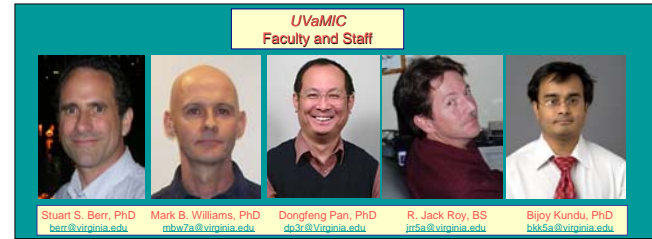


The UVa Molecular Imaging Core Lab (UVaMIC)



Stuart S. Berr, Ph.D., Laboratory Director;
Mark B. Williams, Ph.D., Faculty Director



Background

The UVa Molecular Imaging Core Lab began 17 years ago. It began as a facility for imaging intact small animals, in particular mice and rats. We have since added capabilities for the synthesis of targeted imaging agents. There is an expressed need on the part of medical researchers for *in vivo* assessment of genetically altered mice. The genetic code of mice is similar to humans as are the spontaneous genetic abnormalities they undergo, and there are a number of well characterized existing genetically altered mice. These genetically altered mice include several immuno-compromised lines which are useful for growing human cancer cells lines *in vivo* that would be rejected by normal mouse models. Using traditional histological means of analysis, our ability to characterize efficiency and location of applied gene therapy, to screen for genetic mutations, and to assess physiological changes caused by genetic alterations is inefficient and limited. Development in these areas is greatly facilitated by the availability of noninvasive imaging techniques. Imaging mice requires tools designed specifically for this task.

Services

The UVaMIC provides:

- Consultation on small animal imaging projects
- Magnetic resonance imaging and spectroscopy
- Dual modality X-Ray CT and Single Gamma Computed Tomographic (SPECT) Imaging
- Positron Emission Tomography (PET)
- Bioluminescence and Fluorescence Imaging
- Production of custom targeted imaging agents
- Image processing
- Training in the operation of the imaging equipment

Recent Highlights

- Receipt of NIH-NCRR High End Instrumentation (\$1,980,000, May 2005) for purchase of High Field MRI
- Acquisition of 5 new major instruments (see Equipment/Resources)
- Renovation of MR imaging suite in MR4 to make space for the new high field imaging system
- An institutional investment of approximately \$1,330,000 funded renovation of space and purchase of new imaging equipment.
- Excluding annual support for the operating budget, the total support for the SAMMIC since 1999 (equipment and renovations) is \$3,310,000, with 60% of this coming from the NIH.

Advisory Committee

Sarah Parsons, Ph.D., Professor of Microbiology and Associate Director Of Laboratory Research, Cancer Center
G. Paul Matherne, M.D., Professor of Pediatrics, Chair for Pediatric Research
Brian Duling, Ph.D., Professor of Molecular Physics and Biophysics

ClinScan 7.0T MRI



Xenogen IVIS Bioluminescence / Fluorescence



Equipment/Resources

MRI. Siemens/Bruker 7.0T ClinScan High Field small animal MRI/MRS system (Installed April 2007: \$2M NIH-NCRR High End Instrumentation Grant)

MRI. Varian Direct Drive 4.7 Tesla MRI with Magnex magnet and gradients

Micro-PET. Siemens Focus 120 Micro PET Scanner.

Bioluminescence/Fluorescence. Xenogen IVIS Scanner.

Dual Modality X-Ray CT and SPECT Scanner. Developed and built in-house by MB Williams, PhD.

Varian 4.7T MRI



Micro PET - Siemens CTI Focus 120



CT/SPECT Imaging System



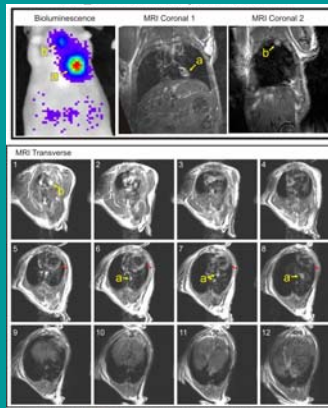
Bioluminescence and MRI

Bladder Cancer Lung Metastasis Model:

Upper left: Bioluminescence image (BLI) in color overlaid on a photograph of the mouse (grayscale) that was acquired with the Xenogen IVIS scanner 20 minutes after injection with luciferin. Animal had been injected 3 weeks prior to imaging via tail-vein with 10^5 LUC-tagged EJ bladder cancer cells injected in 100mL via tail vein.

Top Middle and Left, and lower panels: Gd-DTPA enhanced magnetic resonance images (MRI). Top: of coronal planes at two different spatial positions indicate two tumors located within the lungs. Lower panels are transverse MR images that confirm the tumors are not in the heart (red arrows indicate the heart). Corresponding lesions between the BLI and MRI are indicated by the letters (a and b) on the images.

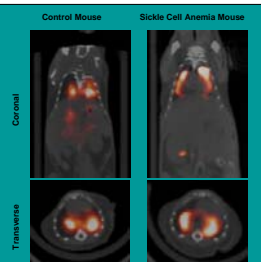
Acknowledgments: Kevin McRoberts BSc, Yimin Wu, PhD, and Dan Theodorescu MD PhD



CT-SPECT

This set of SPECT-CT images compares the lung vascularity of a normal (control) mouse with that of a mouse with sickle cell anemia using the intravenously injected tracer ^{99m}Tc -MAA (macroaggregated albumin). The images demonstrate that, compared to the normal mouse, the tracer distribution (shown in color) in the sickle cell mouse was confined to the lateral portion of the lungs, with little medial penetration. This suggests poor medial vascular structure, which was confirmed by pathology.

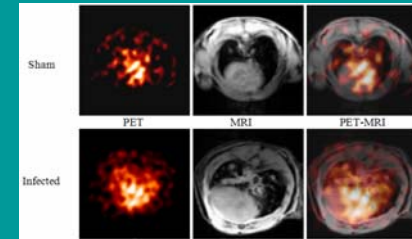
Acknowledgments: Joel Linden, David Glover, Kori Wallace, Joe Pole, Mark B Williams



Targeted Imaging Agents

The UVaMIC chemistry lab produces radiolabeled targeted imaging agents. In this example, we synthesized neutrophil-specific peptide agent for PET imaging of inflammation caused by infection. The PET agent was cinnamoyl-F(D)LF(D)LF-PolyEthyleneGlycol- ^{64}Cu (cFLFLF-PEG- ^{64}Cu). PEG was added to decrease liver uptake. Respiratory gated PET images were acquired with the Focus 120, and MRI with the ClinScan MRI. Pneumonia was induced in C57Bl/6 mice by oropharyngeal aspiration under light inhalational anesthesia of 10^6 colony forming units of *Klebsiella pneumoniae*. A significant difference in uptake was noted between the infected and control mice.

Acknowledgments: Dongfeng Pan, Landon Locke, Bijoy Kundu, Yi Zhang, Karen Fairchild, Stuart Berr, Joel Linden.

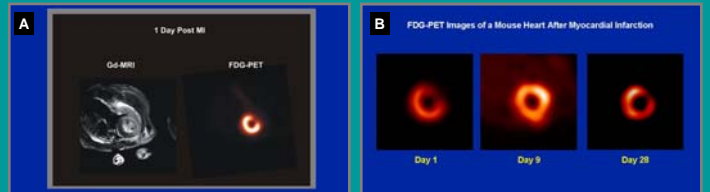


PET and MRI

Myocardial Infarction in Mice

Methods have been established in the SAMMIC to image the mouse heart using magnetic resonance and PET with ^{18}F fluorodeoxy glucose (FDG). **A.** The images below were acquired from the same mouse on the same day, one day after ischemia-reperfusion (IR) injury. The infarcted area becomes bright in the MR image after injection of Gd-DTPA. FDG does not accumulate in the infarction, and results in an area of hypointensity in the PET image. **B.** Nine days after IR, the area of infarction (confirmed by MRI) becomes hyperintense due to the utilization of glucose by infiltrating macrophages. After 28 days, the macrophages are no longer active in the infarction, and the PET image again become hypointense.

Acknowledgments: Stuart Berr, Brent French, Fred Epstein, Bijoy Kundu, Jack Roy, Mark Williams.



PET, X-Ray CT, Optical

Metastatic spine disease with Human Breast Cancer Cells. Sagittal micro-PET (left) and microCT (middle) images. Note the advanced L5-L6 osteolytic spine tumor with extension into the posterior surrounding soft tissue on CT. This corresponds to the increased ^{18}F -FDG uptake on micro-PET (arrows). Bioluminescence imaging (extreme right) with luciferase-labeled MDA-MB-231 cells (MDA-MB-231-D3H1) on post-operative day 5. The signal is in the proximity of L5-L6 vertebral body.

Acknowledgments: Shen-Ying Ma, Francis Shen, Luke Choi, Christopher McKenna, Bijoy K. Kundu, Xudong Li, Khalid Mohammad, Theresa Guise, The European Spine Journal (submitted), 2007.

