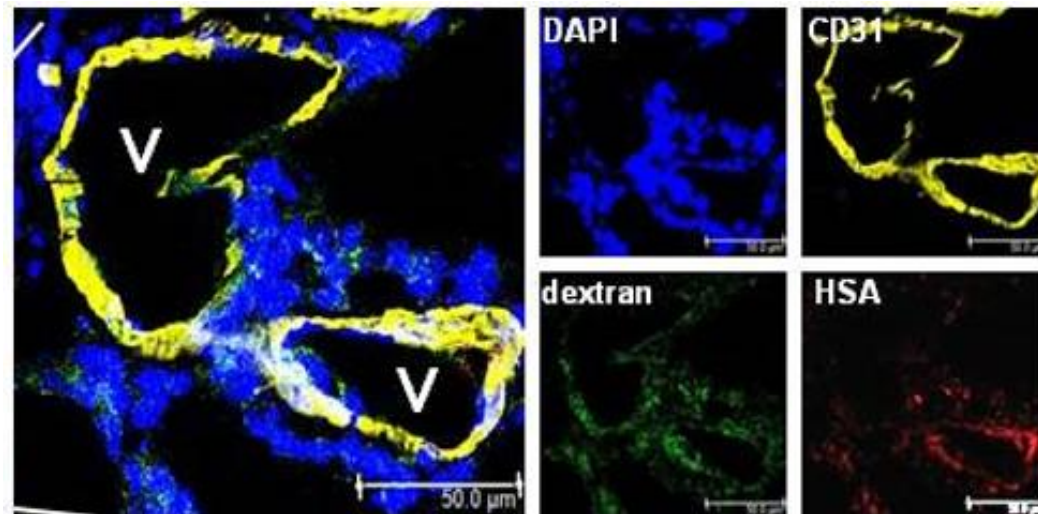
U87MG  
6.0 x 6.3 mm<sup>2</sup>

# *ex vivo* fluorescent imaging

**U87MG**



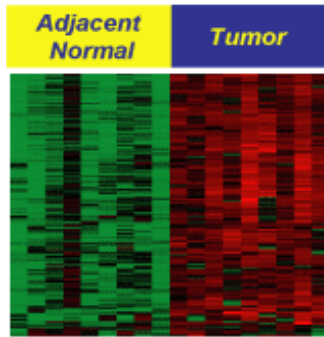
**U87MG  
-SPARC KD**



\*V: blood vessel



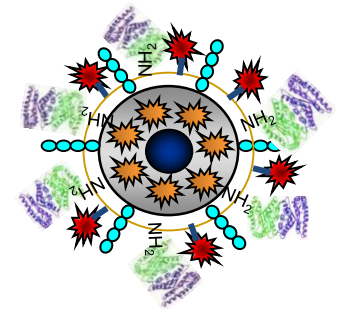
# Precision nanomedicine using molecular imaging



Genomics



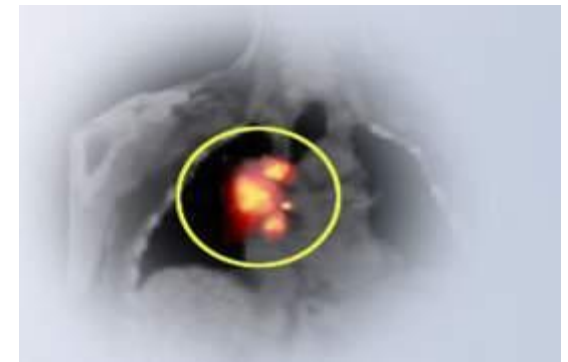
Targeting biomarker



Nano-carrier



In vivo molecular imaging

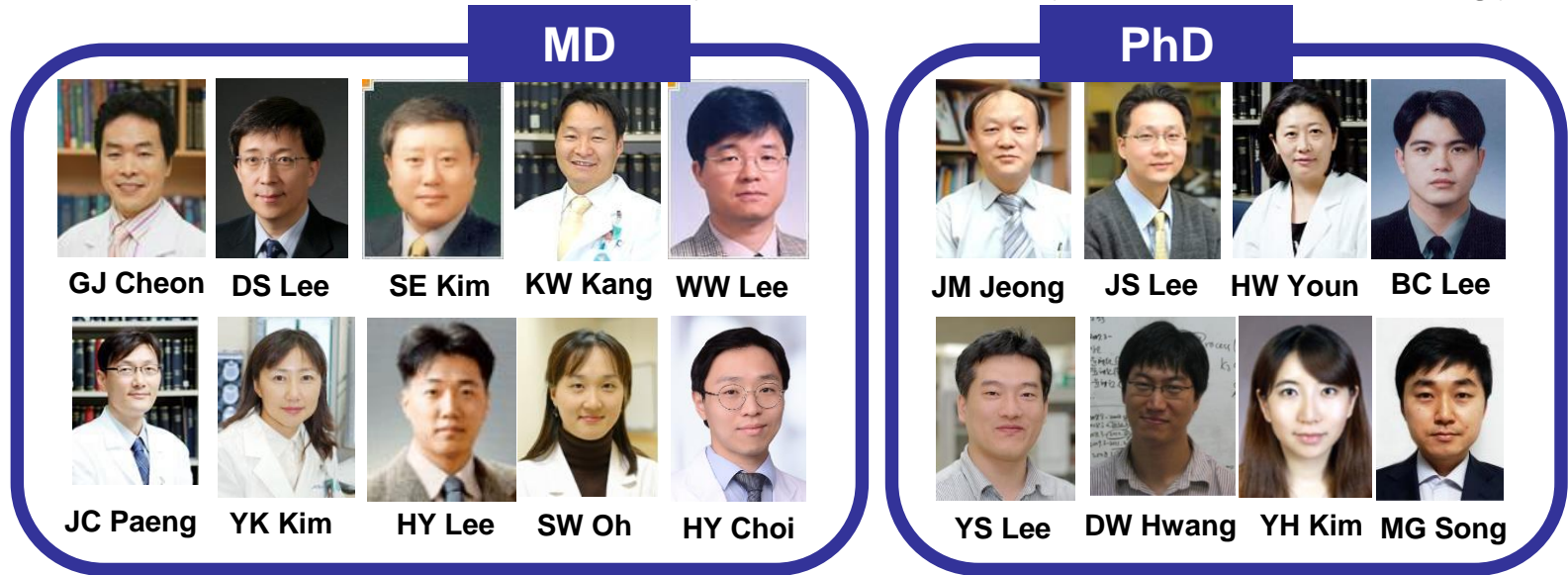


Precision theranostics

# Nuclear Medicine, SNU

■ Faculties: 22

■ MD: 12 / PhD: 10 (Physics, Chemistry, Molecular Biology)



■ Researchers: 42