SPARTAN RESEARCH CORES

MICHIGAN STATE UNIVERSITY

SPARTAN RESEARCH CORES

Shared Research Resources at Michigan State University

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.

Spartans Will.

At **Michigan State University**, research thrives through shared access to cutting-edge tools and expertise. MSU's network of shared resources and cores enables discovery, creativity, and innovation across disciplines.

More than infrastructure, these resources reflect a culture of collaboration and momentum. Together, Spartans push boundaries, build on shared strengths, and **turn discovery into impact**.

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

LOCATION

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

CONTACT INFORMATION

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

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
- CRISRP 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

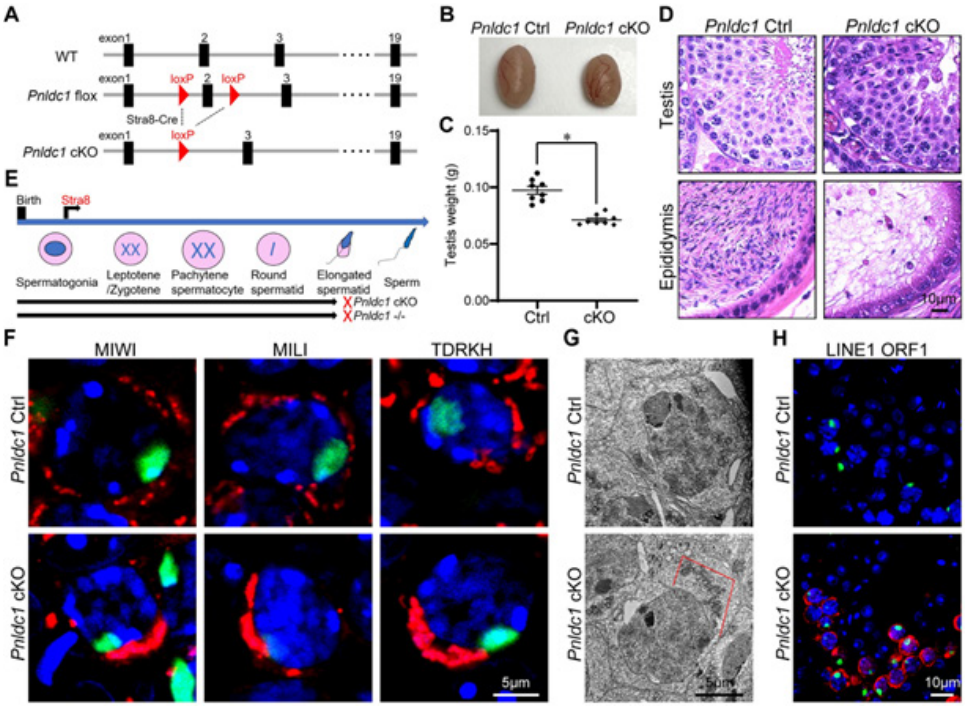
Additional Rodent Services:

- 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

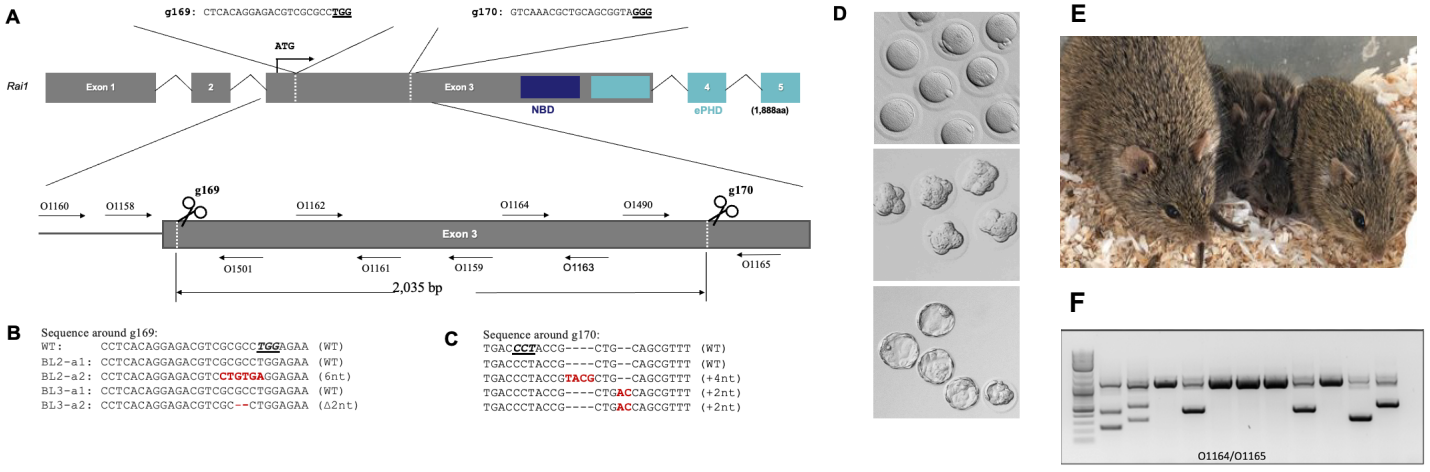
Conditional Deletion of Pnldc1 in Postnatal Germ Cells Causes Defective piRNA Trimming, LINE1 Upregulation, and Male Infertility



(A) Gene targeting strategy for the generation of Pnldc1 cKO. Cre-mediated deletion removed the exon 2 of Pndlc1. **(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.

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

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

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.

EQUIPMENT

AVITI sequencing instruments

- **Illumina-style short read sequencing**
- DNA, DNA methylation & RNA sequencing
- Uses regular Illumina-style libraries
- Multiple read formats
  - 2x75, 1x150, 2x150, 2x300
- Multiple flow cell capacities
  - 100 M to 1,000 M read pair outputs

10X Genomics Chromium X

- **Single-cell library preparation instrument**
- 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
- IDT xGen DNA-methylation library prep
- Watchmaker RNA-seq library prep
- Watchmaker RNA-seq w/ FastSelect rRNA/globin depletion
- 10X Genomics single cell library preparations
- Lexogen QuantSeq 3' mRNA-seq library prep
- Lexogen small RNA-seq library prep
- 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
- Combined RNA-seq, ChIP-seq or 16S V4 amplicon sequencing plus bioinformatics
  - Flat-rate sequencing plus bioinformatics in cooperation with the MSU Bioinformatics Core

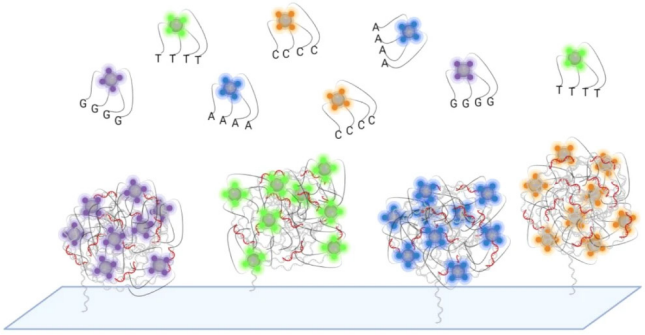
LOCATION

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

CONTACT INFORMATION

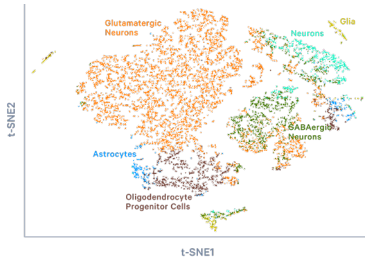
web: rtsf.natsci.msu.edu/genomics
email: gtsf@msu.edu

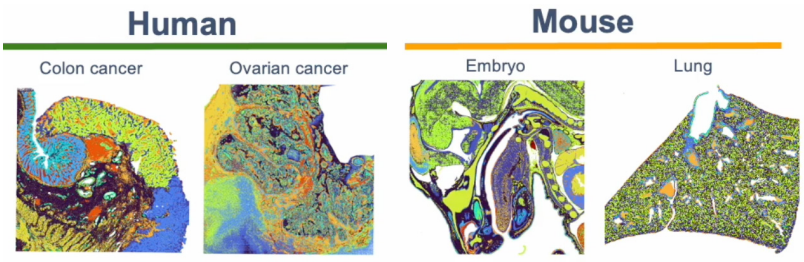
AVITI Short Read Sequencing



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.

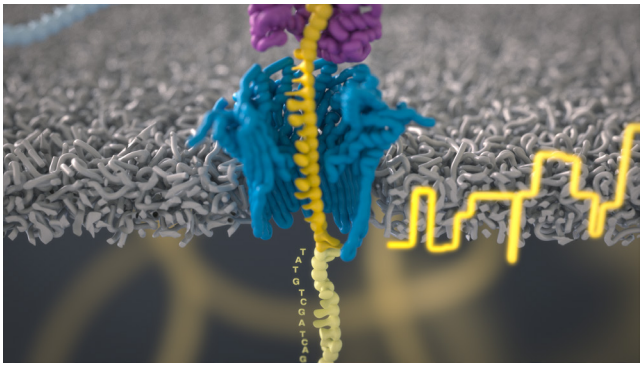
10X Genomics Single Cell and Spatial Omics





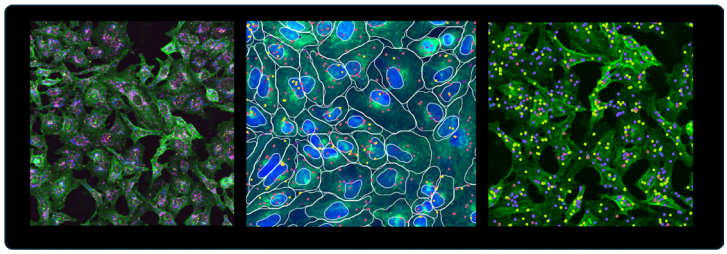
Single cell and single nuclei libraries are prepared with our Chromium X instrument from 10X Genomics. 5' and 3' RNA-seq libraries, ATAC-seq libraries and new human/mouse specific probe-based libraries can be prepared. Spatial transcriptomics can be performed with our Visium CytAssist from 10X Genomics 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 cm^2. Both spatial and dynamic relationships can be recognized in cell cultures and soon in fixed tissue sections. Images from Element Biosciences.

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

CONTACT INFORMATION
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 imagining capabilities and low fmol level sensitivity.
- **HTX M3+ matrix sprayer**
  Automated MALDI imagining sample preparation system.

QUANTITATIVE/TANDEM QUADRUPOLE MASS SPECTROMETERS

- **Waters TQ-D UPLC/MS/MS**
- **Waters TQ-S UPLC/MS/MS**
- **Waters 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

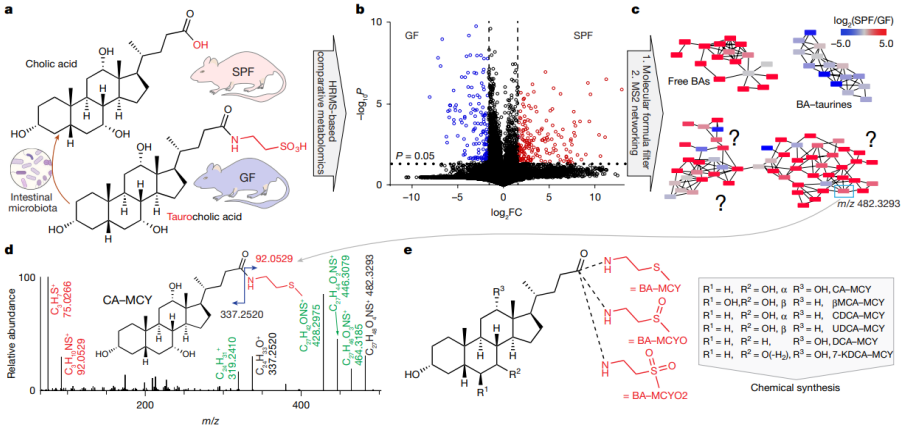
- **Thermo Compound Discoverer 3.3**
- **Waters Progenesis QI**
- **A gamut of open-source software including XCMS, MZmine, MetaboLyzer, MS-DIAL, MetaboAnalyst, GNPS suite of tools**
- **In-house bioinformatics and specialized tools**
- **Multi-omics analysis and pathway enrichment analysis**

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

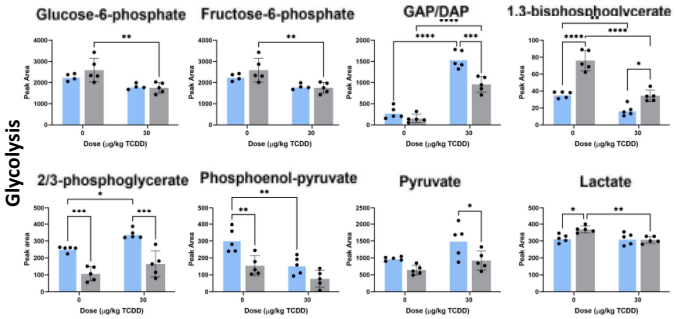
Untargeted Metabolomics: Comprehensive Profiling, Accurate Metabolite Annotation and Full Bioinformatics Analysis

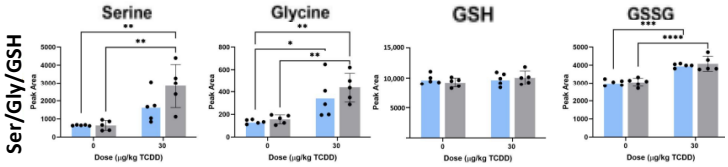
Identification of novel conjugates of bile acids (BAs) via mass spectrometry (MS), regulated by host and gut microbiota. MS data revealed clusters representing free BAs, BA–taurine conjugates and previously unannotated BA–MCY conjugates. The red and blue nodes are downregulated and upregulated, respectively, 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. PMID: 39779854; PMCID: PMC11886927.

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

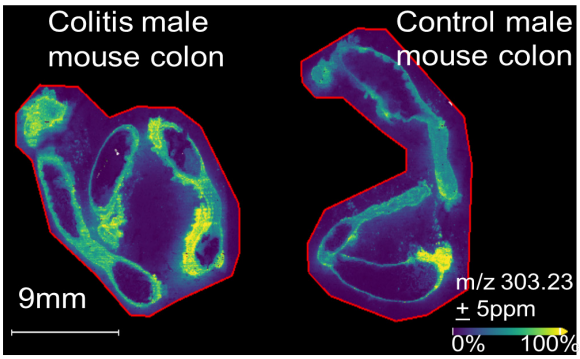




Orlowska K, Nault R, Zacharewski T. Loss of Dioxin Response Element-Mediated Induction of PKM2 Reprograms Hepatic Metabolism in Response to TCDD. ***Int J Mol Sci.*** 2025; 26(22):10853. DOI: 10.3390/ijms262210853. PMID: 41303339; PMCID: PMC12652037.

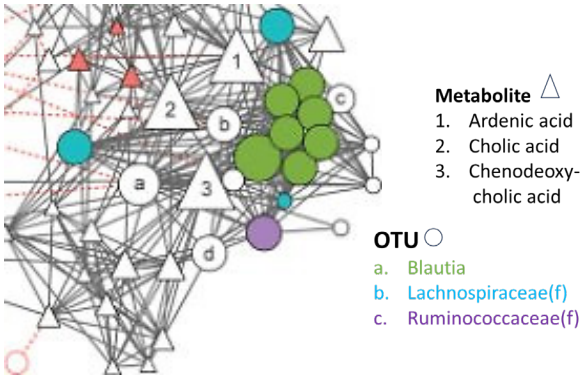
Levels of glycolytic and Ser/Gly/GSH metabolites in WT (blue) and PkmΔDRE (grey) mice treated with sesame oil (vehicle) or dioxin-like compound (30 μg/kg TCDD) every 4 day for 28 days.

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 metabotypes associated with predisease risk state in inflammatory bowel disease (IBD): An inter'omic network of OTU-type–associated microbes and metabotype-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. PMID: 28174747; PMCID: PMC5247316.

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.

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

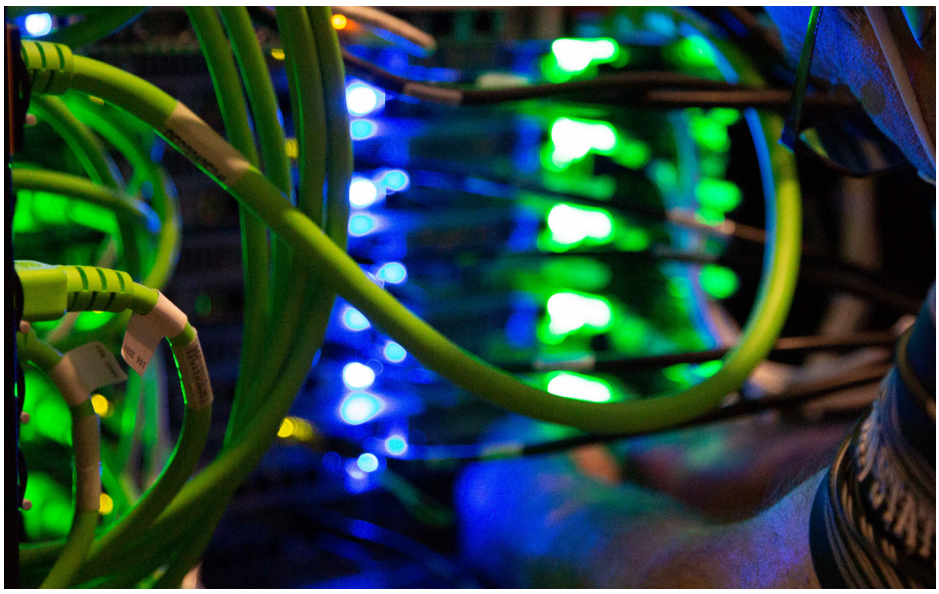
Short term projects
Discrete omics data analysis projects with well-defined deliverables. Charged per sample or per hour.

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



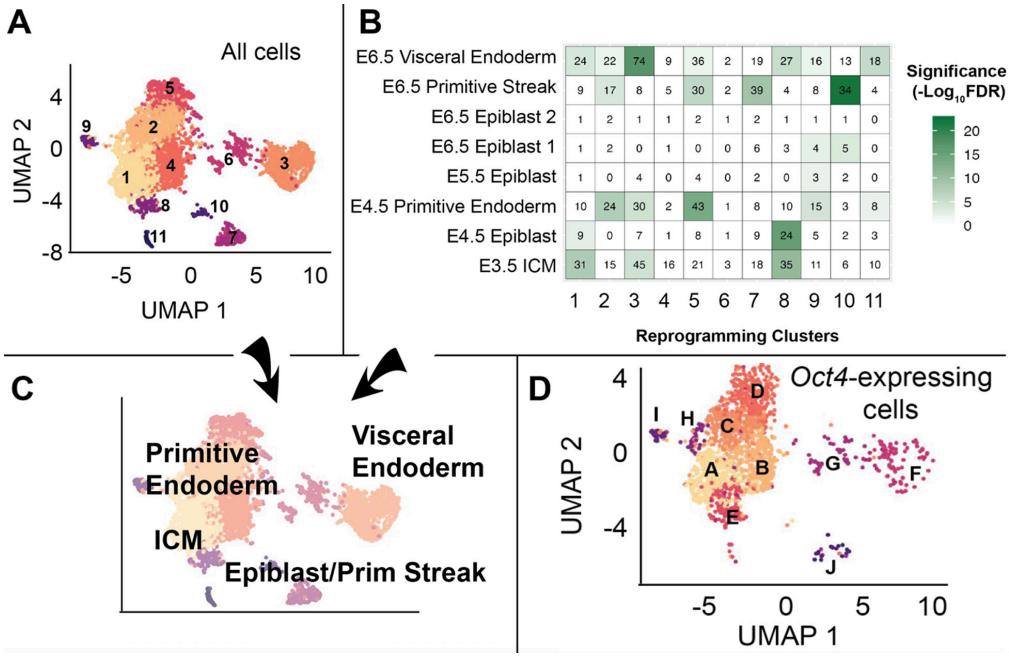
LOCATION

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

CONTACT INFORMATION

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

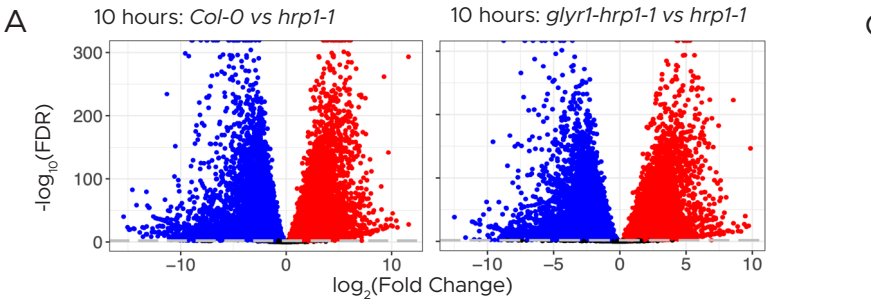
Identification of Oct4-Expressing Cells with Primitive Endoderm Character during OSKM Reprogramming by Single-Cell RNA-Sequencing

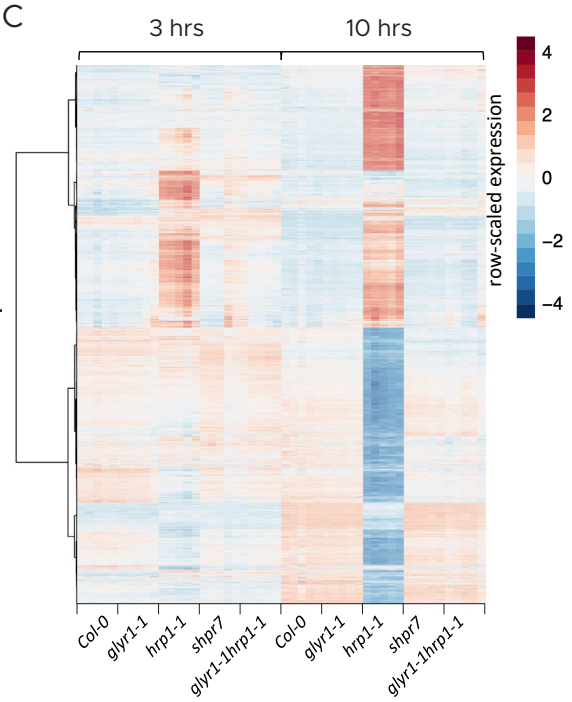


(A) UMAP visualization of scRNA-seq data derived from cells on day 17 of OSKM reprogramming reveals eleven major clusters (numbered 1-11). **(B)** Overlap of Clusters 1-11 from panel A with single-cell transcriptomes from early embryos (Mohammed et al., 2017) shows significant enrichment (green) of embryonic cell type gene expression within several clusters. ICM = inner cell mass. **(C)** For the purposes of visualization, enrichments from panel B were overlayed on cluster map from panel A. **(D)** Cells expressing Oct4 were reclustered, producing Clusters A-J.

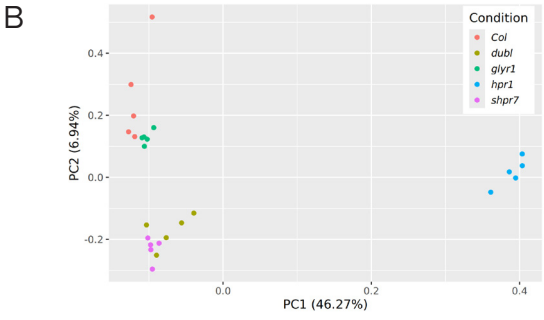
Adapted from: Moauro, A., Hickey, S.L., Halbisen, M.A., Parenti, A., Ralston, A., 2024. OCT4 is expressed in extraembryonic endoderm stem (XEN) cell progenitors during somatic cell reprogramming. https://doi.org/10.1101/2024.01.22.576724

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





Adapted from: Jiang, X., Koenig, A.M., Walker, B.J., Hu, J., 2024. A photorespiratory glyoxylate shunt in the cytosol supports photosynthesis and plant growth under high light conditions in Arabidopsis. https://doi.org/10.1101/2024.12.03.626664



Plants were grown for 3 weeks under high CO_2 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.

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

CONTACT INFORMATION

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

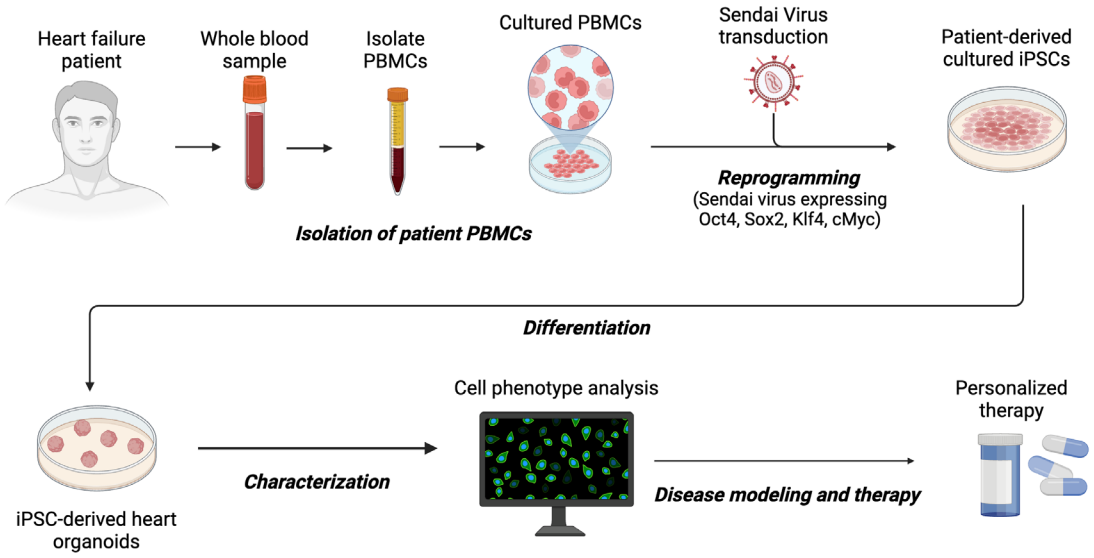
MODEL SYSTEM DEVELOPMENT & TECHNICAL SUPPORT

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

CONSULTATION & GRANT SUPPORT

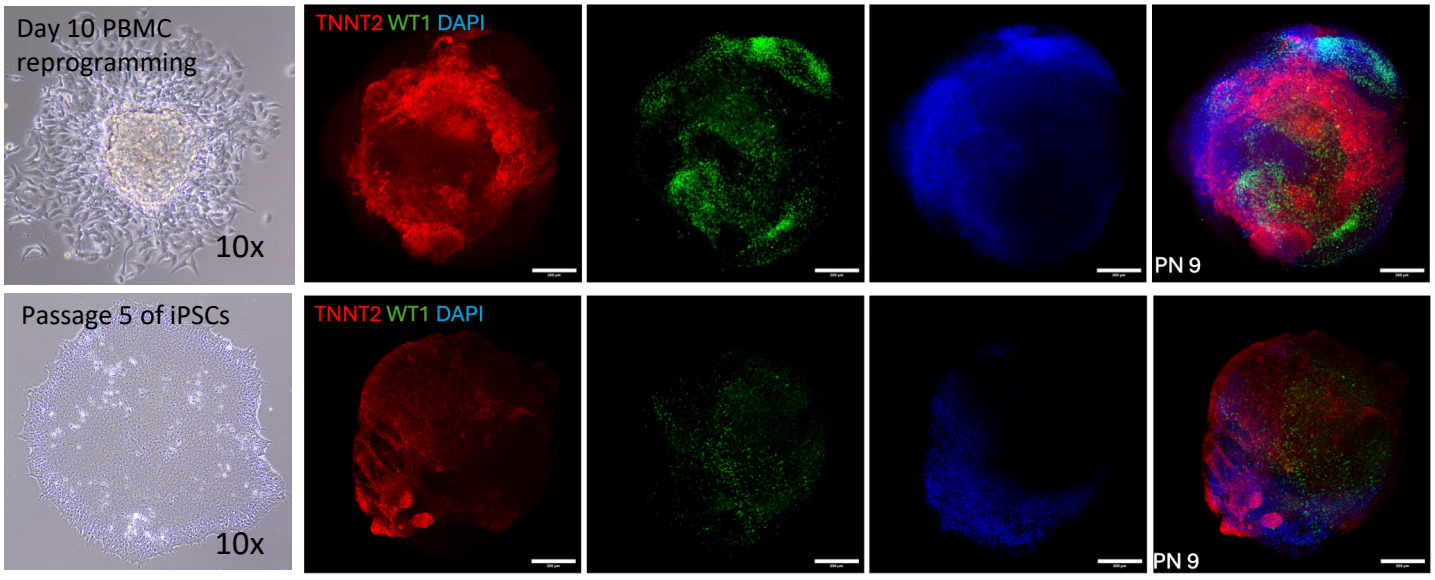
- Experimental design guidance for SC projects
- Pre-award proposal support
- Editing of stem cell-related grant research sections
- Letters of support available upon request

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.

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.

EQUIPMENT

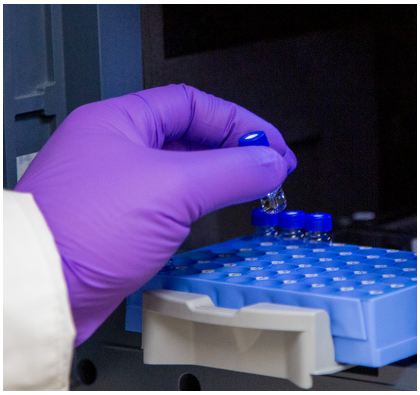
MASS SPECTROMETERS

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.



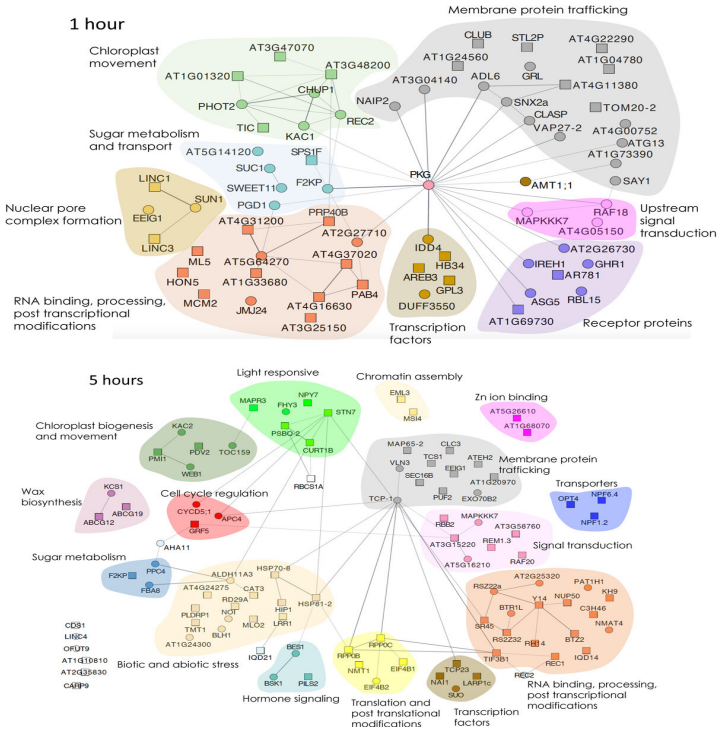
SERVICES

- 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

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

CONTACT INFORMATION
web: rtsf.natsci.msu.edu/proteomics
email: rtsf.proteomics@msu.edu

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



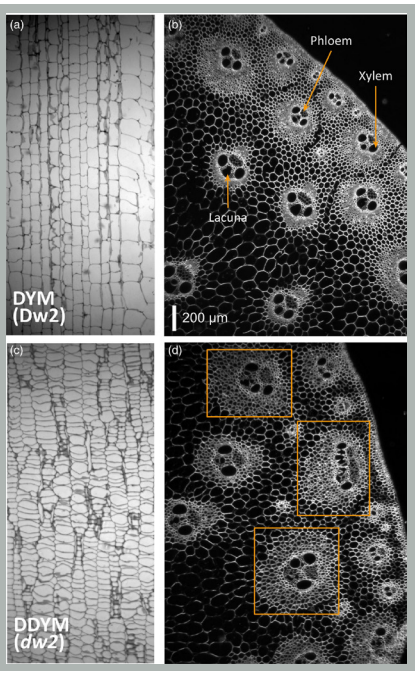
Important biological functions of differentially expressed phosphoproteins in *Arabidopsis* leaves fumigated with isoprene. STRING protein–protein interactions are shown for phosphoproteins differentially expressed in response to fumigation with 1 (top) or 5 (bottom) with isoprene. The nodes represent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

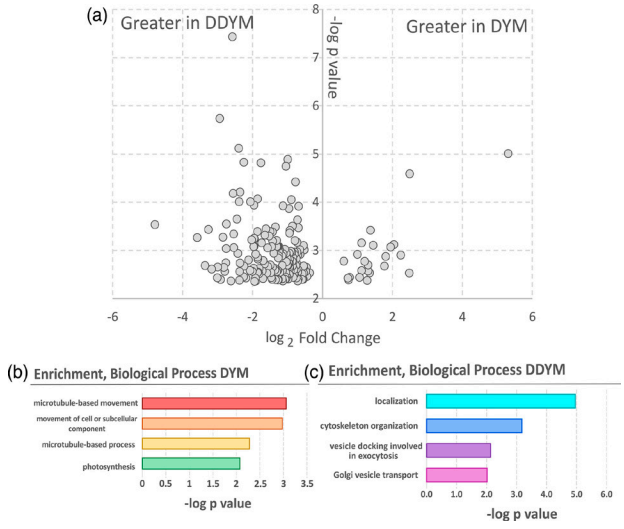
Adapted from: Weraduwage, S.M., Whitten, D., Kulke, M., Sahu, A., Vermaas, J.V. & Sharkey, T.D. (2024) **The isoprene-responsive phosphoproteome provides new insights into the putative signaling pathways and novel roles of isoprene.** Plant, Cell & Environment, 47, 1099–1117. https://doi.org/10.1111/pce.14776

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

Dw2 causes uniform cell morphology and vascular bundles (VBs). **(a,c)** Longitudinal sections of mature internodes in DYM **(a)** and DDYM (*dw2*) **(c)** plants. Cells in DYM show uniform cell files and morphology, whereas mutant plants show irregular cell shapes and compromised cell files. **(b,d)** Horizontal sections of mature internodes in DYM **(b)** and DDYM **(d)** plants. DYM plants show typical monocot VB morphology, whereas DDYM plants show aberrations in VB morphology (orange boxes). Scale bar is the same for all images.



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/tpj.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.

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.

LOCATION

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

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

CONTACT INFORMATION

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, CO_2, O_2), 2x – 60x objectives, free AI/machine learning analysis software

CELL SORTERS

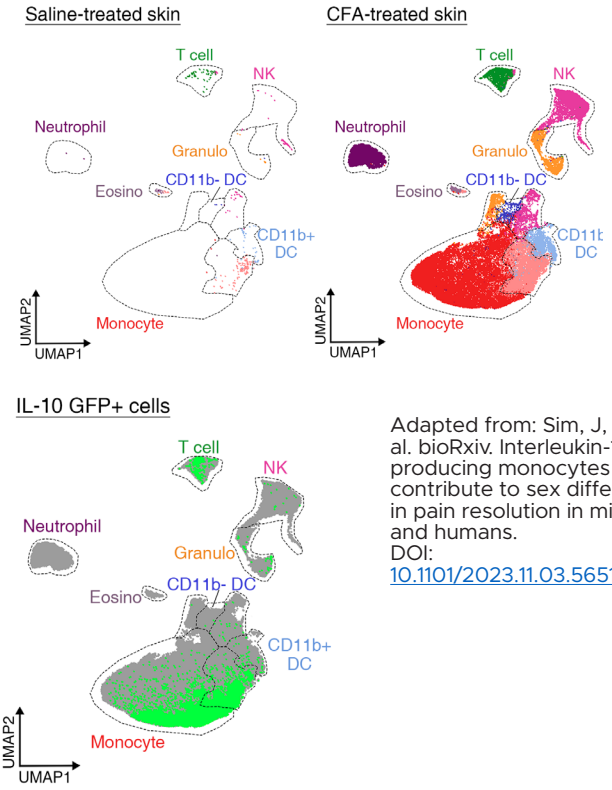
SONY MA900 (SONY Biotechnology)
- Features automatic setup, calibration, and cleaning for ease of use

BD FACSAria 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

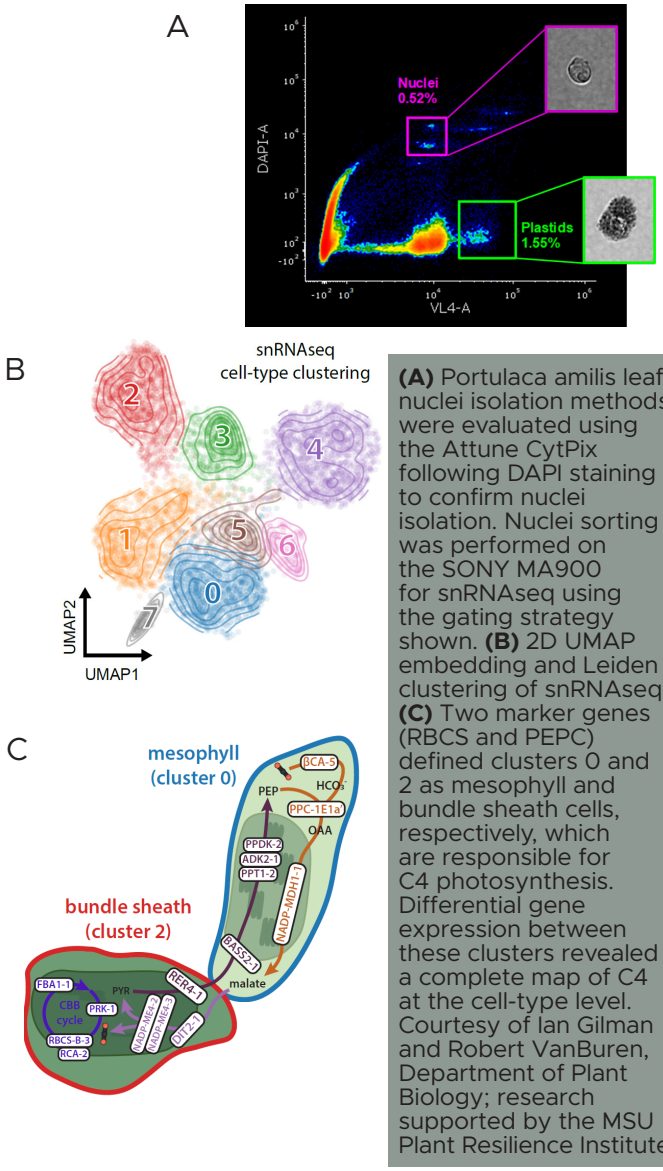
Spectral Cytometric Immunophenotyping in a Mouse Model of Inflammatory Pain



Adapted from: Sim, J, et al. bioRxiv. Interleukin-10-producing monocytes contribute to sex differences in pain resolution in mice and humans.
DOI: 10.1101/2023.11.03.565129

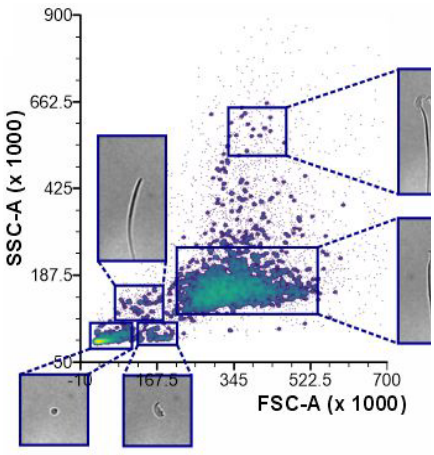
Intraplantar immune populations were evaluated from IL-10 GFP reporter mice using a Cytek Aurora spectral cytometer following saline (left) or Complete Freund's Adjuvant (CFA; middle) administration. A dimensionality reduction (UMAP) and clustering pipeline was used to identify CD11b+Ly6C+Ly6G-F4/80^{mid} 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

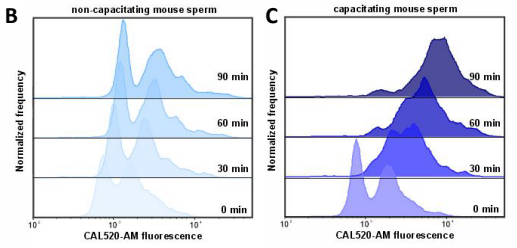
Developing a Single-Nuclei RNAseq-based Model of C_4 Photosynthesis in Portulaca amilis



(A) Portulaca amilis leaf nuclei isolation methods were evaluated using the Attune CytPix following DAPI staining to confirm nuclei isolation. Nuclei sorting was performed on the SONY MA900 for snRNAseq using the gating strategy shown. **(B)** 2D UMAP embedding and Leiden clustering of snRNAseq **(C)** Two marker genes (RBCS and PEPC) defined clusters 0 and 2 as mesophyll and bundle sheath cells, respectively, which are responsible for C4 photosynthesis. Differential gene expression between these clusters revealed a complete map of C4 at the cell-type level. Courtesy of Ian Gilman and Robert VanBuren, Department of Plant Biology; research supported by the MSU Plant Resilience Institute

Dynamic Monitoring of Intracellular Ca^{2+} Levels in Mouse Sperm





Calcium (Ca^{2+}) is a critical regulator of sperm motility, fertilization capacity, and potentially metabolism. **(A)** Morphometric evaluation of mouse sperm using the Attune CytPix. Intracellular Ca^{2+} mobilization was assessed using Cal-520 AM (AAT Bioquest) in single intact sperm over a period of 90 min. Representative histograms show Ca^{2+} levels measured following incubation in TYH buffer alone **(B)** and in the presence of HCO_3^- **(C)**, which induces capacitation. Courtesy of Melanie Balbach, Department of Biochemistry & Molecular Biology

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

CONTACT INFORMATION

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

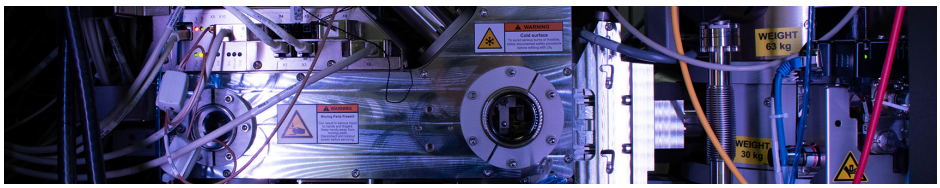
EasiGlow (Pelco) & GloQube Plus (Quorum)
Glow discharger for grid preparation

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 Pressue Freezer (CryoCapCell)
Freezing device for thick tissue samples

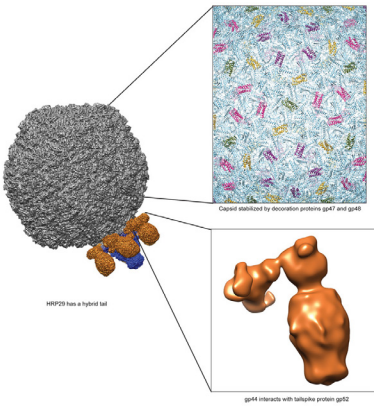


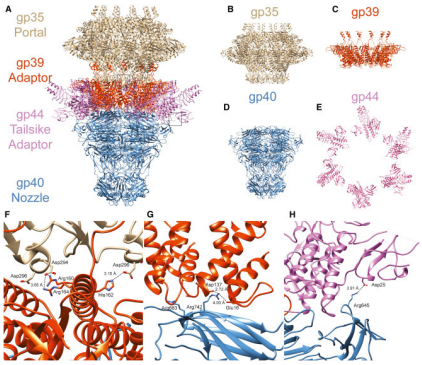
SERVICES

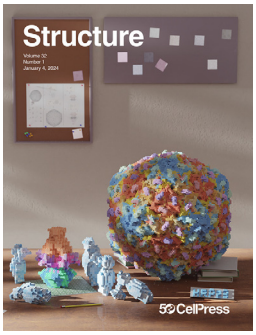
Cryo-EM imaging including:
- Single particle analysis
- Cryo-tomography
- FIB-Milling
- Micro-ED

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





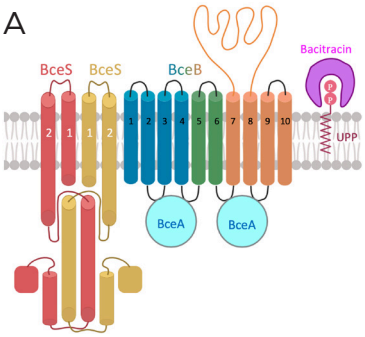


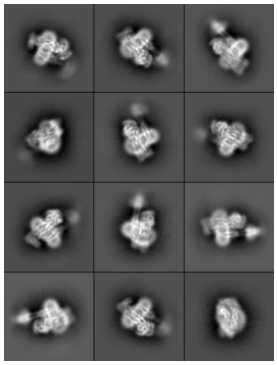
Adapted from: Subramanian, S., Bergland Drarvik, S.M., Tinney, K.R., and Parent, K.N. (2024) Cryo-EM structure of a Shigella podophage reveals a hybrid tail and novel decoration proteins Structure, 32(1):24-34

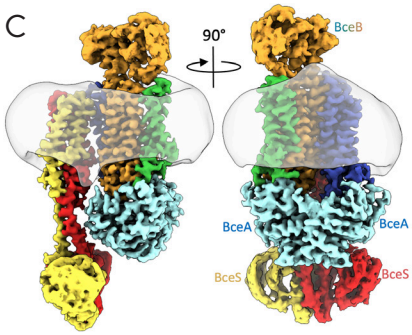
https://doi.org/10.1016/j.str.2023.10.007

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





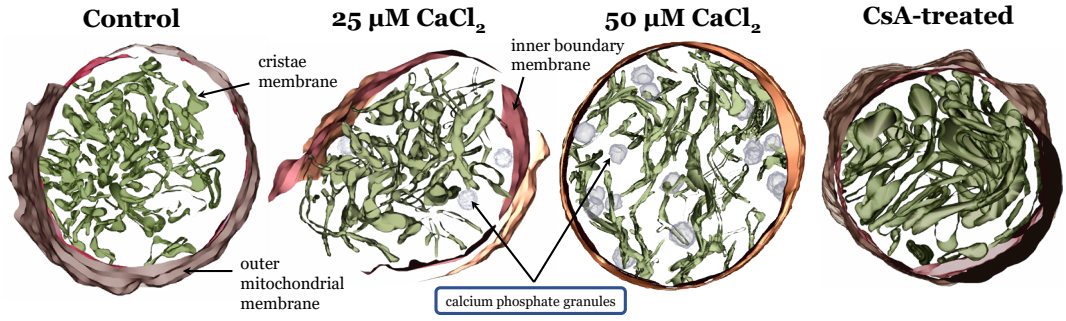


Adapted from: George, N.L. and Orlando, B.J. Architecture of a complete Bce-type antimicrobial peptide resistance module. Nature Communications. 14, 3896 (2023).

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 400 MSU researchers per year from 40 different University departments, as well as many off-campus customers.

LOCATION

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

CONTACT INFORMATION

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

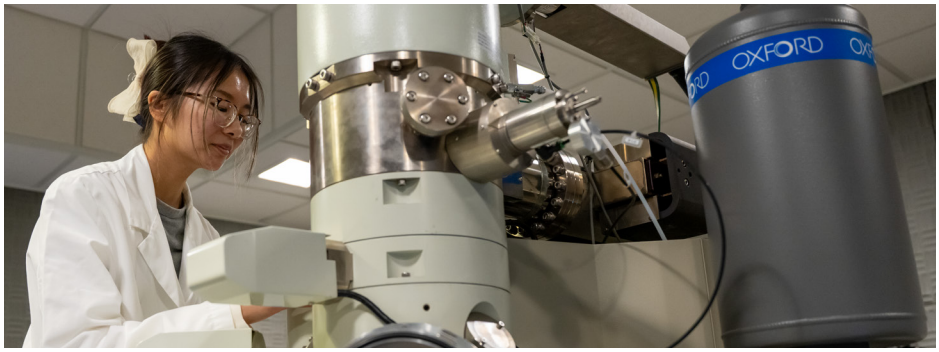
Digital Light Microscopy
- Keyence VHX-6000 Digital Microscope

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)

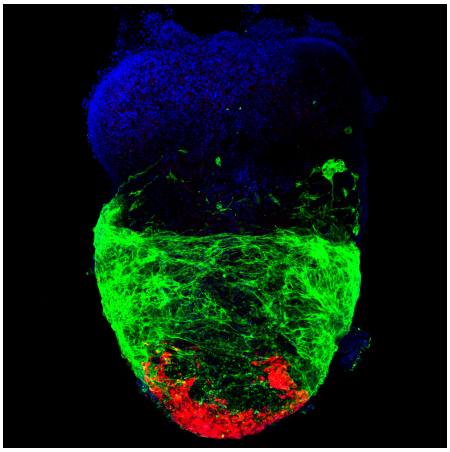
Sample Preparation
- State-of-the-art ultramicrotomy
- Many coaters (C, Au, Ir, Os, Pt)
- Critical point drying and freeze-drying
- Cryostat
- Disc cutter, dimple grinder, ion mill

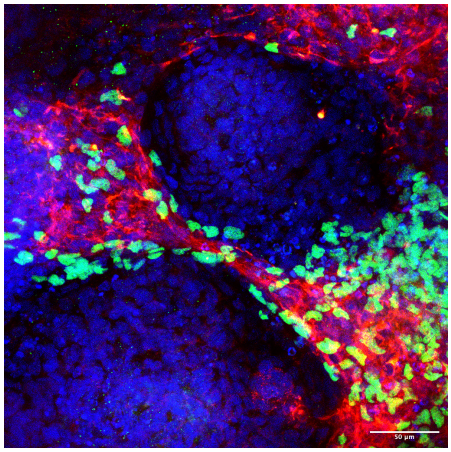


SERVICES

- 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

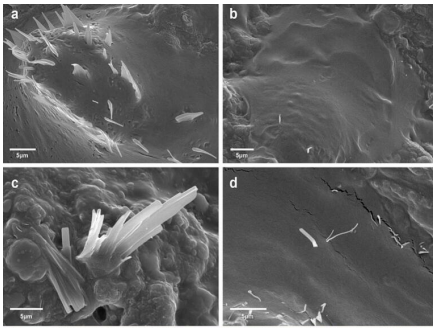


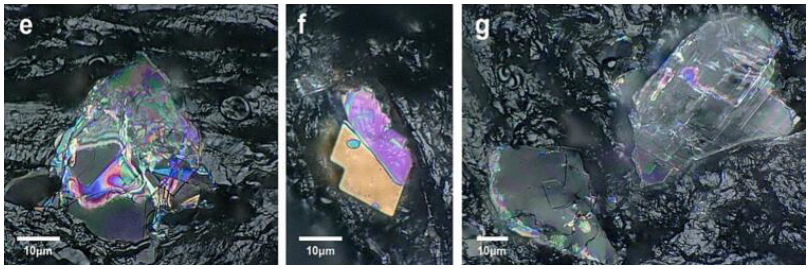


Thanks to advancements in the development of patented synthetic human-like hearts first created at MSU, researchers can study human heart development and congenital heart disease on highly accurate models.
Left: A heart organoid with a well-developed ventricle (green) and cardiac neural crest cells (mCherry) 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





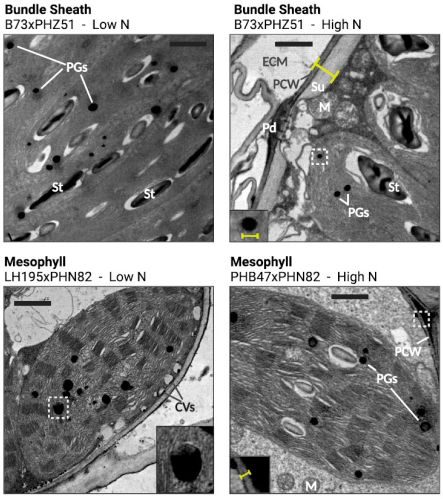
Research from the Abela lab. For details: Abela GS et al. Am Heart J Plus. PMID: 37981958.

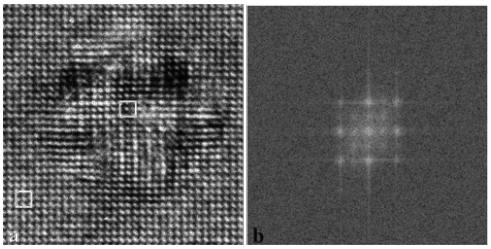
Scanning and 3D-digital microscopy of colon cancer and marginal tissue: Scanning electron micrographs of colon cancer **(a, c)** and matching marginal tissue **(b, d)** demonstrate larger and prominent cholesterol crystal formations in the cancer but not in the normal marginal tissue. CCs are seen traumatizing 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)**.

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 plastogobules (PGs). Regions highlighted in the insets are marked with dashed white boxes. All scale bars indicate 1 µm. 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.

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

CONTACT INFORMATION

web: phmtox.msu.edu/facilities/medchem

EQUIPMENT

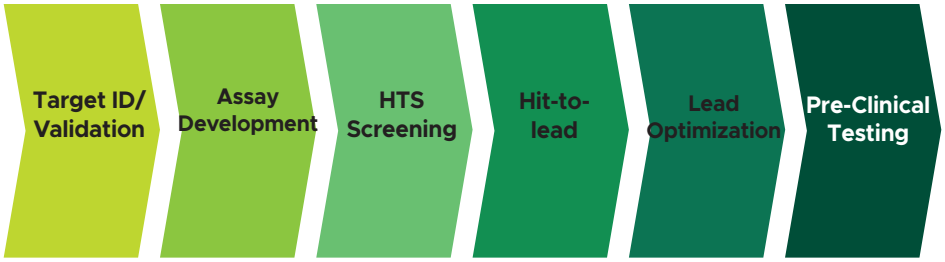
LCMS (Advion)
Low resolution liquid chromatography mass spec. Enables synthetic efforts by monitoring reactions progress and isolation of compounds of interest.

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.



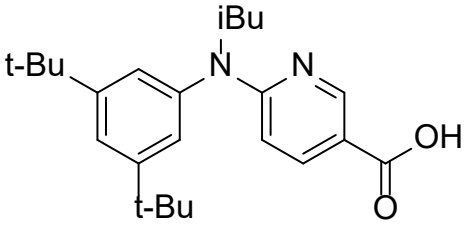
SERVICES

- 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 medicated 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



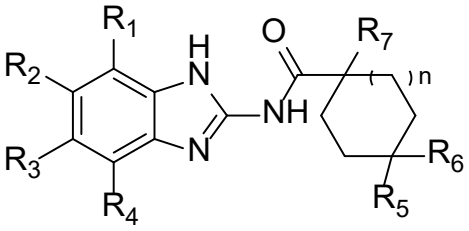
MSU-42011

Pei-Yu Hung, Jessica A. Moerland, Ana S. Leal, Bilal Aleiwi, 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.

MmpL$_3$ for TB and NTM Infections

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

- **MmpL$_3$ 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

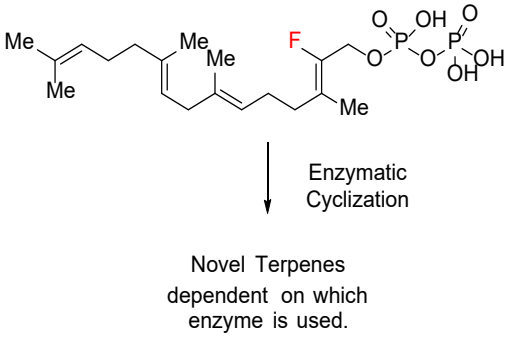


Williams JT, Giletto M, Haiderer ER, Aleiwi B, Krieger-Burke T, Ellsworth E, Abramovitch RB. The *Mycobacterium tuberculosis* MmpL3 inhibitor MSU-43085 is active in a mouse model of infection. *Microbiol. Spectr.* **2024**,12(1): e0367723. doi: 10.1128/spectrum.03677-23.

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)

Assay Development & Drug Repurposing Core

The Department of Pharmacology & Toxicology ADDRC bridges the drug discovery gap that often exists between research and preclinical drug development. The ADDRC is a campus-wide resource, providing expertise in adapting biological and biochemical bench-top assays into high-throughput screening (HTS)-compatible assays and generating screening data with the goal of identifying chemical probes to further interrogate a particular biological process or potential leads for drug development.

LOCATION

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

CONTACT INFORMATION

web: drugdiscovery.msu.edu/facilities/addrc

DDRC
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

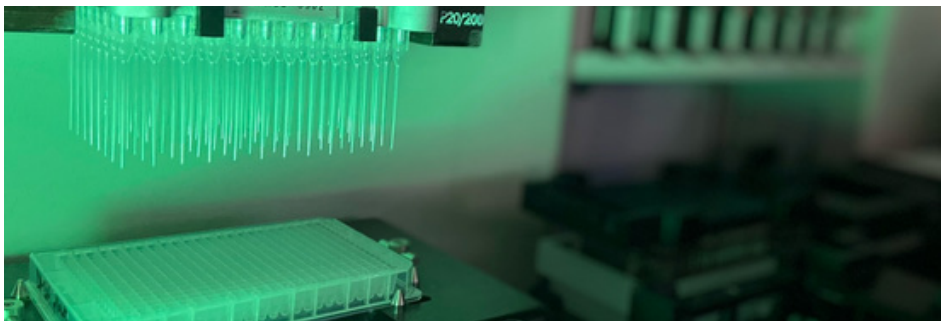
Hamamatsu Function Drug Screening System
Fluorescence/Luminescence plate imager with simultaneous addition and reading of plates

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 (Ka, Kd)

Microcal VP-ITC
Directly measure mM to nM affinities, no labeling or immobilization required

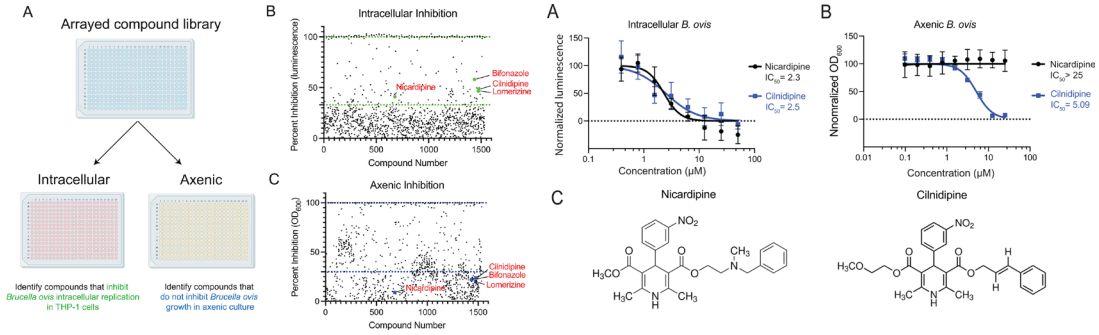
Biomek
Robot liquid handling system for high-throughput workflows



SERVICES

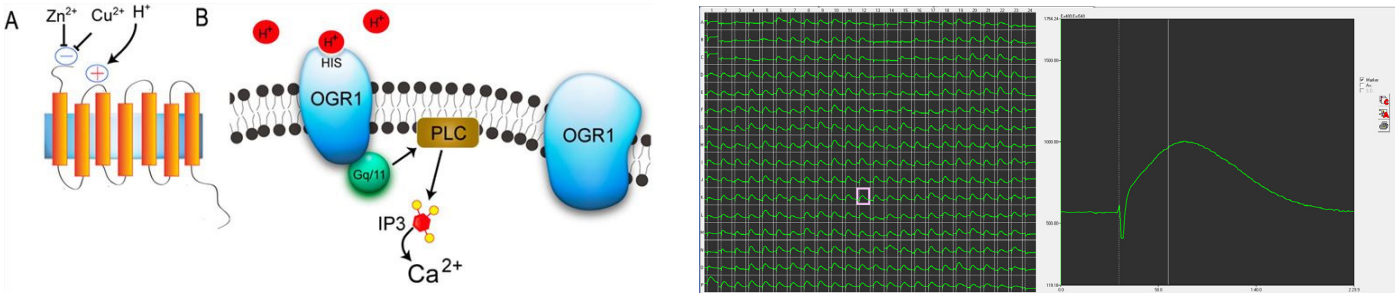
- High-Throughput Screening (HTS) Assay Development and Validation
- Small/Large Scale Chemical Screens
- HTS Data Analysis and Management
- Hit Picking and Dose Response Follow-up
- Core Instrument Operation Training
- Access to Compound Libraries
- Access to Automated Laboratory Robotics
- Grant Support

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



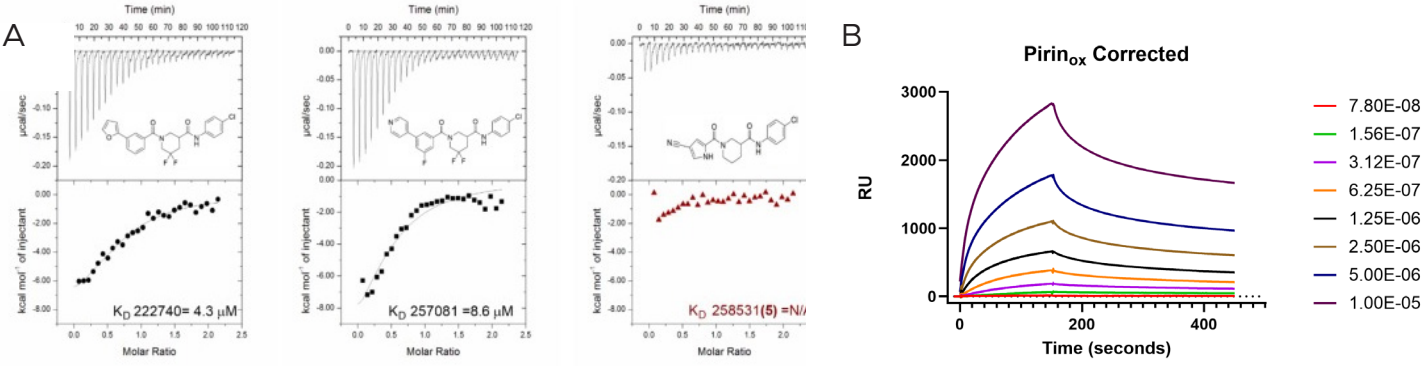
Left panel: (A) Diagram of the drug screening pipeline for the identification of small molecules that selectively inhibit *B. ovis* intracellular growth with minimal axenic activity. **(B and C)** Intracellular inhibition of all tested small molecules, shown as percentage of luminescence emitted by *B. ovis* cells harboring the *lux* operon. Highlighted in green are drug candidates that inhibited *B. ovis* intracellular growth in THP-1 macrophages and highlighted in blue are ones that inhibited growth in Axenic culture. **Right panel: (A)** Intracellular inhibitory activities of nicardipine and cilnidipine during *B. ovis* THP-1 macrophage infection. *B. ovis* luminescence was measured 48 h post-treatment and normalized to signal from infected untreated cells. IC_{50} values based on curve fits are shown. **(B)** Axenic inhibitory activity of nicardipine and cilnidipine during *B. ovis* growth in liquid medium. Optical densities at 600 nm were measured after 48 h of growth and normalized to untreated cultures. **(C)** Chemical structures of nicardipine and cilnidipine. **"Reversion of a RND transporter pseudogene reveals latent stress resistance potential in Brucella ovis" Kim et al,** 10.1371/journal.pgen.1011795

High-throughput Calcium assay to examine GPR68 Structure Activity Relationships



GPR68 is a class A GPCR that is activated by pH [EC50 = 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 (Ca2+), cAMP, and Rho. In developing the first GPR68 inhibitor, OGM, we used Chem1-OGR1(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://wwtransfectedw.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/acsptsci.8b00048

Metabolic Phenotyping & Preclinical Imaging Core

The MPPI Core provides comprehensive expertise, rigorous training, and high-quality technological resources that support non-invasive, multidimensional *in vivo* analysis of disease onset, progression, and therapeutic response. Through the application of advanced bioluminescence and fluorescence imaging systems (IVIS Spectrum) and integrated metabolic instrumentation, including the TSE PhenoMaster NG, Bruker LF90II, and X-RAD320, the facility supports investigators engaged in preclinical research on metabolic disease, cancer, and aging.

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

CONTACT INFORMATION

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

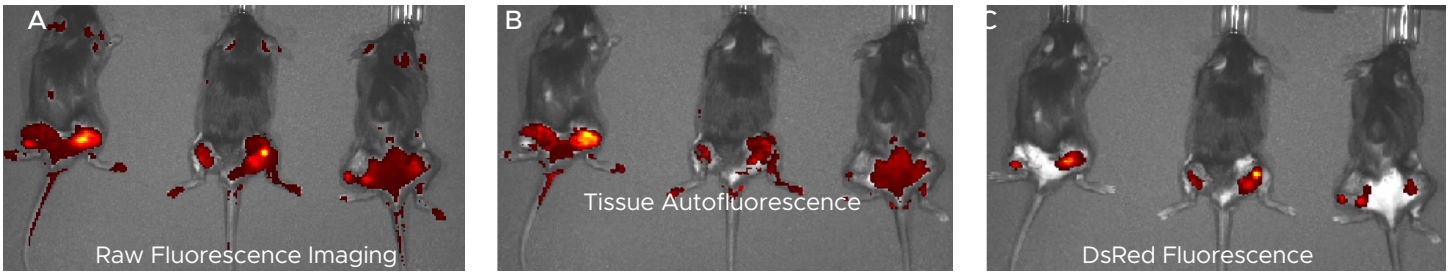
Located in the imaging suite and adjoining animal facility

- 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

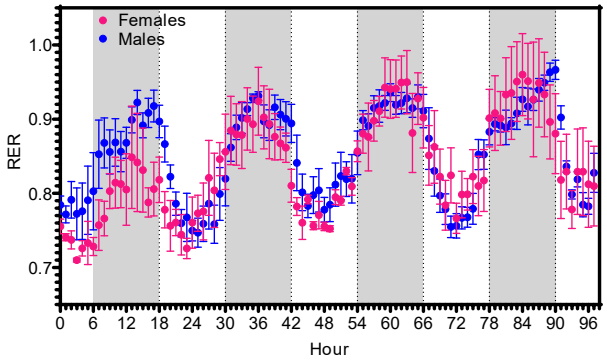
Optimizing *In Vivo* Fluorescence Imaging: The Importance of Mouse Strain Selection

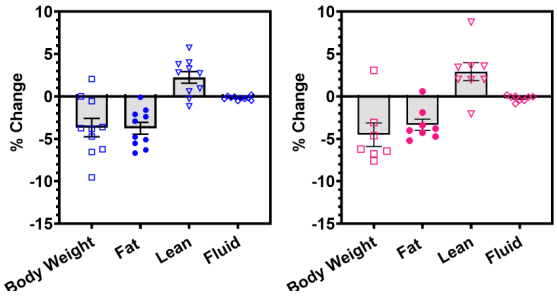


DsRed-expressing mouse pancreatic tumor cells were injected subcutaneously into the flank of C57BL/6 mice. Prior to imaging, fur at the injection site was removed to minimize background signal. Fluorescence imaging was performed using the IVIS Spectrum imaging system **(A)**. Spectral unmixing enabled 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 pattens, 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.

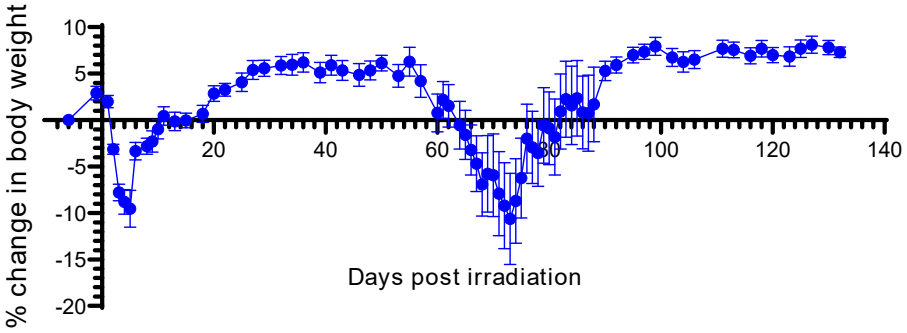




The Bruker LF90II enables non-invasive, longitudinal quantification of rodent body composition. The representative graphs to the left show fat and lean mass measurements after short-term (3-day) housing in TSE PhenoMaster NG metabolic cages equipped with voluntary running wheels. The decrease in fat 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.



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