UAB SAIF ISSUE 7 2020
SMALL ANIMAL IMAGING FACILITY

NEWS & UPDATES

IMAGING IMMUNE RESPONSE
IN PRECLINICAL MODELS

The Small Animal Imaging Facility provides a centralized environment for researchers with various instrumentation dedicated to in vitro and noninvasive in vivo imaging. These imaging methods enable further insight into the biological processes and behavioral compositions of certain diseases, contributing viable data for research in disease progression and treatment development. Imaging the immune system and associated response has been of particular interest in a wide variety of diseases.

Noninvasive imaging methods, such as molecular imaging with PET/CT and optical imaging, have helped in development and observation of immunogenic, cell-targeted and virologic forms of therapeutic treatments. Preclinical studies have been carried out to look at immune response through autoimmune cell tracking, white blood cell labeling, and observe the biological impact of immunotherapeutic approaches, which can provide detailed information on disease mechanisms. These methods have made it possible to observe regulatory pathways and characteristics of adaptive immunity to potentially alter disease progression.

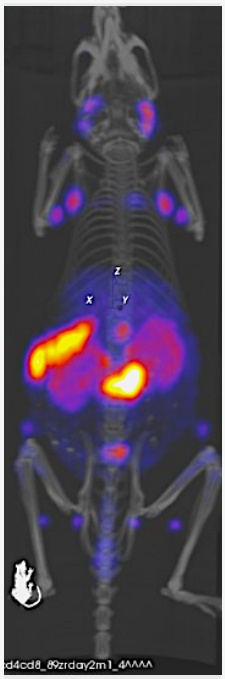


Figure 1: Biodistribution of ^{89}Zr with CD4 minibody to show accumulation in lymph nodes and spleen 24-hours post-injection. (Dr. Suzanne Lapi's Lab/Dr. Hailey Houson, UAB)

White blood cells recruited at the onset of a triggered immune response can be used for autoimmune cell tracking and analyzing roles of endogenous cells in homeostatic maintenance and immune defense. Through the use of radionuclide imaging (e.g. PET), cytologic behaviors can be observed and delineated because of high sensitivity with anatomical information provided from high-resolution CT. PET imaging offers absolute quantification and higher sensitivity, making it capable of in vivo cell tracking.[1] Indirect cell labeling can be achieved by using the PET isotope Zirconium-89 (^{89}Zr), which is bound to radiometal complexed hydroxyquinoline (oxine) chelators that induce cellular uptake via diffusion or transport mediated processes. With the use of this PET tracer, researchers can gain insight into the role modulation of these immune cells (or other labeled cells of choice) and their correlative effects on disease progression, providing information to devise rational therapeutic strategies in longitudinal experimental settings.[2]

PET imaging techniques can be used to further assess immune response and the efficacy of immunotherapy through tracer targeted methods including Granzyme B, a serine protease released by CD8+ T-cells and natural killer cells when actively engaged. In an oncological study, ^{68}Ga-NOTA-GZP, a recently developed tracer by an investigator at UAB, binds to Granzyme B and detects the protease through tumoral uptake of the PET tracer, allowing visualization of potential cytotoxic T-cell activity within tumor sites. These results indicate the significant role of Granzyme B as a biomarker of active cytotoxic immune response and in the interrogation of multiple tumor sites to predict immune response to therapeutic treatments.[3]

Preclinical use of bioluminescent (BLI) and fluorescent optical imaging provide additional approaches to observing immune response. Both BLI and fluorescent imaging allow investigators to monitor cellular activity and offer capabilities to track cells integral to tumor development and related immuno-oncology. Targeting fluorescent imaging probes or cells tagged with luciferase reporters are effectively detected using a highly sensitive camera that converts emitted signal into pseudo-colors of varying intensities. Preclinical oncologic and bacterial or virologic models permit investigation into immune-specific pathways and the effects of immunotherapeutic treatments. Optical imaging can assist in visualizing and providing semi-quantification of cellular or protein accumulation or dissipation in specific regions correlating to immune response, as well as *in vitro* analysis of cytologic activity. This imaging technique can allow a better understanding, from an in vivo standpoint, of immune infiltration of cancerous cells and the role that the immune system plays in tumor development, while also enabling the ability to gather useful information regarding specific cellular characteristics *in vitro*.

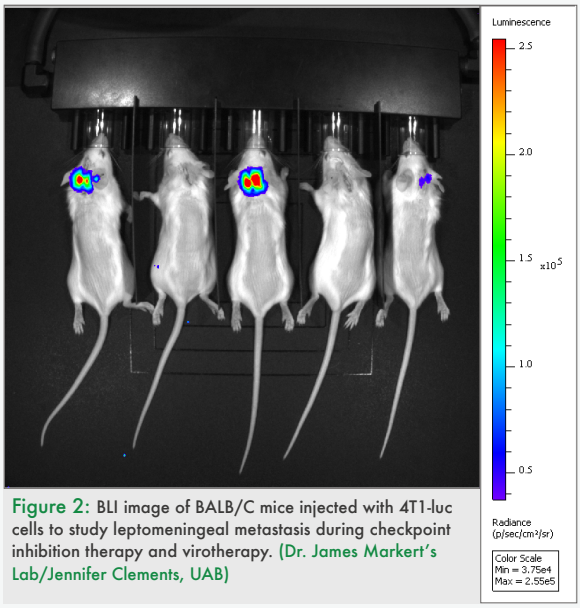


Figure 2: BLI image of BALB/C mice injected with 4T1-luc cells to study leptomeningeal metastasis during checkpoint inhibition therapy and virotherapy. (Dr. James Markert's Lab/Jennifer Clements, UAB)

With the ability to isolate and observe various components of the immune system through radionuclide labeling and optical imaging, experimental approaches encourage development of treatment plans and formulation of pharmaceuticals to address biological mechanisms. Through appropriate integration of preclinical imaging techniques alongside sound experimental procedures, effective data can be collected to investigate probable treatment strategies for infectious and non-infectious diseases.

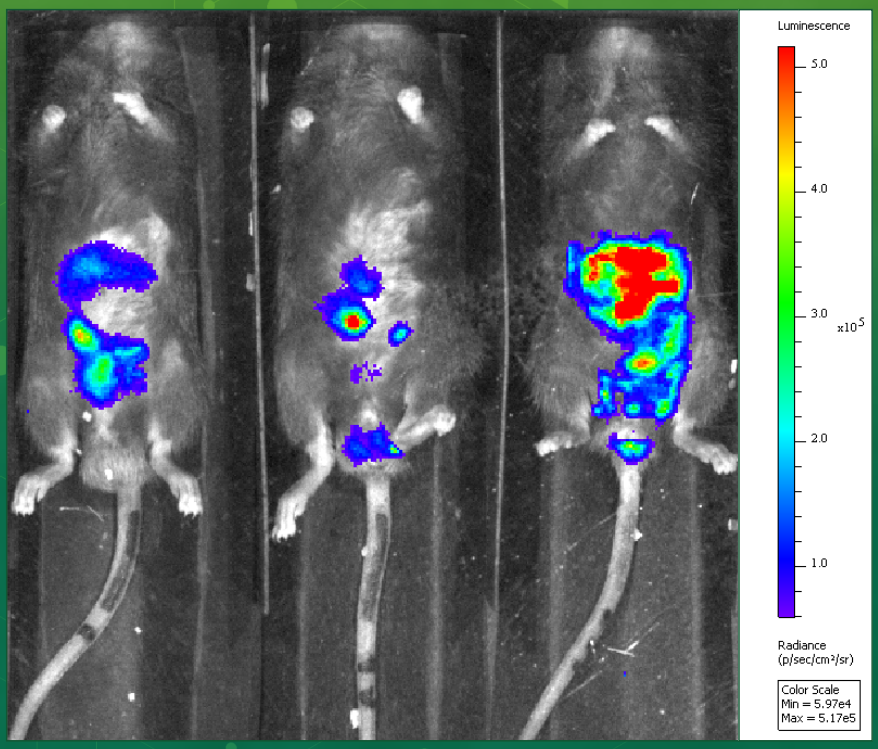
1.Iafrate, M. and G.O. Fruhwirth, How Non-invasive in vivo Cell Tracking Supports the Development and Translation of Cancer Immunotherapies. Frontiers in Physiology, 2020. 11(154).
2. Fairclough, M., et al., A new technique for the radiolabelling of mixed leukocytes with zirconium-89 for inflammation imaging with positron emission tomography. Journal of Labelled Compounds and Radiopharmaceuticals, 2016. 59(7): p. 270-276.
3. Larimer, B., et al., Granzyme B PET Imaging as a Predictive Biomarker of Immunotherapy Response. Cancer Research, 2017. 77: p. 2318-2327.

Please acknowledge support of SAIF services in grants and publications by citing the O'Neal Cancer Center Grant P30CA013148.

For data obtained with the IVIS Lumina III systems, please cite S10 instrumentation grant 1S10OD021697.

For kidney related imaging, cite the grant DK079337 and acknowledge UAB-UCSD O'Brien Center support.

FEATURED IMAGE OF THE QUARTER



NEUTROPHILIC RESPONSE TO CITROBACTER RODENTIUM (C.R)

A bioluminescent (BLI) image acquired using the IVIS Lumina that depicts Cybb knockout (KO) mice infected with *Citrobacter rodentium* luciferase strain localized in the gut. Cybb is part of the NADPH oxidase complex involved in reactive oxygen species (ROS) production. Many immune cells, including neutrophils, utilize ROS to kill the bacteria during host immune response. The goal of this study was to monitor the effects of Cybb knockout on the host immune response against *Citrobacter rodentium* bacteria.

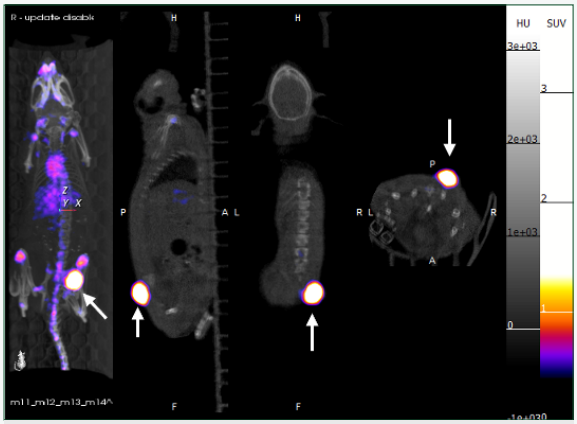
IMAGING CREDIT: Dr. Casey Weaver
Baiyi Cai, Graduate Research Assistant

FEATURE SPOTLIGHT

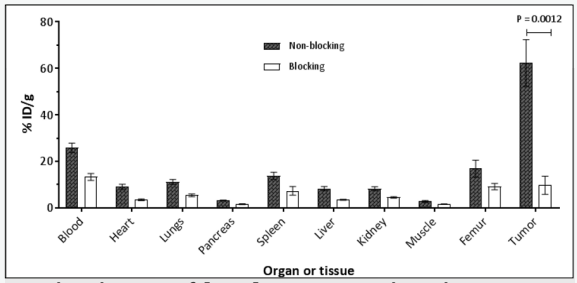
BIODISTRIBUTION

Dosimetry, or accumulation of radio-compounds in organs and tissues of preclinical models, can be quantified through biodistribution. This procedure relies on the radioactive compound to be injected into the preclinical model (usually via intravenous injection) followed by euthanasia and extraction of organs of interest at specific time-points post-injection. The organs are then weighed and radioactivity measured in a gamma-counter to assemble data pertinent for observing quantifiable trends related to absorption and accumulation of specific compounds and pharmaceuticals.

Small Animal Imaging Facility personnel are capable of performing biodistributions and dissecting a vast number of organs. This can provide investigators with information for understanding compound secretion and mechanistic details regarding their models.



PET-CT image of [89Zr]Panitumumab acquired 7 days post-injection in nude mice bearing PDX tumor EGFR+ (white arrows). Images and biodistribution done for Dr. Hope Amm.



Biodistribution of [89Zr]Panitumumab 7 days post-injection. Images and biodistribution done for Dr. Hope Amm.

USEFUL LINKS

↗ PRE-CLINICAL IMAGING CALENDAR
Check for any available time slots for imaging modalities.

↗ TRAINING FORMS
Download training material for submission prior to scheduling imaging.

↗ PERKIN ELMER RESOURCES
Educational material related to the IVIS Lumina III.

↗ DEPARTMENT OF RADIOLOGY
Homepage for UAB's Department of Radiology.

↗ O'NEAL COMPREHENSIVE CANCER CENTER
Homepage for O'Neal Comprehensive Cancer Center at UAB.

↗ O'BRIEN CENTER
Homepage for O'Brien Center for Acute Kidney Injury Research.

↗ UAB CYCLOTRON FACILITY
Homepage for UAB's Cyclotron Facility.

DID YOU KNOW?

In the modified business model, there are changes currently being implemented within the **Small Animal Imaging Facility**. A few of those changes include the following:

- Remote training
- New cleaning procedures for staff and facility users
- Imaging schedule changes (required 15-minute gaps between appointments
- Social distancing of six feet required for both staff and facility users. **Experiments requiring more than one individual working together require both PI and Core Director Approval**
- Required PPE within facility space

For more information, please feel free to contact SAIF Core Personnel.

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MAIN LAB

Volker Hall Laboratory
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IMAGING FACILITIES

WTI Imaging Suite
WTI 630D

MRI 9.4T Imaging Suite
LHL B15, 934-0265

Volker Hall Imaging Suite
VH B21A, 975-6466

SAIF MODALITY PRICING

*Labor charges are $40 per hour (for each personnel), when assisted during imaging.

Prices effective 11/1/2018.

*Training is available on some modalities, free of charge.

MODALITY	COST	INSTRUMENT
Bioluminescence	$7/mouse OR $55/hour (re-agent dependent)	IVIS Lumina III
Fluorescence	$55/hour	Custom Leica microscope with Nuance CRI spectral camera
		IVIS Lumina III
Ultrasound	$75/hour	Vevo 660
MRI	$125/hour	Bruker 9.4T
SPECT/CT	$100/hour + dosing	XSPECT system
PET/CT	$200/hour + dosing	Sofie GNEXT PET/CT
Gamma Camera	$20/hour + dosing	Picker Camera with Numa computer
Specialty Fluorescent Imaging	$100/hour	Li-Cor Pearl Impulse
		Luna/SPY Systems
		FMT 4000
Staff Image Analysis	$40/hour	

*NON-CANCELLATION POLICY:
If user is not present at scheduled appointment time without prior notification of cancellation, user will be charged an hourly-use fee for that instrument.

IMAGE SUBMISSIONS

Submit images that you would like featured in the newsletter to **erikanmc@uab.edu.** Please include PI's name, modality, brief experiment summary, and species.

PUBLICATION REFERENCE

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