In Vivo Imaging Technologies in Basic and Preclinical Research

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PerkinElmer In Vivo Small Animal Imaging Instrument Portfolio

Optical – Bioluminescence/Fluorescence

microCT, Ultrasound

Functional/Molecular

Anatomical

3D Tomographic

2D – Low Throughput

2D – High Throughput

IVIS® Lumina™ Platform

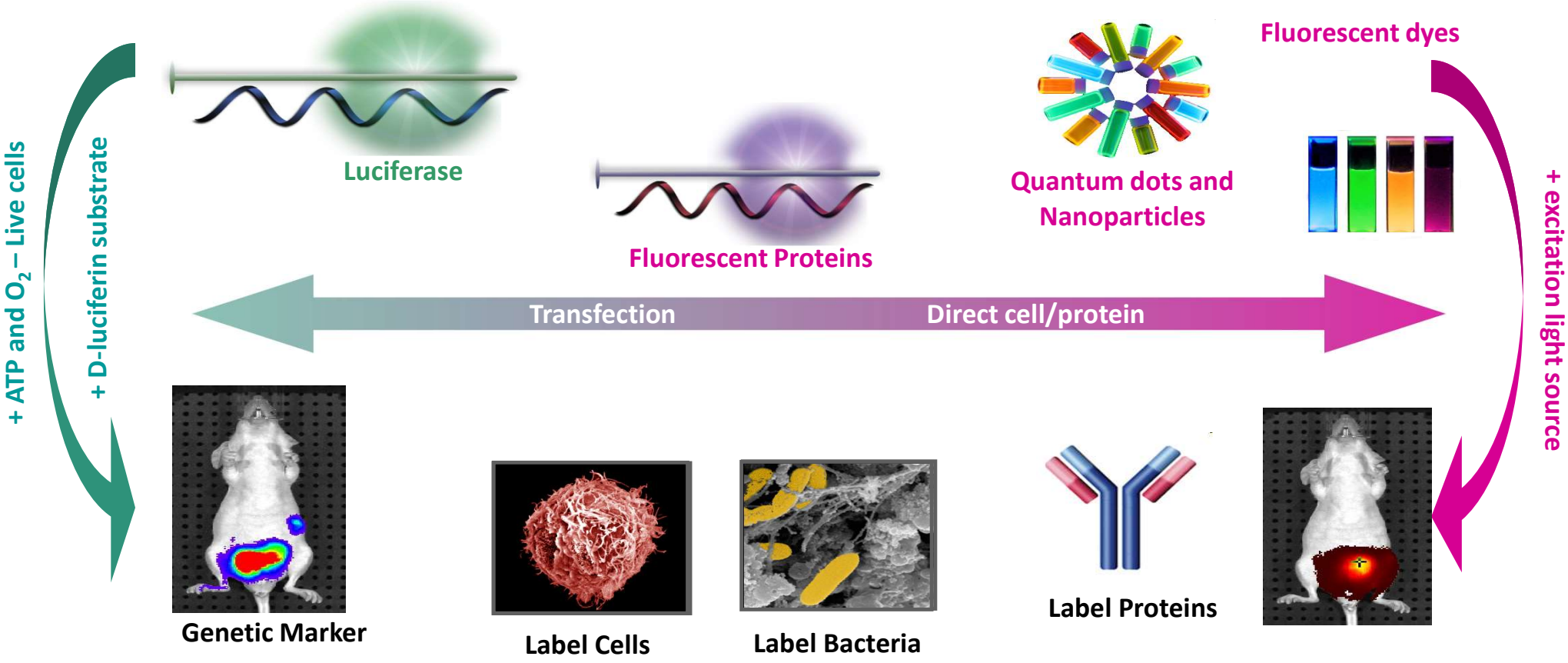
IVIS® Lumina S5™ and X5™

IVIS® Spectrum™ Platform

Vega®

Quantum GX2

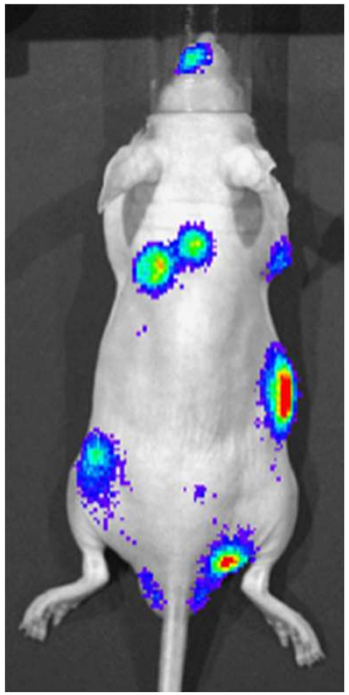
The Power of Optical Imaging



Why Optical Imaging?

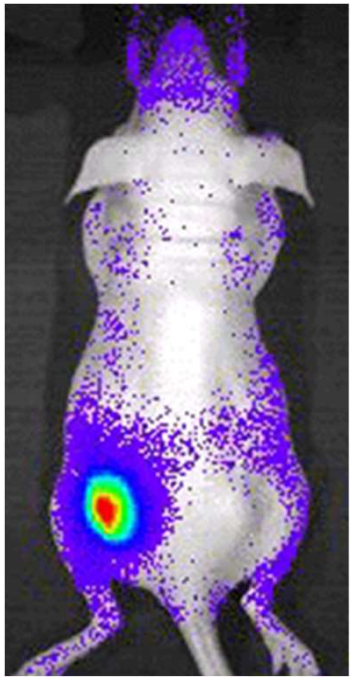
- **In vivo tracking and monitoring of tumor cells, stem cells, bacteria**
- **Study of gene function**
  - Light producing transgenic animals
- **Ideal for small animal imaging**
  - Small tissue depths
  - Relatively simple instrumentation
  - no hazardous radiation
  - easy to learn
- **Quantitative - light output is proportional to number of labeled cells**

BIOLUMINESCENCE



B16F10-luc melanoma metastases

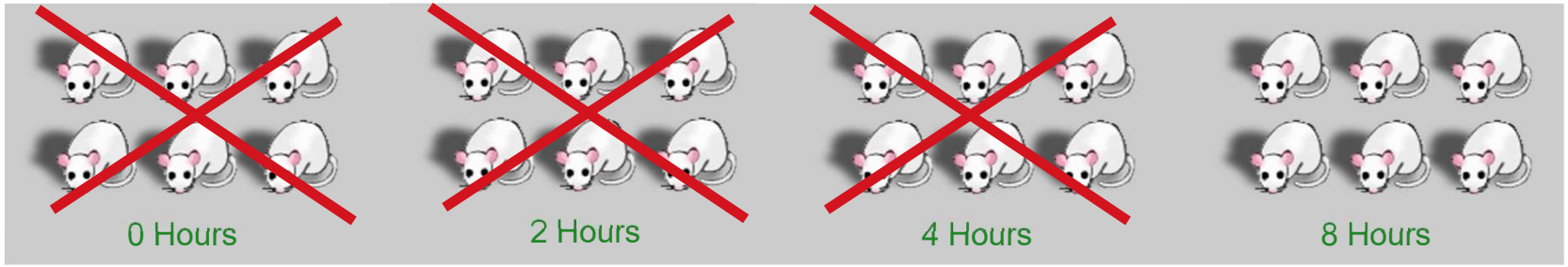
FLUORESCENCE



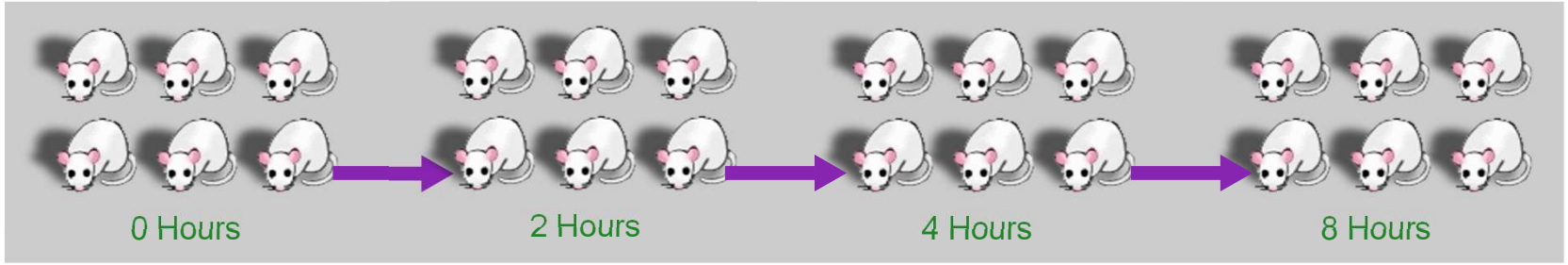
PC3M cells labeled with PKH-26 dye

Histology vs. In Vivo Optical Imaging

CURRENT METHODOLOGY = 24 ANIMALS OVER FOUR TREATMENT POINTS

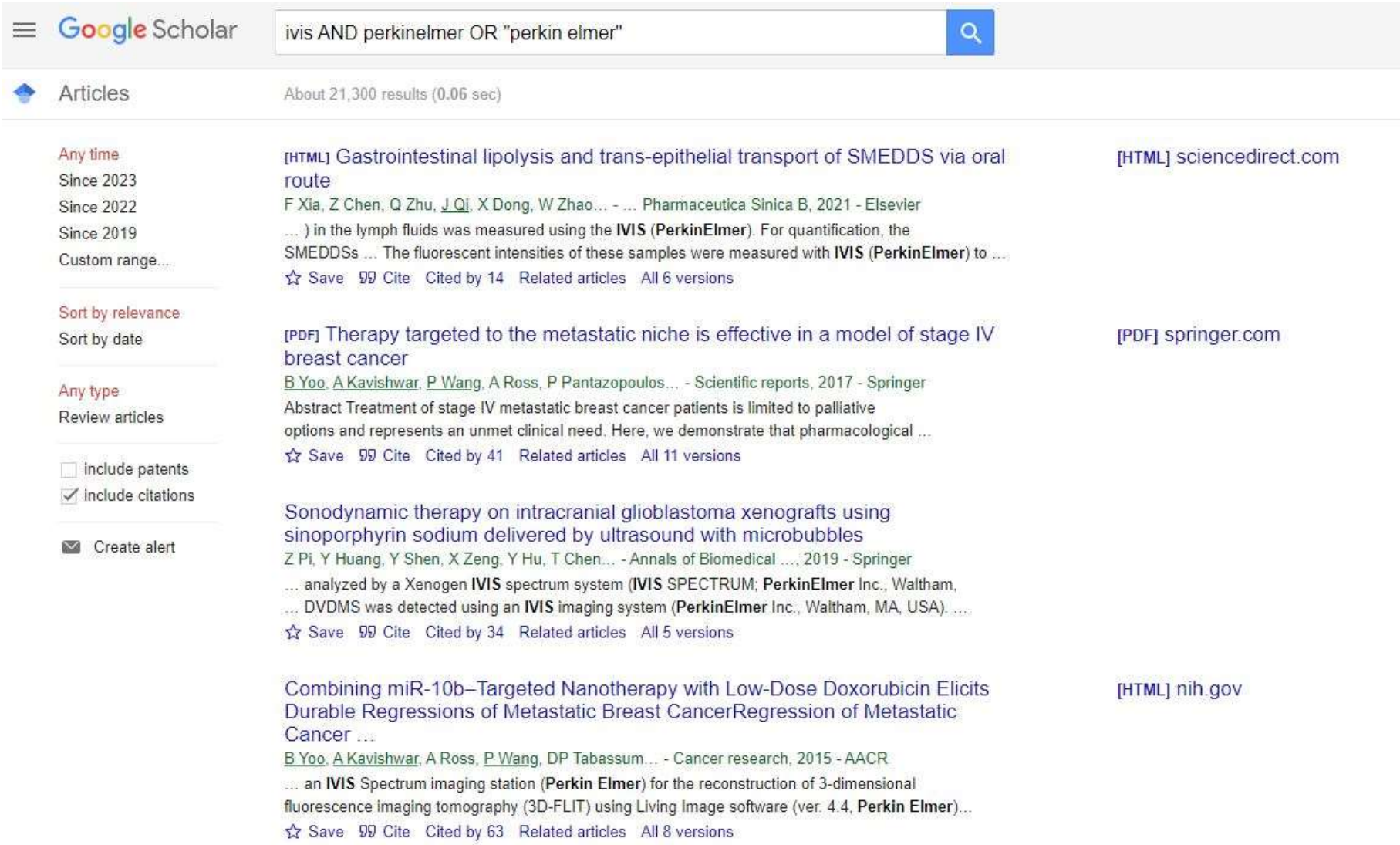


IN VIVO IMAGING METHODOLOGY = THE SAME 6 ANIMALS OVER FOUR TREATMENT POINTS



Same group of anesthetized test animals at each time point of an experiment uses far fewer animals than current methodology. By using the same set of animals at each time point yields improved statistical relevance.

Additionally: earlier and more precise detection


Google Scholar
ivis AND perkinelmer OR "perkin elmer"
Articles
About 21,300 results (0.06 sec)
Any time
Since 2023
Since 2022
Since 2019
Custom range...
Sort by relevance
Sort by date
Any type
Review articles
include patents
include citations
Create alert
[HTML] Gastrointestinal lipolysis and trans-epithelial transport of SMEDDS via oral route
F Xia, Z Chen, Q Zhu, J Qi, X Dong, W Zhao... - ... Pharmaceutica Sinica B, 2021 - Elsevier
...) in the lymph fluids was measured using the IVIS (PerkinElmer). For quantification, the SMEDDSs ... The fluorescent intensities of these samples were measured with IVIS (PerkinElmer) to ...
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[HTML] sciencedirect.com
[PDF] Therapy targeted to the metastatic niche is effective in a model of stage IV breast cancer
B Yoo, A Kavishwar, P Wang, A Ross, P Pantazopoulos... - Scientific reports, 2017 - Springer
Abstract Treatment of stage IV metastatic breast cancer patients is limited to palliative options and represents an unmet clinical need. Here, we demonstrate that pharmacological ...
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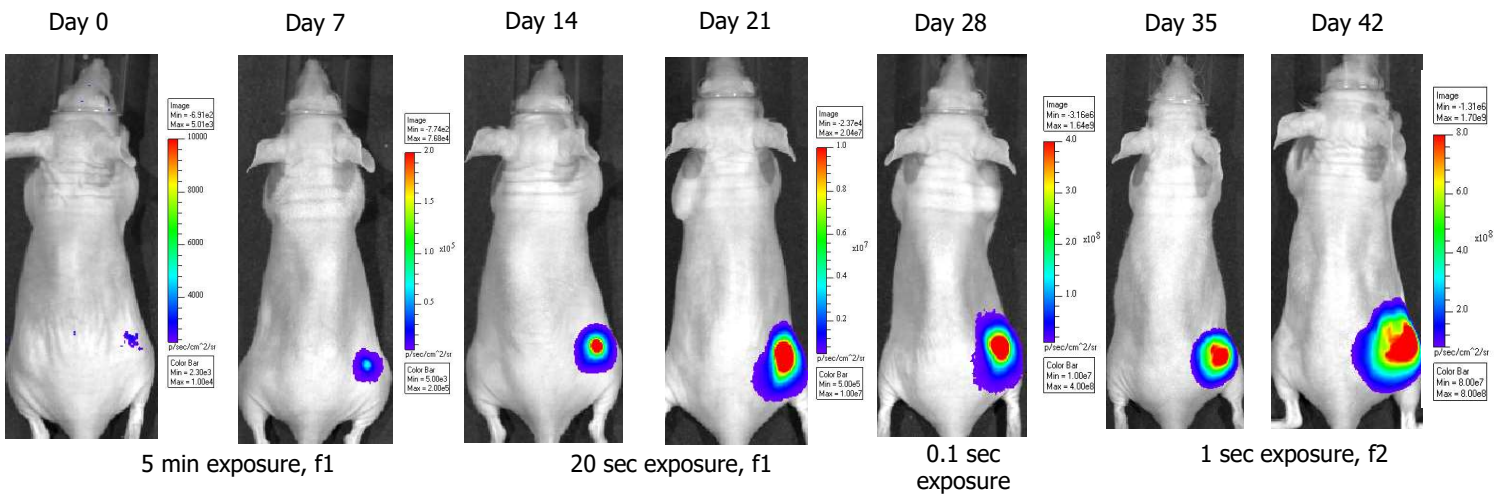
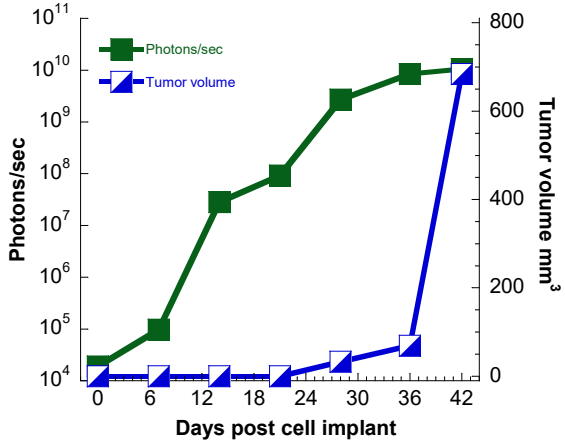
[PDF] springer.com
Sonodynamic therapy on intracranial glioblastoma xenografts using sinoporphyrin sodium delivered by ultrasound with microbubbles
Z Pi, Y Huang, Y Shen, X Zeng, Y Hu, T Chen... - Annals of Biomedical ..., 2019 - Springer
... analyzed by a Xenogen IVIS spectrum system (IVIS SPECTRUM; PerkinElmer Inc., Waltham, ... DVDMS was detected using an IVIS imaging system (PerkinElmer Inc., Waltham, MA, USA). ...
Save Cite Cited by 34 Related articles All 5 versions
Combining miR-10b–Targeted Nanotherapy with Low-Dose Doxorubicin Elicits Durable Regressions of Metastatic Breast CancerRegression of Metastatic Cancer ...
B Yoo, A Kavishwar, A Ross, P Wang, DP Tabassum... - Cancer research, 2015 - AACR
... an IVIS Spectrum imaging station (Perkin Elmer) for the reconstruction of 3-dimensional fluorescence imaging tomography (3D-FLIT) using Living Image software (ver. 4.4, Perkin Elmer)...
Save Cite Cited by 63 Related articles All 8 versions
[HTML] nih.gov

Luminescence - Cell Tracking

Quantifying Tumor Growth with Bioluminescent Cell Lines

LONGITUDINAL STUDIES REQUIRE CALIBRATION IN PHYSICAL UNITS





- Five 4T1-luc2-1A4 cells injected on day 0 in a nu/nu mouse

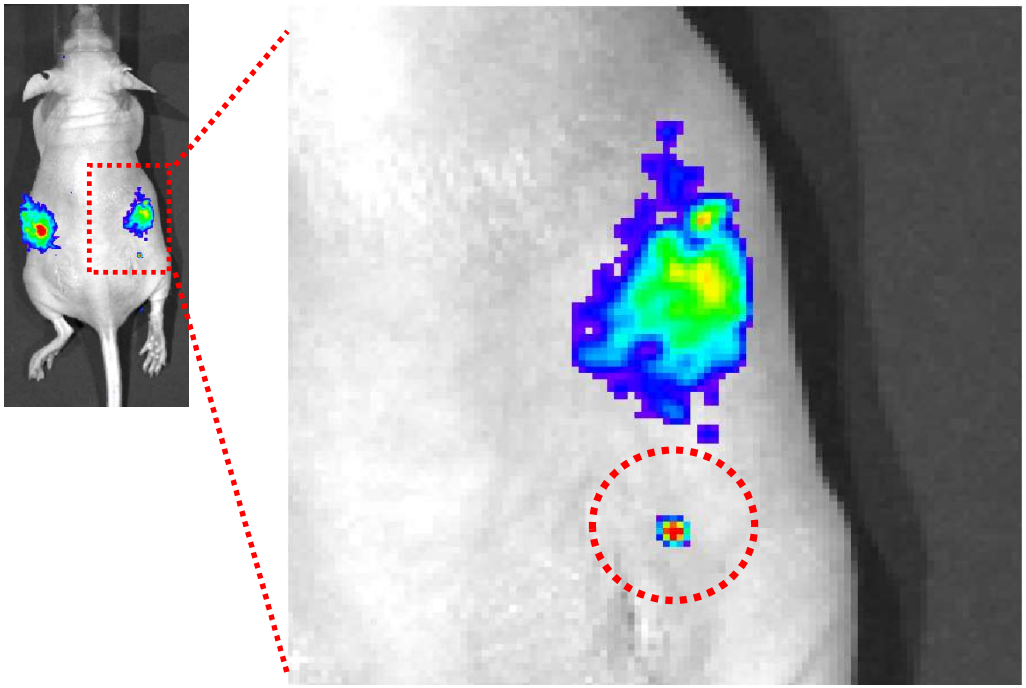
Brightness of Revvity Cell Lines

HT1080-Red-Fluc	Human Fibrosarcoma Cancer Cell line.	> 30,000 p/s/c	BW 128092
4T1-Red-Fluc	Murine Breast Cancer Cell line	> 15,000 p/s/c	BW 124087
MDA-MB-231-Red-Fluc	Human Breast Cancer Cell line, ideal for experimental metastasis model	> 4,000 p/s/c	BW 124319
GL261-Red-Fluc	Murine Glioma Cell line	> 15,000 p/s/c	BW 134246
HepG2-Red-Fluc	Human Hepatic Cancer cell line	> 35,000 p/s/c	BW 134280
PC-3M-Red-Fluc	Human Prostate Cancer Cell line, orthotopic, intracardiac tumor models	> 30,000 p/s/c	BW 124089
PC-3-Red-Fluc	Human Prostate Cancer Cell line	> 30,000 p/s/c	BW 128444
LnCaP-Red-Fluc	Human Prostate Cancer Cell line	> 3,000 p/s/c	BW 125055
B16-F10-Red-Fluc	Murine Melanoma Cancer Cell line	> 6,000 p/s/c	BW 124734
HCT-116-Red-Fluc	Human Colorectal Cancer Cell line	> 4,000 p/s/c	BW 124318
HT-29-Red-Fluc	Human Colorectal Cancer Cell line	> 30,000 p/s/c	BW 124353
Colo205-Red-Fluc	Human Colorectal Cancer Cell line	> 6,000 p/s/c	BW 124317
U-87 MG-Red-Fluc	Human Brain Cancer Cell line, ideal for glioblastoma models	> 8,000 p/s/c	BW 124577
NCI-H460-Red-Fluc	Human Lung Cancer Cell line, ideal for orthotopic lung tumor models	> 4,000 p/s/c	BW 124316
K-562-Red-Fluc	Human Leukemia Cell line	> 4,000 p/s/c	BW 124735
BxPC3-Red-Fluc	Human Pancreatic Cancer Cell	> 15,000 p/s/c	BW 125058
MCF-7-lRed-Fluc	Human Breast Cancer	> 10,000 p/s/c	BW 119262
A549-Red-Fluc	Human Lung Cancer	> 25,000 p/s/c	BW 119266
LL/2-Red-Fluc	Murine Lung Cancer	> 5,000 p/s/c	BW 119267
SKOV3-Red-Fluc	Human Ovarian Cancer	> 10,000 p/s/c	BW 119276
4T1-Red-Fluc-GFP	Murine Breast cancer cell line dual labeled with Luciferase and GFP	> 15,000 p/s/c	BW 128090
MDA-MB-231-Red-Fluc-GFP	Human Breast cancer cell line dual labeled with Luciferase and GFP	> 10,000 p/s/c	BW 128442
PC-3-Red-Fluc-GFP	Human Prostate cancer cell line dual labeled with Luciferase and GFP	> 8,000 p/s/c	BW 133416

Non-invasive imaging of a single 4T1-luc2 cell in nu/nu mouse

4T1: ADENOCARCINOMA CELLS – 6500 PHOTONS/S/CELL

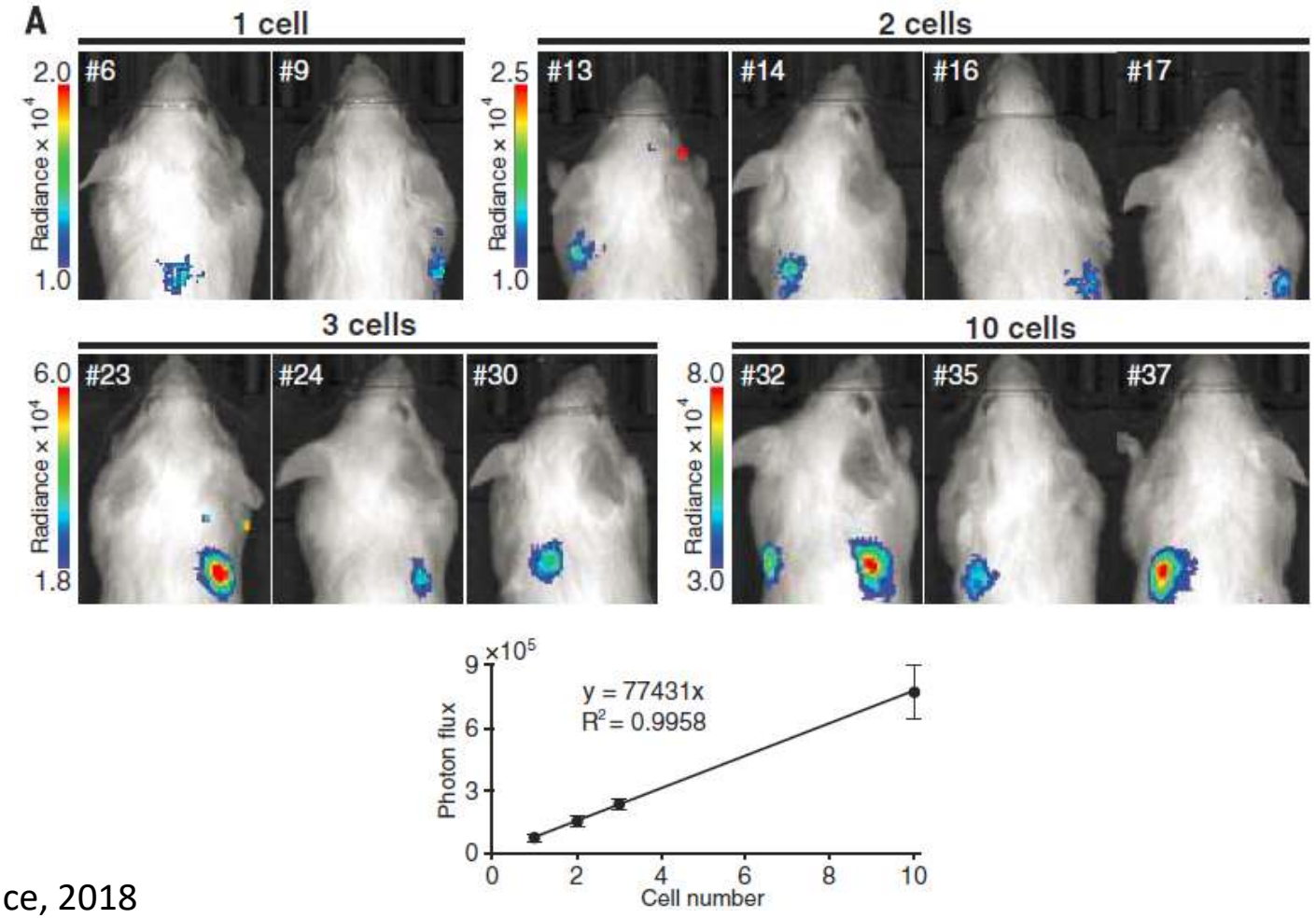
Transduced using lentivirus containing luciferase 2 gene under the control of human ubiquitin C promoter



Kim et al., PLoS ONE, 2010

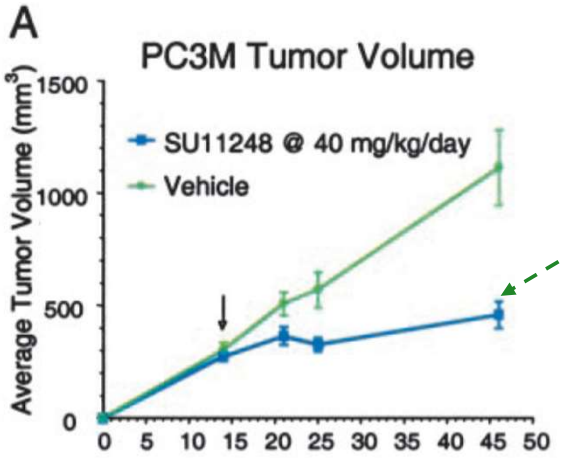
Deep Tissue Imaging with AkaLumine and AkaLuc

Detection of bioluminescence from a small number of Akaluc-expressing HeLa cells trapped in the mouse **lung**.

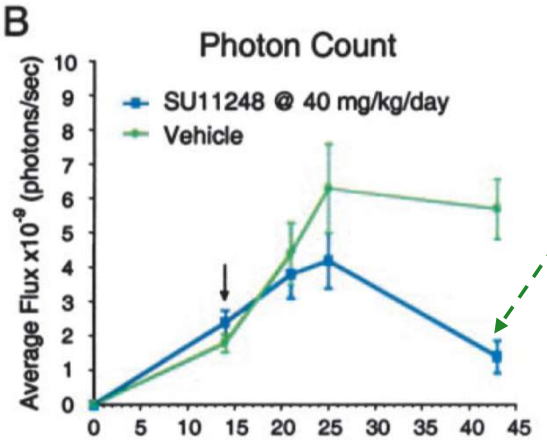


Iwano et al., Science, 2018

Sutent – Fast Tracked FDA Approval

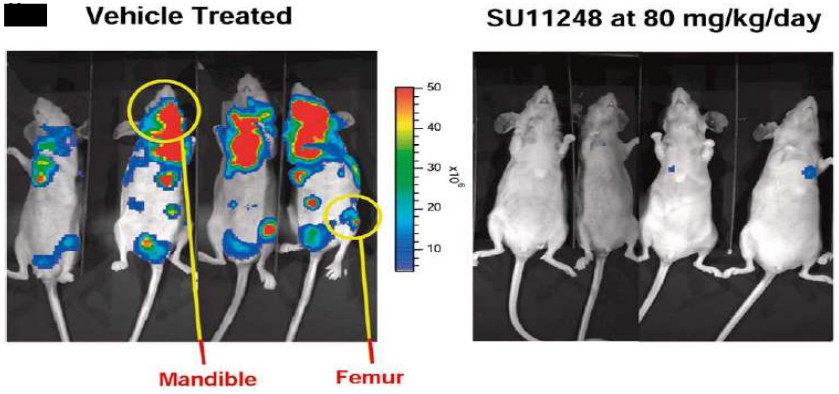


Physical measurement
(tumor still getting bigger)



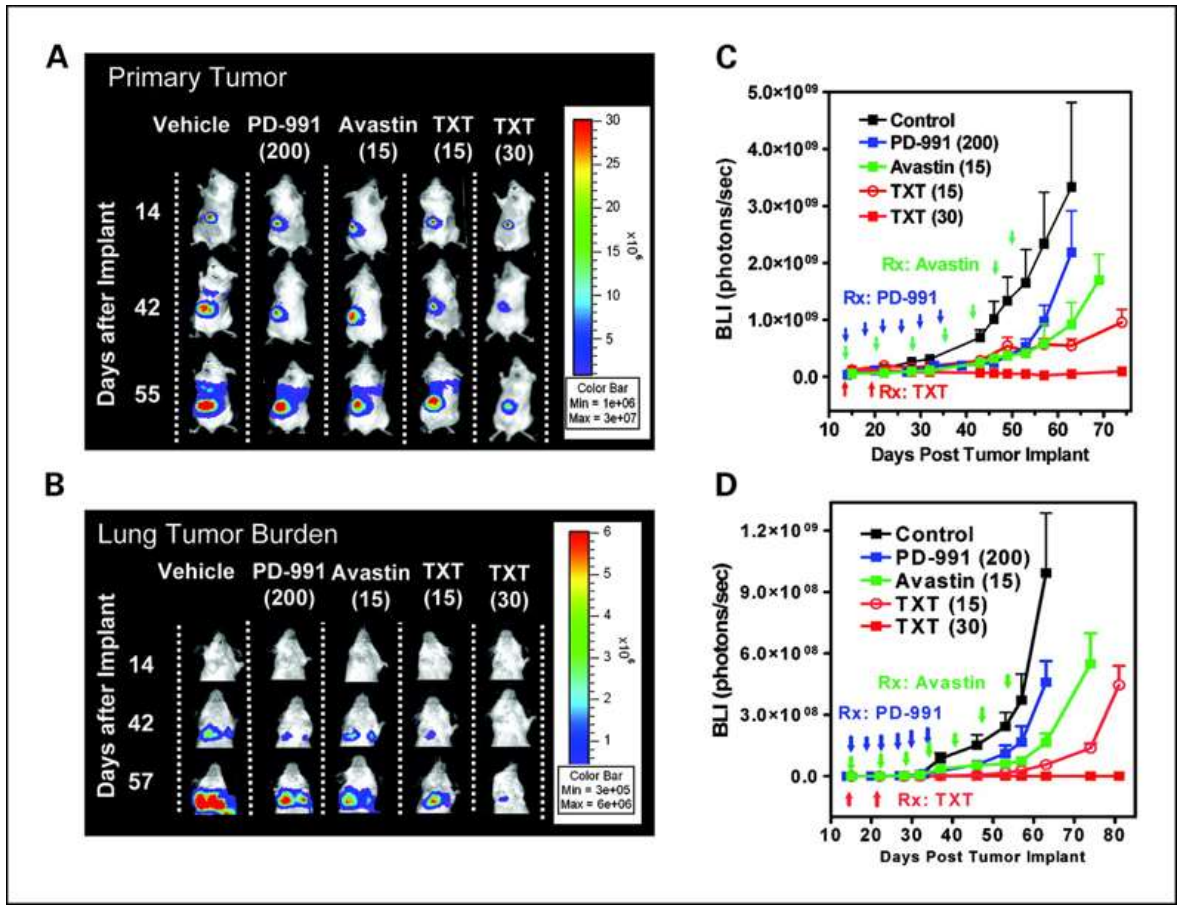
Biophotonic imaging
(tumor cells being killed)

Mendel *et al* 2003



Murray *et al* 2003

Therapeutic Development in a SRC Implantation Model



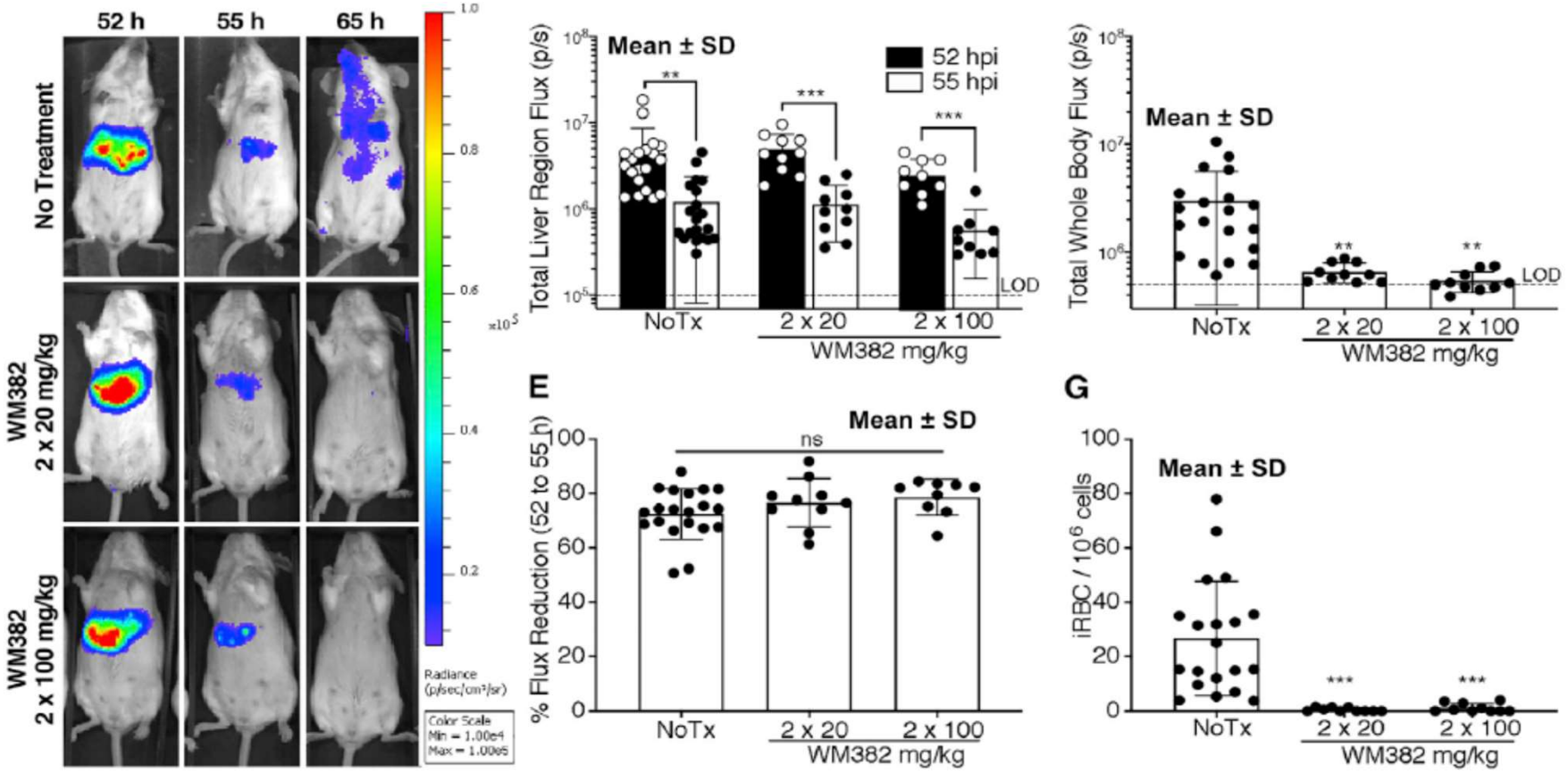
BENEFITS

- Expedites progress towards clinical trials
- Measurable economic benefits include reduced animal costs and personnel
- Simultaneous insights into drug efficacy, kinetics, target, mechanism
- Superior statistics and data reproducibility

Zhang et al, Clin Cancer Res., 2009

Luminescence - Infectious Diseases

In Vivo Imaging Shows Inhibition of *P. falciparum* Blood Stage

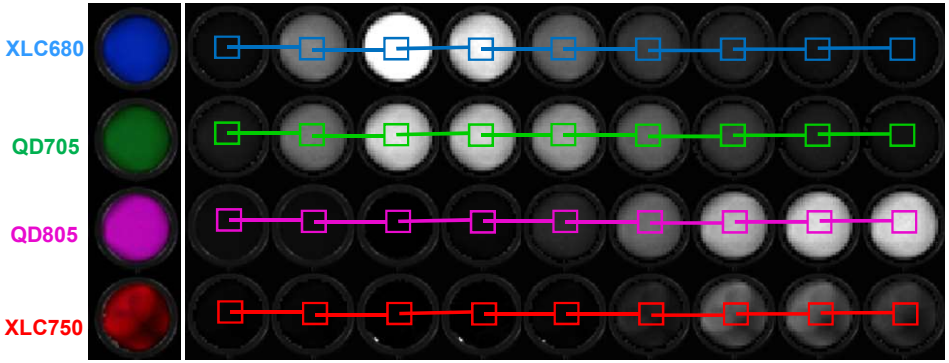


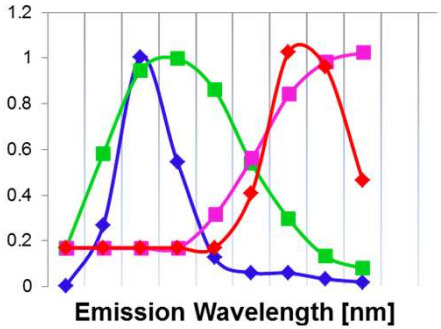
Favuzza et al., Cell Host & Microbe, 2020

Fluorescence - Spectral Unmixing

Spectral Imaging is Essential for Spectral Unmixing

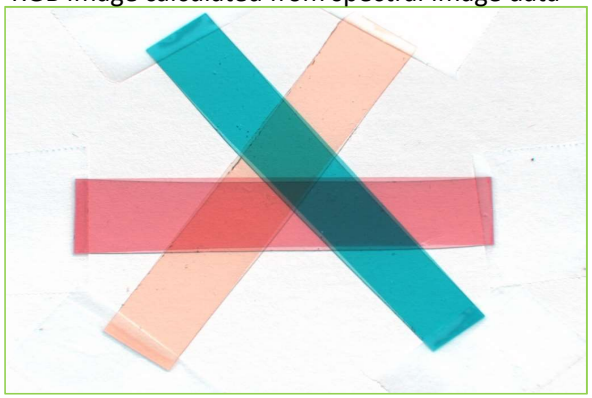
- IMAGES ACQUIRED AT MULTIPLE WAVELENGTHS FOR A SPECTRAL SCAN (EVERY 20 nm)
- BUILDING A SPECTRAL LIBRARY

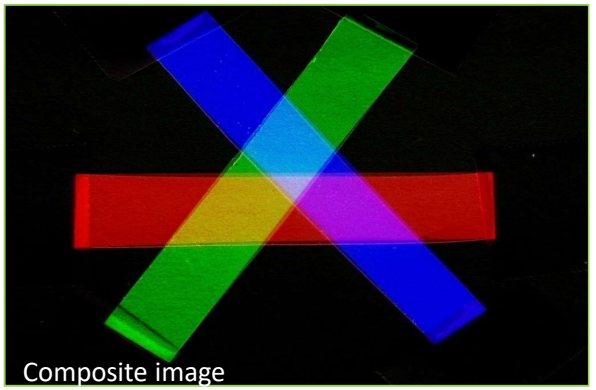




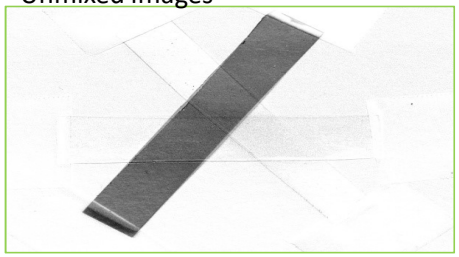
How is Spectral Unmixing accomplished?

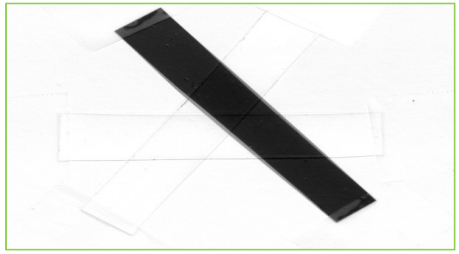
RGB image calculated from spectral image data

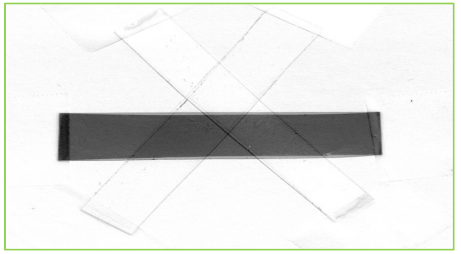




Unmixed images





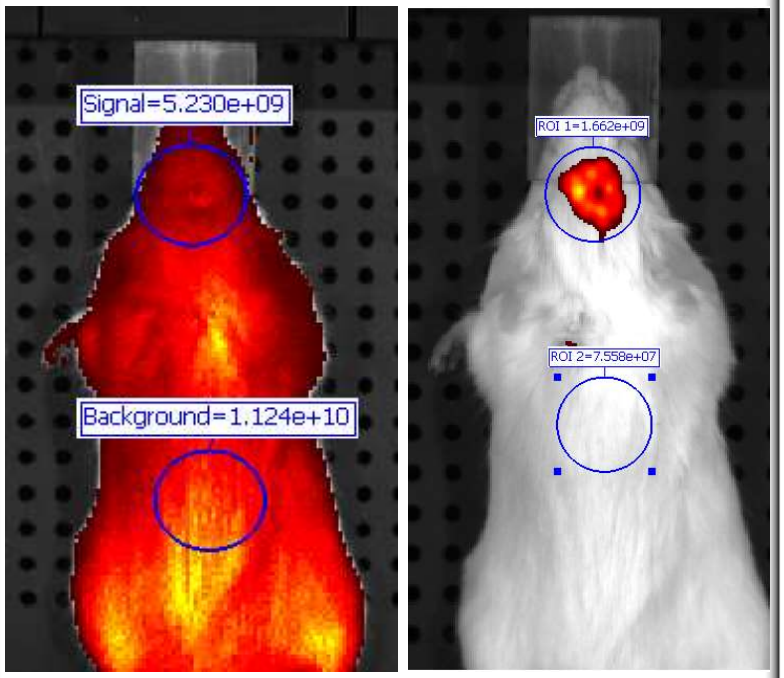


When is Spectral Unmixing Most Useful?

Reduce Autofluorescence to Increase Signal to Noise

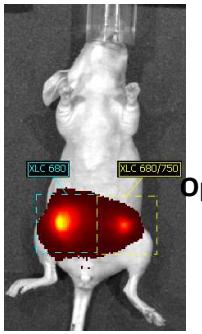
S/N = .46

Unmixed S/N = 22



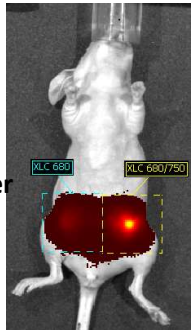
Separate Colocalized Components

XLC 680 left and right
XLC 750 right
Signals indistinguishable
Significant overlap



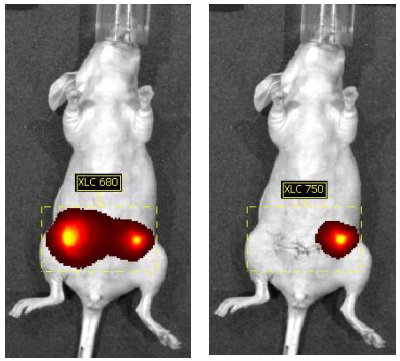
XLC 680 Optimal Filter Pair

XLC 750 Optimal Filter Pair



Unmix

Quantification of Individual Components Possible

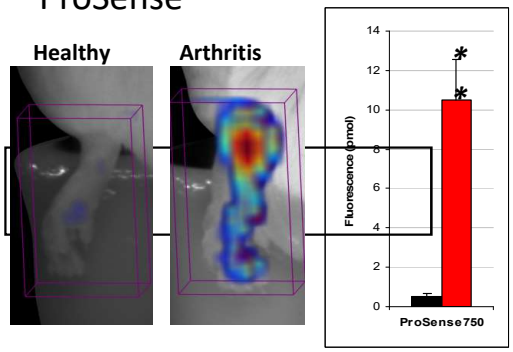


Fluorescent Probes

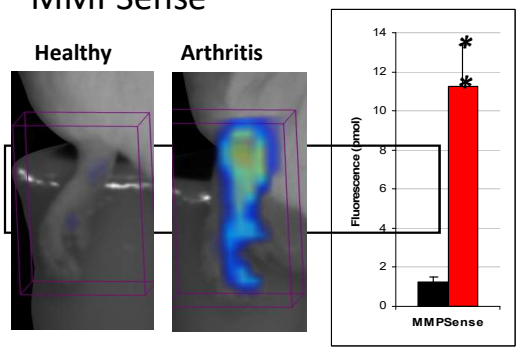
Different Revvity Agents for Imaging Arthritis Biology

INFLAMMATION PROTEASE ACTIVITY

ProSense

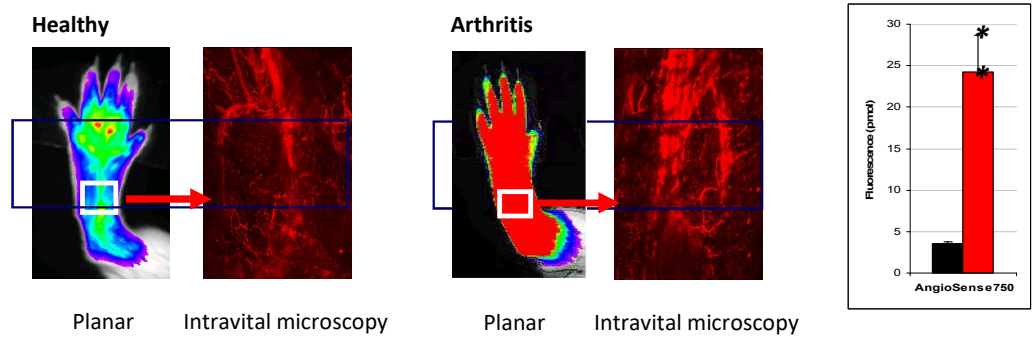


MMPSense



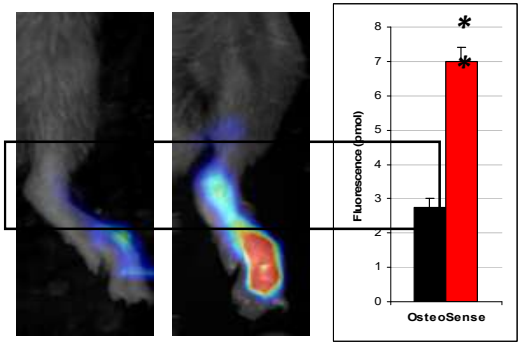
VASCULAR LEAK

AngioSense

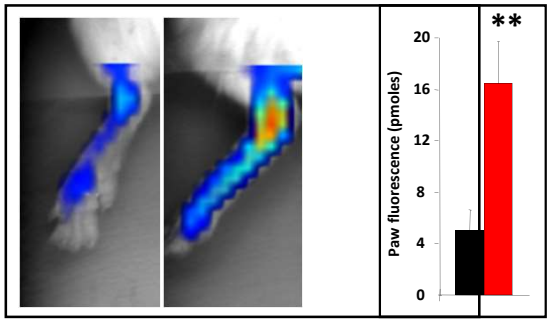


BONE CHANGES

OsteoSense

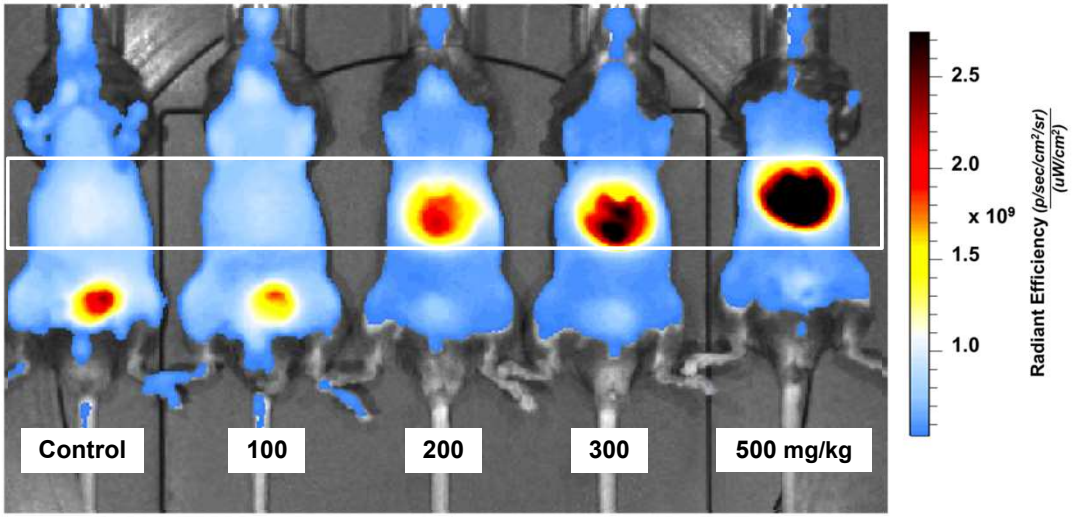


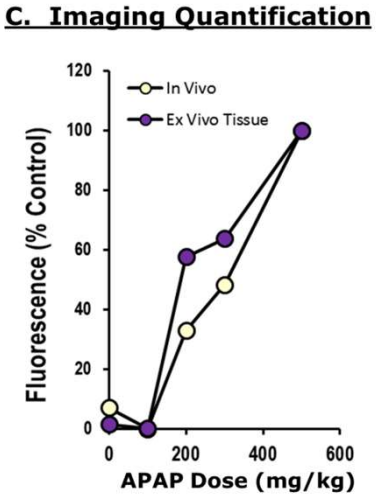
Cat K FAST 680



Toxicology Imaging: Drug Induced Liver Injury

IN VIVO IMAGING





Dose-responsive effects of Acetaminophen/Paracetamol on Annexin-Vivo 750 accumulation in the liver

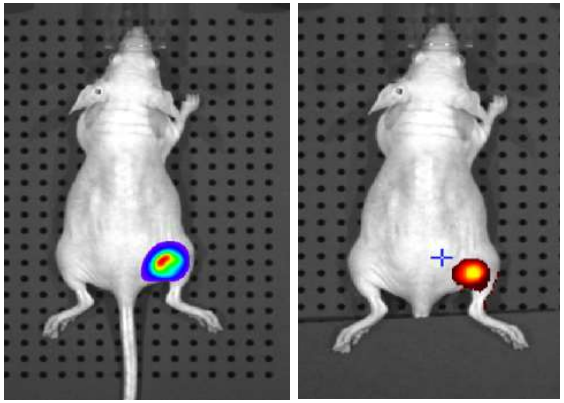
- Normal Annexin-Vivo 750 kidney/bladder clearance altered with increased phosphatidyl serine exposure in the liver
- Ex vivo tissue FL intensity correlates well with in vivo imaging, supporting a robust non-invasive approach to imaging liver tox

Vasquez & Peterson, J Pharmacol Exp Ther., 2017

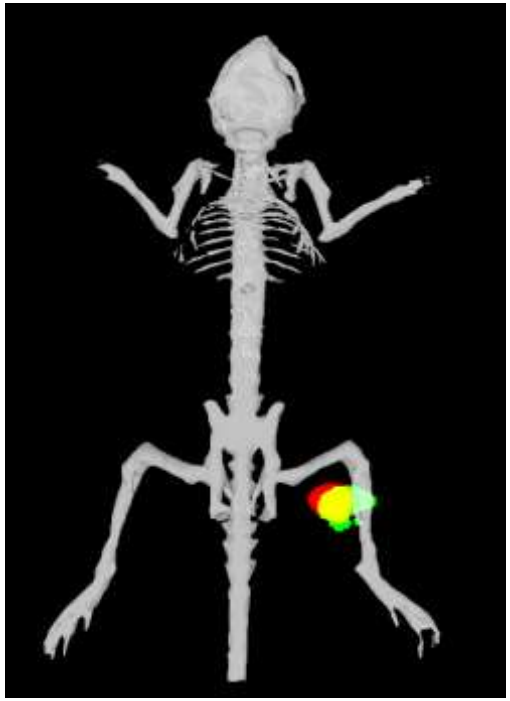
Bioluminescence & Fluorescence - Tomography (3D)

Imaging MMP Activity in Mammary Tumors

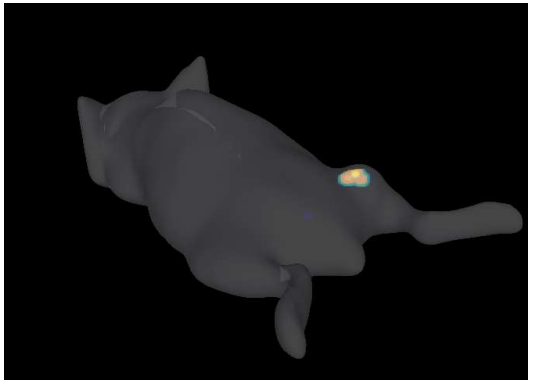
FLANK IMPLANTATION OF MD231 TUMOR TARGETED WITH MMPSENSE680



Bioluminescence Fluorescence



Tomographic Bioluminescence & Fluorescence co-registered with the mouse atlas



Reconstruction with animal surface rendering

Data Courtesy of Andrew Kung, Dana Farber Cancer Institute, Boston MA

Mouse Imaging Shuttle for Co-Registration

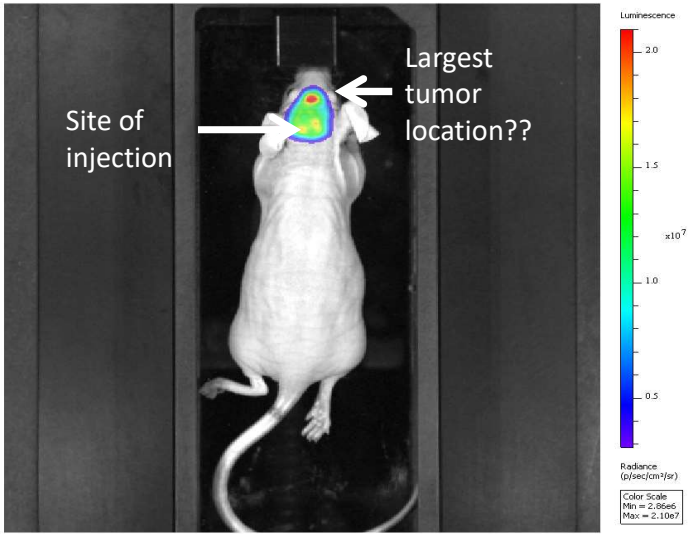
Shuttle Heights:
10, 12, 14 & 25 mm

Optical: IVIS Spectrum

µCT: Quantum GX2

Brain Tumor Model – Absolute Quantification

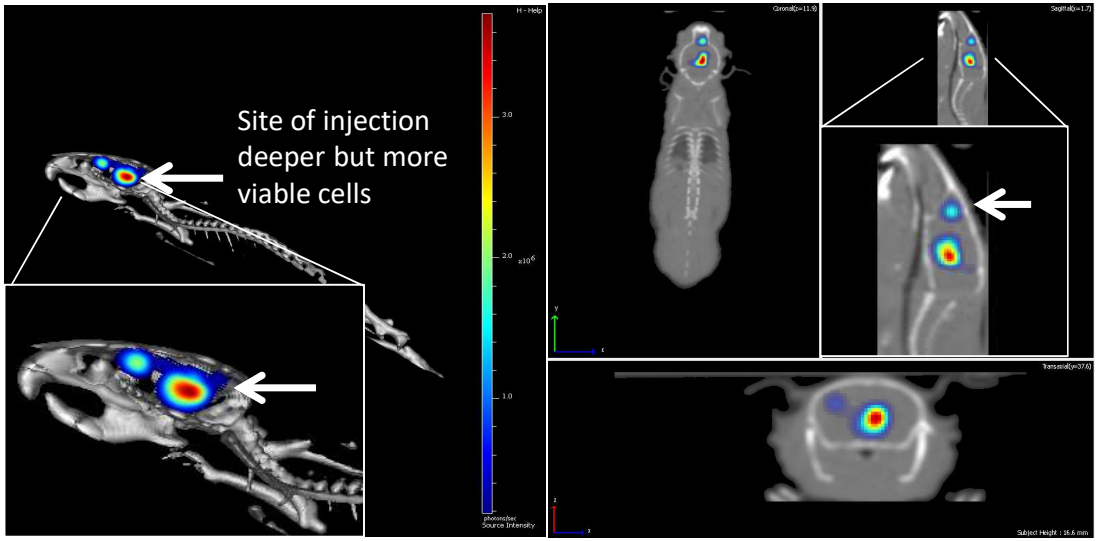
2 D



- 2D acquisition excels at quick high throug-put quantitation over time accurately determining growth, viability and efficacy
- However focal points of signal are dependent on depth of source

3 D

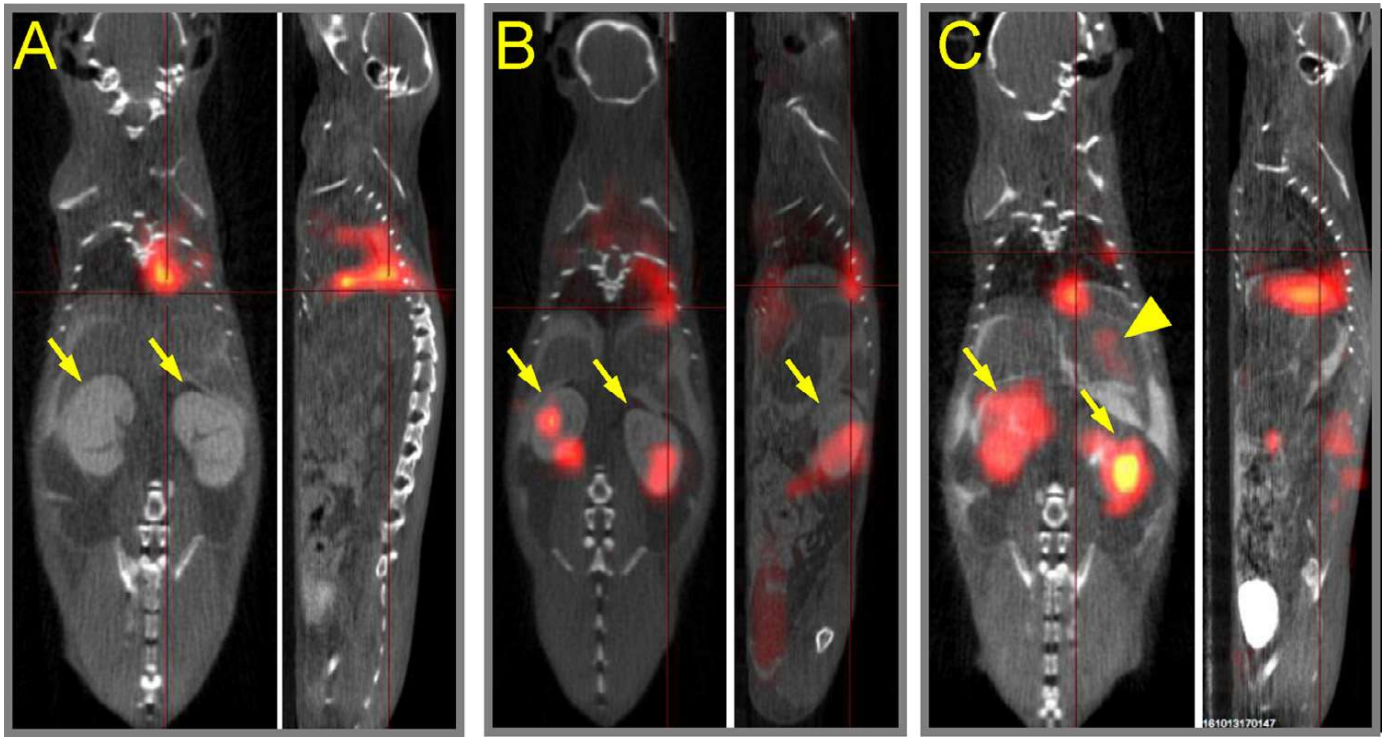
Metastatic lesion shallower thus more intense in 2D however fewer viable cells



- 3D analysis factors in attenuation, scattering, and diffusion
- Pixels clustered based on resultant emission curve thus elucidating differences in depth and intensity more accurately
- 3D imaging can shed lght on both pinpoint localization and depth of source
- Resultant data more representative of actual tumor locations in brain
- Individual tumor locations can be monitored with ease

Biodistribution

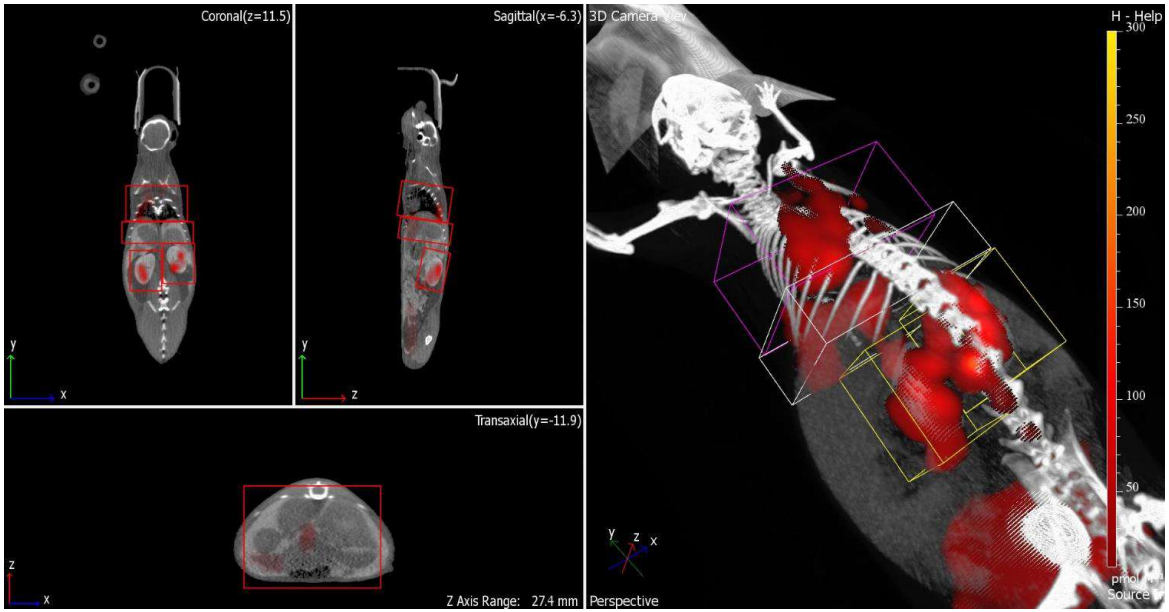
Biodistribution of siRNA after Intratracheal Application in Mice



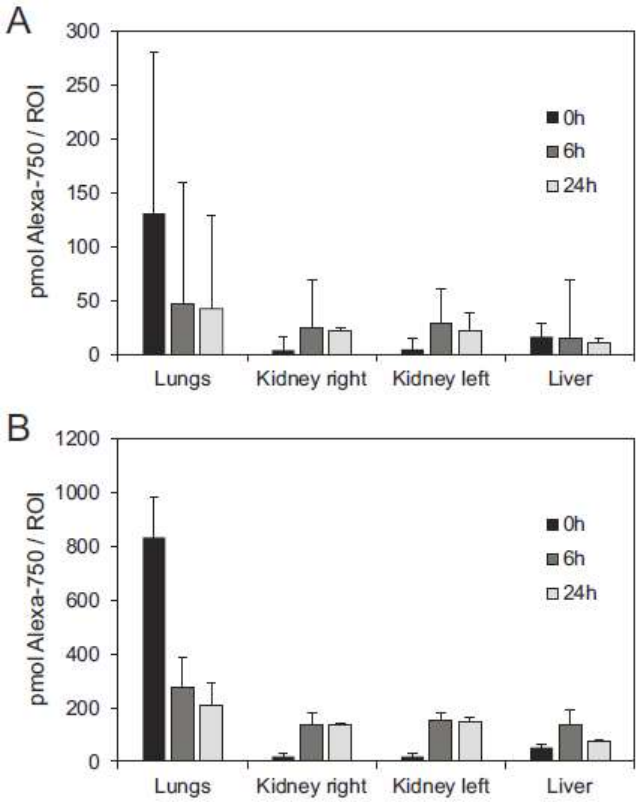
CT/FLIT IMAGING OF AF750-siRNA BIODISTRIBUTION BALB/C MICE

Geyer A et al., Int. J. Pharm., 2017

Biodistribution of siRNA after Intratracheal Application in Mice



CT/FLIT IMAGING OF AF750-siRNA BIODISTRIBUTION BALB/C MICE

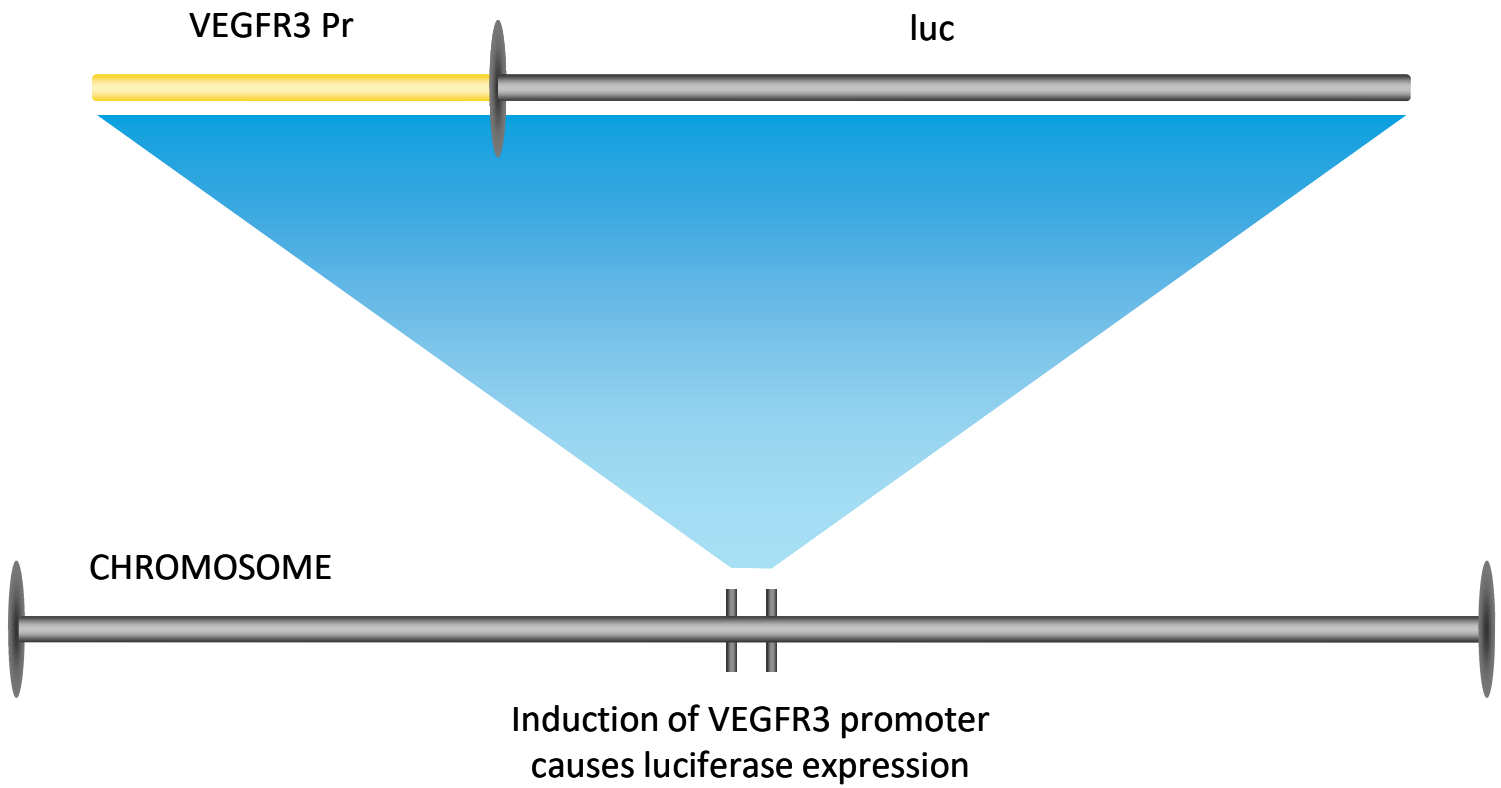


Molecular quantification of AF750 labeled siRNA by FLIT
A: 2.5µg B: 10µg

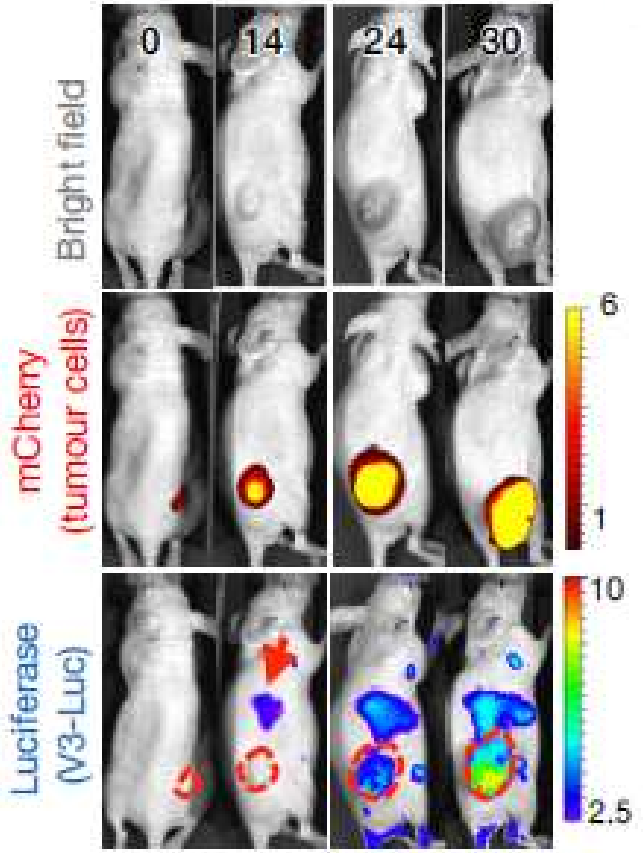
Geyer A et al., Int. J. Pharm., 2017

Transgenic Animals – Molecular Mechanisms

Transgenic Animals:
Vascular Endothelial Cell Growth Factor Receptor 3



Vegfr3^{Luc} Reporter Mice for Imaging of Neo-Lymphangiogenesis



Xenografts of mCherry–SK-Mel-147 cells, imaged in Vegfr3^{Luc} reporter mice for wholebody analysis.

Metastatic relapses were found at later time points (involving skin, lymph node and lung metastases) and were invariably preceded by V3-Luc emission.

Proteomic analyses identify midkine (MDK) as new prolymphangiogenic and pro-metastatic factor.

The heparin-binding factor midkine is a systemic inducer of neo-lymphangiogenesis that defines patient prognosis.

Olmeda et al., Nature, 2017

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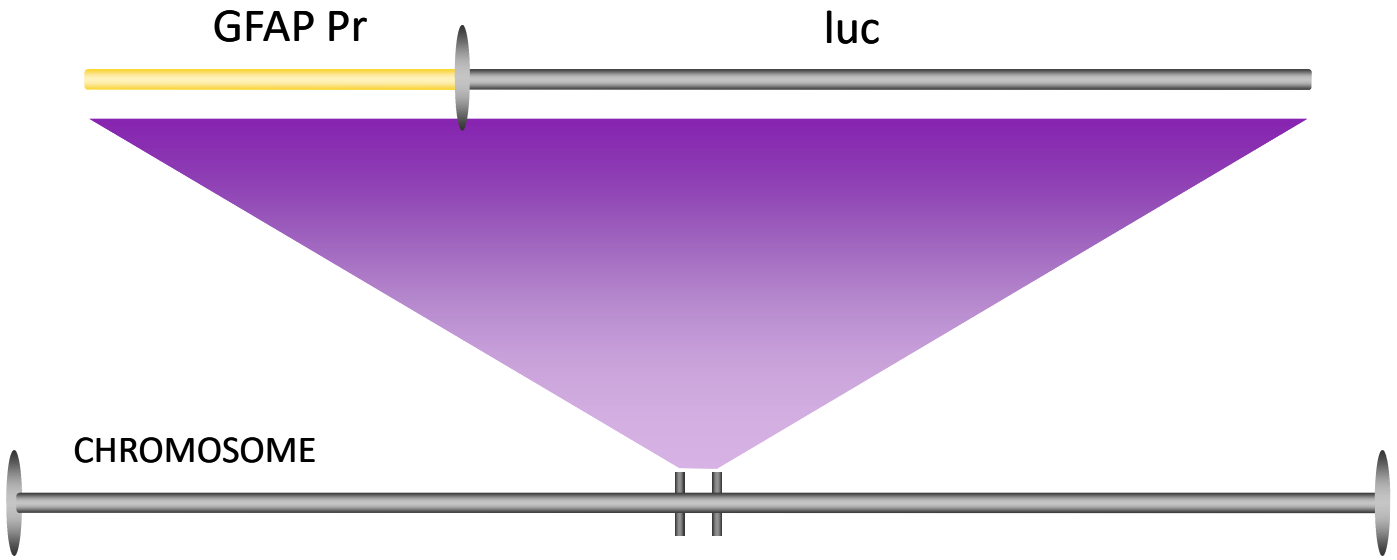
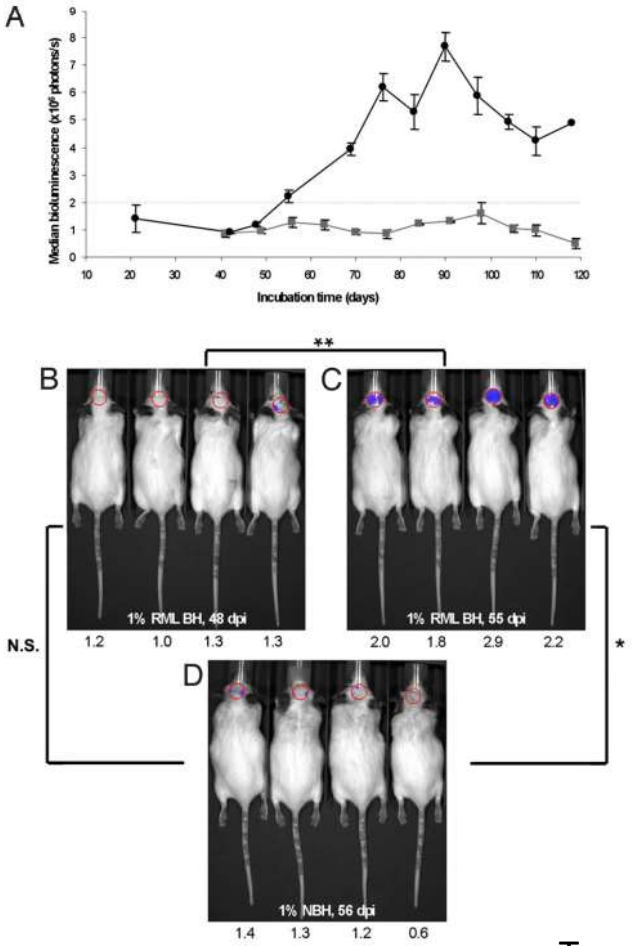
Transgenic Animals:
Glial Fibrillary Acidic Protein - Luc



Intermediate Filament Protein Expressed in Astrocytes
of the CNS Induced by Neuronal Brain Injury

GFAP as a marker for prion disease



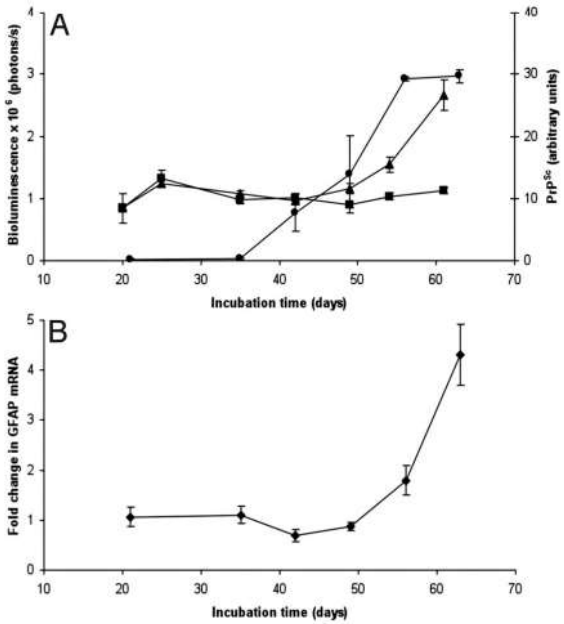


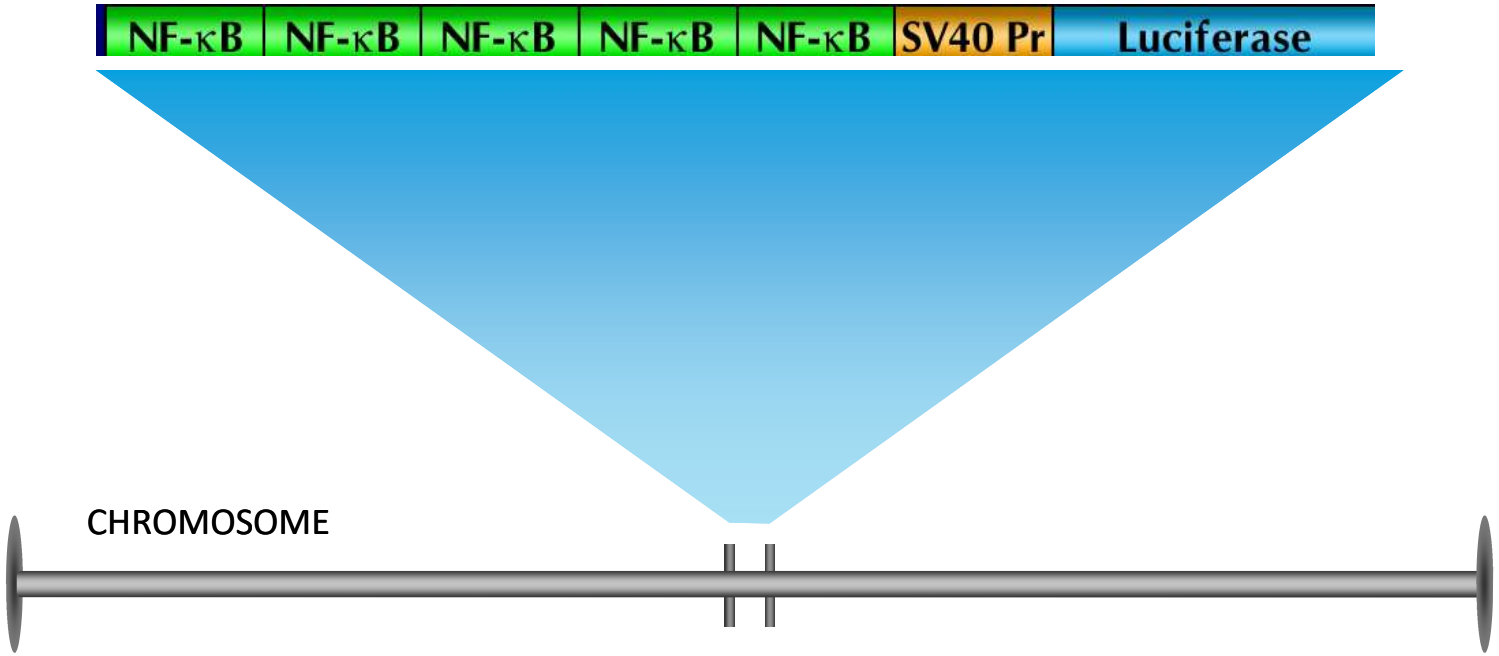
Fig. 2. During prion infection, increases in PrP^{Sc} preceded increases in BL (*A*) and GFAP mRNA (*B*). (*A*) Protease-resistant PrP^{Sc} (circles, right ordinate) in the brains of RML-infected Tg(*Gfap*-luc) mice began to accumulate at 42 dpi and increased steadily. PrP^{Sc} levels were quantified at each time point by densitometry of Western blottings. BL (triangles, left ordinate) in the brains of infected Tg(*Gfap*-luc) mice increased beginning at 56 dpi, ≈14 d after PrP^{Sc} accumulation. BL measured from the brains of control mice inoculated with 1% NBH did not increase (squares). (*B*) Correlating with an increase of BL, GFAP mRNA also increased at ≈56 dpi. Error bars indicate the SE, based on at least 9 mice for BL measurements and 3 mice for all other measurements.

- Tg(Gfap-luc) mice
- Detection of light 55 days post inoculation
- 62 days before appearance of neurological deficits

"BLI bioassays were as or more sensitive than those determined by the onset of neurological dysfunction, and were completed in approximately half the time."

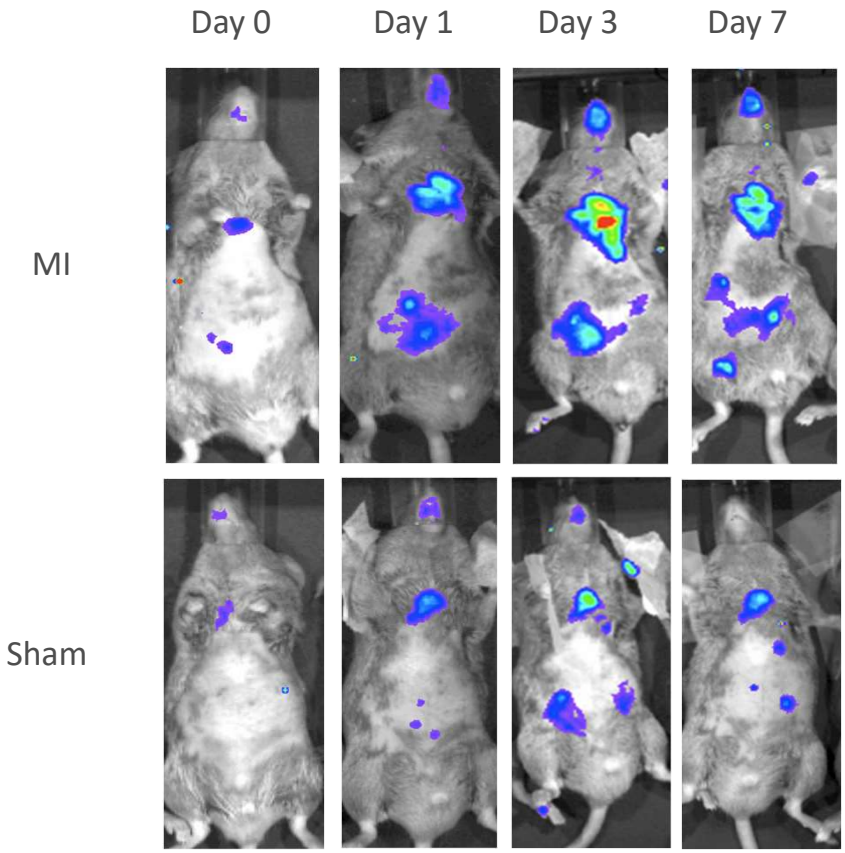
Tamgüney et al., PNAS, 2009

Transgenic Animals:
NF-κB-RE-luc



- Immune Cell Regulation
- Cytokine Signaling
- Inflammation

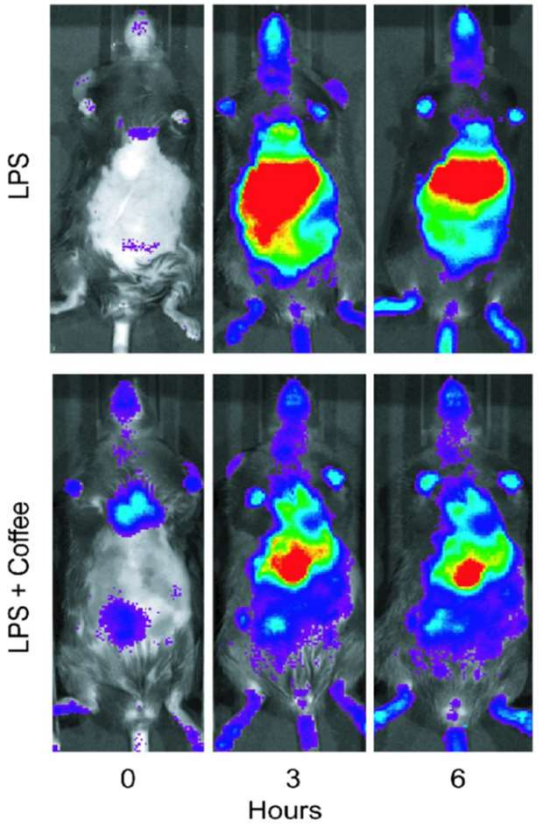
NF-κB is Increased After Myocardial Infarction

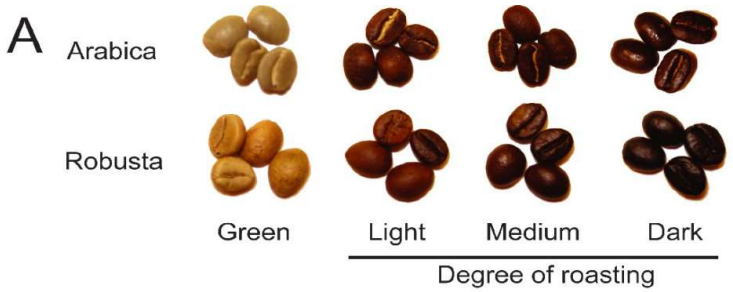


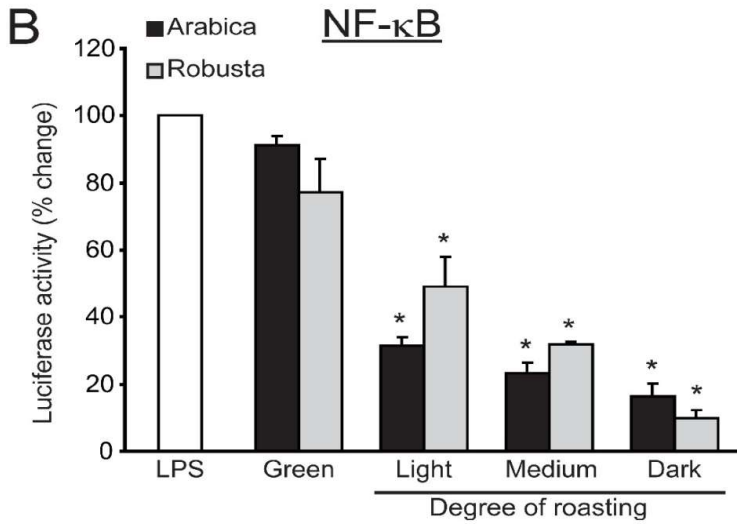
Tillmans et al, Biophys. Biochem. Res. Comm., 2006

Effects of Coffee on NF-κB Activity

Transgenic NF-kB reporter mice were given a single dose of coffee extract by oral gavage 3h prior to s.c. LPS injection (at 0h). A) The luciferase activity was measured by *in vivo* imaging at 0h, 3h and 6h







Paur et al., Free Radical Biology and Medicine, 2010

revvity