

SPARTAN RESEARCH CORES



MICHIGAN STATE
UNIVERSITY

SPARTAN

Research Cores

*Shared Research Resources at
Michigan State University*

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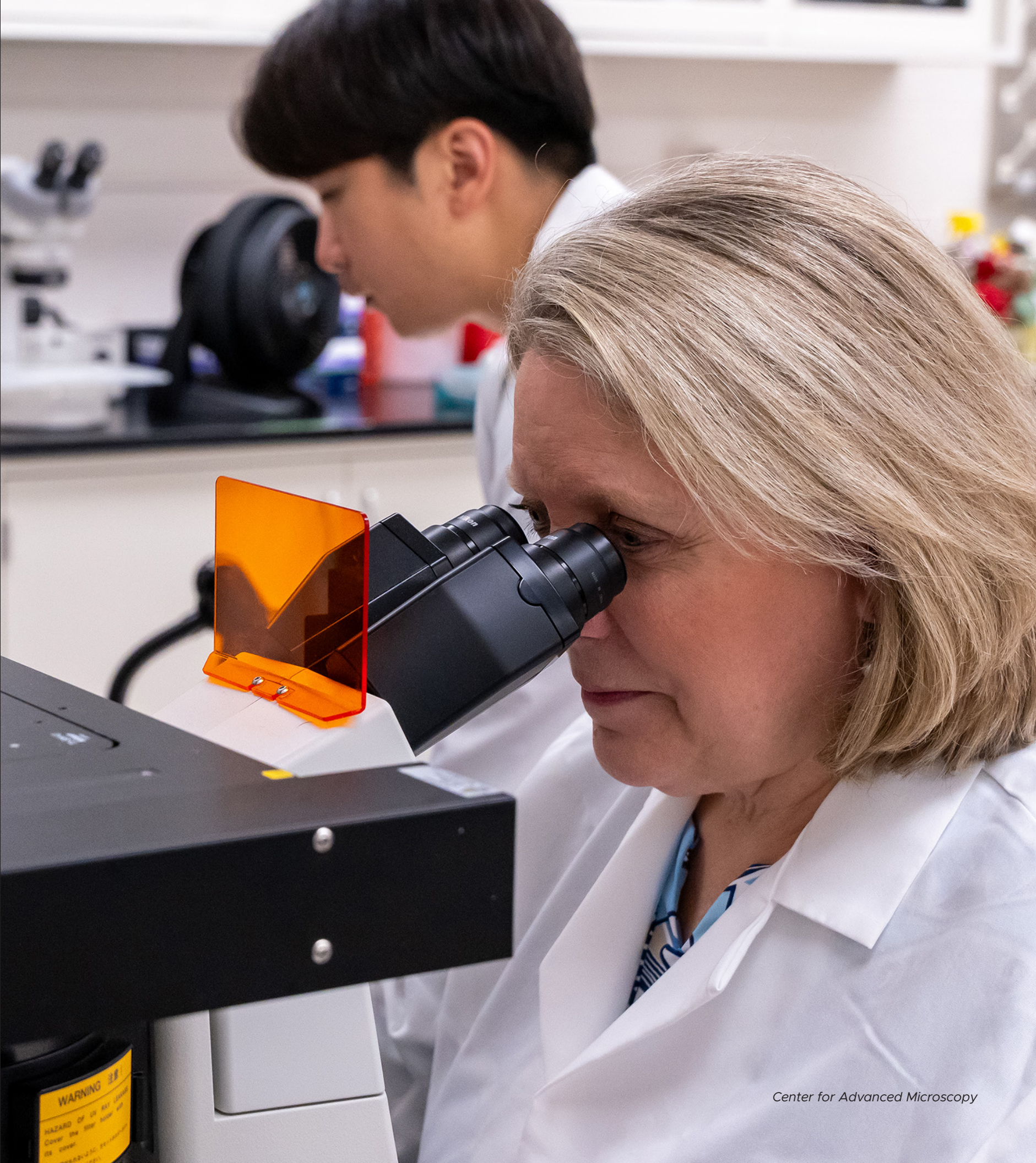
This booklet highlights a selection of Michigan State University’s shared research resources, offering a snapshot of the tools, expertise, and capabilities that support collaborative research.

View the **Shared Research Resources Webpage** for a comprehensive listing of resources available to MSU researchers.
research.msu.edu/srr



Spartans Will.

*Design: Tanya Bakija
Photography: Tanya Bakija, Michelle David
Project Lead: Matthew Bernard
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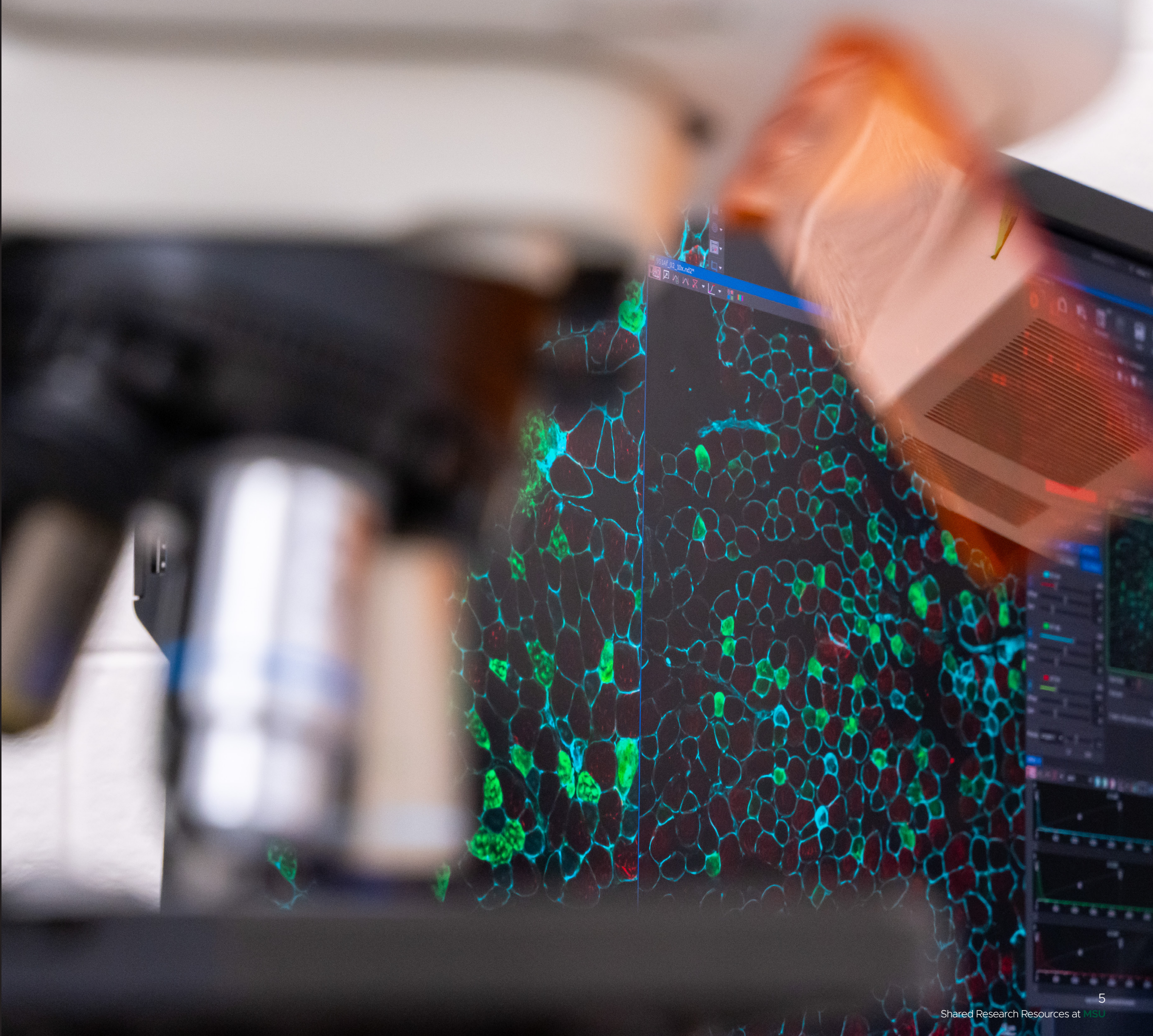


Imaging & Visualization

Go deeper than the surface.

From molecules to living systems, advanced tools bring hidden structure and function into focus.

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Cryo-EM Core Facility

The Cryo-EM Core Facility provides investigators with access to cutting-edge cryo-electron microscopy instrumentation, as well as support in training and experimental consultation. Cryo-electron microscopy is extensively used for determining structures of biological materials such as isolated proteins and complexes, small particles including viruses and bacteria, isolated organelles, whole cells, and FIB-milled tissues.



LOCATION
Engineering Research Complex
1449 Engineering Research Ct.
Room D122
East Lansing, MI 48824

CONNECT
web: cryo-em.natsci.msu.edu
email: RTSF.cryoEM@msu.edu

EQUIPMENT MAIN MICROSCOPES

Talos Arctica (ThermoFisher)

The Arctica is a 200 keV cryo-electron microscope equipped with an autoloader, a Selectris energy filter and a Falcon 4i camera. It is great for sample screening and data collection of specimens using single particle analysis.

Titan Krios (ThermoFisher)

The Krios is a 300 keV cryo-electron microscope equipped with an autoloader, a Selectris X energy filter and a Falcon 4i camera. It is great for high resolution data collection using single particle analysis. In addition is great for cryo-electron tomography and micro-electron diffraction.

Helios Hydra Bio (ThermoFisher)

The Helios is a FIB-SEM electron microscope used for focused ion beam milling of cryogenic specimens. The Helios is also capable of correlated light and electron microscopy.

AUXILIARY EQUIPMENT

EasiGlow (Pelco) & GloQube Plus (Quorum)

Glow discharger for grid preparation

ACE-600 carbon coater (Leica)

Carbon coating and metal shadowing

Vitrobot Mark IV (ThermoFisher) & GP2 (Leica)

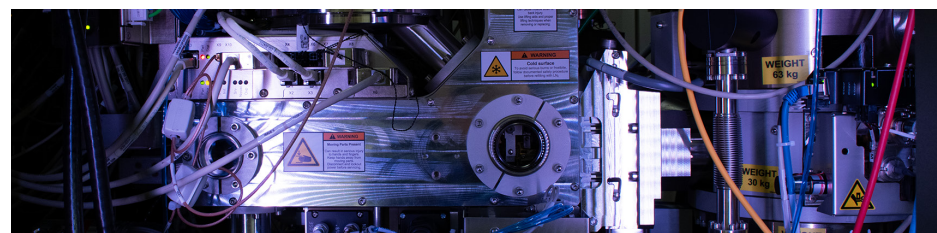
Robotic plunge freezing device for cryo-EM grid preparation

Compresstome (Precisionary)

Vibratome for tissue sectioning

High Pressure Freezer (CryoCapCell)

Freezing device for thick tissue samples



SERVICES

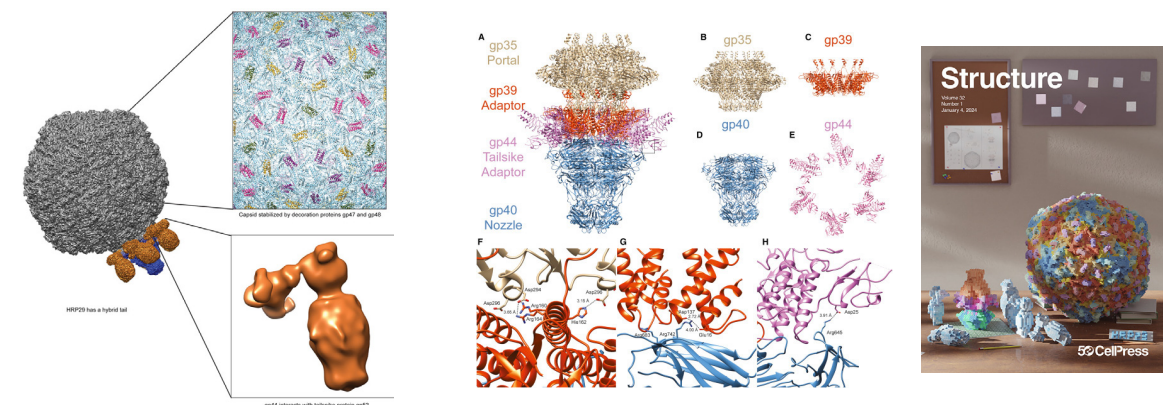
Cryo-EM imaging including:

- Single particle analysis
- Cryo-tomography
- FIB-Milling
- Micro-ED

Computational support including:

- Live image processing
- Access to computers with standard image processing programs (RELION, cryoSPARC, IMOD, etc.)
- Raw data storage for 30 days

Cryo-EM Structure of an Entire Bacteriophage with a Hybrid Tail

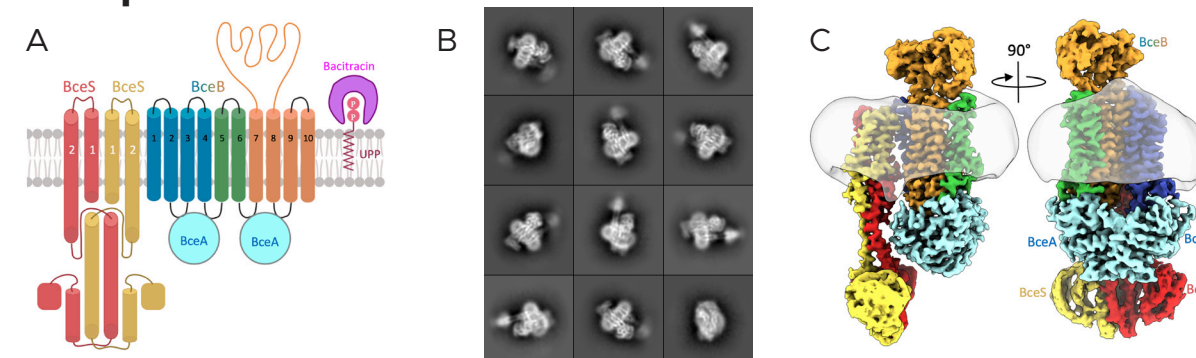


Adapted from:
Subramanian, S., Bergland Drarvik, S.M., Tinney, K.R., and Parent, K.N. (2024)
Cryo-EM structure of a Shigella podophage reveals a hybrid tail and novel decoration proteins Structure, 32(1):24-34

<https://doi.org/10.1016/j.str.2023.10.007>

There is a paucity of high-resolution structures of phages infecting Shigella, a human pathogen and a serious threat to global health. HRP29 is a Shigella podophage belonging to the Autographivirinae family, and has very low sequence identity to other known phages. Single particle analysis cryo-EM was used to resolve the structure of the entire phage HRP29 virion. These results show that Phage HRP29 has a highly unusual tail, which is a fusion of a T7-like tail tube and P22-like tailspikes mediated by interactions from a novel tailspike adaptor protein. Understanding phage tail structures is critical as they mediate hosts interactions.

Structure of an Antimicrobial Peptide Sensing and Detoxification Complex

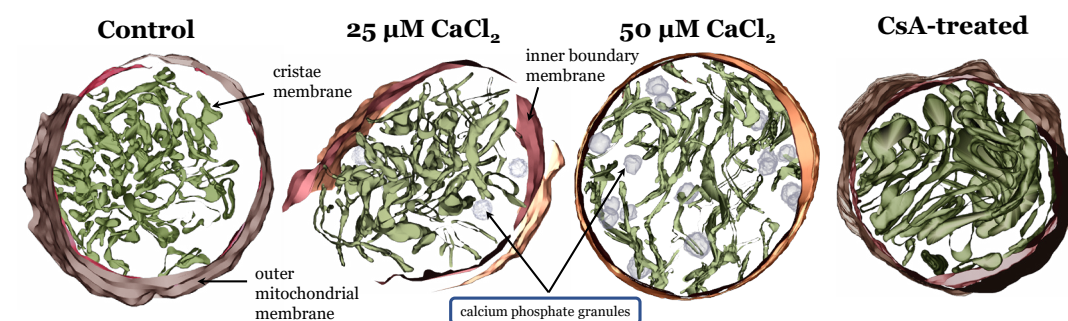


Adapted from:
George, N.L. and Orlando, B.J. Architecture of a complete Bce-type antimicrobial peptide resistance module. Nature Communications. 14, 3896 (2023).

<https://doi.org/10.1038/s41467-023-39678-w>

Antibiotic resistance is a growing global health problem. Most Gram-positive bacteria contain membrane protein complexes known as Bce modules (A) that consist of an ABC transporter working in tandem with a histidine kinase to sense and mediate resistance against diverse antimicrobial peptides. Single-particle cryo-EM was used to visualize the structure and dynamics (B & C) of the prototypical Bce module BceABRS from *B. subtilis*. These structures provide key insight into the assembly and dynamics of Bce modules, and the first ever structure of a full-length membrane embedded histidine kinase.

How Structure Impacts Mitochondrial Function in Health and Disease



Adapted from:
Subramanian, S., Bergland Drarvik, S.M., Tinney, K.R., and Parent, K.N. (2024)
Cryo-EM structure of a Shigella podophage reveals a hybrid tail and novel decoration proteins Structure, 32(1):24-34

<https://doi.org/10.1016/j.str.2023.10.007>

Mitochondrial ultrastructural changes associated with calcium overload will reveal the answer to an over 50-year-old question, and cryo-EM is currently the best way to visualize them with minimal disturbance to native states. Mitochondrial reconstructions from cryo-EM data reveal striking and newly discovered ultrastructural effects of calcium and a mitoprotectant called CsA. Calcium causes a decrease in cristae volume in a titratable manner, and CsA leads to an expanded cristae volume and altered outer membrane morphology. These images help inspire new perspectives on this 50-year-old question.

Center for Advanced Microscopy

The Center for Advanced Microscopy is the central microscopy laboratory for the East Lansing campus. We provide MSU researchers with formal graduate level instruction and 24/7 access to scanning electron microscopes, transmission electron microscopes, a digital light microscope, and confocal laser scanning microscopes.

We support all research disciplines, and we serve more than 500 MSU researchers per year from 40 different University departments, as well as many off-campus researchers.



LOCATION
Center for Integrated Plant Sciences Building
578 Wilson Road
Room B2
East Lansing, MI 48824

CONNECT
web: cam.msu.edu
email: cam.microscopy@msu.edu

EQUIPMENT

Confocal Laser Scanning Microscopy (CLSM)

- 3i Spinning Disk, live-cell or tissue incubation
- Leica Stellaris 5 with white light laser
- Nikon A1Rsi with TIRF and STORM
- Nikon AXR upright / large FOV
- Nikon C2+
- Olympus Fluoview 1000 Spectral
- Zeiss 980 with Airyscan 2 super resolution

Digital Light Microscopy

- Keyence VHX-6000 Digital Microscope

Laser Capture Microscopy

- Zeiss Palm MicroBeam IV

Scanning Electron Microscopy (SEM)

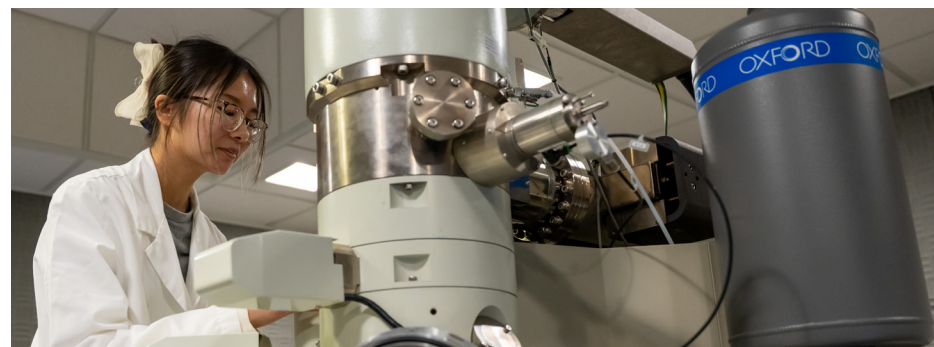
- JEOL 6610LV with Oxford EDS, includes low-vac
- JEOL 7500F with Oxford EDS, high resolution

Transmission Electron Microscopy (TEM)

- JEOL 1400 'Flash', 120 kV
- JEOL 2200FS, 200kV with EDS
- ThermoFisher probe-corrected Spectra 200 STEM with EDS and EELS (coming 2027)

Sample Preparation

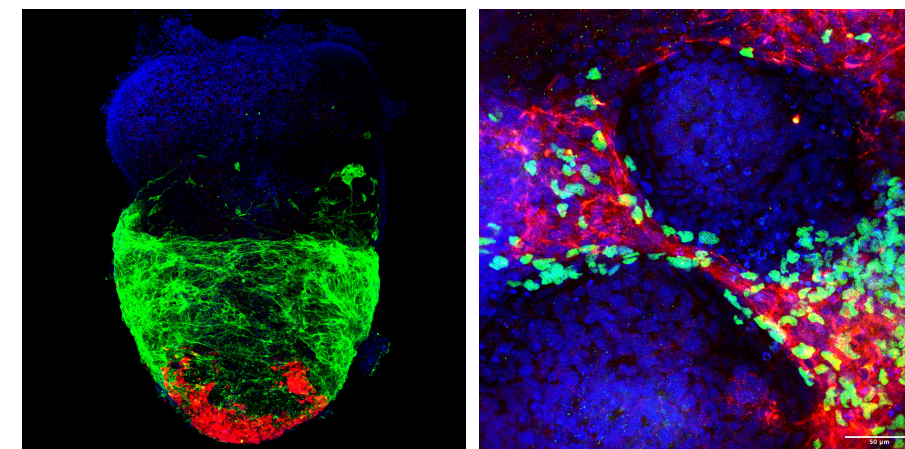
- State-of-the-art ultramicrotomy
- Many coaters (C, Au, Ir, Os, Pt)
- Critical point drying and freeze-drying
- Cryostat
- Disc cutter, dimple grinder, ion mill



SERVICES

- Graduate-level microscopy courses and training
- Confocal microscopy applications including: Multi-channel fluorescence imaging, high speed imaging, live-cell, FLIM, FRAP, FRET, BiFC, spectral imaging, high-resolution large area scanning, TIRF, super resolution (Airyscan, lightning, STORM), heating / cooling incubation, etc.
- Biological and soft-matter TEM services, including fixation and embedding, negative staining, immunogold experiments, and TEM imaging / data collection.
- Sample preparation, imaging, and analysis of a wide range of samples for SEM-EDS
- Physical sciences TEM-EDS services
- Experimental design, image acquisition and analysis
- Assistance with grant planning and writing

Confocal Laser Scanning Microscopy (CLSM) and Transmission Electron Microscopy Contribute to the Development of More Realistic Human Heart Model Systems



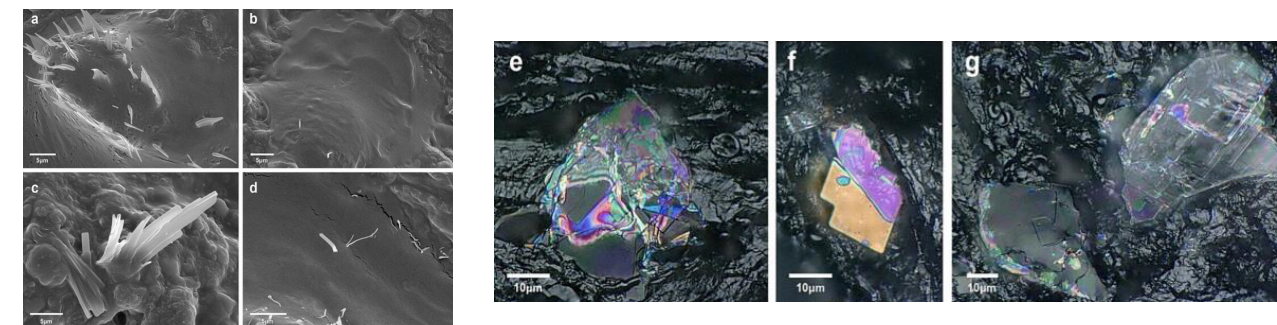
Thanks to advancements in the development of patented synthetic human-like hearts first created at MSU, researchers can study human heart development and congenital heart disease on highly accurate models.

Left: A heart organoid with a well-developed ventricle (green) and cardiac neural crest cells (mCherry) incorporating to the structure. Blue is cell nuclei.

Right: Neural crest cells in green (SOX10) migrating along red cardiomyocytes (TNNT2) in a developing heart organoid. Blue is cell nuclei. Scale bar 10 microns. Collected on the CAM Nikon A1 CLSM.

Research from the Aguirre lab; for details see: Volmert et al. Nat Commun 14, 8245 and MSU Today 2024 issue 02.

Scanning Electron Microscopy (SEM), Digital Optical Microscopy, and CLSM Demonstrate Cholesterol Crystals Induce Damage in Solid Cancers as in Arterial Plaques



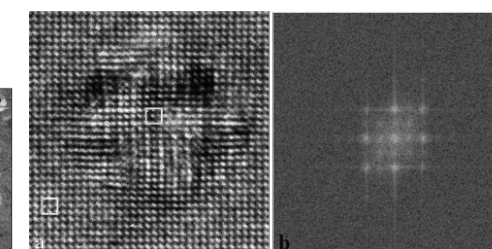
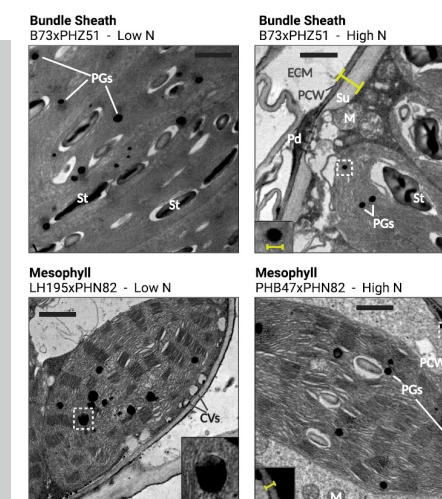
Scanning and 3D-digital microscopy of colon cancer and marginal tissue: Scanning electron micrographs of colon cancer (a, c) and matching marginal tissue (b, d) demonstrate larger and prominent cholesterol crystal formations in the cancer but not in the normal marginal tissue. CCs are seen traumatizing and perforating the tumor surface. Digital microscopy of fresh unprocessed tissue demonstrates the presence of large cholesterol crystal formations in the colon cancer (e, f, g).

Research from the Abela lab. For details: Abela GS et al. Am Heart J Plus. PMID: 37981958.

Transmission Electron Microscopy (TEM) Advances Plant Resilience and Materials Research

Thickening of maize hybrid mesophyll and bundle sheath cell walls occurs as a general response to low N, increases in plastoglobuli size and abundance, and unusual plastoglobule features. Yellow markings indicate how cell wall thickness and plastoglobule diameter were measured. Extracellular matrix (ECM), primary cell wall (PCW), the suberin layer of the cell wall (Su), starch grains (St), mitochondria (M), plasmodesmal pits (Pd), cytosolic vesicles (CVs), and plastoglobules (PGs). Regions highlighted in the insets are marked with dashed white boxes. All scale bars indicate 1 μ m. Lunquist lab.

For details, see: Plant Physiology, "Multi-scale physiological responses to nitrogen supplementation of maize hybrids"



High-resolution TEM image from a Lead Antimony Silver Tellurium (LAST)-18 sample (a) and the corresponding FFT's from nanocrystal (b). The electron beam is parallel to one of the [100] directions. The results reported here provide experimental evidence for a conceptual basis that could be employed when designing high performance thermoelectric materials and dispel the decades long belief that these systems are solid solutions. JACS 127(25) 9177-9190.

IQ Microscopy Core Facility

The IQ Microscopy Core facility provides researchers with some of the most advanced fluorescence-based microscopes for imaging a wide range of biological samples including live cells and tissues in vivo. The microscopy core staff provide training and consultation to new users and support internal and external investigators.



LOCATION
IQ/Bioengineering Building
775 Woodlot Drive
East Lansing, MI 48824

CONNECT
web: microscopy.iq.msu.edu
email: iq@msu.edu

EQUIPMENT

WIDE-FIELD MICROSCOPE

Leica Thunder Imager

A 3D cell culture imaging system that features a computational clearing method to remove out-of-focus blur; equipped with eight excitation wavelengths (LED source) and an environmental chamber for controlling the temperature and CO₂.

CONFOCAL MICROSCOPES

Leica Stellaris 5

An inverted laser scanning confocal microscope with white light laser (WLL) from 485 nm to 685 nm and up to eight excitation lines that can be used simultaneously; equipped with an environmental chamber for controlling the temperature and CO₂.

Leica SP8

An upright laser scanning confocal microscope with WLL from 470 nm to 670 nm and up to eight excitation lines that can be used simultaneously.

MULTI-PHOTON MICROSCOPE

Leica SP8 Dive two-photon

An upright two-photon and laser scanning confocal microscope well-suited for imaging thick tissues and live animal imaging. The second harmonic generation capability of the instrument enables label-free imaging of specific samples (e.g., collagen).

TIRF SUPER RESOLUTION

Olympus TIRF/HiLo

An inverted microscope equipped with a TIRF/HiLo illumination system and four laser lines (405 nm, 488 nm, 561 nm, and 647 nm). An environmental chamber (cellVivo) is included to control humidity, temperature, and CO₂ level for live cell imaging.

RAMAN

HORIBA

A Raman with two lasers (532 and 785 nm), four motorized gratings, independent slit and confocal pinhole that is ideal for non-destructive identification of a wide range of samples.

HYPERSPPECTRAL DARK-FIELD MICROSCOPE

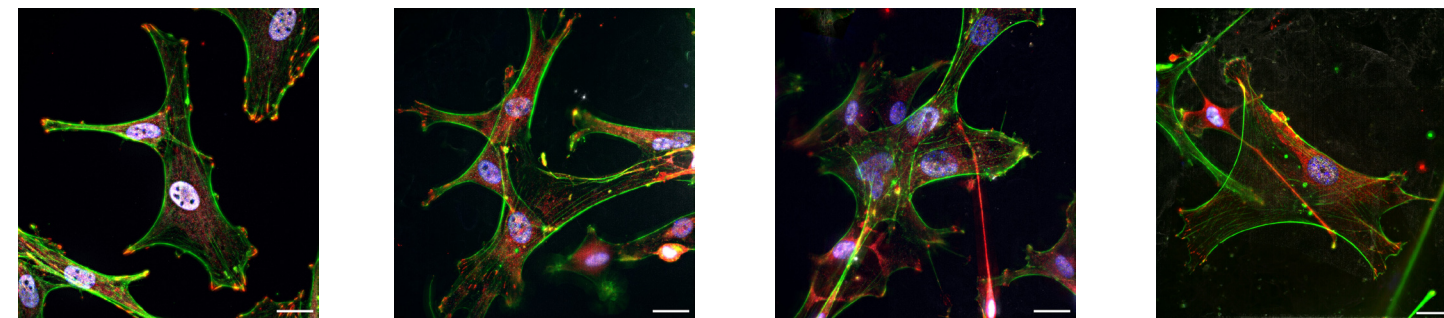
CytoViva

An upright microscope with enhanced dark-field capability that can be utilized for hyperspectral imaging to detect nanoparticles as small as 10 nm.

SERVICES

- Comprehensive training provided for new users
- Consultation (sample preparation, designing experiments)
- Imaging samples provided by researchers
- Manuscript/grant review

Leica Thunder Fluorescence Imaging (wide-field)



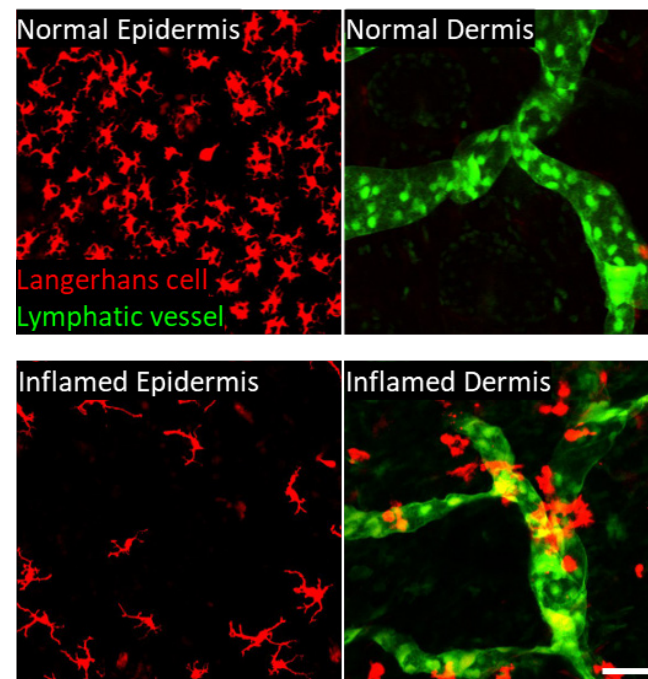
Mouse Schwann cells one day post-seeding on various substrates: (a) glass, (b) microporous polycaprolactone (PCL), (c) microporous poly(lactide-co-glycolide) (PLGA) 85:15, and (d) microporous PLGA 50:50. Blue: nucleus (DAPI), green: cytoskeleton (actin), red: paxillin, white: sox10. Scale bar: 25 μ m.

Courtesy of Dr. Kendell Pawelec

Two-photon Fluorescence Imaging

Egress of Langerhans cells to lymphatic vessels. Barrier disruption by the skin inflammation activates Langerhans cells. Three days after the skin inflammation, activated Langerhans cells leave the epidermis and egress to the lymphatic vessels in the dermis. Scale bar: 50 μ m.

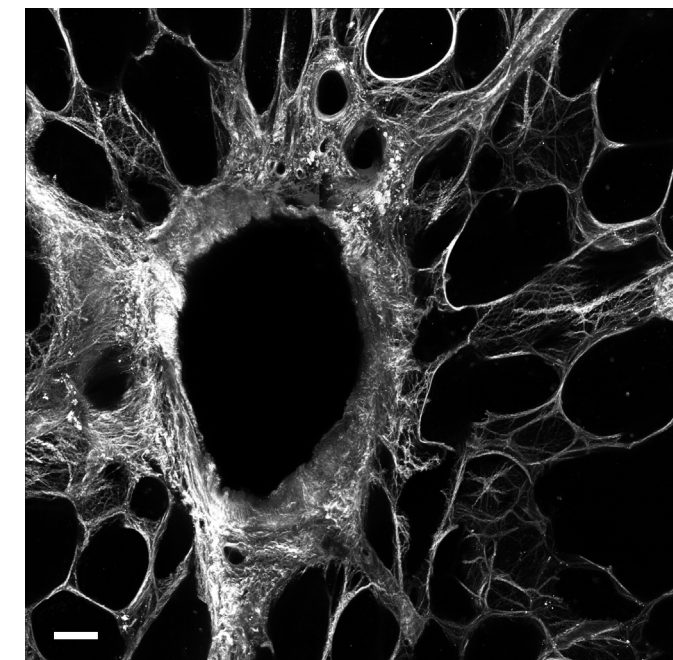
Courtesy of Dr. Sangbum Park



Two-photon SHG (label-free) Imaging

Small airway in a human lung sample. This is a label-free, second harmonic generation (SHG) image captured using the Leica SP8 Dive two-photon microscope with a 25x magnification. The collagen structure is shown without any fluorescence labeling. Scale bar: 100 μ m.

Image was captured by Dr. Sara Makaremi. The lung sample was provided by Dr. Xiaopeng Li from Grand Rapids Research Center



Flow Cytometry Core Facility

The MSU Flow Cytometry Core Facility provides investigators with access to cutting-edge analytical flow cytometry instrumentation and cell sorting services, as well as training and experimental consultation. Flow cytometry is extensively used for a variety of applications including evaluation of viability/apoptosis, immunophenotyping, intracellular cytokines/transcription factors, ROS, cell cycle, ploidy, kinetics, protein-protein interactions, and RNA transcript levels.



LOCATIONS
North Campus Hub
Biomedical & Physical Sciences Building
 567 Wilson Road
 Rooms 4120 & 5115
 East Lansing, MI

South Campus Hub
IQ/Bioengineering Building
 775 Woodlot Drive
 Rooms 2521 & 2522
 East Lansing, MI

CONNECT
web: facs.iq.msu.edu
email: FACS@msu.edu



EQUIPMENT BENCHTOP ANALYZERS

Attune CytPix (ThermoFisher Scientific)

- Brightfield imaging capable cytometer, image acquisition ≤6,000 events/second; machine learning-based image analysis tools

Cytek Aurora (Cytek Biosciences)

- Spectral for high parameter panel acquisition (>45 fluorescent parameters); autofluorescence extraction; and identification of unique autofluorescent signatures with ≤97% similarity

ZetaView NTA (ParticleMetrix)

- Small particle (nanoparticles, extracellular vesicles) size (50nm – 1µm), fluorescence, & concentration

Luminex 200 (Luminex)

- 96-well based multiplex analysis of cytokines; growth factors; signaling proteins

IMAGING

CQ1 Cell Voyager (Yokogawa)

- Automated high content spinning disk confocal imaging (96-well plate in 4 min), environmental control (Temp, CO₂, O₂), 2x – 60x objectives, free AI/machine learning analysis software

CELL SORTERS

SONY MA900 (SONY Biotechnology)

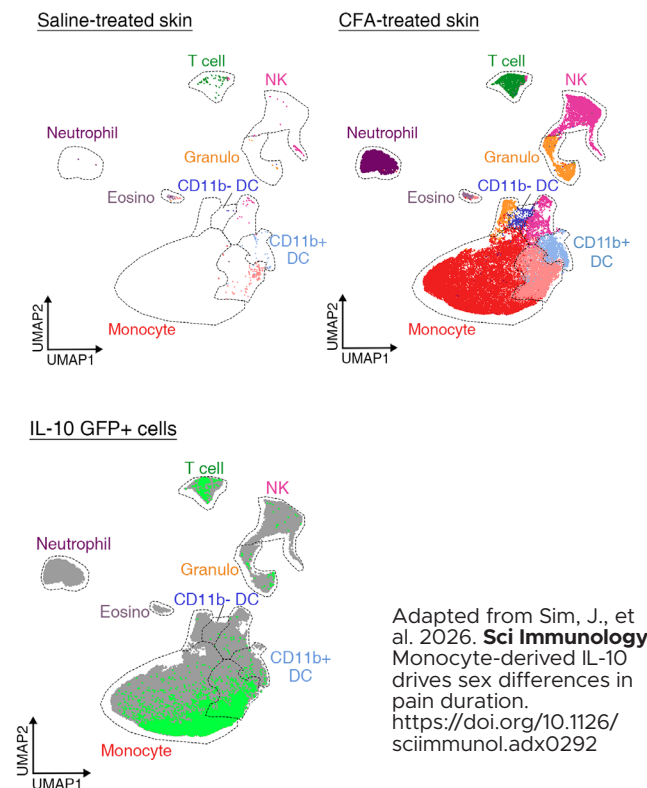
- Features automatic setup, calibration, and cleaning for ease of use

BD FACSria IIu (BD Biosciences)

SERVICES

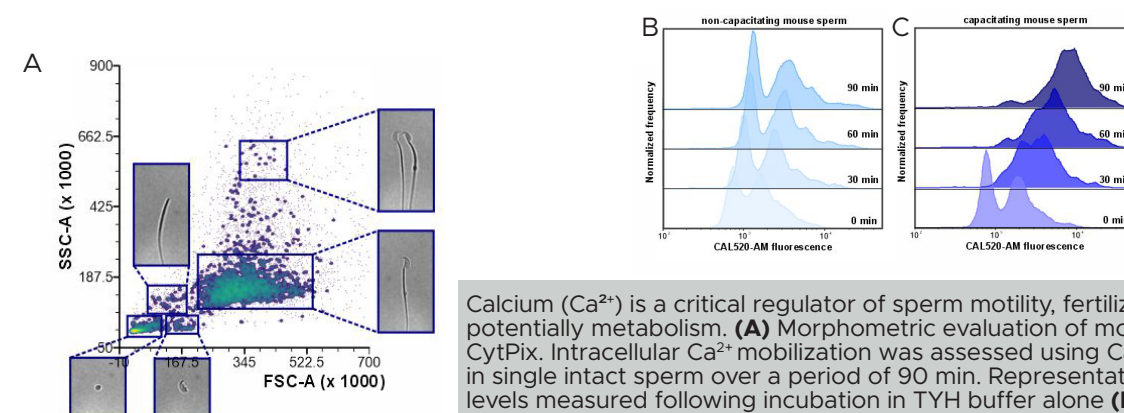
- Comprehensive training program to support development of independent flow cytometrists
- Full-Service Cell Sorting
- Assay Development & Experimental Design
- Multi-parameter Panel Design
- Access to data analysis software for Core Users
- Manuscript/Grant Review

Spectral Cytometric Immunophenotyping in a Mouse Model of Inflammatory Pain



Intraplantar immune populations were evaluated from IL-10 GFP reporter mice using a Cytek Aurora spectral cytometer following saline (left) or Complete Freund's Adjuvant (CFA; middle) administration. A dimensionality reduction (UMAP) and clustering pipeline was used to identify CD11b+Ly6C+Ly6G-F4/80^{mid} monocytes as one of the major immune cell source of IL-10 (right), a cytokine that plays a role in pain resolution. Flow cytometric assessment of immune cell subsets revealed elevated levels of IL-10 producing monocytes in males compared to females that correlated with improved pain resolution rate, demonstrating sexual dimorphism of pain resolution. Courtesy of Geoffroy Laumet, Department of Physiology

Dynamic Monitoring of Intracellular Ca²⁺ Levels in Mouse Sperm



Calcium (Ca²⁺) is a critical regulator of sperm motility, fertilization capacity, and potentially metabolism. (A) Morphometric evaluation of mouse sperm using the Attune CytPix. Intracellular Ca²⁺ mobilization was assessed using Cal-520 AM (AAT Bioquest) in single intact sperm over a period of 90 min. Representative histograms show Ca²⁺ levels measured following incubation in TYH buffer alone (B) and in the presence of HCO₃⁻ (C), which induces capacitation. Courtesy of Melanie Balbach, Department of Biochemistry & Molecular Biology

Advanced Molecular Imaging Facility

Our facility provides a variety of preclinical imaging instruments: we can image small animals using optical imaging (fluorescence and bioluminescence), PET/MRI, μ CT, opto-acoustic imaging and magnetic particle imaging. We have a space for surgeries, and a suite of computers for image analysis. For all modalities, we will assist with experimental design and animal protocols, and either train users on image acquisition or acquire images for you.



LOCATION
IQ/Bioengineering Building
775 Woodlot Drive
Rooms 1700-1706
East Lansing, MI 48824

CONNECT
web: imaging.iq.msu.edu

EQUIPMENT

PET/MRI (Bruker 7 T)

- Full set of built in preclinical MRI sequences and coils for dedicated brain and body MRI with simultaneous PET acquisition
- Anatomical imaging eg tumor size, cardiac imaging, neuro-imaging (fMRI, diffusion tensor imaging, perfusion), liver and brain PET-MRI

μ CT (Revvity Quantum GX)

- High resolution or anatomical co-registration at low x-ray dose.
- Bone density, scaffold degradation, fat quantification, quality control of manufactured parts
- Resolution as low as 4.5 μ m, typically $\sim$ 100 μ m

Fluorescence and Bioluminescence

- (Revvity IVIS and Licor Pearl Trilogy)
- Tumor growth, bioluminescent bacteria, nanoparticle tracking, implanted organoids

Magnetic Particle Imaging (Magnetic Insight Momentum Scanner)

- 2D and 3D imaging for nanoparticle and macrophage tracking to tumors, drug delivery, lung imaging
- Coregister with μ CT

3D Cryofluorescence Tomography (EMIT Xerra)

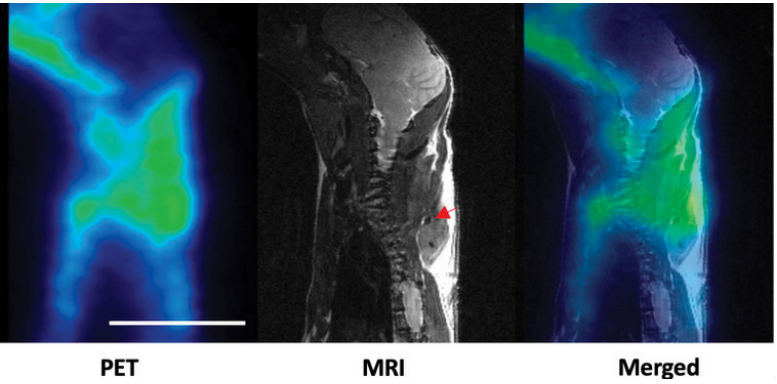
- Ex vivo cryosectioning and imaging of whole mice and rats, or organs
- 7 fluorescent channels and white light
- Gene expression in mouse models, nanoparticle distribution

SERVICES

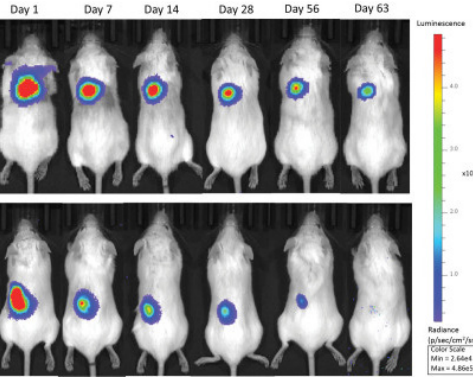
- Experimental design, image acquisition and analysis
- Training
- Animal procedures
- Full study
- Assistance with IACUC submissions, grant planning



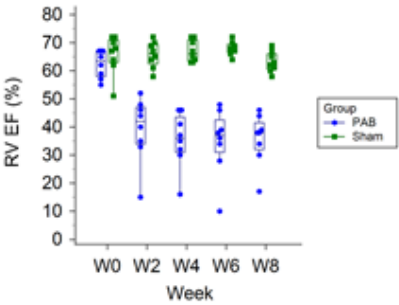
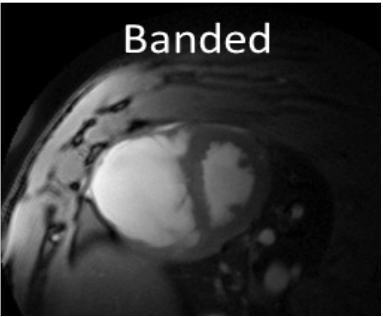
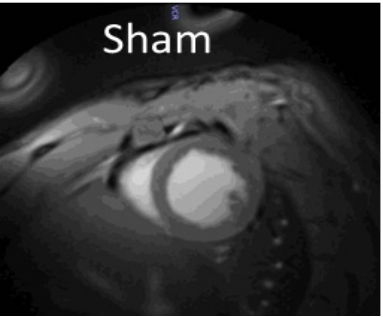
Survival of Transplanted Islet Organoids with PET/MRI and Bioluminescence



Brown adipose tissue (BAT) was evaluated as a transplant location for islet organoids. Placement in the brown fat was confirmed by labeling the islets with an iron oxide nanoparticle, then imaging by MRI and PET. The red arrow shows the signal void caused by the iron oxide nanoparticles, and the PET signal shows the location of the scapular BAT after cooled mice were injected with FDG. Bioluminescence imaging confirms that islets in the BAT survive longer than those in the kidney capsule. Sun et al Transplantation Direct. 2024 Jul; 10(7): e1658.

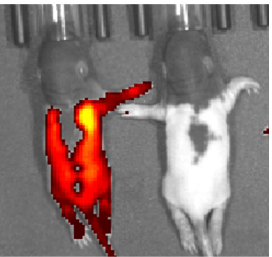


Cardiac Magnetic Resonance Imaging

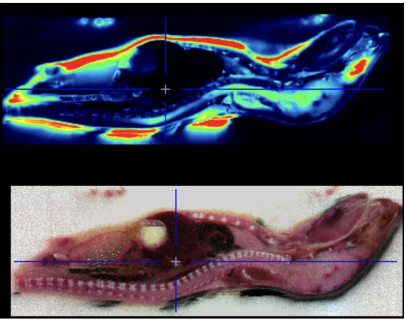


The pulmonary artery was banded in rats, to examine the effect on tricuspid valve regurgitation and the timeline of functional and anatomical changes. Rats were scanned by MRI at baseline and every 2 weeks after surgery to measure the progression of functional changes in the heart such as ejection fraction and ventricular strain, as well as anatomical changes like valve size. The changes are apparent on the MRI images – the right ventricle is much bigger on the banded animal. These changes were detectable even 2 weeks after banding, for example, the right ventricle ejection fraction was significantly different from the sham at 2 weeks. This study was a collaboration with investigators at Corewell Health in Grand Rapids and the In Vivo Facility at MSU. (Tomasz Timek lab, Corewell Health/MSU. Manuscript in preparation, used with permission.)

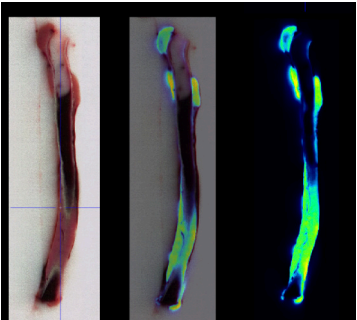
Phenotyping with In Vivo Imaging and Ex Vivo Cryofluorescence Tomography



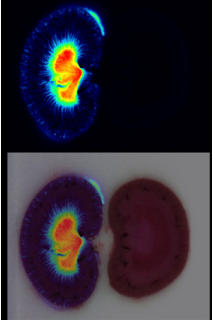
In vivo fluorescence



Whole body, P10 pup



PVAT, adult



Kidney, adult

The transgenic core developed a mouse model for studying fat. In this model TdTomato was expressed using an adiponectin promoter. Homozygous mice had high expression of TdTomato as seen by in vivo fluorescence imaging at P4 (left). Whole pups at P10 were sectioned by automated cryofluorescence tomography, and fat expressed TdTomato. In adult rats, perivascular adipose tissue and kidney (among other tissues) expressed TdTomato. (Elena Demireva, Huirong Xie, Stephanie Watts and the PVAT PPG at MSU.)

Investigative HistoPathology Lab

The Investigative HistoPathology Core supports MSU investigators by providing routine and custom tissue processing, staining, and imaging services, including paraffin and frozen sectioning, special stains, immunohistochemistry, and TUNEL, to advance a wide range of research projects. Through one-on-one consultations, the core assists with study design, troubleshooting, and optimal use of research materials, enriching faculty research programs and supporting education for lab staff and students.

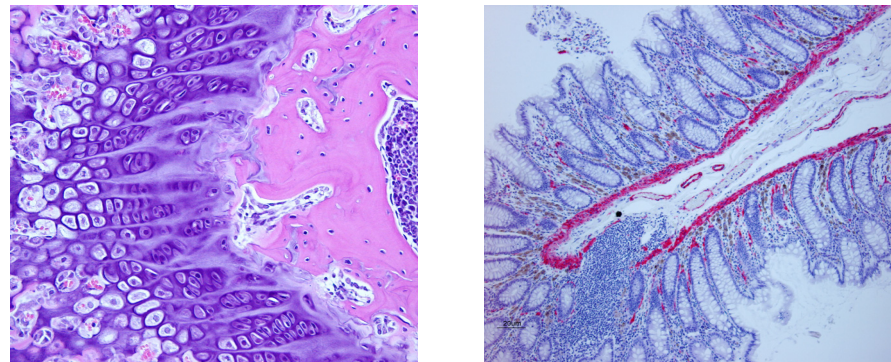


LOCATION
Biomedical Physical Sciences Building
567 Wilson Road
2133 - Secure Hall
East Lansing, MI 48824

CONNECT
web: sites.google.com/msu.edu/ihpl/home

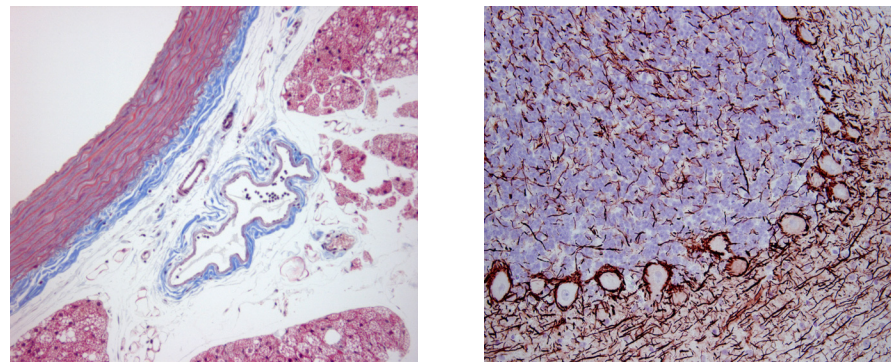
EQUIPMENT

- Leica ASP300 Tissue Processor
- Tissue Tek VIP Tissue Processor
- Leica EG1160 Embedding Center
- ThermoFisher HistoCentre III Embedding Center
- Rotary Microtomes
- *Reichert Jung 2030, Leica RM2235, Leica RM2255*
- Leica AutoStainer XL
- *Consistent Automated Hematoxylin & Eosin Staining*
- Biocare intelliPath Flex
- *Open platform for use with reagents from multiple vendors for FFPE and FS staining for Immunohistochemistry utilizing brightfield or fluorescent techniques*
- Thermo-Fisher Gross Station
- *Available for scheduled use to trim in research subjects*



SERVICES

- One-on-One consults regarding research studies
- Goal of project & design
 - Potential pitfalls with histology
 - Maximize use of research materials
-
- Formalin/PFA fixed tissues for paraffin embedding
 - Fresh Frozen & Fixed Frozen tissue
 - Routine & Custom Protocols for:
 - Hematoxylin & Eosin Staining
 - Special staining to identify cellular structures
 - Immunohistochemistry – Brightfield & Immunofluorescence
 - TUNEL



Von Willebrand Factor Delays Liver Repair After Acetaminophen-induced Acute Liver Injury in Mice

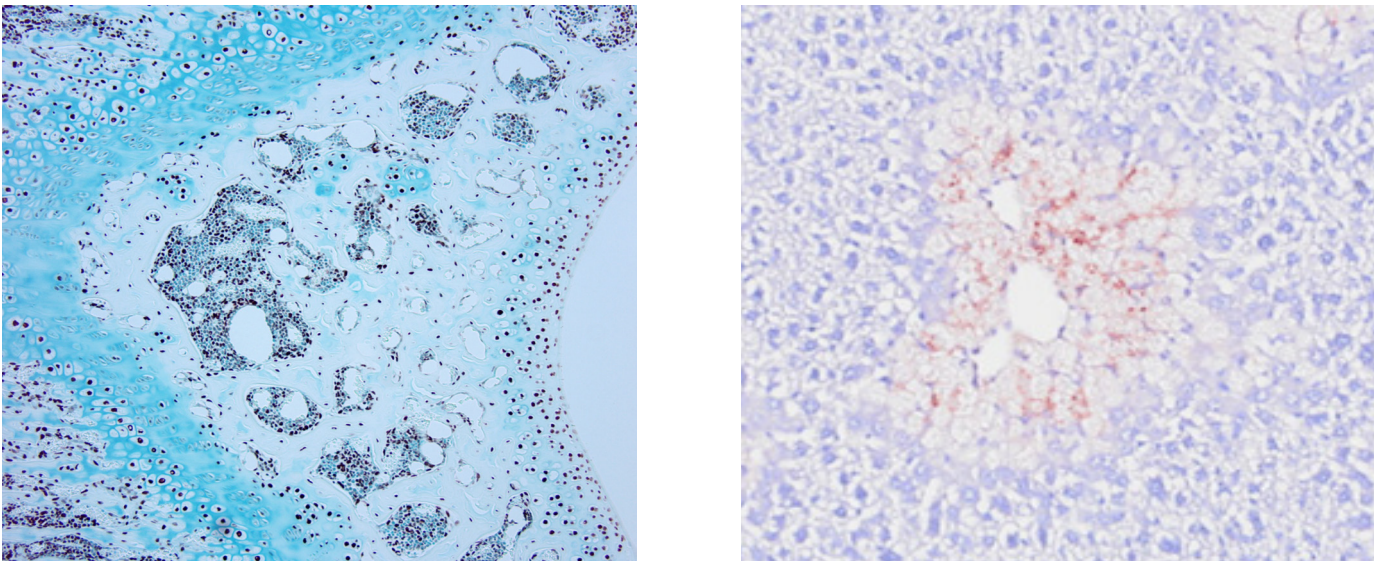
This publication in *Journal of Hepatology* features results, products of the Investigative Histopathology Laboratory, which among other results produced by Amy Porter’s team, led to receipt of a 2.8-million-dollar R01 grant in which the laboratory figures centrally. Histological analyses driven by related immunohistochemical stains led to grant support for clinical-translational science supported by the Tetrad grant program. Moreover, presentation of these results at leading edge conferences prompted investigators external to MSU to send sections to the laboratory for processing for these specific stains, based largely on the exceptional quality provide by the IHP Lab team.
DOI: <https://doi.org/10.1016/j.jhep.2019.09.030>
James (Jim) P. Luyendyk, PhD, Albert C. and Lois E. Dehn Chair, Professor, Department of Pathobiology and Diagnostic Investigation, College of Veterinary Medicine, Michigan State University

Divergent Pathogenetic Outcomes in BALB/c Mice Following Omicron Subvariant Infection

“The Laboratory of Investigative Histopathology at Michigan State University has provided us with invaluable histology services for thirty years that has resulted in 225 peer-reviewed publications in pathology, toxicology and infectious disease, as well as over 10 million dollars in extramural federal funding. Their high-quality production of whole glass slides with exquisitely prepared histochemical and immunohistochemical stained tissue sections is essential for our designed-based, unbiased, quantitative histopathology analyses. Examples of their work are found in these selected scientific articles.”
DOI: <https://doi.org/10.1016/j.virusres.2024.199319>
Jack Harkema, DVM, PhD, DACVP, ATSF, University Distinguished Professor, Department of Pathobiology and Diagnostic Investigation, College of Veterinary Medicine, Michigan State University

Insight into Mammary Gland Development and Tumor Progression in an E2F5 Conditional Knockout Mouse Model

This publication in the *Journal Oncogene* features images generated from H&E as well as immunohistochemistry (IHC) by the IHP Labs team in several of the figures. This was indispensable for publication, from the routine H&E to the IHC that required the lab to go through multiple rounds of testing to determine the optimal staining conditions. This publication is the first of the publications stemming from an R01 from the NICHD, which also featured a number of these images. Amy Porter and the histopathology lab are intricately involved in the majority of the projects in the lab , with many new antibodies being profiled in tumor development by the IHP Lab team.
DOI: <https://doi.org/10.1038/s41388-024-03172-4>



MSU Digital Slide Scanning Core

The mission of Michigan State University's (MSU) Digital Slide Scanning Core Facility is to provide high-resolution and high-throughput digital scans (virtual images) of whole glass slides containing tissues or cells for advanced microscopy research and education.

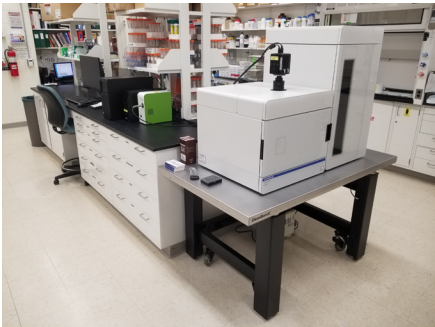
LOCATION
Food Safety and Toxicology Building
 1129 Farm Lane
 Room 218G
 East Lansing, MI 48824

CONNECT
email: harkemaj@msu.edu

EQUIPMENT

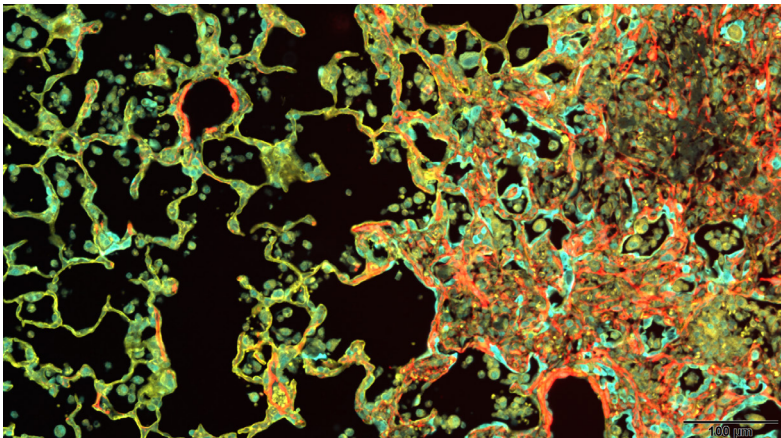
SLIDEVIEW (formally Olympus) VS200 slide scanner

- Converts high-resolution microscopic images of biologic tissues or cells on whole glass slides into digitized images through a fully automated high-speed scanning and tiling process
- Provides flexibility with five imaging modes, multiplexing capabilities, and multiple magnifications up to 60X
- Generates high quality digitized images for accurate quantitative and spatial analyses

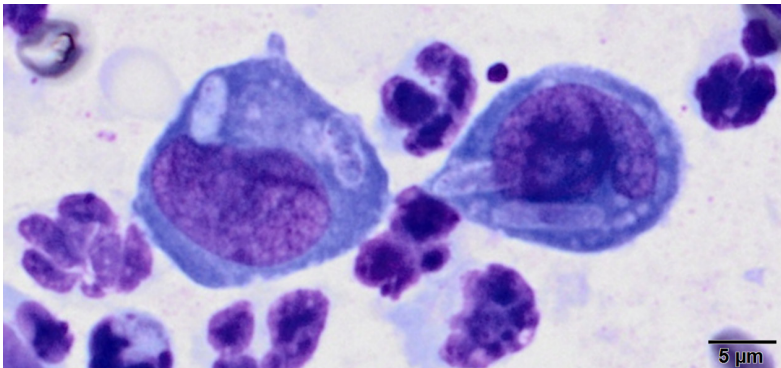


SERVICES

- Digitization of whole glass slides
- Multiple imaging modes: Brightfield, darkfield, fluorescence, polarization and phase contrast
- 20x or 40x magnification for histologic scans, and 60x oil for cytologic scans
- Scanning of 1 x 3 in. or 2 x 3 in. glass slides

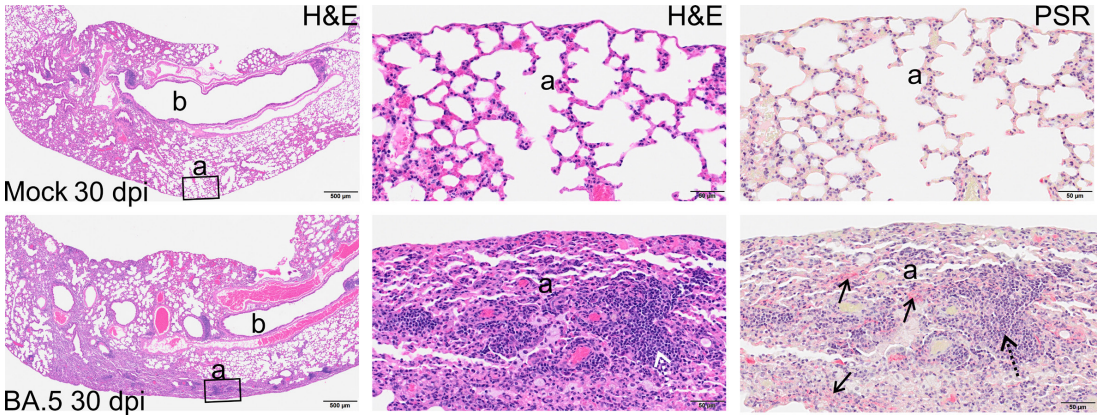


Immunofluorescence, Histologic Digital Scan



60x Oil, Brightfield, Cytologic Digital Scan

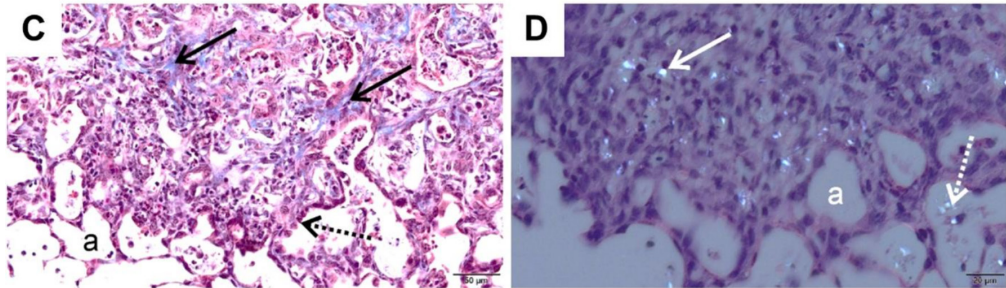
Mouse-Adapted SARS-CoV-2 Omicron BA.5 Infection Induces Post-Acute Lung Fibrosis in BALB/c Mice



Light photomicrographs, at low (scale bar 500 μ m) or high magnifications (scale bar 50 μ m), of left lung lobe tissue sections stained with hematoxylin and eosin (H&E) or Picrosirius red (PSR). Lung lobes were taken at 30 days post infection(dpi) from mock-infected mice (controls) or mice intranasally instilled with BA.5. Pulmonary histopathology was not observed in mock-infected mice. In contrast, BA.5 mice at 30 dpi had subpleural chronic alveolitis with scattered tertiary lymphoid structures (stippled arrows) and areas of PSR-stained interstitial fibrosis in the alveolar parenchyma (a). (b) bronchiolar airways; small rectangular boxes, location of the photos taken at high magnification.

Powers JM, Leist SR, Suryadevara N, Zost SJ . . . Harkema JR, Baric RS. J Virol. 2025 Nov 25;99(11): e0140625.

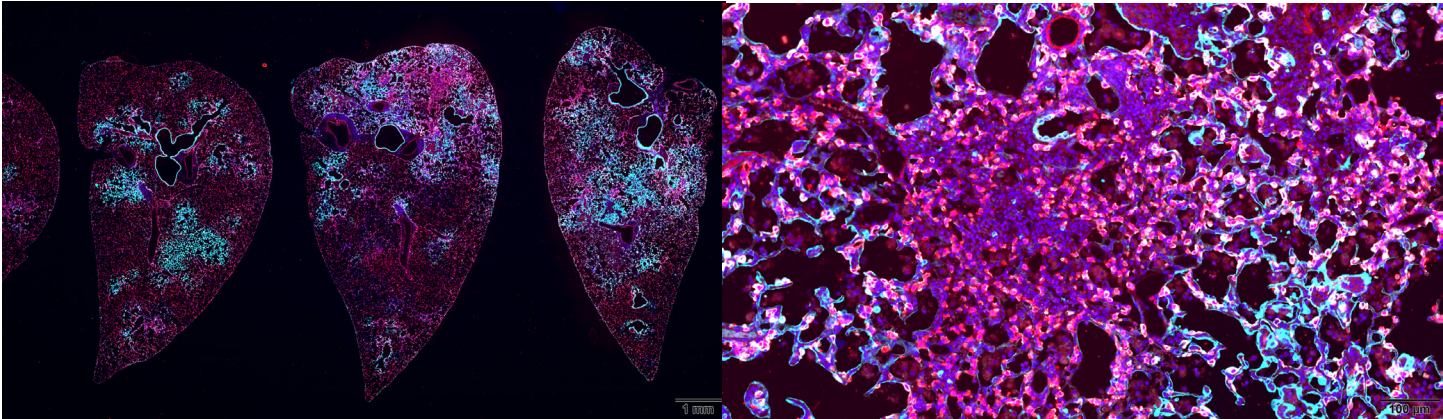
Impact of Soluble Epoxide Hydrolase Inhibition on Silica-Induced Pulmonary Fibrosis, Ectopic Lymphoid Neogenesis, and Autoantibody Production in Lupus-Prone Mice



(C) Centriacinar lung lesion (7 days post infection) stained with Masson's trichrome illustrating areas of interstitial fibrosis (blue stain; solid black arrows). (D) H&E-stained centriacinar lung lesion taken with polarized light exposing birefringent cSiO2 particles embedded in the fibrotic lesion (solid white arrow) and associated with degenerating and necrotic phagocytic cells in alveolar airspaces (stippled white arrows).

McDonald OF, Wagner JG, Lewandowski RP, Heine LK, Estrada V, Pourmand E, Singhal M, Harkema JR, Lee KSS, Pestka JJ. Inhal Toxicol. 2024 Aug-Sep;36(7-8):442-460.

Immunofluorescent Imaging of Pulmonary Histopathology After Air Pollutant Exposure



Immunofluorescent imaging of murine pulmonary tissue from KKAY diabetic mice repeatedly exposed to 1 ppm ozone. Exposed mice had persistent injury and early fibrotic lesions in alveolar parenchyma with epithelial remodeling: Type 2 alveolar epithelial cells (AEC2, Red), Krt-8 Transitional AEC (Cyan), and DAPI nuclear stain (blue)

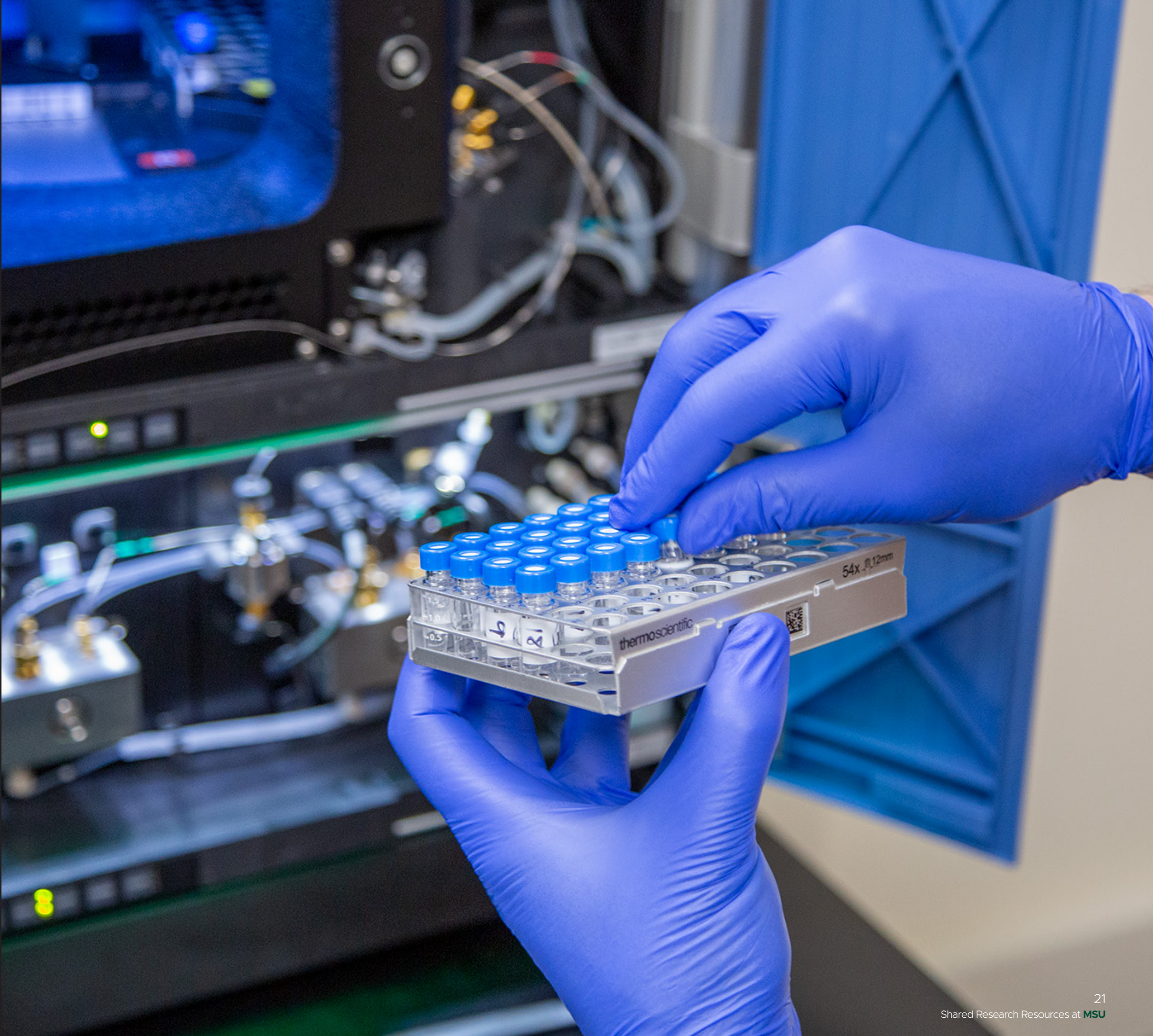
Elemental, Molecular, and Structural Analysis



Break matter down.
Build understanding
up.

Advanced technologies
reveal molecular composition,
chemistry, and structure.

Quantitative Bio Element Analysis and Mapping.....	22
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Proteomics Core Facility.....	26
Mass Spectrometry & Metabolomics Core.....	28



Quantitative Bio Element Analysis & Mapping (QBEAM)

QBEAM provides researchers with a comprehensive suite of state-of-the-art elemental analysis and imaging equipment allowing for ultra trace analysis, isotopic measurement, speciation analysis, and quantitative elemental imaging of biological, biomedical, agricultural, environmental, and materials research samples. By integrating advanced mass spectrometry, X-ray imaging, and custom informatics workflows, QBEAM enables investigators to determine the elemental composition of a variety of sample types including cells, tissues, soils, plants, and advanced materials.



LOCATION

Interdisciplinary Science and Technology Building
766 Service Road
Offices 1100 | Labs 1307 and 1308
East Lansing, MI 48824

CONNECT
web: qbeam.ehi.msu.edu

EQUIPMENT

ELEMENTAL/METALS ANALYSIS

ICP-QQQ-MS (Agilent 8900)

Equipped with a valve system, autosampler, and H, He, and O₂ gases for fine control of reaction chemistry capable of ppt levels of detection. Can be equipped with a HPLC, laser ablation, or single cell autosampler.

ICP-OES (Agilent 5800)

A vertical dual view (VDV) system equipped with a valve and autosampler that allows analysis in radial or axial views over the full 167 to 785 nm wavelength range from ppb to ppm with up to 10% TDS.

HPLC (Agilent 1260 Infinity II Bioinert)

A metal-free flow path HPLC capable of low volume sampling or speciation analysis of a variety of elements including As, Hg, Fe, Zn, etc. when connected to the Agilent 8900 ICP-QQQ-MS.

Combustion Analysis for C, H, N, O (Thermo FlashSmart Elemental Analyzer)

A combustion analyzer with a 120-sample capacity autosampler capable of C, H, N, O, and S analysis.

Single Particle (SP)/Single Cell (SC) Autosampler (ESI microFAST SingleCell)

Autosampling system equipped with CytoSpray spray chamber and CytoNeb low flow nebulizer for single cell/particle analysis using either ICP-TOF-MS (full spectrum) or ICP-QQQ-MS (high sensitivity).

ELEMENTAL/HIGH THROUGHPUT IMAGING

(2) LA-ICP-TOF-MS (Tofwerk S2 ICP-TOF-MS w/ ESL BioImage 266 nm Laser Ablation)

State-of-the-art systems that allow for full spectrum coverage (~13 μs). Can be coupled to a 1000 Hz Nd:YAG 266 nm laser ablation system or single cell autosampler.

iXRF Atlas Apex M

Energy Dispersive X-ray Fluorescence (EDXRF) Spectrometer for non-destructive elemental mapping, hyperspectral XRF imaging, and quantitative micro-scale down to 10 μm spot sizes.

Zeiss Axioscan 7 High Throughput Slide Scanner

A high-throughput whole slide scanner (100 slide capacity) for brightfield, color, and multispectral fluorescence imaging. 4 objectives (5x, 10x, 20x, and 40x) and HE, GFP, Cy3, Cy5, and Cy7 filters.

SAMPLE PREPARATION

Acid Distillation (Savillex)

Sub boiling point distillation that produces ultra-trace acids such as HF, HCl, HNO₃, and H₂O.

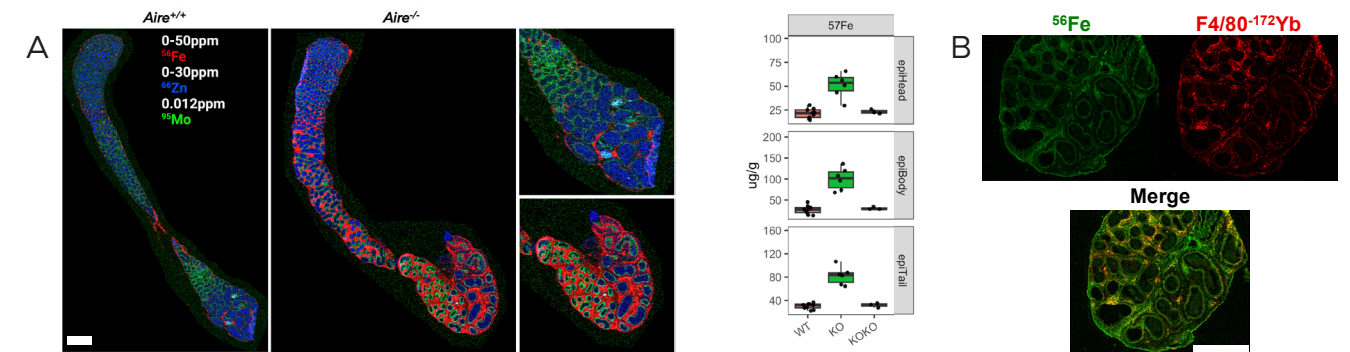
Microwave Digestion (CEM MARS6)

Closed-vessel acid digestion system with up to 300 °C and 1500 psi.

SERVICES

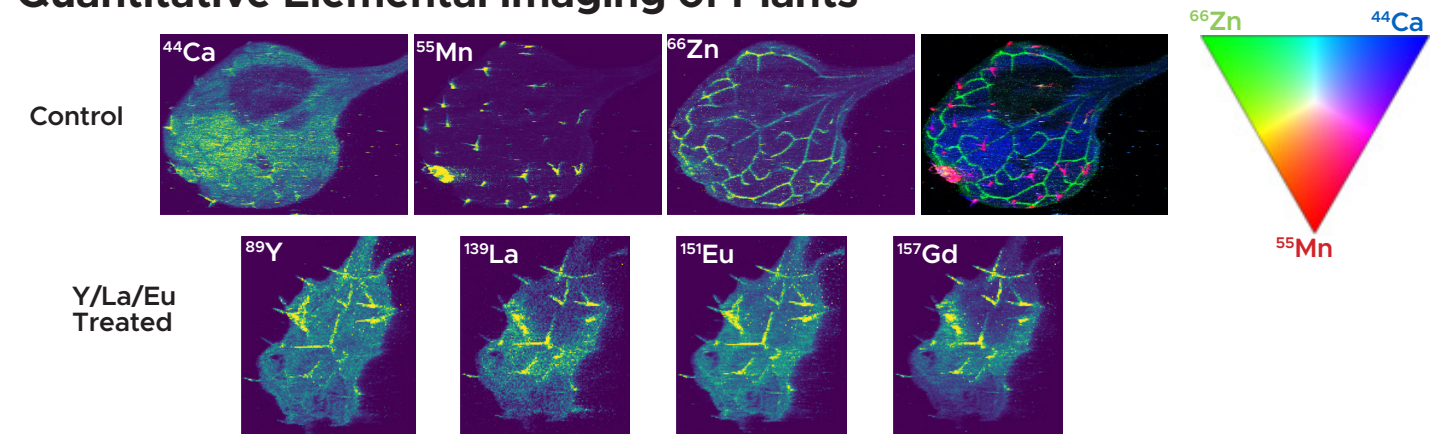
- Hands-on graduate level chemistry and biology course (MGI991/CEM913)
- Comprehensive training program to develop independent analytical chemists
- Full-service analytical chemistry including sample preparation, data acquisition, and analysis
- Experimental design and method development
- Training, workshops, and user support
- Access to data analysis software on 2 high end workstations
- Manuscript/grant review

Elemental Imaging Reveals Metal Dysregulation in Autoimmune Disease



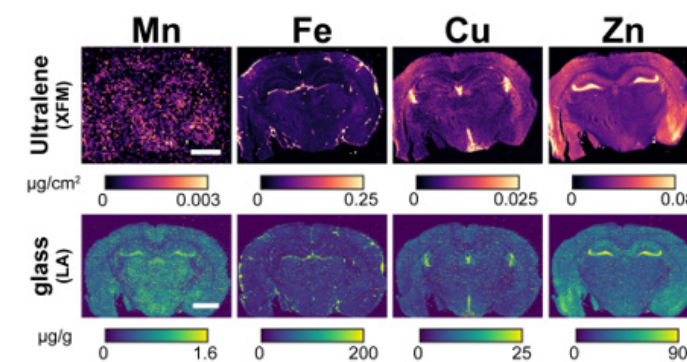
Quantitative elemental imaging was used to investigate how autoimmunity alters the reproductive microenvironment. **(A)** Iron accumulation and zinc depletion were observed throughout the epididymis of autoimmune mice. **(B)** Fibrosis was associated with macrophage infiltration using an Yb-tagged antibody for F4/80+ macrophages. These results demonstrate how elemental imaging can uncover disease-associated changes. Scale bar = 1000 μm. Adapted from: Ahn, S.H. et al. J. Immunol. DOI: 10.1093/jimmun/vkaf054.

Quantitative Elemental Imaging of Plants



Elemental distribution in plants helps explain inorganic physiology and plant health. The elemental composition of the soil and surrounding environment are the main contributors to plant physiology. An elemental map of a control Arabidopsis thaliana leaf from a plant grown in a growth chamber as well as a A thaliana leaf after exposure to Y/La/Eu in soil. Scale bar = 200 μm.

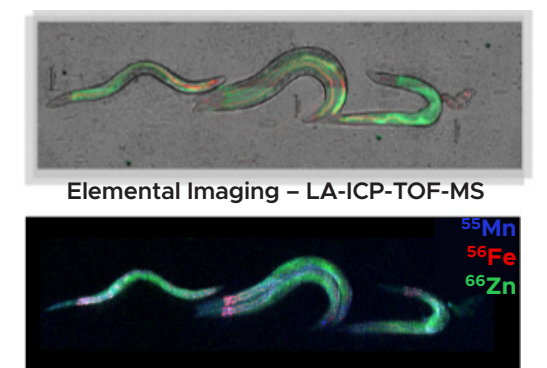
Multimodal Elemental Imaging



20 μm thick mouse brain sections imaged using XFM at APS and LA-ICP-TOF-MS at QBEAM. Scale bar = 1000 μm. Adapted from: Zee, D.Z. et al. J. Anal. At. Spectrom. DOI: 10.1039/D5JA00371G

QBEAM develops analytical workflows and through systematic evaluation of substrates, researchers established robust approaches for correlative LA-ICP-TOF-MS and XFM. These advances improve data quality and expand opportunities for multimodal elemental imaging studies.

Brightfield & Autofluorescence



Whole *C. elegans* prepared using petrolatum and imaged via LA-ICP-TOF-MS at QBEAM. Scale bar = 100 μm. Adapted from: Reynolds, A.J. et al. bioRxiv DOI: 10.64898/2026.01.08.698490

QBEAM develops sample preparation methods to enable elemental imaging of whole intact organisms such as *C. elegans* (Pictured above). Through evaluation of sample preparation protocols, researchers established a novel method for *C. elegans* allowing for accurate assessment of elemental distributions.

Genomics Core

The MSU Genomics Core provides DNA and RNA library preparation and sequencing services for researchers. Our mission is to keep pace with the world of genomics technology and to provide the best possible advice to researchers about their projects. The Genomics Core maintains an ever-changing portfolio of state-of-the-art instruments and services.



LOCATION
Plant Biology Building
612 Wilson Road
Room S-18
East Lansing, MI 48824

CONNECT
web: rtsf.natsci.msu.edu/genomics
email: gtsf@msu.edu

EQUIPMENT

AVITI sequencing instruments

- **Illumina-style short read sequencing**
- DNA, DNA methylation & RNA sequencing
- Multiple read formats
 - 2x75, 1x150, 2x150, 2x300
- Multiple flow cell capacities
 - 100 M to 1,500 M read pair outputs

10X Genomics

- **Single-cell library preparation and spatial transcriptomics**
- RNA-seq, ATAC-seq & multiomic library preparation
- Species agnostic

Nanopore Promethion P2 instruments

- **Long read sequencing**
- Read lengths of 1 kbp to 50 kbp
- DNA, cDNA, RNA & amplicon sequencing

TapeStation

- **Automated, high-throughput DNA/RNA electrophoresis**
- Provides quality control for samples and libraries

Qubit Flex

- **Accurate quantification of DNA & RNA**
- For high-throughput projects

Qubit Single Channel

- **Accurate quantification of DNA & RNA**
- Self-service instrument

Covaris Sonicator

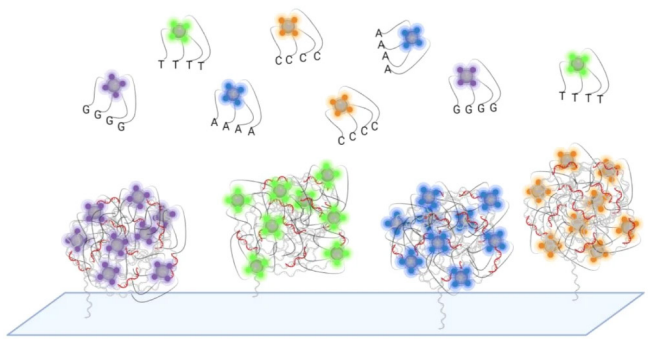
- **Ultrasonic fragmentation of DNA**
- Highly reproducible and isothermal shearing
- Used for fragmentation of DNA
- Self-service instrument

SERVICES

- Consulting on project design
- Self-serve Qubit DNA/RNA quantification
- High throughput Qubit DNA/RNA quantification
- DNA/RNA TapeStation QC assays
- Flat-rate DNA/RNA library prep + sequencing
- Quantabio SparQ DNA-seq library prep
- Low cost, ultra high throughput DNA library preparations with Twist FlexPrep
- IDT xGen DNA-methylation library prep
- Watchmaker RNA-seq library prep
- Qiagen QIAseq RNA-Seq with FastSelect rRNA depletion
- 10X Genomics single cell library preparations
- 10X Visium spatial transcriptomics assays
- Lexogen QuantSeq 3' mRNA-seq library prep
- Lexogen small RNA-seq library prep with or without unique molecular identifiers
- 16S V4 amplicon library prep
- Amplicon barcoding library prep
- Short-read sequencing of user-prepared libraries
- Oxford Nanopore long-read libraries w/ PromethION sequencing
 - DNA ligation libraries
 - Native and rapid barcoding libraries
 - cDNA libraries w/ or w/o barcoding
 - Direct sequencing of RNA libraries

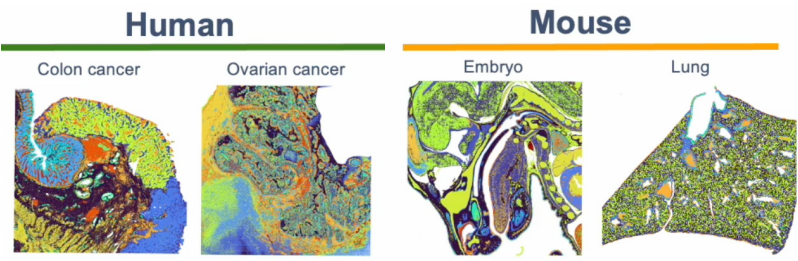
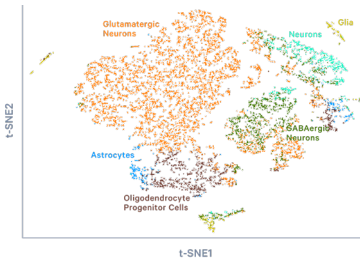


AVITI Short Read Sequencing



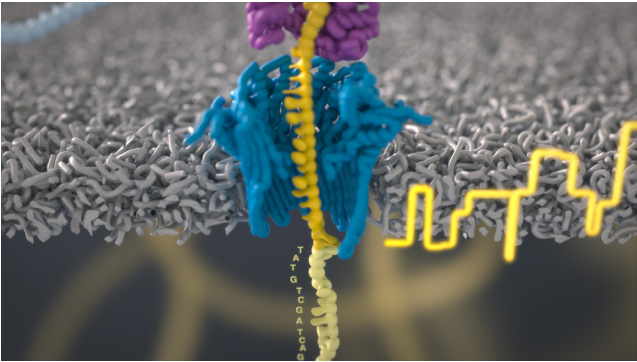
AVITI short read sequencing uses regular Illumina-style libraries and produces regular fastq output files. Existing bioinformatic pipelines can be used for data analysis. Before sequencing, library fragments are amplified on the flow cell using rolling-circle amplification to form a hairball-like polony. AVITI sequencing makes use of avidites containing a central fluorescent signal molecule tethered to several nucleotides. Sequencing involves multiple tethered nucleotides annealing within polymerase binding pockets. Avidite fluorescence on the polony allows base detection. Single base extension with ddNTPs is separate from base detection. Images from Element Biosciences.

10X Genomics Single Cell and Spatial Omics



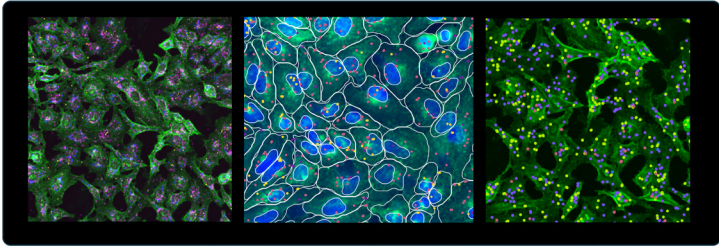
Single cell and single nuclei libraries are prepared with our Chromium X instrument from 10X Genomics. 5' and 3' RNA-seq libraries, ATAC-seq libraries and new human/mouse specific probe-based libraries can be prepared. Spatial transcriptomics can be performed with our Visium CytAssist from 10X Genomics using panels of human or mouse probes or with species-agnostic mRNA capture and sequencing. Images from 10X Genomics.

Oxford Nanopore Long Read Sequencing



Long read sequencing in the Genomics Core is performed on our PromethION P2. Nanopore flow cells contain thousands of protein pores within isolated membranes. As single stranded DNA or RNA passes through each pore, a changing current is decoded into fastq sequences. Image from Oxford Nanopore.

AVITI24 Spatial Omics



Our AVITI24 sequencer can perform multiomic analyses in the flow cell. Morphology, protein and RNA can be detected in a single assay. The detection area is 10 cm². Both spatial and dynamic relationships can be recognized in cell cultures and soon in fixed tissue sections. Images from Element Biosciences.

Proteomics Core Facility

The MSU Proteomics Facility provides expertise and advanced mass spectrometry resources for protein identification, characterization, and quantitative proteomics. We support projects ranging from purified protein characterization to deep proteome profiling, post-translational modification analysis, and quantitative studies in complex biological samples. We're happy to consult with investigators, at no charge, to help design the best experimental strategy for each project.



LOCATION
Biochemistry Building
603 Wilson Road
Rooms 5 and 17C
East Lansing, MI 48824

CONNECT
web: rtsf.natsci.msu.edu/proteomics
email: rtsf.proteomics@msu.edu

EQUIPMENT

MASS SPECTROMETERS

ThermoScientific Excedion Pro

Hybrid quadrupole-Orbitrap with high-capacity transfer tube and electrodynamic ion funnel. High scan speed, ultra-high mass resolution, and high sensitivity support deep proteome coverage, confident peptide identification, and analysis of low-abundance species in complex biological samples.

ThermoScientific Q-Exactive

Hybrid quadrupole-Orbitrap well suited for peptide mapping, and routine analysis of purified proteins and simpler samples, while also supporting high-resolution MS workflows for a broad range of protein and peptide applications.



SOFTWARE TOOLS

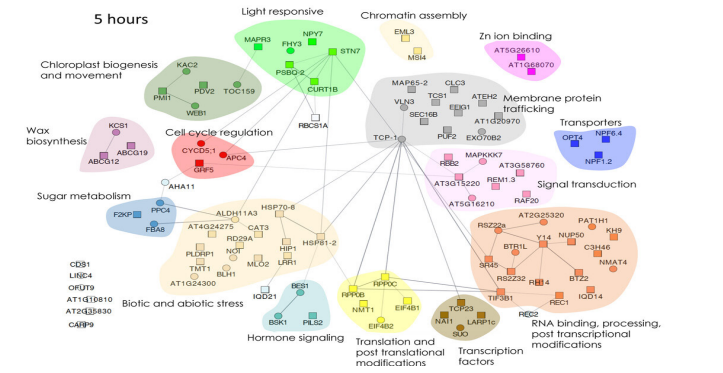
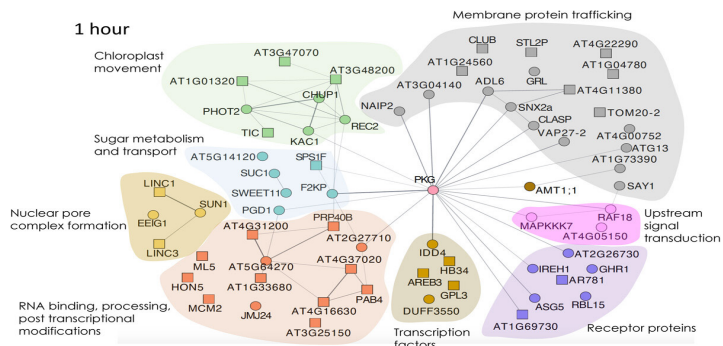
We provide end-to-end data analysis using widely adopted proteomics software for peptide identification, quantification, DIA analysis, statistical interpretation, and visualization.

SERVICES

- Purified protein characterization
- Peptide mapping
- Protein and peptide identification (DDA and DIA)
- Protein/peptide quantification (Label-free, SILAC and TMT)
- Interaction Proteomics (AP-MS)
- Post Translational Modification (PTM) analysis
- Experimental design and consultation
- Data analysis support
- Grant application support



The Isoprene-Responsive Phosphoproteome Provides New Insights into the Putative Signaling Pathways and Novel Roles of Isoprene

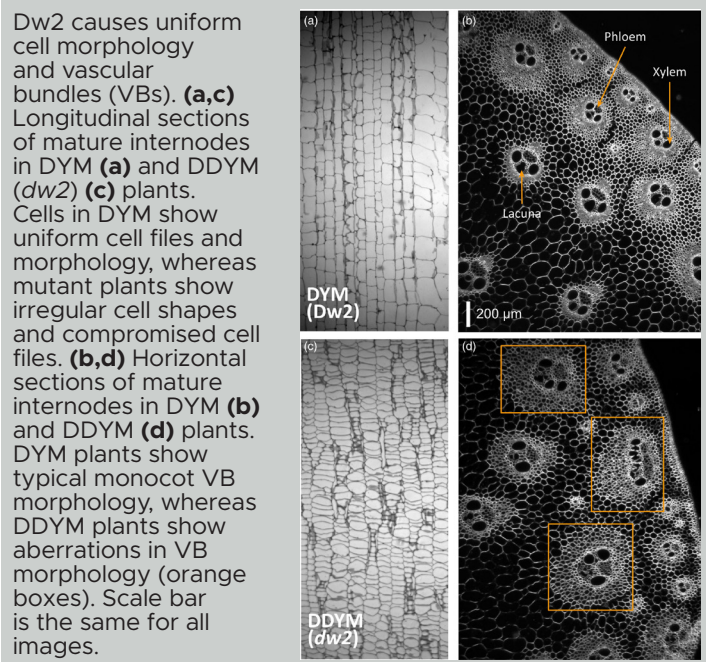


Important biological functions of differentially expressed phosphoproteins in *Arabidopsis* leaves fumigated with isoprene. STRING protein-protein interactions are shown for phosphoproteins differentially expressed in response to fumigation with 1 (top) or 5 (bottom) with isoprene. The nodes represent phosphopeptides upregulated (spheres) or downregulated (squares) in expression.

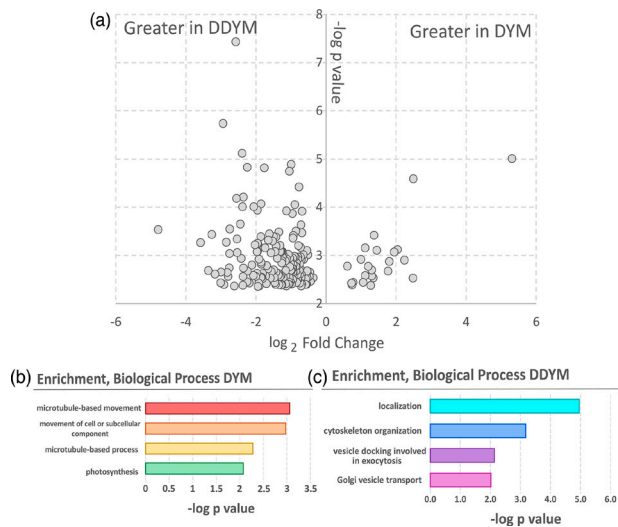
Edges or the lines connecting nodes represent evidence supporting interactions between a pair of proteins; thicker the edge stronger the evidence supporting an interaction. Nodes sharing the same color represent a cluster of phosphoproteins with similar biological functions.

Adapted from: Weraduwege, S.M., Whitten, D., Kulke, M., Sahu, A., Vermaas, J.V. & Sharkey, T.D. (2024) **The isoprene-responsive phosphoproteome provides new insights into the putative signaling pathways and novel roles of isoprene.** *Plant, Cell & Environment*, 47, 1099–1117. <https://doi.org/10.1111/pce.14776>

The AGCVIII Kinase Dw2 Modulates Cell Proliferation, Endomembrane Trafficking, and MLG/Xylan Cell Wall Localization in Elongating Stem Internodes of Sorghum Bicolor



Adapted from: Oliver J, Fan M, McKinley B, Zemelis-Durfee S, Brandizzi F, Wilkerson C, Mullet JE. **The AGCVIII kinase Dw2 modulates cell proliferation, endomembrane trafficking, and MLG/xylan cell wall localization in elongating stem internodes of Sorghum bicolor.** *Plant J.* 2021 Feb;105(4):1053-1071. doi: 10.1111/tj.15086



Phosphoproteomics of internode tissue revealing endomembrane and cytoskeleton proteins. (a) Volcano plot of the phosphoproteomic experiment on growing Int(P5) tissue. Most differential phosphorylation events occur in DDYM (Dw2) tissue. (b) GO enrichment analysis of the phosphoproteins in the right section of (a). Significant enrichment is observed for many processes involved in cytoskeletal maintenance. (c) GO enrichment analysis of the phosphoproteins in the left section of (a). Significant enrichment is observed for cytoskeletal organization, as well as localization, exocytosis, and vesicle transport. A complete list of enriched terms for both phosphoprotein datasets can be found in the supplementary information.

Mass Spectrometry & Metabolomics Core

The MSMC integrates state-of-the-art mass spectrometry and advanced bioinformatics to reveal biochemical networks across human health, plant and soil biology, environmental systems, agriculture, nutrition, veterinary medicine and more. We help researchers uncover hidden metabolites, identify biomarkers, and define molecular mechanisms across diverse biological systems.



LOCATION
Biochemistry Building
603 Wilson Road
Room 11
East Lansing, MI 48824

CONNECT
web: rtsf.natsci.msu.edu/mass-spectrometry
email: RTSF.MassSpec@msu.edu

EQUIPMENT

HIGH RESOLUTION MASS SPECTROMETERS

- **SCIEX ZenoTOF 7600**
The only high resolution TOF instrument with EAD capability providing sensitive and highly specific molecular structures.
- **ThermoScientific Q-Exactive**
Hybrid quadrupole-Orbitrap with resolution up to 140,000 allowing for robust global profiling and quantitative analysis.
- **Waters Xevo G2-XS**
Quadrupole TOF providing most comprehensive and high-quality data on the broadest range of compounds in complex matrices.
- **LECO GC-HRT+ GC-TOFMS**
High performance GCMS capable of full range allowing for high-confidence compound identification.

IMAGING MASS SPECTROMETER

- **Bruker ultrafleXtreme MALDI-TOF/TOF**
Next generation MALDI-TOF/TOF with imaging capabilities and low fmol level sensitivity.
- **HTX M3+ matrix sprayer**
Automated MALDI imaging sample preparation system.

QUANTITATIVE/TANDEM QUADRUPOLE MASS SPECTROMETERS

- **Waters Xevo TQ Absolute XR UPLC/MS/MS**
- **Waters Xevo TQ-S UPLC/MS/M**
- **Waters Xevo TQ-XS UPLC/MS/MS**
- **Waters Xevo TQ-S Micro UPLC/MS/MS**
A fleet of LC/MS/MS instruments for absolute quantitation of compounds in various complex matrices.

GCMS

- **Agilent 5975 single quad GCMS**
- **Agilent 7010 triple quad GCMS**
- **LECO GC-HRT+ TOFMS**
Robust and quantitative analysis of known panels of metabolites from various metabolic pathways.

SOFTWARE TOOLS

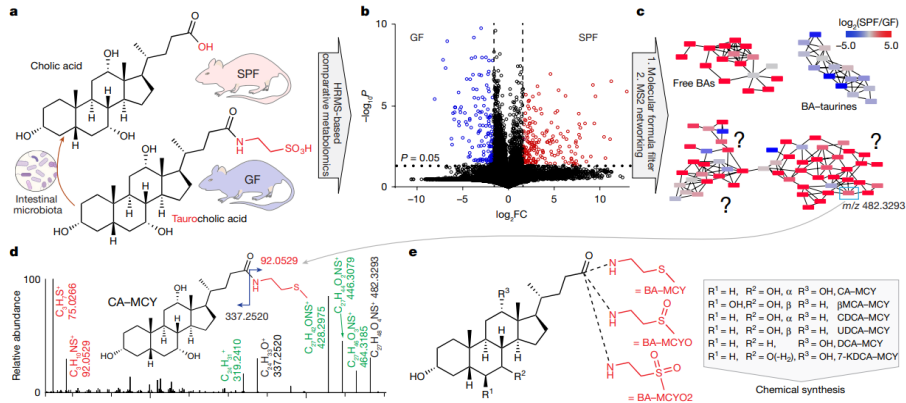
- Thermo Compound Discoverer 3.3
- Waters Progenesis Q1
- A gamut of open-source software including XCMS, MZmine, MetaboLyzer, MS-DIAL, MetaboAnalyst, GNPS suite of tools
- In-house bioinformatics and specialized tools
- Multi-omics analysis and pathway enrichment analysis

SERVICES

- **Comprehensive** metabolite profiling (targeted & untargeted)
- **Quantitative** metabolite measurement
- **Imaging** mass spectrometry (MALDI-TOF/TOF)
- Advanced LC-MS/MS and GC-MS capabilities
- **Bioinformatics** support and data integration
- Experimental design and method development consultations
- Manuscript and grant proposal preparation
- Lipidomics and microbiome analysis

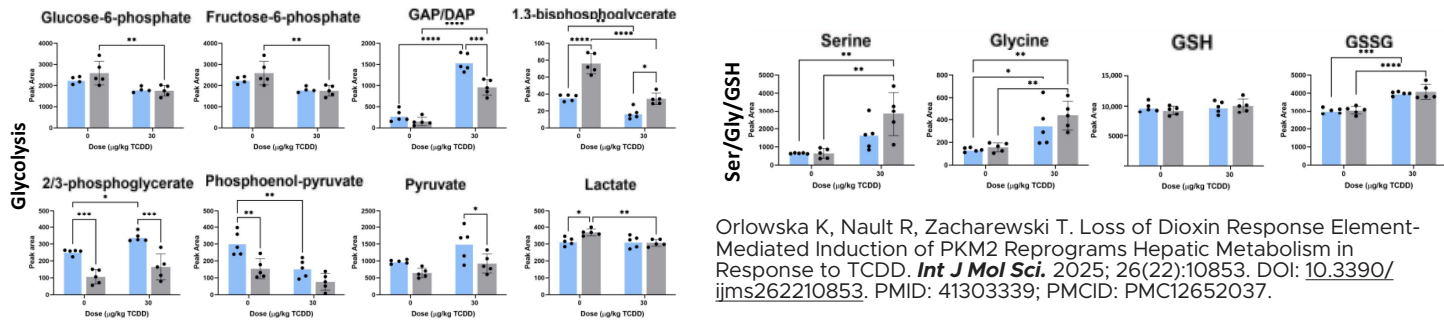
Untargeted Metabolomics: Comprehensive Profiling, Accurate Metabolite Annotation and Full Bioinformatics Analysis

Identification of novel conjugates of bile acids (BAs) via mass spectrometry (MS), regulated by host and gut microbiota. MS data revealed clusters representing free BAs, BA-aurine conjugates and previously unannotated BA-MCY conjugates. The red and blue nodes are downregulated and upregulated, respectively, in serum of germ-free (GF) compared with SPF mice.



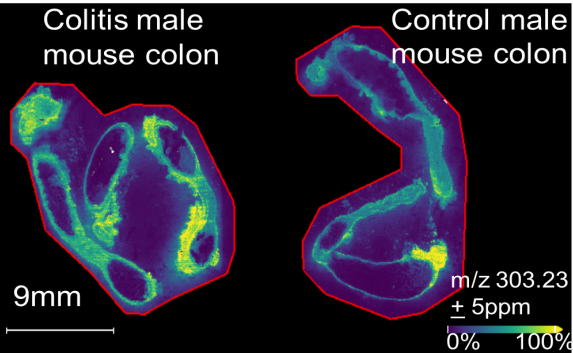
Won TH, Arifuzzaman M, Parkhurst CN, et al. Host metabolism balances microbial regulation of bile acid signaling. *Nature*. 2025; 638(8049):216-224. DOI: [10.1038/s41586-024-08379-9](https://doi.org/10.1038/s41586-024-08379-9). PMID: 39779854; PMCID: PMC11886927.

Targeted Metabolomics: Quantitation, 20+ Validated Assays, Novel Assay Development and Full Data Processing



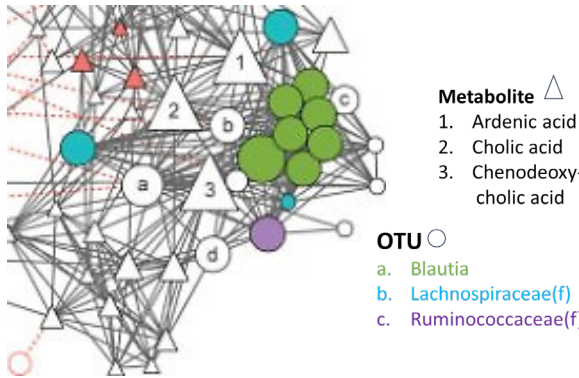
Levels of glycolytic and Ser/Gly/GSH metabolites in WT (blue) and PkmΔDRE (grey) mice treated with sesame oil (vehicle) or dioxin-like compound (30 µg/kg TCDD) every 4 days for 28 days.

Imaging Mass Spectrometry



Ion image heatmap of m/z 303.2329, putatively annotated as arachidonic acid, in colon of mice with DSS-induced colitis. [unpublished]

Multi-Omics and Pathway Analysis



Identifying metabolotypes associated with predisease risk state in inflammatory bowel disease (IBD): An inter-omic network of OTU-type-associated microbes and metabolite-associated metabolites in a children with IBD and their healthy siblings/parents.

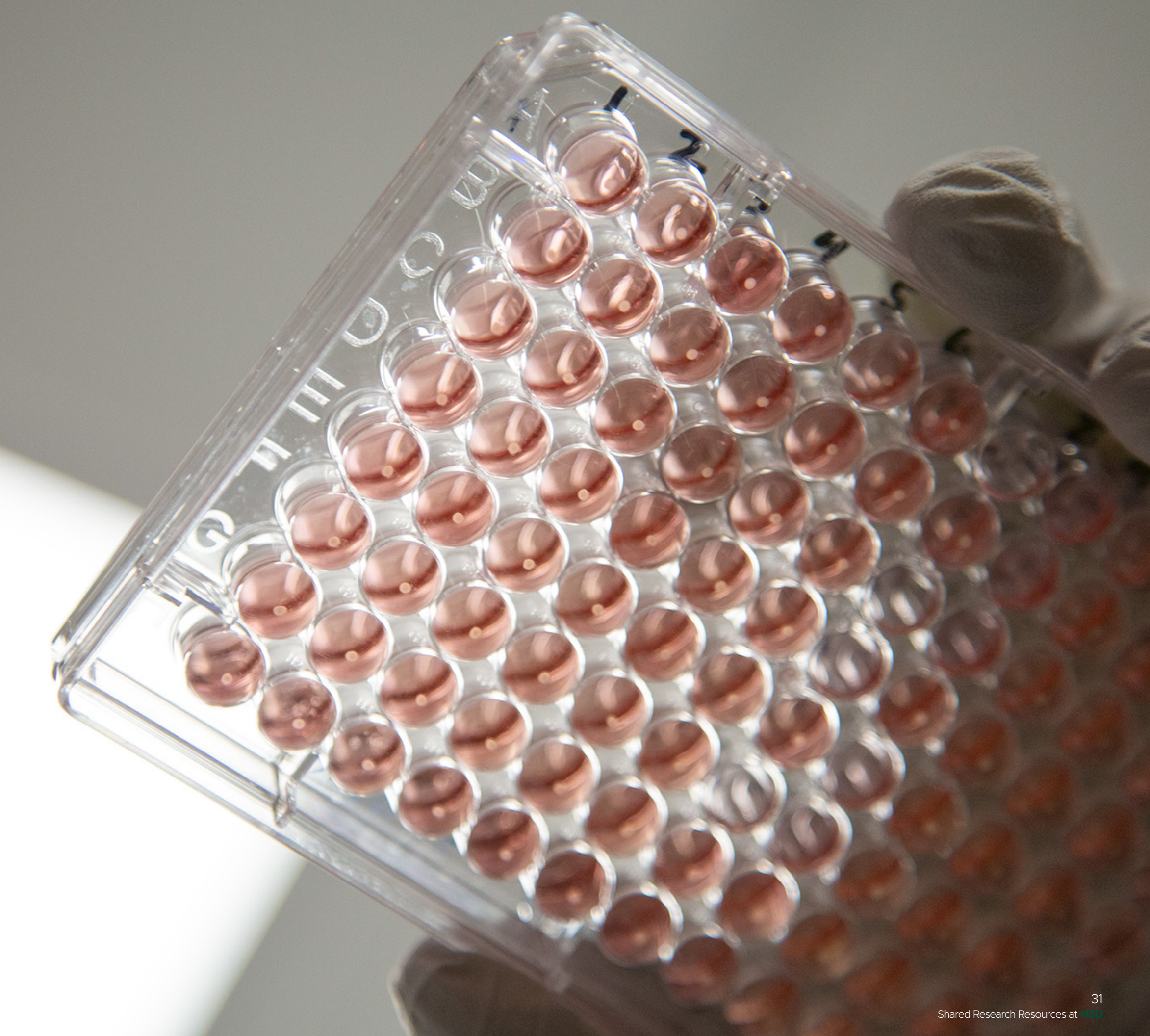
Jacobs JP, Goudarzi M, Singh N, et al. A Disease-Associated Microbial and Metabolomics State in Relatives of Pediatric Inflammatory Bowel Disease Patients. *Cell Mol Gastroenterol Hepatol*. 2016; 2(6):750-766. DOI: [10.1016/j.jcmgh.2016.06.004](https://doi.org/10.1016/j.jcmgh.2016.06.004). PMID: 28174747; PMCID: PMC5247316.

Biomedical, Clinical & Translational Resources

Where discovery becomes medicine.

Integrated capabilities
accelerate translational research
and drug discovery to improve
human and animal health.

Assay Development and Drug Repurposing Core.....	32
Medicinal Chemistry Facility.....	34
Radiochemistry and Radiopharmacy Solutions	36
Stem Cell Core.....	38
Transgenic and Genome Editing Facility.....	40
Metabolic Phenotyping & Preclinical Imaging Core.....	42



Assay Development & Drug Repurposing Core



EQUIPMENT

Biotek Synergy Neo

Multi-mode microplate reader: Fluorescence, Luminescence, AlphaScreen, UV/Vis Absorbance, FP & BRET

Biotek Cytation 3

Wide-field imaging system providing live cell imaging capabilities, temperature/gas control, automated cell counting, subpopulation analysis, image statistics

Hamamatsu Function Drug Screening System

Fluorescence/Luminescence plate imager with simultaneous addition and reading of plates

Akta Pure 25M

FPLC System with 6 column holders, 3 wavelength detection, sample pump, and fraction collector

Pioneer SPR

Measure high affinity binding in labeled or unlabeled biologics and produce high quality kinetic data (K_a , K_d)

Microcal VP-ITC

Directly measure mM to nM affinities, no labeling or immobilization required

Biomek

Robot liquid handling system for high-throughput workflows



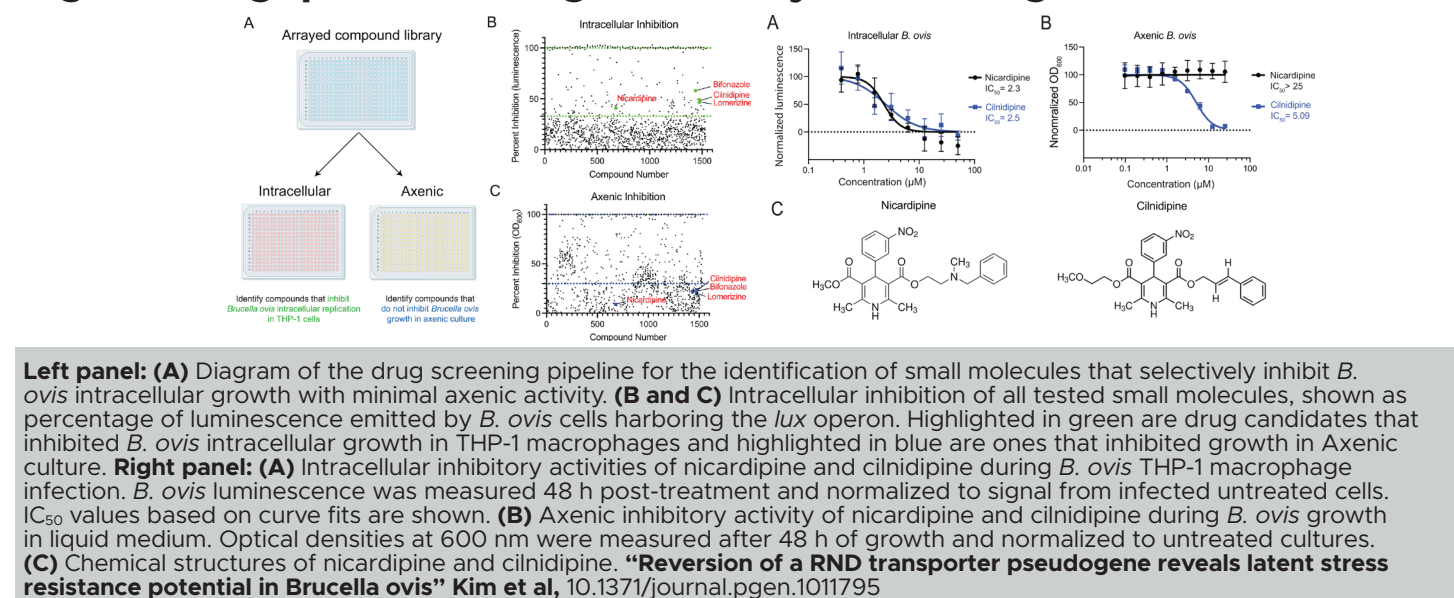
SERVICES

- High-Throughput Screening (HTS) Assay Development and Validation
- Small/Large Scale Chemical Screens
- HTS Data Analysis and Management
- Hit Picking and Dose Response Follow-up
- Core Instrument Operation Training
- Access to Compound Libraries
- Access to Automated Laboratory Robotics
- Grant Support

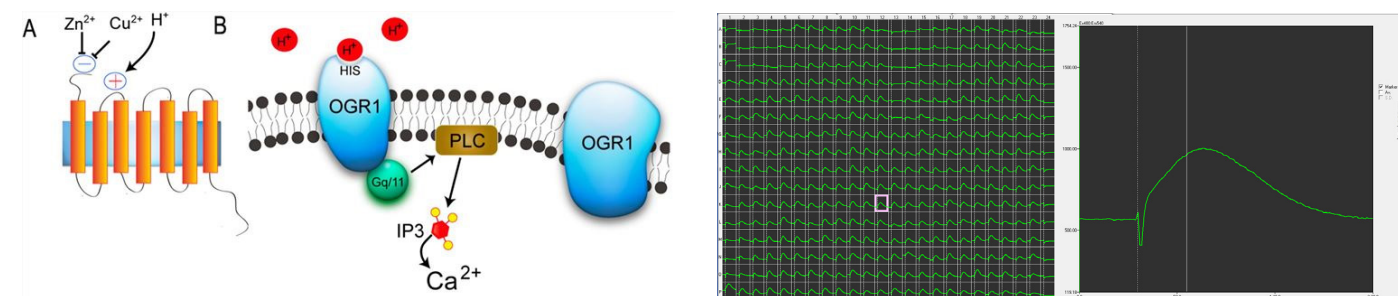
LOCATION
Life Sciences Building
1355 Bogue Street
Room B338
East Lansing, MI 48824

CONNECT
web: drugdiscovery.msu.edu/facilities/addrc

High-Throughput Screening to Identify Novel Targets in *Brucella Ovis*

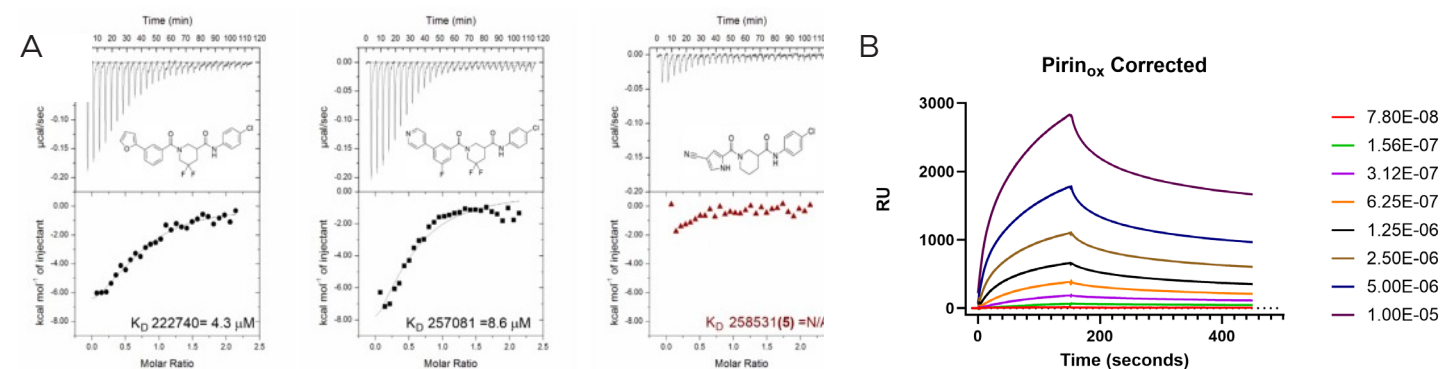


High-throughput Calcium assay to examine GPR68 Structure Activity Relationships



GPR68 is a class A GPCR that is activated by pH [EC_{50} = pH 6.8]. GPCRs can couple to many G-proteins, resulting in a plethora of second messengers, including (but not limited to) inositol phosphate, calcium ions (Ca^{2+}), cAMP, and Rho. In developing the first GPR68 inhibitor, OGM, we used Chem1-OGRI(GPR68) [Millipore] cells, that when activated, results in Ca^{2+} release from the endoplasmic reticulum, and GPR68. Real time calcium traces were measured using the Hamamatsu FDSS uCell in a 384-well format and varying concentrations of novel inhibitors were used. Data courtesy of the Hong Lab. <https://www.transfectedw.creative-biolabs.com/gpr68-membrane-protein-introduction.html>

Binding of small molecules to protein targets using ITC and SPR



(A) Isotherm generated by ITC shows that CCG-222740 (left) and CCG-257081 (middle) have greater enthalpy changes upon binding to pirin, as compared to that of CCG-258531 (right), indicative of better binding to recombinant pirin. **(B)** SPR sensograms of binding of recombinant pirin to an immobilized CCG-257081 analog **“Identification of Pirin as a Molecular Target of the CCG-1423/CCG-203971 Series of Antifibrotic and Antimetastatic Compounds” Lisabeth et al, ACS Pharmacol Transl Sci. 2019 Apr 12;2(2):92-100. doi: 10.1021/acspstsci.8b00048**

Medicinal Chemistry Facility

The Department of Pharmacology & Toxicology Medicinal Chemistry Facility contributes to the universal mission of MSU to enhance human health via drug discovery and chemical biology efforts. It partners on multidisciplinary projects by advancing the discovery and development of novel therapeutics. The medicinal chemistry team uses a variety of research resources that aid in the design, synthesis, scale up, optimization of bioactive compounds, and ADME and pharmacokinetic studies. It offers research support services for university and outside researchers.



LOCATION
Life Science Building
 1355 Bogue Street
 Rooms B347, B331
 East Lansing, MI, 48824

CONNECT
web: phmtox.msu.edu/facilities/medchem

EQUIPMENT

LCMS (Advion)

Low resolution liquid chromatography mass spec. Enables synthetic efforts by monitoring reactions progress and isolation of compounds of interest.

Microwave reactor (Anton Parr)

Useful for running reactions safely at higher pressure and temperature conditions leading to improved reaction efficiency. It has proved to be a great tool for enhancing reactions yields for difficult chemistries.

Analytical HPLC (Agilent)

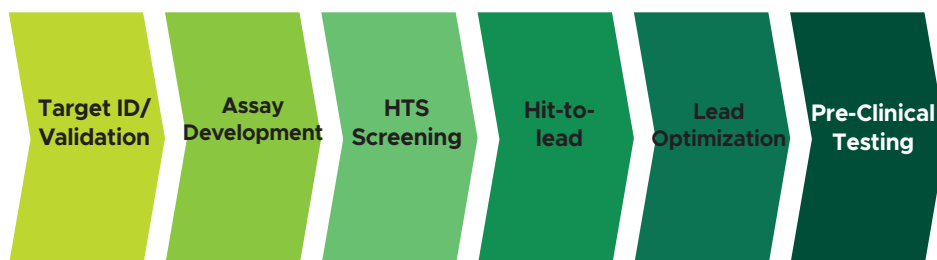
High pressure liquid chromatography. Utilized for purity analysis and separation/purification of reaction mixtures and final products. This instrument is equipped with semi-prep. column for small and medium scale separations.

CombiFlash Purification MPLC systems (Teledyne ISCO)

Moderate pressure liquid chromatography for purification of small to large scale quantities (up to few hundred grams). Operates under normal phase and reverse phase conditions. Uses UV-VIS detection and operates in a semi-robotic fashion.

Lyophilizer (LABCONCO)

Operates at lower temperature and pressure for larger water amounts removal under freeze dry conditions. Complements very well with the reverse phase purification techniques.



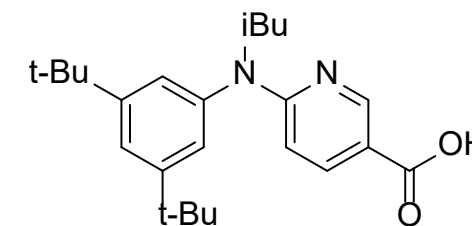
SERVICES

- Drug discovery and medicinal chemistry support
- Chemical biology support
- Proposal and grant preparation
- Series triage-High throughput screening
- Custom compound synthesis and scale-up
- Analytical separation and purifications
- in vitro ADME
- Pharmacokinetic studies
- Metabolite ID studies
- IP/ patent development / early company formation

RXR Agonists for Treatment of Various Cancers

In collaboration with Karen Liby (Department of Pharmacology and Toxicology)

- **RXR agonists:** New series of immunomodulatory that modulate PD-L1 (macrophages) that were active against KRAS mediated Cancers (Lung, Pancreatic, Colorectal, NFI cancers)
- Over **200** analogs have been prepared
- Current lead drug (MSU-42011) is in preclinical characterization for *Investigational new drug* IND



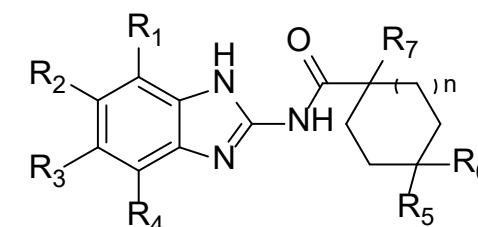
MSU-42011

Pei-Yu Hung, Jessica A. Moerland, Ana S. Leal, Bilal Alewi, Edmund Ellsworth, D Wade Clapp, Verena Staedtke, Renyuan Bai, Karen T. Liby. The RXR agonist MSU-42011 is effective for the treatment of preclinical NF1-deficient models. *Cancers*, 2025, 17(12), 1920.

MmpL₃ for TB and NTM Infections

In collaboration with Robert Abramovitch (Department of Microbiology, Genetics, & Immunology)

- **MmpL₃ inhibitors:** Has proven to be excellent drug target for the treatment of mycobacterial infections
- Over **500** analogs have been prepared
- Current leads are in preclinical characterization for *Investigational new drug* IND

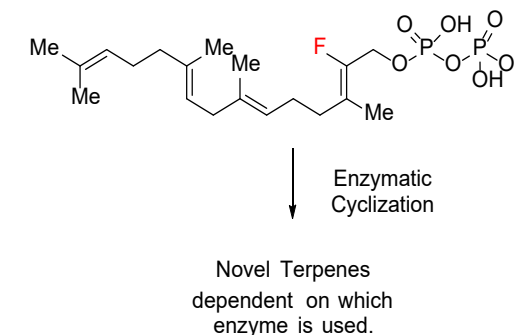


Williams JT, Giletto M, Haiderer ER, Alewi B, Krieger-Burke T, Ellsworth E, Abramovitch RB. The *Mycobacterium tuberculosis* MmpL3 inhibitor MSU-43085 is active in a mouse model of infection. *Microbiol. Spectr.* **2024**,12(1): e0367723. doi: 10.1128/spectrum.03677-23.

Preparation of Non-Natural Terpene Products

In collaboration with Prof. Bjoern Hamberger (Department of Biochemistry & Molecular Biology)

- Discovery of plant pathways for bioactive diterpenoids found in medicinal plant species.
- Preparation of substrates for the biosynthesis of non-natural terpene products.



U.S. Patent Application Serial No.: 62/930,898
 Title: BIOSYNTHESIS OF CHEMICALLY DIVERSIFIED NON-NATURAL TERPENE PRODUCTS
 Inventors Ellsworth, Giletto, Hamberger, Miller, Neubig (November 2019, provisional)

Radiochemistry & Radiopharmacy Solutions (RadCore)

The RadCore provides synthesis of drugs and radiolabeled agents for imaging and therapeutic applications in animals and humans. The core serves as a central resource for drug manufacturing, radiolabeling services, and regulatory support to researchers engaged in in vitro, preclinical, and clinical trials. The RadCore meets FDA guidelines (cGMP compliant) under 21 CFR parts 210, 211, 212, and USP <797>.



LOCATIONS
Radiochemistry Labs
 IQ/Bioengineering Building
 775 Woodlot Drive
 Room 1S
 East Lansing, MI, 48824

Radiopharmacy
 Clinical Center East – D Wing
 840 Service Road
 Suite E20
 East Lansing, MI, 48824

CONNECT
web: radcore.msu.edu
email: radiopharmacy@msu.edu

EQUIPMENT

cGMP-COMPLIANT MANUFACTURING

- **Clean Room** (ISO5 areas inside ISO7)
Siemens Desigo-monitored gowning room, anteroom, and clean room for temperature, humidity, and pressure differentials with 24/7 alarms; biannual ISO certifications and environmental monitoring. Monitored refrigerator and freezer.
- **Radiosynthesis Modules** (Synthra GmbH)
RN-Plus automated radiosynthesizers for complex synthesis of small molecules and drugs
- **Lead-Shielded Hot cells** (Van Gahlen)
Two large shielded hot cells with manipulators for safe handling of high levels of radioactivity (10 Ci)
- **Radiation Detection Instruments**
Dose calibrators, well counter, HPLC radiation detectors, Radio iTLC scanner, CZT detector for gamma-ray spectroscopy; all to enable accurate measurements of radioactivity & purity.

QUALITY CONTROL AND RELEASE TESTING

- **HPLC:** For Identity & purity of drug substance
- **Gas Chromatography:** For Residual Solvent Analyses following synthesis & safety
- **Endotoxin and Sterility testing:** For safety
- **Potency Assays:** For biological activity after radiolabeling
- **Stability testing:** To determine expiration date

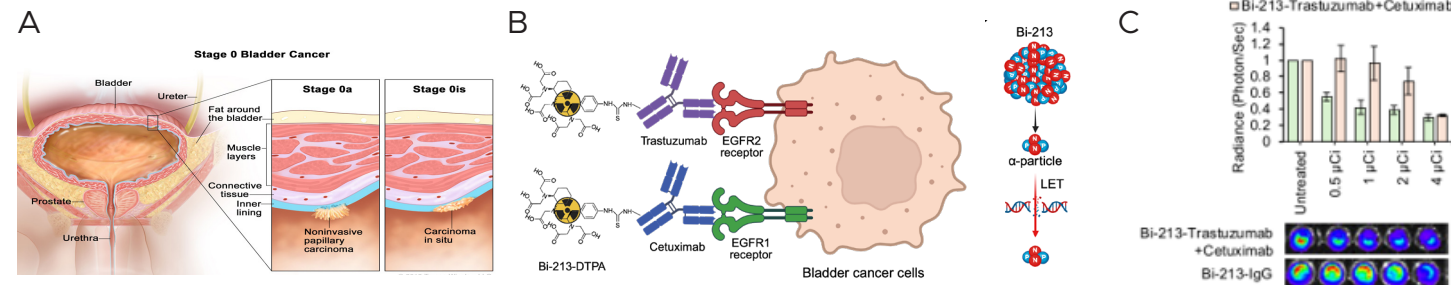


SERVICES

- Manufacturing radiopharmaceuticals for binding assays, preclinical studies, and clinical studies
- Radiolabeling small molecules, peptides and proteins (e.g., antibodies) with a wide array of different radioisotopes: F-18, Tc-99m, Cu-64, Ga-68, Zr-89, Y-86/90, Lu-177, Pb-203, Pb-212, Bi-213, Pb-214/Bi-214, Ac-225,
- Manufacturing non-radioactive drugs/precursors
- Quality control and release testing for manufactured compounds
- Preparation of Chemical Manufacturing and Control (CMC) section of IND for clinical trial
- Extensive Training Program

A Prospective, Open-Label, Phase 1 Study of Safety, Tolerability, and Efficacy of Intravesical Radiolabeled-Trastuzumab/Cetuximab Therapy in Patients with Non-Muscle Invasive Bladder Cancer

Dr. Kurt Zinn with Corewell Health Partner, Dr. Conrad Tobert

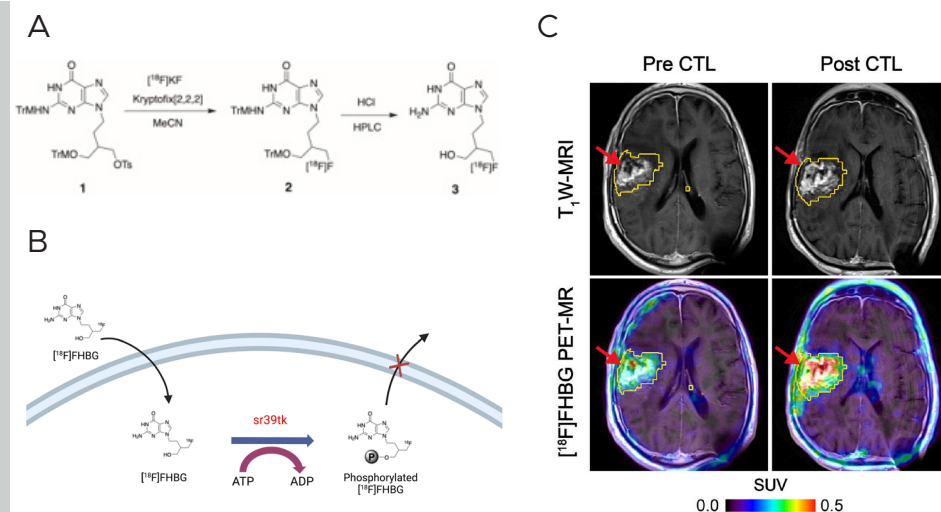


This collaborative project (Corewell, MSU, Niowave) addresses the lack of effective treatments for bladder cancer by creating a novel radiopharmaceutical for effective and safe targeted radiation therapy. The standard of care treatment for high-grade, non-muscle-invasive bladder cancer (A) is immunotherapy with BCG (Bacillus Calmette-Guerin, a bacterium to “turn on” the immune system) administered into the bladder. Intravesical BCG is relatively well-tolerated but is effective in only two-thirds of patients. To provide a better treatment, we attached alpha-particle emitting Bi-213 to trastuzumab and cetuximab, two FDA-approved antibodies that target EGFR1/2 that are overexpressed on bladder cancer (B). As shown (C), this treatment is highly effectively in killing human bladder cancer cells (SCaBER) compared Bi-213 attached to a control, non-targeted isotype antibody (C). A phase I clinical trial is planned.

Cancer Gene Therapy and [F-18]FHBG PET Imaging of HSV1-sr39tk gene expression

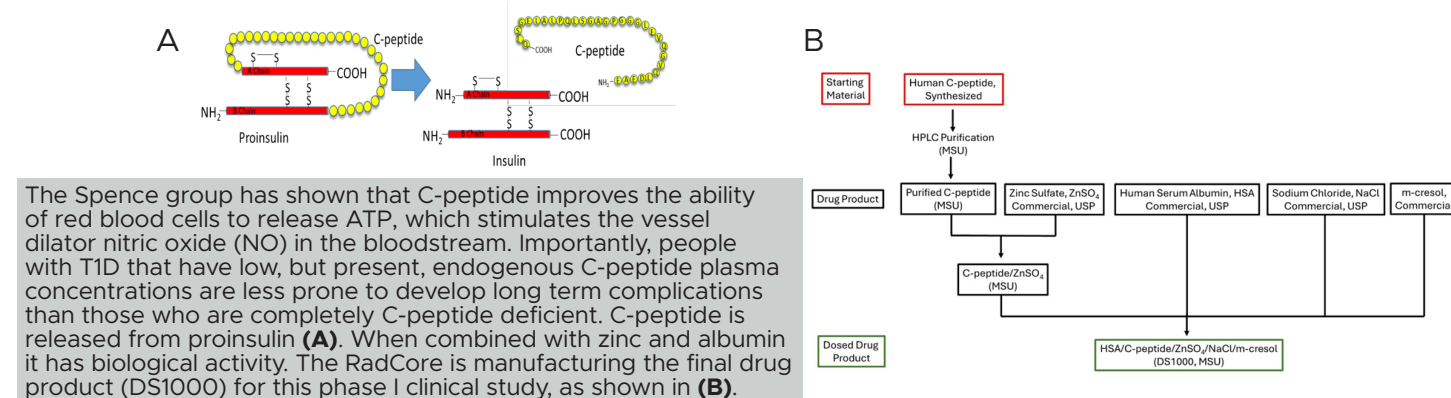
Dr. Jinda Fan with Henry Ford Health Partner, Dr. Tobias Walbert

This project focuses on developing a robust automated radiosynthesis method to produce and purify [F-18] FHBG, a small-molecule substrate for the HSV1-sr39tk (thymidine kinase) reporter enzyme. The synthesis steps are shown (A). Following injection in the human patient undergoing gene therapy for cancer, the [F-18]FHBG is trapped (B) and provides contrast for non-invasive imaging with Positron Emission Tomography (PET) to show the areas of gene transfer and HSV-sr39tk expression (C). The example in (C) is from a Stanford group[#] after CTL (CD8+ cytotoxic T lymphocytes) were given as glioma therapy and followed by PET/MRI.
[#]Sci Transl Med. 2017 January 18; 9 (373): doi:10.1126/scitranslmed.aag2196. Fig. 4



A Prospective, Open-Label, Phase 1 Study of Safety, Tolerability, and Efficacy of DS1000 in people with type 1 diabetes (T1D)

Dr. Dana Spence and Dr. Kurt Zinn are co-PIs of the project and are collaborating with clinical partner Dr. Littlejohn, Sparrow-Michigan Health (Funded by Helmsley Charitable Trust)



The Spence group has shown that C-peptide improves the ability of red blood cells to release ATP, which stimulates the vessel dilator nitric oxide (NO) in the bloodstream. Importantly, people with T1D that have low, but present, endogenous C-peptide plasma concentrations are less prone to develop long term complications than those who are completely C-peptide deficient. C-peptide is released from proinsulin (A). When combined with zinc and albumin it has biological activity. The RadCore is manufacturing the final drug product (DS1000) for this phase I clinical study, as shown in (B).

Stem Cell Core

The mission of the SCC is to advance the in-house adoption of stem cell approaches for both basic and translational research and to accelerate their application to biomedical and regenerative therapies. SCC provides faculty with comprehensive expertise, resources, and support in stem cell culture, reprogramming, genome engineering, and lineage-specific differentiation.



LOCATION
IQ/Engineering Building
775 Woodlot Drive
Room 3114
East Lansing, MI 48824

CONNECT
web: stemcells.iq.msu.edu

CORE SERVICES

Training and Education Services

- We provide hands-on training in human iPSC culture for researchers at all experience levels.
- Hands-on training in human iPSC culture, techniques include expansion, maintenance, passaging, cryopreservation, and recovery. Introductory and advanced skill development available.
- Training conducted in the Stem Cell Core tissue culture facilities.

Cryo Banking of Stem Cell Lines

- Cryo-banking for stem cell lines (limited PI storage available)
- Access to a repository of select publicly available hESC and hiPSC lines

iPSC Reprogramming Services

- Somatic cell reprogramming to iPSCs (human and select animal species)
- Reprogramming from PBMCs or fibroblasts
- Multiple vector platforms available: episomal, Sendai virus, lentiviral, and RNA-based
- Patient-derived hiPSC model generation support

Genome Editing of Stem Cell Lines

- CRISPR RNP-based gene editing for knockouts and small modifications
- Assistance with design, screening, and clonal validation workflows



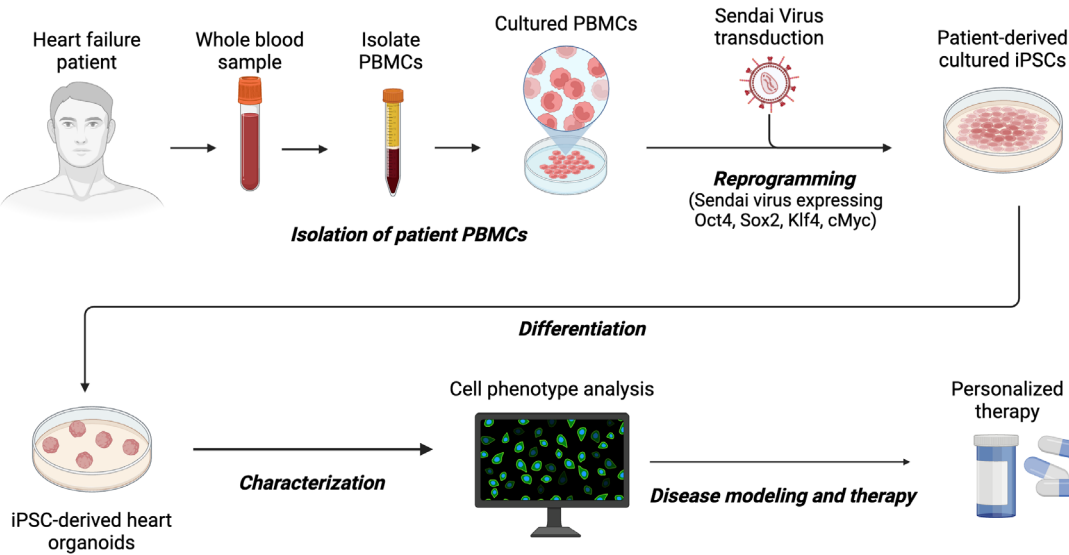
MODEL SYSTEM DEVELOPMENT & TECHNICAL SUPPORT

- Differentiation protocol selection, optimization, and troubleshooting
- Organoid and assembloid culture guidance
- Support in adapting and implementing new reprogramming and differentiation methodologies

CONSULTATION & GRANT SUPPORT

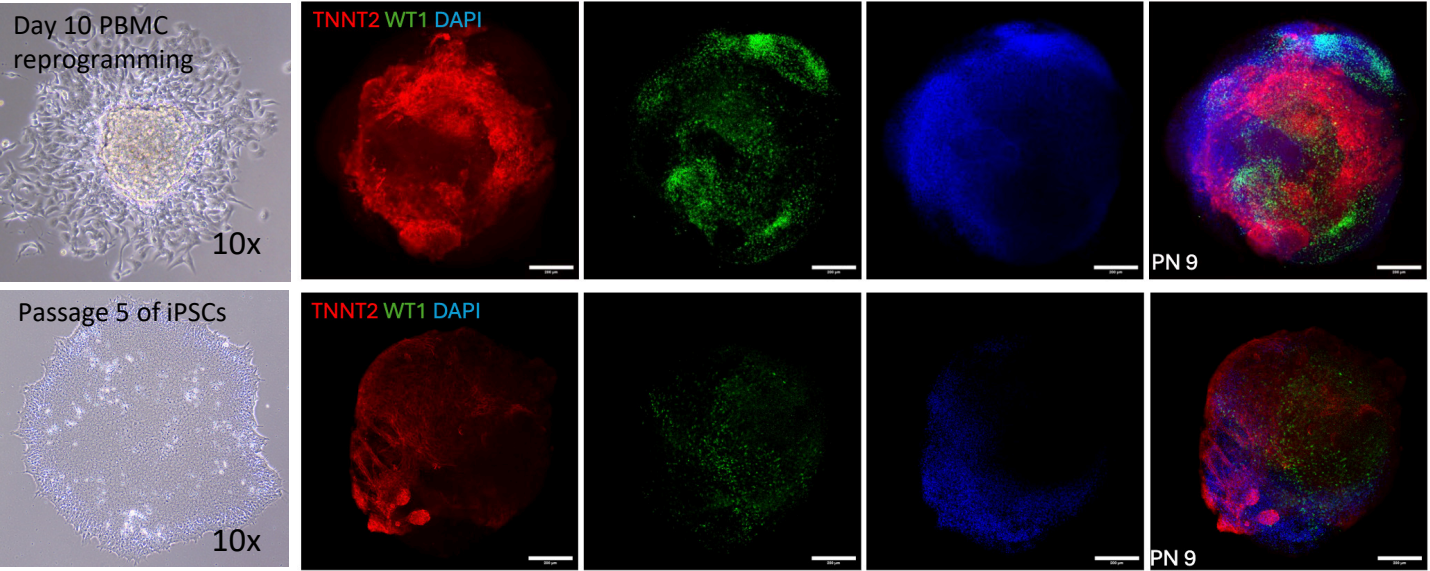
- Experimental design guidance for SC projects
- Pre-award proposal support
- Editing of stem cell-related grant research sections
- Letters of support available upon request

PBMC Reprogramming for Generation of iPSC-Derived Cardiac Organoids



Patient-to-organoid pipeline for investigating GDMT responsiveness in heart failure using iPSC-derived heart organoids. Peripheral blood mononuclear cells (PBMCs) are isolated from a heart-failure patient's whole blood, cultured, and reprogrammed with non-integrating Sendai virus vectors expressing OCT4, SOX2, KLF4, and c-MYC to generate patient-derived induced pluripotent stem cells (iPSCs). iPSCs are then differentiated into cardiac lineages and assembled into iPSC-derived heart organoids. The organoids are characterized and their cellular phenotypes analyzed for disease modeling and drug testing, with results used to guide personalized therapy.

Cardiac Organoids from Reprogrammed iPSCs from GDMT Non-Responder Heart Failure Patients



The goal of this project is to establish a patient-specific *in vitro* model of heart failure to study responsiveness to guideline-directed medical therapy (GDMT). To that end, we have begun collecting blood from heart-failure patients classified as GDMT responders or non-responders. Patient-specific hiPSC lines are generated by reprogramming PBMCs isolated from these samples at MSU's Stem Cell Core. The Aguirre lab differentiates the hiPSCs to produce patient-specific heart organoids, which will be used for downstream phenotyping, including assessment of neurohumoral responses characteristic of heart failure with reduced ejection fraction (HFrEF), such as activation of the renin-angiotensin-aldosterone and sympathetic (adrenaline) axes.

Transgenic & Genome Editing Facility

- The TGEF provides Genome Editing services of multiple experimental systems (animals, cell-lines, in-vivo)
- Comprehensive 'start-to-finish' pipeline from targeting design to genotyped edited organisms, as well as modular service offerings for individual project stages
- Serves as a knowledge hub for faculty interested in using genome or epigenome editing approaches

CAPABILITIES

ANIMAL MODELS SUPPORTED

- CRISPR editing of *Mouse, Rat, African Grass Rat*
- CRISPR Small Modification (knockout, point mutation, small knockin, small deletion) and large deletion
- CRISPR Conditional knockout (loxP/Cre or Flp/FRT)
- CRISPR large insertions or replacements
- Conventional transgenic generation

EMBRYO MANIPULATION SERVICES

- Microinjection (pronuclear or cytoplasmic): zygote, 2-cell embryo, or blastocyst ESC
- Embryo electroporation: in vivo and in vitro
- Consultation on non-mammalian embryo microinjection

MOLECULAR SERVICES

Gene Editing & Molecular Cloning

- CRISPR targeting and molecular cloning design
- Genome editing with nucleases (CRISPR-Cas), recombinases (Cre, FLP), and conditional/inducible systems: construct and component design and cloning
- gRNA design and validation for CRISPR-Cas targeting
- GE modification screening strategies
- Genotyping and optimization

New CRISPR Technology Testing and Adoption

- In vivo delivery of CRISPR components
- Transcriptional and epigenetic regulation
- Base editors, Prime editing and new Cas variants
- Pooled CRISPR library screens

SERVICES

Cryopreservation and Cryorecovery Services:

- Cryopreservation of sperm and fertilized embryos
- Rat and mouse cryorecovery from frozen embryos
- Mouse cryorecovery from sperm
- Frozen germplasm banking, export and import

Additional Rodent Services:

- Rederivation of mouse or rat lines on campus (both for imports and internal, small and large scale)
- Rodent import/export assistance: fresh or cryopreserved sperm/embryo
- Speed congenics and speed expansion
- Mouseline - IVF, ICSI

CONSULTATION & GRANT SUPPORT

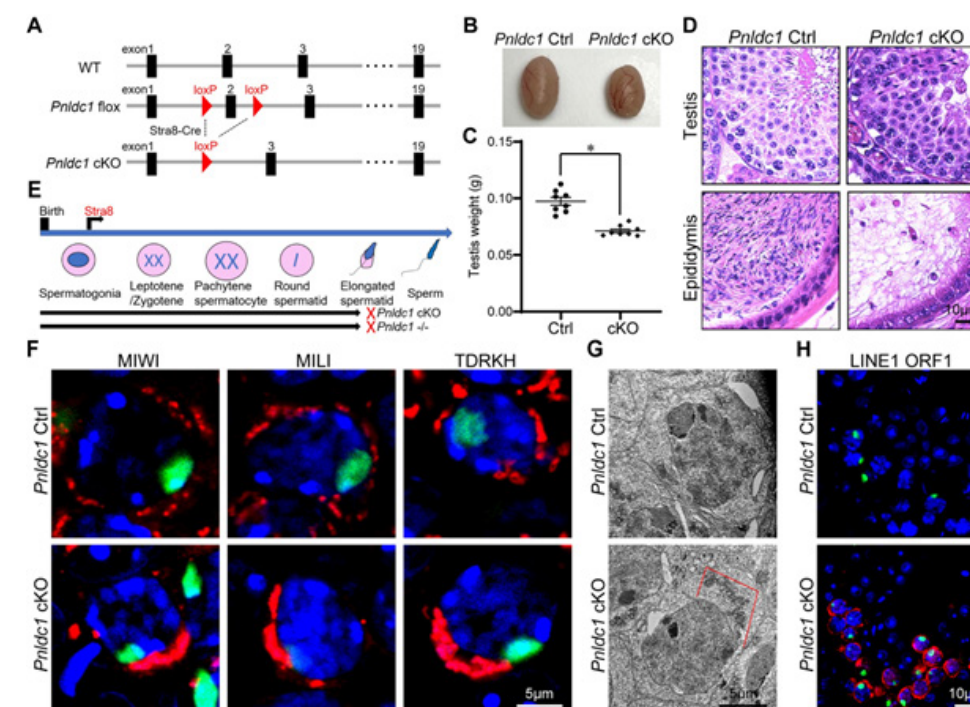
- Project and experimental design consultation
- Information on available GE resources and tools
- Training on molecular, GE and reproductive bio approaches
- Grant editing related to GE approaches
- Letters of support for grant applications
- Publication/manuscript editing
- Genotyping strategy development and support



LOCATION
IQ/Bioengineering Building
775 Woodlot Drive
Room 3114
East Lansing, MI 48824

CONNECT
web: tgef.iq.msu.edu
email: tgef@msu.edu

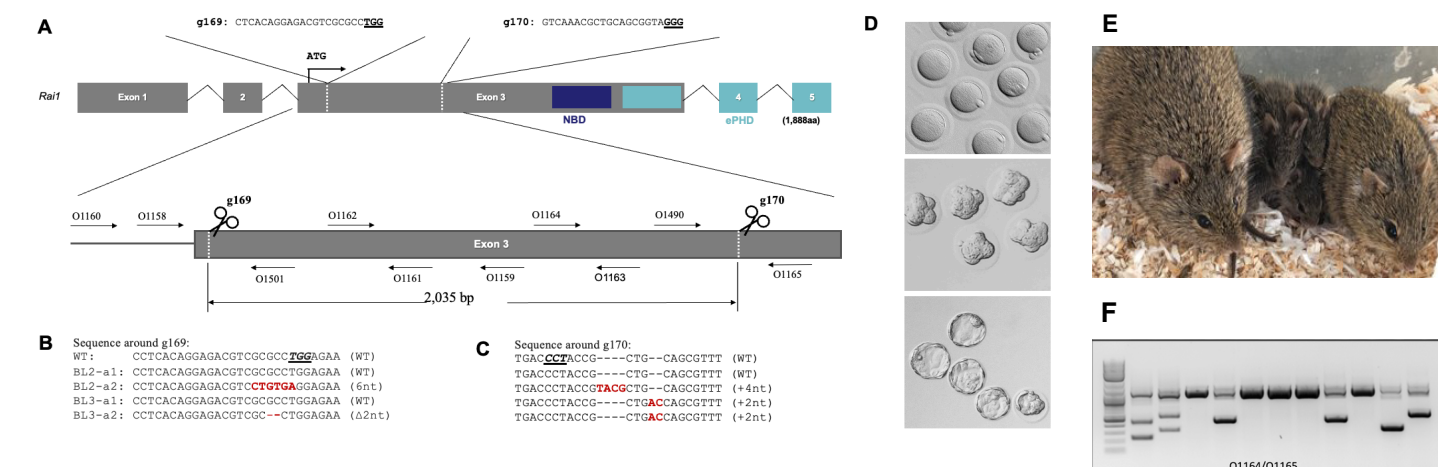
Conditional Deletion of Pnldc1 in Postnatal Germ Cells Causes Defective piRNA Trimming, LINE1 Upregulation, and Male Infertility



Wei et al. 2024. PNLDC1 catalysis and postnatal germline function are required for piRNA trimming, LINE1 silencing, and spermatogenesis in mice. *PLoS Genetics* 20(9):e1011429. PMID: 38234819

(A) Gene targeting strategy for the generation of Pnldc1 cKO. Cre-mediated deletion removed the exon 2 of Pnldc1. (B) Images of adult control and Pnldc1 cKO testes. (C) Testis weights of adult control and Pnldc1 cKO mice. (D) Hematoxylin and eosin-stained testis and epididymis sections from adult control and Pnldc1 cKO mice. (E) Spermatogenic arrest stage in Pnldc1 cKO and Pnldc1 KO mice. (F) Co-immunostaining of MIWI, MILI, or TDRKH (red) with γH2AX (green) in adult control and Pnldc1 cKO spermatocytes. (G) Transmission electron microscopy was performed on pachytene spermatocytes from adult control and Pnldc1 cKO testes. The mitochondria aggregation is indicated by red line. (H) Co-immunostaining of LINE1 ORF1 (red) with γH2AX (green) in adult control and Pnldc1 cKO spermatocytes. DNA was stained with DAPI.

First Successful Demonstration of CRISPR Editing in the African Grass Rat



CRISPR-Cas9 Mediated Deletion of the Rai1 Gene in the Nile Grass Rat, *Arvicanthis niloticus*

(A) A locus map denoting the targeting strategy for generation Rai1 KO grass rat. (B) and (C) Alignments with reference genome demonstrate the presence of indel mutations around CRISPR gRNA targeting sites. (D) Grass rat embryos that were cultured in vitro were able to develop to blastocyst stage. (E) A litter of Nile grass rats. (F) PCR demonstrating that multiple deletions from 2 Rai1 KO founders were transmitted to G1 offspring.

Xie et al. 2023 CRISPR-based Genome Editing of a Diurnal Rodent, Nile Grass Rat (*Arvicanthis niloticus*). *BMC Biology* 22(1):144. doi: 10.1186/s12915-024-01943-9. PMID: 37662225

Metabolic Phenotyping & Preclinical Imaging Core

The mission of the Metabolic Phenotyping & Preclinical Imaging Core is to advance biomedical discovery by providing investigators with access to specialized expertise, rigorous training, and cutting-edge imaging and metabolic phenotyping technologies. Through non-invasive *in vivo* assessment of physiological function, disease progression, and treatment response, the Core supports innovative preclinical research in metabolic disease, cancer, aging, and other health-related fields.



LOCATION
IVIS & X-RAD320
Biomedical Physical Sciences
567 Wilson Road
East Lansing, MI 48824

TSE SYSTEM/BRUKER MINISPEC
Interdisciplinary Science and Technology Building
766 Service Road
East Lansing, MI 48824

CONNECT
email: rtsf.ivis@msu.edu

EQUIPMENT

PRECLINICAL OPTICAL IMAGER

IVIS Spectrum (Revvity)

A versatile, advanced *in vivo* bioluminescent and fluorescent pre-clinical imaging system combining high-throughput and full tomographic optical imaging in one platform.

Features include:

- Light tight imaging chamber, heated stage with integrated gas anesthesia
- High throughput screening – 5 position manifold
- Versatile field of view – high sensitivity, high resolution
- Spectral un-mixing algorithms – 28 high efficiency filters spanning 430-850nm – visualize multiple reporters in the same animal
- 3D Reconstruction – DLIT, FLIT
- Living Image Software – seamless workflow from image acquisition to data analysis

METABOLIC CAGES

PhenoMaster NG (TSE Systems)

A sophisticated, modular platform designed for automated, non-invasive monitoring of mice in a stress-free home cage environment. Enables simultaneous tracking of:

- Metabolic parameters via Indirect Calorimetry: VO_2 , VCO_2 , RER, Energy Expenditure
- Ingestive Behavior – tracks food and liquid intake
- Activity and Exercise – spontaneous locomotor activity, voluntary running wheel
- This integrated system supports detailed phenotyping by capturing metabolic function, behavior and activity patterns in real-time under minimally stressful conditions

BODY COMPOSITION ANALYSIS

Minispec LF90II (Bruker)

A state-of-the-art Body Composition Analyzer for measuring lean tissue, fat, and fluid in live animals; excised organs/tissue.

The LF90II probe in probe design permits measurement in: Rats up to 700g; Mice and organs up to 130g; Biopsies from 50mg to 500mg

BIOLOGICAL IRRADIATOR

X-RAD320 (Precision X-Ray)

High-precision, self-contained biological X-Ray irradiator for cellular (e.g., survival curves, preparation of feeder layers), and small animal studies (e.g., whole-body irradiation with adoptive transfer). User friendly TouchRAD Control Panel. Pre-programmed password protected Lab accounts.

ANCILLARY EQUIPMENT

Located in the imaging suite and adjoining animal facility

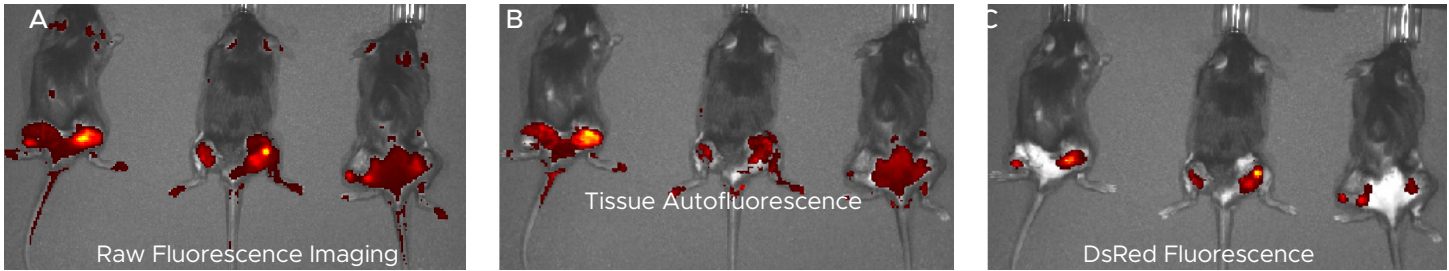
- 4ft Class II Type A2 Biosafety cabinet with UV light (Labconco)
- SMZ-800 Stereo Microscope with boom stand (Nikon)
- SMZ-745T Stereo Microscope with DS-Vi1 2 Megapixel high speed color Digital Camera (Nikon)
- Benchtop Non-Rebreathing Anesthesia Machine with 6 position manifold (Supera Anesthesia Innovations formerly LEI Medical)
- RT7 Plus Centrifuge with adaptors (Sorvall)

SERVICES

- Comprehensive hands-on training provided for IVIS Spectrum, X-RAD320, and Bruker LF90II
- Assistance with:
 - Study design, image acquisition and analysis
 - Animal handling techniques, manipulations, procedures & colony management
 - Information for IACUC submissions
 - Letters of support for grant applications



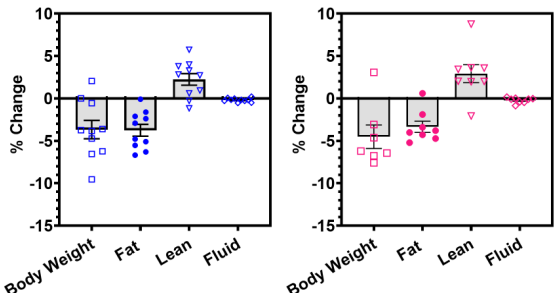
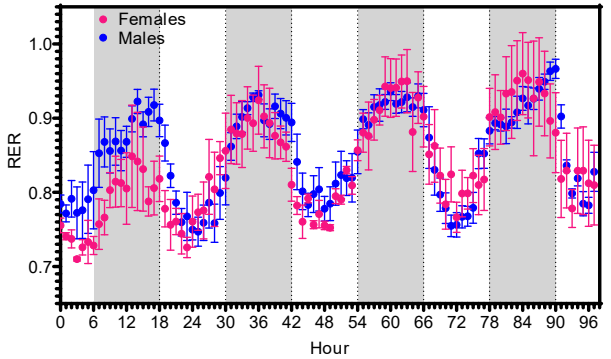
Optimizing *In Vivo* Fluorescence Imaging: The Importance of Mouse Strain Selection



DsRed-expressing mouse pancreatic tumor cells were injected subcutaneously into the flank of C57BL/6 mice. Prior to imaging, fur at the injection site was removed to minimize background signal. Fluorescence imaging was performed using the IVIS Spectrum imaging system (A). Spectral unmixing enabled separation of endogenous tissue autofluorescence (B) from the true DsRed fluorescence signal (C). These images illustrate that dark fur and melanin-rich skin can markedly attenuate fluorescence signal detection, underscoring the importance of strategic mouse strain selection to achieve sensitive *in vivo* fluorescence imaging.

Metabolic Phenotyping (TSE systems) & Body Composition Analysis (Bruker LF90II)

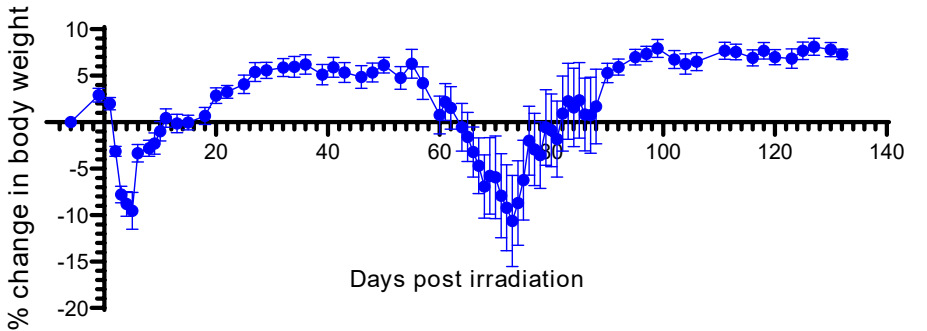
The TSE PhenoMaster NG System is an integrated, modular platform for metabolic, behavioral, and physiological phenotyping in rodents. Enabling continuous monitoring of indirect calorimetry (VO_2 , VCO_2 , RER), ingestive behavior (meal patterns, food and water intake), and locomotor activity within a low-stress home-cage environment. The representative plot illustrates Respiratory Exchange Ratio (RER) measurements collected over a 96-hour period, showing characteristic diurnal fluctuations in substrate utilization across this time course.



The Bruker LF90II enables non-invasive, longitudinal quantification of rodent body composition. The representative graphs to the left show fat and lean mass measurements after short-term (3-day) housing in TSE PhenoMaster NG metabolic cages equipped with voluntary running wheels. The decrease in fat mass accompanied by an increase in lean mass indicates a shift toward a more metabolically active state, consistent with increased physical activity during the monitoring period.

Murine Total-Body Irradiation and Bone Marrow Transplantation

C57BL/6 mice received 11 Gy total-body irradiation using the X-RAD320 Biological Irradiator (two 5.5 Gy fractions, 3 hours apart) followed by adoptive transfer of bone marrow transplant 18–24 hours later. Mice showed early weight loss days 1–5 (consistent with radiation-induced gastrointestinal injury), recovery by days 7–10, coat color changes around days 40–45, and a second weight-loss phase around days 65–70 consistent with hematopoietic dysfunction.



Data Science & Informatics



Turn data into insight.

Expertise and computational infrastructure support study design, omics analysis, and interpretation to advance discovery.

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Center for Statistical Training and Analysis.....48



Bioinformatics Core

The Bioinformatics Core brings together expertise from across MSU to support research through advanced omics data analysis, grant proposal assistance, and tailored training for researchers at all career stages.



LOCATION
Biomedical Physical Sciences Building
567 Wilson Road
Room 1440
East Lansing, MI 48824

CONNECT
email: bioinformatics@msu.edu
web: bioinformatics.msu.edu

CAPABILITIES

- Bulk and single-cell RNA-seq
- Bulk and single-cell ATAC-seq
- Single-cell multi-omics
- ChIP-seq and CUT&RUN
- Genome-wide methylation analysis
- Metagenomics/microbiome analyses
- Variant calling
- Causal variant prediction
- Population genomics
- Genome assembly

SERVICES

Short term projects
Discrete omics data analysis projects with well-defined deliverables. Charged per sample or per hour.

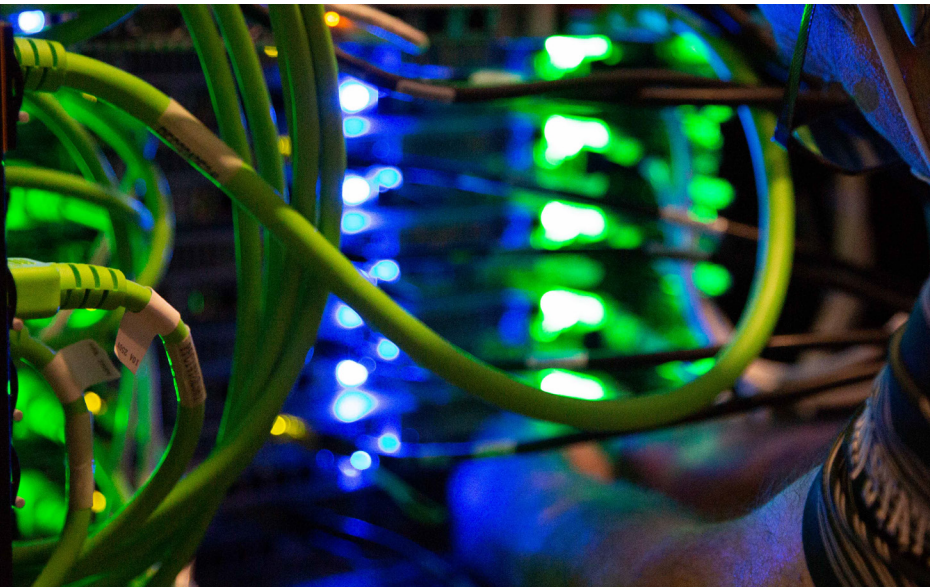
Long-term collaborations
Complex or exploratory projects that necessitate flexible, long-term collaborations for a % FTE/year.

Proposal support

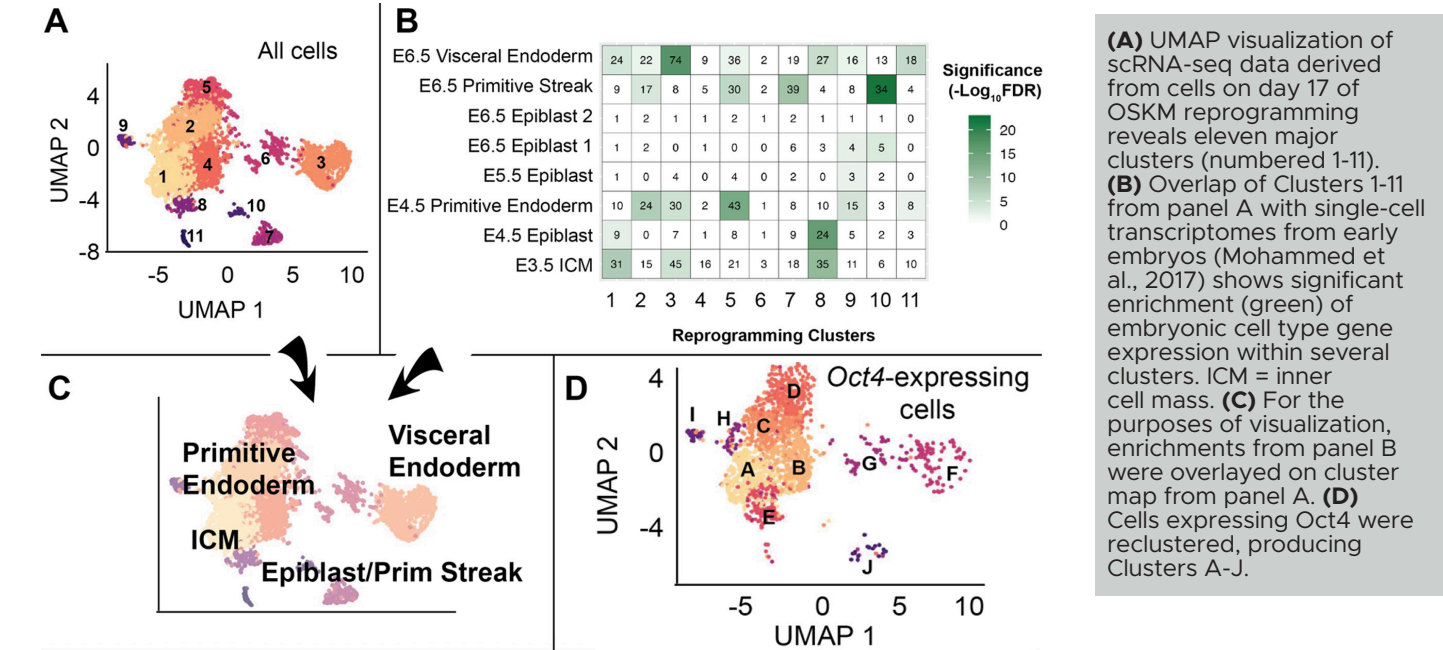
- Experimental design and methods consultation
- Letters of support
- Facilities statements
- Budget planning

Training
We provide individualized training on custom omics analysis pipelines

Virtual help desk and office hours
Encountering challenges with your own bioinformatics analysis? Message our Microsoft Teams Virtual Help Desk channel for free guidance from expert consultants, on demand. Or visit our weekly in-person office hours. For more information see <https://bioinformatics.msu.edu/help-desk>

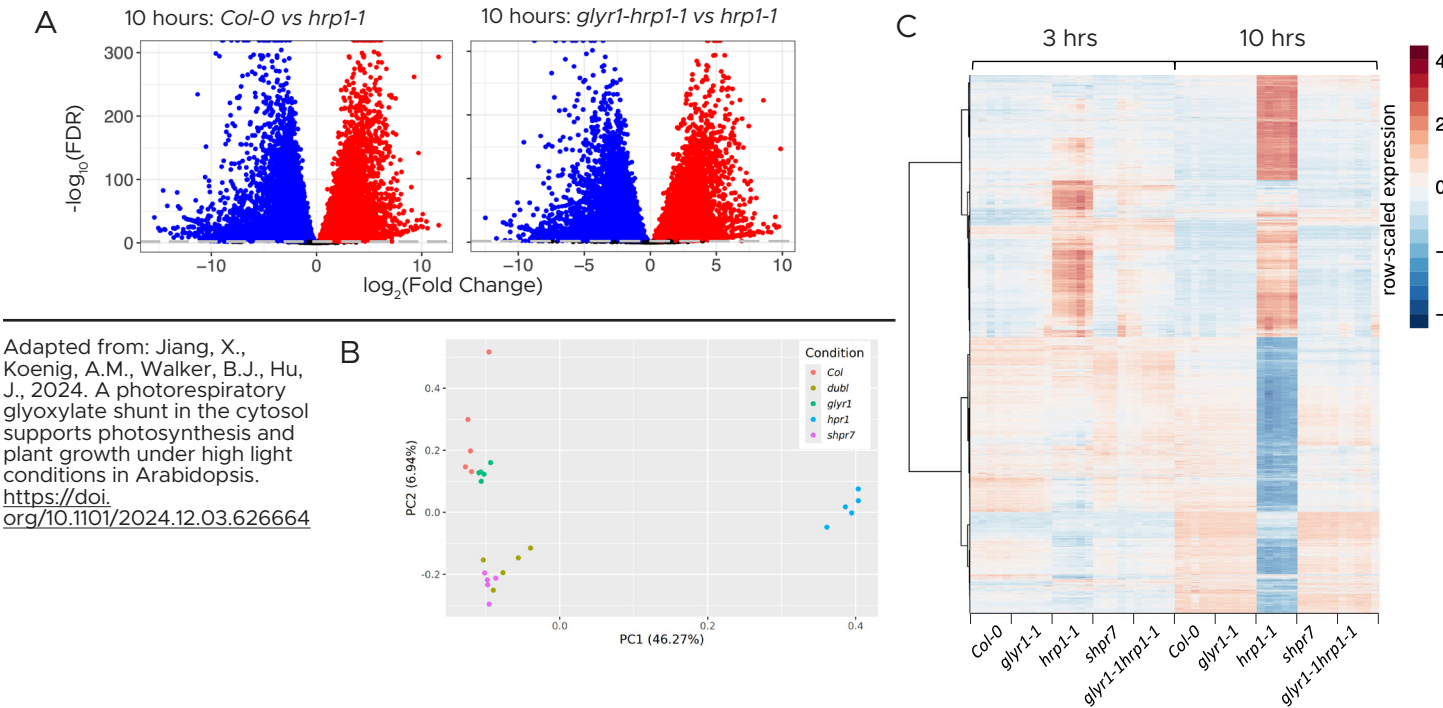


Identification of Oct4-Expressing Cells with Primitive Endoderm Character during OSKM Reprogramming by Single-Cell RNA-Sequencing



Adapted from: Moauro, A., Hickey, S.L., Halbisen, M.A., Parenti, A., Ralston, A., 2024. OCT4 is expressed in extraembryonic endoderm stem (XEN) cell progenitors during somatic cell reprogramming. <https://doi.org/10.1101/2024.01.22.576724>

Deficient GLYR1 Largely Reverts the Transcriptional Reprogramming in Arabidopsis *hpr1-1* Mutants



Plants were grown for 3 weeks under high CO₂ in normal light and then transferred to ambient air and high light during the dark period. Leaf tissue was sampled after 3 h and 10 h for RNA-seq. Biological replicates: n=5. (A) Volcano plots displaying differentially expressed genes (DEGs) in *glyr1-1* vs. Col-0, and *glyr1-1 hpr1-1* vs. *hpr1-1* at 10 h. (B) Principal Component Analysis (PCA) at 10 h. Col-0 and *glyr1-1* cluster together and *shpr7* and *glyr1-1 hpr1-1* (*dubl*) cluster together, with both groups clustering discretely from *hpr1-1*. (C) A heatmap in which *hpr1-1* shows dramatic transcriptional reprogramming that is restored to near Col-0 levels in *glyr1-1 hpr1-1* (*dubl*) and *shpr7*. Genes with at least a 4-fold change in the Col-0 vs. *hpr1-1* are represented.

Center for Statistical Training & Consulting (CSTAT)

At CSTAT we are dedicated to helping researchers thrive by collaborating on research projects and providing accessible and accurate guidance in study design and statistical analysis. We provide statistical expertise to MSU faculty, research staff, and graduate students, as well as off-campus clients.



LOCATION
Giltner Hall
293 Farm Lane
Room 100
East Lansing, MI 48824

CONNECT
web: cstat.msu.edu
email: cstatinf@msu.edu

OUR ROLE

Statisticians play a critical role in comprehensive study design and statistical analysis as well as interpretation and dissemination of ethical, reproducible, and high-quality research.

High quality and impactful research does not emerge in isolated environments but rather thrives from diverse input, communication, and cultivating partnerships.

KEY ACTIVITIES

- We provide expertise and guidance on **study design** and **statistical methods**.
- We **conduct statistical analyses** and provide accurate interpretation of results.
- We advise on **machine learning, AI, large language models** from algorithmic selection to model training, validation, and interpretation of output.
- We participate in **grant proposal** development and serve as **key personnel**.
- We collaborate on **manuscripts** and serve as co-authors.
- We provide **research data management** services.
- We offer **seminars** and workshops



Access and Partnership models

CSTAT is funded by contracts and grants and by contributions from the Office of Research and Innovation, colleges, departments, and programs. CSTAT team members collaborate on research projects and provide statistical expertise to MSU-affiliated faculty, research staff, and graduate students, and off-campus clients.

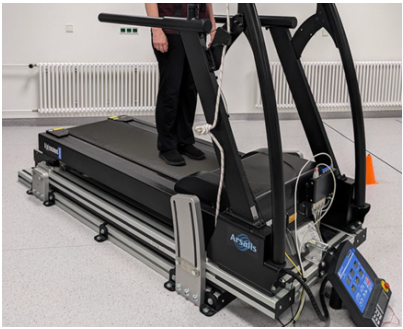
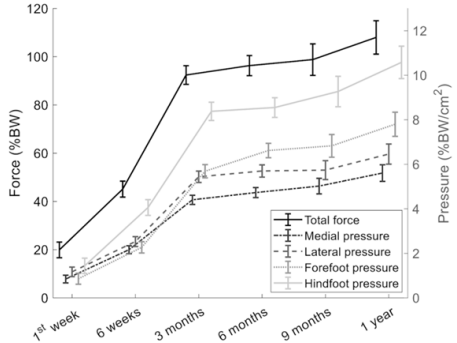
Partner units engage with CSTAT via joint appointments, staffing agreements, or fixed contributions. Researchers from these units will receive free statistical support as outlined in a memorandum of understanding.

Grant proposal development is free if CSTAT's statisticians are appropriately included in the post-award budget (minimum 5-10% FTE).

MSU graduate students receive free statistical support for their **dissertation research** (9 hours per fiscal year; more hours if they are members of partner colleges or departments).

Post-award grant collaborations or work on **individual projects** not covered by partnerships are subject to hourly fees or percent effort payments.

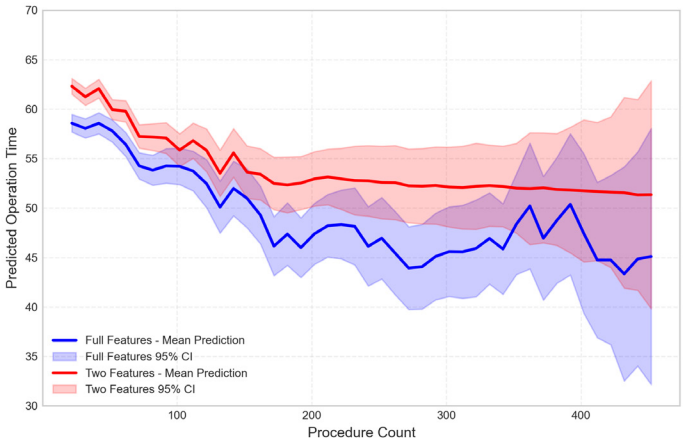
Recovery After Tibial and Malleolar Fractures Measured by Gait Parameters Obtained by Instrumented Insoles and Quality of Life



Adapted from Warmerdam E, Huebner M, Stoll C, Lange AI, Ganse B. Recovery of Patient-Reported Outcome Measures vs Gait Parameters Obtained by Instrumented Insoles After Tibial and Malleolar Fractures: Prospective Longitudinal Observational Study. JMIR Mhealth Uhealth. 2025 Jun 16;13:e71022

Progress of leg fracture healing may be discerned by examining gait parameters (max force, lateral, medial, forefoot, hindfoot) from the injured leg as well as from symmetry indices. Results can be used to guide patients in their recovery or alert clinicians of potential interventions.

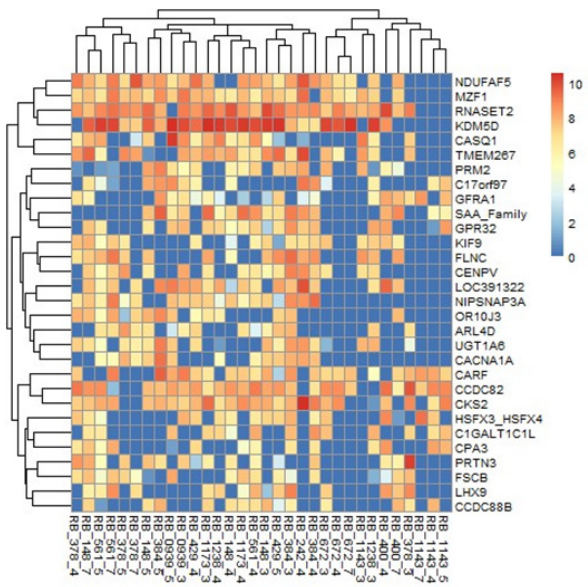
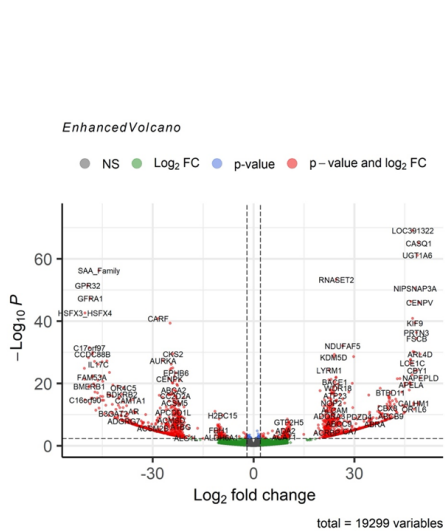
DEEP-LC: Unlocking Surgical Proficiency with AI, Attention-Based Deep Networks, and Memory



Learning curves provide a framework for understanding how learners acquire new skills and knowledge over time. By analyzing learning curves, educators can identify areas for improvement, optimize training strategies, and ensure competency in clinical practice. Focusing on the time-series nature of the data regarding operative time as outcome, we benchmarked several Recurrent Neural Network (RNN) architectures, including the Transformer Encoder, Single-Layer LSTM, Stacked GRU, and a CNN-GRU Hybrid, to model skill advancement as a function of experience. Performance metrics revealed that while the Single-Layer LSTM improved at a rate comparable to other tested algorithms, it notably achieved a lower initial Mean Absolute Error. Credit: Wenjuan Ma, Rayleigh Lei

Decoding the Placental Circadian Clock: Bioinformatics/Biostatistics-Driven Insights into Adverse Pregnancy Outcomes

Shift work and circadian disruption are known risk factors for preterm birth, pre-eclampsia, and other complications. Identifying the molecular underpinnings in the placenta offers a path to precision prevention strategies (e.g., timed interventions, circadian aligned medication delivery). This is accomplished by integrating high throughput transcriptomics, single nucleus RNA sequencing, and spatial profiling and using Bayesian hierarchical clustering of lncRNA expression across cell types, longitudinal mixed model analysis of gene expression dynamics, and structural equation models linking lncRNA, clock gene, and clinical outcomes. Credit: Guoli Zhou





Discovery, without boundaries. Spartans Will.

At Michigan State University, shared research resources remove barriers and expand what's possible. Together, advanced tools, specialized facilities, and expert-led cores form an integrated ecosystem that supports collaboration, accelerates discovery, and strengthens interdisciplinary research.