Transgenic Mouse Facility

UCI Chao Family Comprehensive Cancer Center

Leadership

Grant MacGregor, DPhil
Scientific Director

Shimako Kawauchi, PhD
Managing Director

Further information regarding all offered services can be found at the website:
https://tinyurl.com/yda7q9yy

Mission

Facilitate use of the mouse as a mammalian model genetic system to investigate mechanisms of oncogenesis and testing of cancer therapeutics

To fulfill this mission the **TMF:**

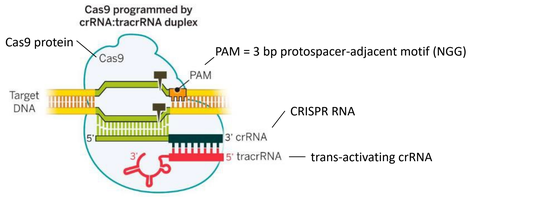
- Provides advice on experimental design and analysis to investigators on the use of genetically modified mice.
- Provides specialized expertise, technical support and obtains reagents required to manipulate the mouse genome and analyze the consequences thereof.
- Develops and communicates awareness of novel mouse-related resources, facilitates their acquisition, and provides practical assistance with their use.

Services

- Consult with, raise awareness and educate Cancer Center members about strategies to modify the mouse genome and to use genetically engineered mouse models in their research programs.
- Genome engineering in mice and ES cells via CRISPR /Cas9.
- Production of gene targeted mouse models using KOMP, EUCOMM ES cells as well as JM8 (C57BL/6N) ES cell-mediated targeting in-house.
- Targeted transgenesis at *Hipp11* (Ch 11) & *ROSA26* (Ch 6).
- Production of small transgene and BAC random-integration transgenic mice.
- Southern analysis of mouse genomic DNA, including probe design and testing.
- Cryopreservation, import, export of mouse embryos and sperm.
- IVF and embryo transfer to re-animate, re-derive, expand or develop large cohorts of identical aged mice for experimental studies.
- Provision of oocytes or pre-implantation embryos for *in vitro* investigation.
- Sourcing of existing mouse models for UCI investigators.
- Molecular genotyping and breeding services.
- Customized services to accommodate investigator.
- Provision of commonly used CRE and FLP expression mice.
- Provision of letters of support for grant applications.
- Provision of materials and methods for manuscripts.

Popular Services (Examples)

CRISPR-mediated Genome Engineering – background and common production pipeline



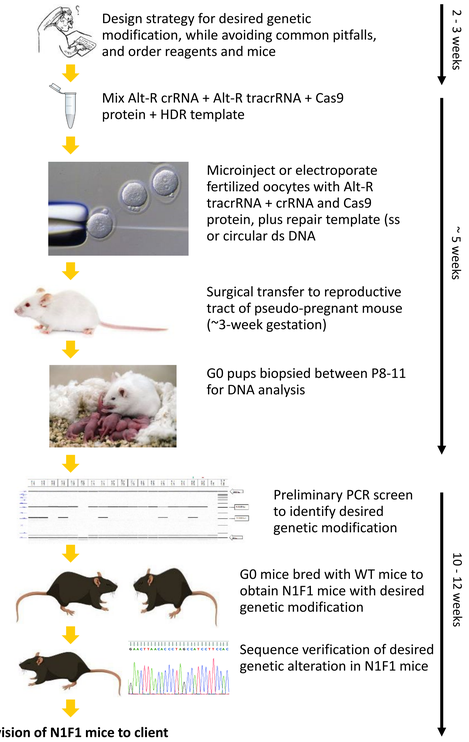
Production of null allele in first generation mice - useful if gene is previously uncharacterized

Repair Template

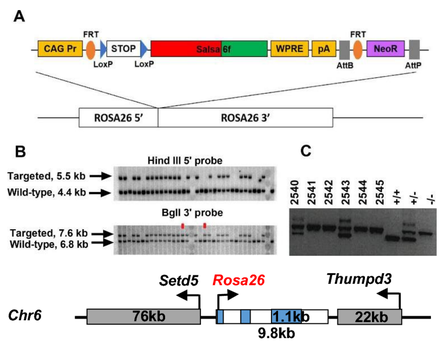
5′ 3′

Examples of HDR templates with commonly requested modifications

- Missense mutation(s)
- Splicing variant
- Enhancer variant
- Floxed allele
- 2A-reporter allele
- 2A-Cre allele
- Humanized exon(s)

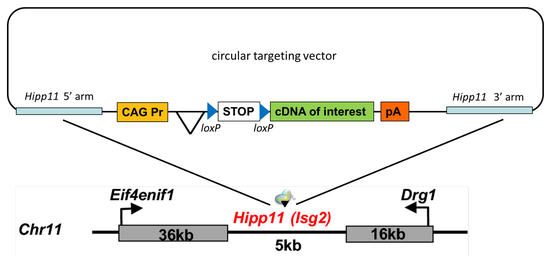


Targeted Transgenesis at *Rosa26* locus in mouse ES cells



Targeted transgenesis at *Hipp11* locus in mouse embryos.

Transgene expression at the *Hipp11* (intergenic) locus can be more consistent than that obtained at *Rosa26* locus. Plasmid transgenes can be targeted with high efficiency (~ 50%) via CRISPR/Cas9. Use of two independent loci enables combination of targeted transgenes.

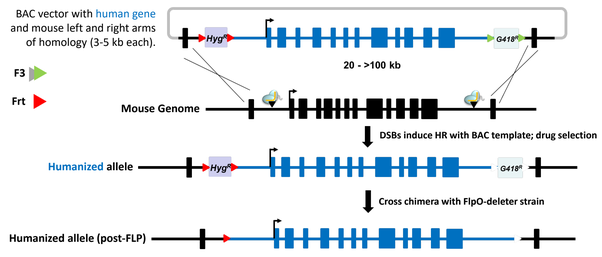


Assisted reproduction to develop large cohorts of mice for experimental studies

- Labs may find it challenging to produce cohorts of age- and sex-matched animals for experimental analysis.
- *In vitro* fertilization (IVF) and embryo transfer (ET) to pseudo-pregnant females can be used to produce mice efficiently for appropriately powered experimental analysis.
- Production of large cohorts of mice for experiments via IVF + ET is a generally under-utilized method to accelerate research using genetically modified mice.

Humanization of mouse loci.

Combining ES cell and CRISPR/CAS9 to substitute mouse genes with their human counterpart.



Key Equipment & Technologies

- Culture and LN_2 cryogenic storage of sperm, embryos, mES cell lines

- Microinjection and electroporation of zygotes / preimplantation embryos

- TaqMan, rhAMP based genotyping via Bio-Rad RT-PCR systems

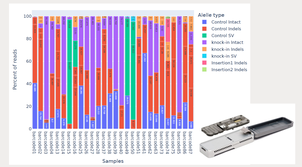
- IVF-based mouse production

- PFGE and Southern analysis using Bio-Rad CHEF Mapper

- High-throughput (3 x 96-well tray) analysis of standard PCR reactions using Agilent zcapillary array Fragment Analyzers

- Multiple animal holding rooms with ventilated cage racks and sterile caging.

- ONT MinION sequencing and Open-source sequence clustering program DAJIN2 analyzes detailed sequence and composition data of CRISPR edits make selection of right founder mice faster.



- Tissue culture suite with incubators, hoods and electroporation apparatus for ES cell culture (not shown)

Under Development

- **Improved production efficiency CRISPR-engineered CRE-conditional (floxed allele) mice via sequential electroporation of pre-implantation embryos.** Electroporation of ssODN containing 1st loxP site at zygote stage, followed by electroporation of 2nd loxP site at 2-cell stage prior to transfer into reproductive tract of pseudo-pregnant female.
- **Faster throughput DNA sequence analysis of targeted ES cells and founder (G0) generation mice generated by CRISPR via targeted sequencing using Oxford Nanopore MinION system.** Applications: Long-range PCR amplicon ligation sequence to identify animals/cells with 2 correct mutations in *cis* (on the same chromosome)

Optical Biology Core

Rahul Warrior, PhD
Director

UCI 趙 Chao Family Comprehensive Cancer Center

Leadership

Adeela Syed, PhD
OBC SUF Manager

Self Use Facility (SUF)

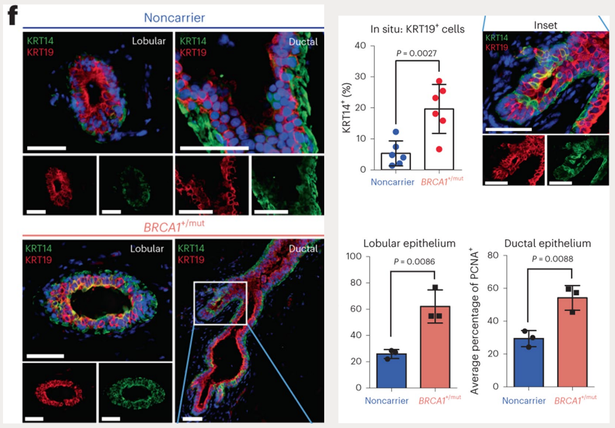
Offers suite of confocal, lightsheet and two photon microscopes that allow everything from deep tissue, whole tissue, confocal, Super Resolution imaging and image analysis

Instruments

- 24/7 access providing comprehensive support, including training, assistance with experimental setup, and data analysis
- 4 confocal microscopes (Zeiss LSM 980, 900, 780 and Leica Sp8) capable of 2 photon microscopy, live imaging,
- Zeiss Z1 Mesoscale Lightsheet for whole tissue imaging
- Zeiss Elyra 7 Super Resolution microscope: Lattice SIM & Single Molecule Localization Microscope
- Workstations for Image Analysis – Imaris, Arivis, ZEN etc

Scientific Highlights

Precancerous stroma in BRCA1+/mut may elevate breast cancer risk through the promotion of epithelial proliferation and an accumulation of luminal progenitor cells with altered differentiation. Nee, K., Ma, D., Nguyen, Q.H. *et al. Nat Genet* 2023 March 13. **55**, 595–606



- **KRT14/KRT19-Positive Cells**: In situ immunofluorescence analysis shows a higher percentage of KRT14/KRT19-double positive cells in BRCA1+/mut tissues compared to noncarriers, indicating increased epithelial changes.
- **PanCK and PCNA Expression**: Immunofluorescence analysis reveals higher expression of pan-cytokeratin and PCNA in ductal and lobular regions of BRCA1+/mut breast tissues, suggesting increased cellular proliferation.
- **PCNA+ Cells**: Bar graphs indicate a significantly higher percentage of PCNA-positive cells in both lobular and ductal regions of BRCA1+/mut patients compared to noncarriers, highlighting elevated proliferative activity.

Leadership

Mihaela Balu, PhD
NLOM Manager

Non-Linear Optics Microscopy (NLOM)

Specializing in multiphoton microscopy-based imaging with large fields of view and rapid scanning, NLOM collaborates on equipment use, development, and protocol design for diagnosing and monitoring skin conditions and therapies.

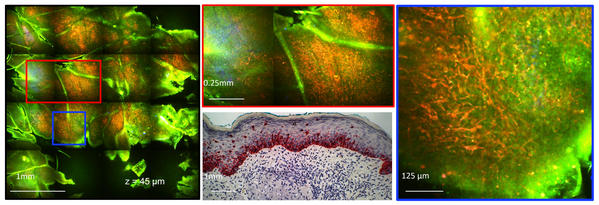
Instruments

Leica SP8 Falcon + coherent anti-Stokes Raman Scattering (CARS) Commercial imaging platform customized to feature the following modalities: confocal fluorescence and two-photon excited fluorescence (TPEF) microscopy, second harmonic generation (SHG), CARS and fluorescence lifetime microscopy.

Scientific Highlights

Label-free non-invasive imaging of melanoma using multiphoton microscopy (MPM): In this study, we investigate the feasibility of a clinical home-built multiphoton microscope (fast, large area multiphoton exoscope: FLAME) to detect non-invasively early melanoma (in situ) in human skin based on label-free molecular contrast provided through time-resolved fluorescence detection from NADH, FAD, melanin, keratin and elastin fibers and second harmonic generation of collagen.

Mihaela Balu, PhD – BIDD & Kristen Kelly, MD – BIDD



FLAME imaging of pagetoid spread in human melanoma. (a) The color coding of the cells is related to their temporal bin detection. Melanocytes and melanoma cells are selectively detected based on the short fluorescence lifetime of eumelanin compared to the fluorescence lifetime of the rest of the fluorophores in human skin. If our current clinical study is successful, this approach will provide a reliable tool for non-invasive, early detection of melanoma in human skin

More Information

Leadership

Michelle Digman, PhD
LFD Manager

Laboratory of Fluorescence Dynamics (LFD)

State-of-the-art research facility dedicated to the development and application of advanced fluorescence microscopy techniques for studying molecular dynamics and interactions in various biological systems.

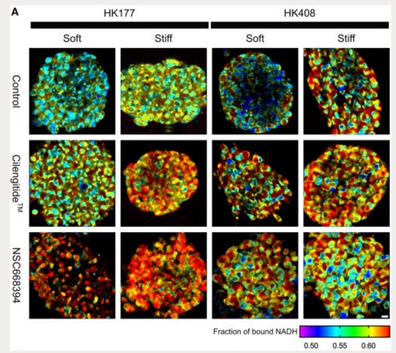
Instruments

National research resource center for biomedical fluorescence spectroscopy with over 12 instruments for dynamic imaging

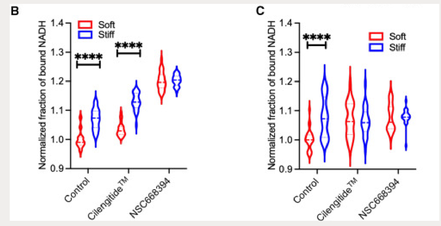
- The LFD designs, tests, and implements advances in the technology of hardware, software, and biomedical applications
- Dynamic imaging modalities include: metabolic Imaging, NADH metabolism, OXPHOS/Glycolysis, Bioluminescent immune reporters and fluorescence metabolic reporters

Scientific Highlights

This study highlights the critical role of tumor mechanics in influencing glioblastoma (GBM) cell behavior and metabolism.
Digman et al., Cell Report. 2023 October 31, Volume 42, Issue 10, 10113175



In HK177 glioblastoma cells, the inhibitor NSC668394 increased oxidative phosphorylation (OXPHOS) activity and eliminated metabolic differences between soft and stiff hydrogels, indicating that CD44-ezrin interactions mediate the shift toward glycolysis in softer environments.



For HK408 glioblastoma cells, both cilengitide (CRGD) and NSC668394 increased OXPHOS activity, suggesting that both integrin engagement and ezrin phosphorylation play roles in the metabolic changes induced by mechanical cues.

IFI Flow Cytometry Facility

UCI Chao Family Comprehensive Cancer Center

Leadership

Michael Hou, PhD
FCF Manager

Eric Pearlman, PhD
IFI Director

NanoCyte Cell Analyzer

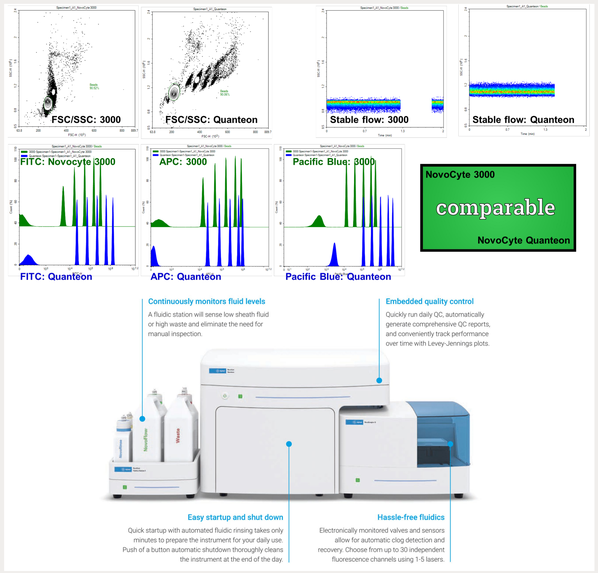
Our facility has 2 high-throughput cell analyzers

- **NovoCyte Quanteon**: 4 lasers with 25 parameter detectors
- **NovoCyte 3000**: 3 lasers with 15 parameter detectors.

The fluidic system is exceptionally stable and has automation for high throughput analysis of multiple plates in addition to support for traditional 5 ml tubes. Startup, shutdown, and other fluidic maintenance procedures are largely automated.

Performance comparison of NovoCyte 3000 and Quanteon using QC/calibration beads

	NovoCyte 3000			NovoCyte Quanteon				
Sextuplicate	1	2	3	4	5	6	Average	% CV
Events	100000	100000	100000	100000	100000	100000	100000	0
Events/Sec	1111	111	1111	1111	1099	1099	1107	0.56
Volume (µl)	98.39	99.21	98.82	98.30	100.22	99.91	99.14	0.80
Time (Sec)	90	90	90	90	91	91	90.33	0.57
Cell Count (µl)	926	919	925	923	907	909	918	0.9

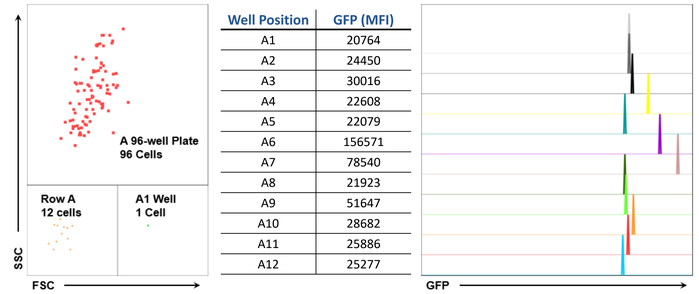


BD FACSAria Fusion Cell Sorter

Our facility houses a BD FACSAria Fusion sorter with 4 lasers and up to 11 fluorescent parameters. The BD FACSAria Fusion allows for 4-way bulk sorting into tubes or one-way sorting of single cells into 6/24/48/96-well plates. This instrument is also equipped with a temperature control system allowing for cooling of the sort chamber and collection device.

Laser	Filter	Preferred Colors
405	450/50	Alexa Fluor 405, Brilliant Violet 421, Pacific Blue, V450
	525/50	Brilliant Violet 510, V500, AmCyan
	610/20	Brilliant Violet 605
488	530/30	FITC, Alexa Fluor 488, GFP
	695/40	PerCP, PerCP-Cy5.5
561	582/15	PE, dsRed
	610/20	PI, PE-Texas Red, mCherry, PE-CF594
	670/14	PE-Cy5, PE-Alexa 647
	780/60	PE-Cy7
640	670/30	APC, Alexa Fluor 647
	780/60	APC-Cy7, APC-H7, APC-Alexa 750, Alexa Fluor 750, DyLight 750

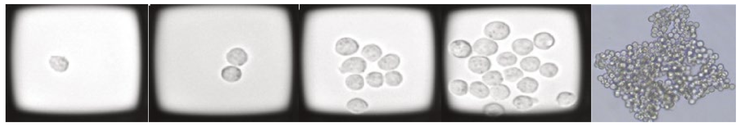
Single cell index sorting allows the isolation of single cells with retrospective identification of each single cell's immune phenotype



Well Position	GFP (MFI)
A1	20764
A2	24450
A3	30016
A4	22608
A5	22079
A6	156571
A7	78540
A8	21923
A9	51647
A10	28682
A11	25886
A12	25277

Index sorting: A method that deposits individual cells from a heterogeneous mixture into wells of 6/24/48/96 plates. Cells are usually sorted using specific fluorochromes and then channeled into an empty well. Cells that do not meet the specified criteria are shunted to a waste tube.

Index sorting for downstream applications: Single cell cloning



Single cell cloning: Separating cells of interest gives scientists the opportunity to culture individual cells in isolation. Single cell sorting is a powerful tool for generating clones with stably genome-integrated transfected genes. (Dr. Marco Bassetto uses this approach)

Index sorting for downstream applications: Single cell analysis

Single cell analysis: When performed on bulk samples, gene expression studies might yield only a limited understanding of complex samples. However, gene expression analyses performed on single cells can offer a powerful method to resolve sample heterogeneity and reveal hidden biology. (Dr. Minji Byun uses this approach)

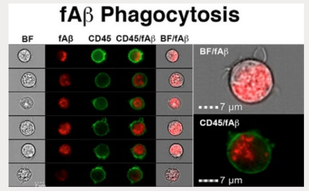
Cytek Amnis ImageStream

- The Cytek Amnis ImageStream MKII combines the phenotyping abilities of flow cytometry with the detailed imagery and functional insights of microscopy.
- There are numerous applications for qualitative and quantitative measurements including cell location, internalization, cell cycle, morphology, cell-cell interaction, and co-localization.

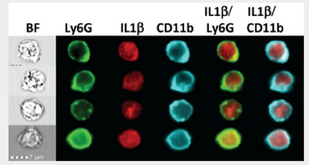
Laser	Filter	Preferred Colors
405	457/45	Alexa Fluor 405, Brilliant Violet 421, Pacific Blue, V450, DAPI
	537/65	Brilliant Violet 510, V500, Pacific Orange, Alexa Fluor 430, Qdot 525
	582/25	Qdot 565, Qdot 585
	610/30	Brilliant Violet 605, Qdot 605, eFluor 605NC
	702/85	Brilliant Violet 711
	762/35	Brilliant Violet 786, Qdot 800
488	528/65	FITC, Alexa Fluor 488, GFP
	577/35	PE, Cy3, dsRed, Alexa Fluor 555
	610/30	PE-Texas Red, PE-Alexa 610, PI, PE-DyLight 594
	702/85	PE-Cy5, PE-Alexa 647, 7-AAD, PI, PerCP, PerCP-Cy5.5, DRAQ 5
	762/35	PE-Cy7, PE-Vio770
642	702/85	APC, Alexa Fluor 647, Alexa Fluor 660, Alexa Fluor 680, Cy5
	762/35	APC-Cy7, APC-H7, APC-Alexa 750, Alexa Fluor 750, DyLight 750

Why use ImageStream?

- If you have a question that requires cell morphology
- If the spatial context of the signal within the cell is important to your research
- If you have rare cell events or short-lived events that are hard to find by normal microscopy.



Human microglial-like cells (iMGLs) phagocytose human brain-derived ingest amyloid β (Aβ). Blurton-Jones. Neuron. 2017 94: 278–293



Representative neutrophils from infected corneas immunostained with antibodies to Ly6G and CD11b, and intracellular IL-1β. Pearlman. J Immunol. 2018; 201: 2767–2775.

Contact Information
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Genomics Research & Technology Hub

UCI Chao Family Comprehensive Cancer Center

Leadership

Suzanne Sandmeyer, PhD
Director
Genomic Technologies

Remi Buisson, PhD
Assistant Director
GRT Hub SR

Melanie Oakes, PhD
Manager
Technical Operations

Jenny Wu, PhD
Director, Bioinformatics
Transcriptomic Analysis

Ivan Chang, PhD
Bioinformatics Engineer
Data Sharing

Mission

To put emerging nucleic acid technologies into the hands of CFCCC investigators and enable bioinformatics analysis through consultation, training and collaboration.

GRT Hub provides:

- Guidance and education throughout the entire experimental process, including experimental design, data analysis and publication.
- In-house staff with professional expertise in genome wide molecular technologies.
- Bioinformatics Consulting Service for experimental design and data analysis staffed by PhD-level scientists experienced in bioinformatics.

Services

- INSE**Illumina iScan beadarray**: linkage analysis, copy number variants, epigenetics
- **Illumina NovaSeq X Plus**: whole human genomes, deep sc sequencing
- **PacBio Revio:** whole genome seq, structural variants, scRNA isoforms
- **BioNano-Saphyr 2**: long-range optical mapping; structural variants
- **Library preparation**: single cell, multi-omic, HiFi, Me-seq, etc
- **NanoString nCounter**: digital quantification of known nucleic acid targets
- **10X Genomics ChromiumX**: scRNA-seq; scATAC-seq; multiome; VD(J) typing
- **Parse Biosciences**: split-seq; reduced cost for 100,000-1 M cells
- **Mission Bio Tapestri**: scDNA and protein typing: tumor lineage mapping; CNV
- **Bruker Isoplexis**: monitoring single cell secreted proteins, e.g. cytokines
- **Digital PCR:** Bio-Rad ddPCR, ThermoFisher Quantstudio Q
- **Nanostring GeoMx and 10x Visium**: spatial transcriptomics on fixed or fresh
- **Data visualization portals:** Publicly accessible web interactive dashboards enabling visual exploration of processed data

Instruments & Research Supported

Epigenome

Iscan: methylome, CNV

Lineage Tracing

Tapestri

Secretome

SC Cytokines: IsoSpark

Digital PCR

Absolute Q

1 | Sequencing: RNA, DNA, multi-omics

Short read

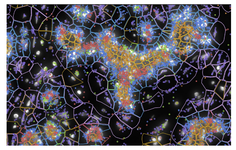
NovaSeq X Plus 30X
human genome:

Long read

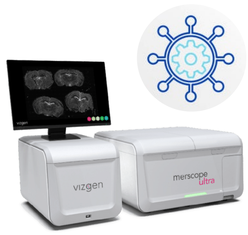
Revio:
long-read, 30X
human genome;
single cell isoform

2 | Sub-Cellular Spatial: FFPE & FF

Xenium:
Segmentation staining;
5000 probes;
post analysis proteomics



Kessenbrock/Lawson
Breast Tissue by Xenium

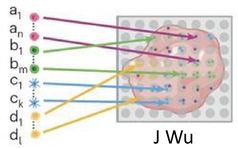


MERFISH Ultra
10,000 probes
3 cm * 3 cm

3 | Analysis and Data Sharing

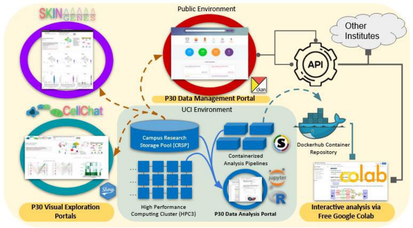
Workshops

Analysis



J Wu

Portal Development



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User Costs

Instrument	Application	Sample	Reagents	Additional cost
iScan Infinium Methylation	Infinium Methylation Screening	Single DNA prep	$90/sample	$425 BeadArray
Tapestri	Lineage analysis of cell populations	DNA & Single cell DNA & Protein	$2,500/sample	$595/sample
IsoSpark	Cytokines		$850/sample	$130/instrument use
Parse single cell	Single cell multiplex seq lib	100,000 cells	$9,800/48 samples	$1,404 staff processing
10X single cell	Single cell multiplex seq lib	20,000 cells	$1,500/sample	$435 first, $140/sample add
Visium<CytAssist FFPE	Low res clinical slide spatial discovery	6.5*6.5mm	$1,600 slide	$686/slide
Xenium	Subcellular resolution	12*11mm	$892 with cell segmentation	$825/run instrument

Plans

1. Expand clinical genomics and epigenetics studies

- Increase ***awareness of clinical community*** with targeted tech discussions for clinical departments
- Increase availability of technology that provides ***personnel and automated support for clinical investigators*** who lack these recourses
- Increase ***economic and technical feasibility of human genome sequencing***
- Participate in clinically focused program grant applications

2. Focus on and expand analysis of Hub data products

- ***Expand bioinformatic staff (underway) support*** for analysis of GRT Hub products
- Repeat and record introductory ***workshops*** and expand advanced topics
- Implement ***commercial pipelines*** to supplement in house analysis
- Build data sharing and data portal resources to foster collaborations
- Collaborate with ***CFCCC Statistics SR for population studies***
- ***Increase recharge rate and throughput*** for bioinformatics sustainability

3. Establish emerging technologies in GRT Hub eo enable insights into biological systems

Publications

CFCCC Investigator	Program	Published Journal	Year
Buisson, R	SPT	*Nat Com*	2024
Buisson, R; Tinoco, R	SPT BIDD	*Nat Com*	2023
Eng, OS; Valerin, JB; Tanjasiri, SP; Seldin MM; Masri, S; Fleischman, AG; Pannunzio, NR	SPT BID CC	*Nat*	2024
Hughes, C	BIDD	*JoVE*	2023
Nie, Q; Lander, AD; Ganesan, AK	SPT BIDD	*BioRxiv*	2024
Pannunzio, NR; Seldin, MM; Marazzi, I; Marangoni, F; Lawson, DA; Kessenbrock, K; Masri, S	SPT	*Nat Immun*	
Sworder, BJ; Wager, LE	SPT	*Cell Stem Cell*	2024

Mass Spectrometry Facility

UCI Chao Family Comprehensive Cancer Center

Leadership

Sergey Pronin, PhD
Director, MS

Felix Grun, PhD
Manager

Mission

To support researchers with expertise and services in mass spectrometric analyses of proteins, oligonucleotides, metabolites and drugs.

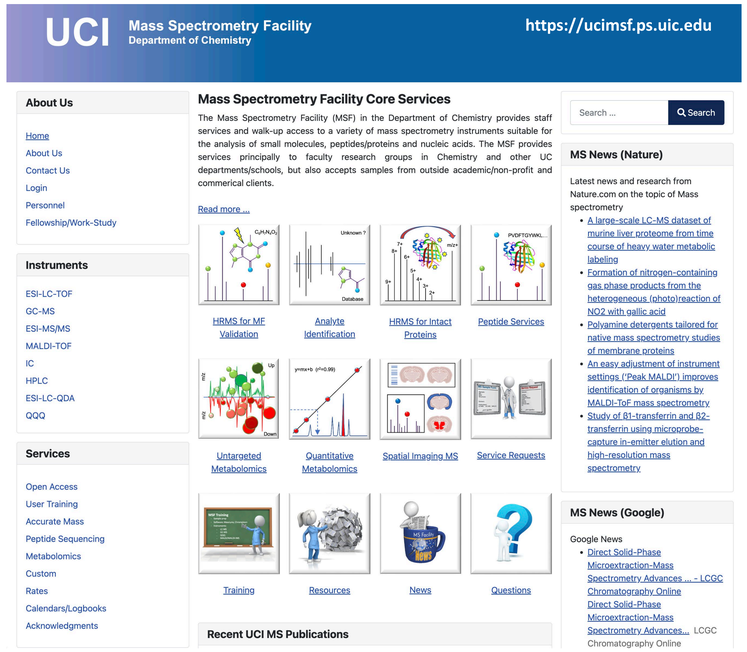
- The MS Facility (Chemistry) provides both walk-up open access and staff services for a wide range of MS applications
- Staff provide weekly user/instrument training
- Additional MS services are available from the High-End Mass Spectrometry Facility (HMSF) and the Nutritional Metabolism & Disease Lab (NMDL)

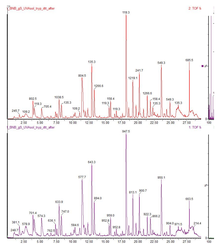
Key Features

- **Open Access:** Available 24/7
- **20 MS Instruments**
- **User-run samples:** 300+ users/yr | 35,000+ samples/yr
- **Low cost:** $2 – $30/sample
- **Service requests:** via Agilent iLab or website
- **Staff support:** Felix Grün, *Director*
  Ben Katz, *Proteomics Specialist*
  Chris Dicksion, *GSR Fellow*

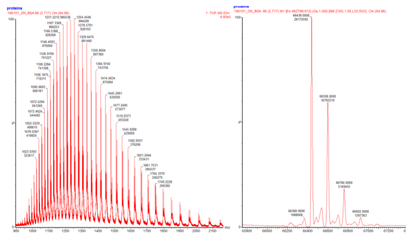
Capabilities

- Small molecule analysis – substrate/product monitoring
- Molecular formula (MF) validation ± 5 ppm
- Isotopic labelling analysis
- Polar/non-polar analyte detection/quantitation
- Air/temperature sensitive analytes
- Quantitation from biological/environmental matrices (targeted metabolomics)
- LC and UV/Vis complex mixture analysis (LC & GC) (global untargeted metabolomics)
- Polymer analysis (oligonucleotides, oligosaccharides)
- Peptide analyses (HRMS; in gel digestion, sequencing, aa modifications, PTMs)
- Intact protein analyses (up to 250 kDa)
- Ion mobility w/ MS (structural discrimination for isobaric species)
- Hydrogen-deuterium exchange (HDX) – protein-protein interactions
- Imaging mass spectrometry (IMS) –5-50 µm pixel res; 40 px/sec
- MS Software: MassLynx, PEAKS Studio 12, Progenesis QI, BioPharmaLynx, MassHunter, Chromeleon 7, mzMine, Sirius, SCiLS Lab Pro, ImageReveal. Remote login/access available

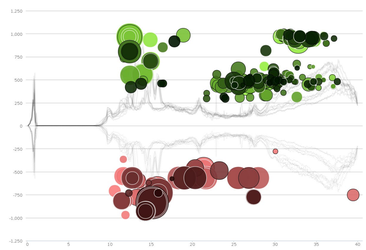


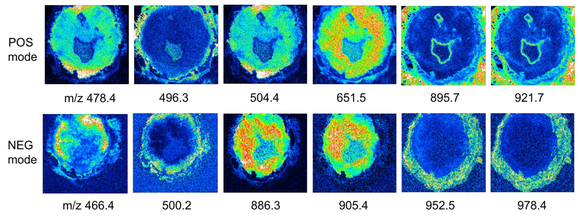


Peptide sequencing
Protein digestion, LC and nanoLC peptide separation, MS and MSMS data acquisition & analysis

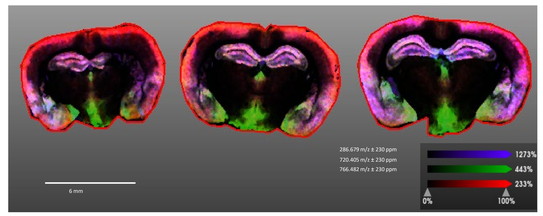


Protein HRMS analysis
Multiple charge state ladder deconvolution of BSA (m/z = 66438); 5 min high-throughput analysis up to 250 kDa, w/ buffer





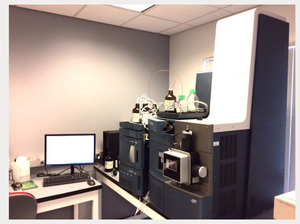
SW480 Tumor Xenograft Metabolic Heterogeneity Revealed by MALDI IMS
SW480 xenografts sectioned fresh frozen at 12 µm onto ITO slides, vacuum dried and matrix applied by sublimation: positive mode DHB (1.5 um), negative mode 9AA (0.9 um). Component features show complementary (mz 478.4 v. 496.3) or strongly correlated (mz 895.7/921.7 and 952.5/978.4) distribution patterns defining distinct zones of metabolite/lipid distributions within the tumor.



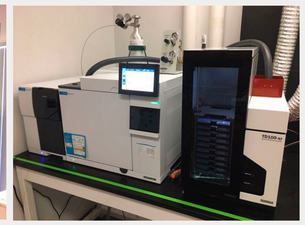
Metabolite/Lipid Imaging of 5xfAD v Control Mouse Brains
C57BL6 (control) or 5xfAD mice (7 months) were fresh frozen at 20 µm onto ITO slides. 9-AA matrix was applied by sublimation/recrystallization. Sections were imaged in reflector negative mode (RN) at 50 µm pixel resolution. False color composite image for three metabolite/lipid m/z markers is shown.

Untargeted metabolomics
Cloud mirror plot of *Anopheles stephensi* v Aedes Chetumal. Circles represent "m/z_rt" features with p-values <0.0001, fold change > 1.5. Green (upper panel) up-regulated in *Aedes*; red (lower half) up-regulated in *Anopheles*. Candidate metabolite IDs were derived by searching METLIN, HMDB and MetaScope databases with exact m/z ± 20 ppm.

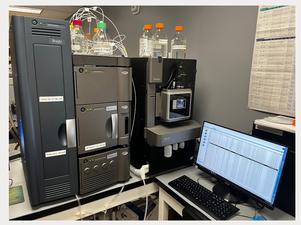
Key Equipment & Technologies



Waters Acquity Xevo G2-XS QTOF
LC-MS/MS; proteomics, metabolomics, sensitivity/quantitation; peptide sequencing,
protein modifications



Agilent TD GC-MS/FID
Thermal desorption GC with MS and FID detectors for volatiles analysis; additional GC-MS instruments available



Waters Acquity TQ-Absolute Premier
UPLC triplequads for targeted quantitation of analytes from complex matrices

ABSciex 5500 & Bruker ultraflextreme
MALDI instruments for protein analysis and imaging mass spectrometry (IMS)

Waters Acquity QDAs
Basic LC-MS/PDA systems for small molecule analyses

Sample prep:
HRMS sample prep for flow-ESI, MALDI targets and LIFDI (e.g. organometallc at -65 °C under inert atmosphere)

Shimadzu iMScope
AP-MALDI QTOF for high-throughput and high resolution IMS

Contact Us

https://ucimsf.ps.uci.edu

UCI High-End Mass Spectrometry Facility

UCI Chao Family Comprehensive Cancer Center

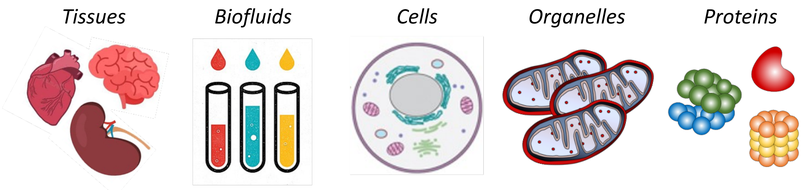
Instrumentation

- Orbitrap Fusion Lumos (ThermoFisher)
- UltiMate 3000 RSLC (ThermoFisher)

- Orbitrap LTQ-XL (ThermoFisher)
- Easy-nLC 1000 (ThermoFisher)

- Agilent 1200 Infinity II HPLCs
- Thermo Scientific Savant SPD131DDA SpeedVac

General proteomics workflow



HMSF Services

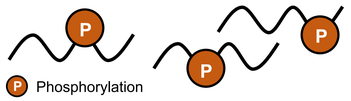
- Qualitative and quantitative profiling of whole proteomes
- Multiplexed, targeted, and label-free quantitative proteomics
- Characterization and quantification of post-translational modifications (PTMs)
- Protein interaction and structural analysis using cross-linking (XL-MS)

HMSF Leadership

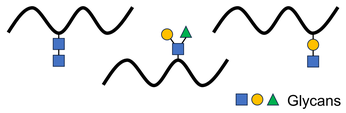
Lan Huang, PhD
Director, High-End MS
lanhuang@uci.edu

Clinton Yu, PhD
Manager
clinton.yu@uci.edu

Post-translational modifications

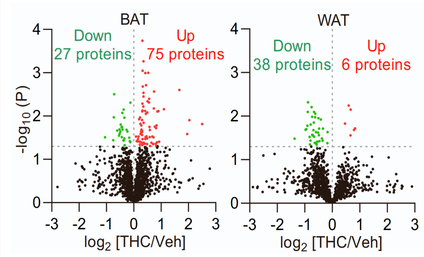


Seo et al., 2023, Molecular Cell 83, 3155–3170
Han et al., 2022. Nat Cell Biol 24, 74–87
Luu et al., 2023. PNAS 120 (19) e2221045120

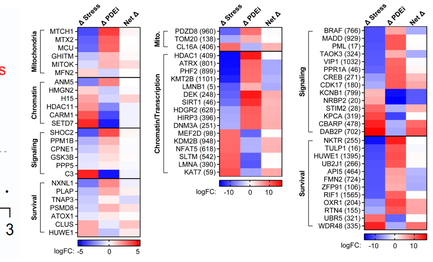


Salom et al., 2019, Journal of Biological Chemistry 294(20) 8123–8133.

Quantitative proteome-wide proteomics

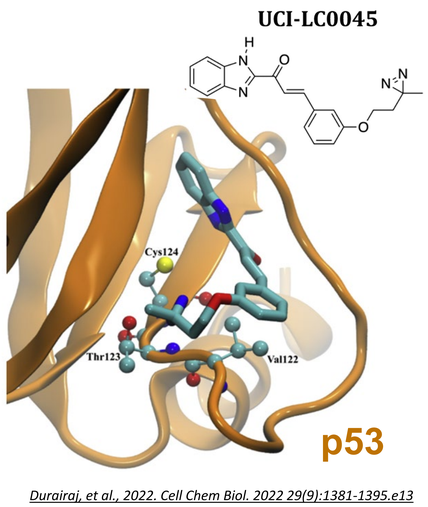


Effects of adolescent THC exposure on BAT proteomes. *Lin et al. 2023. Cell Metabolism, 35(7) 1227 - 1241.e7*



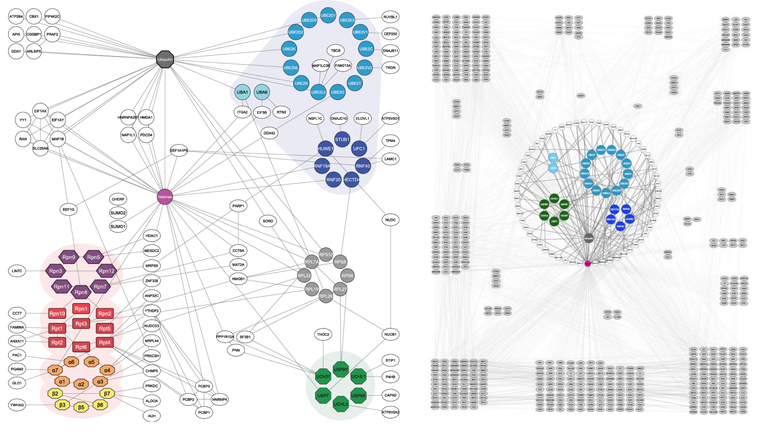
Effects of stress resilience-enhancing drugs on degenerating retina. *Luu et al., 2023. PNAS 120 (19) e2221045120*

Localizing drug interactions



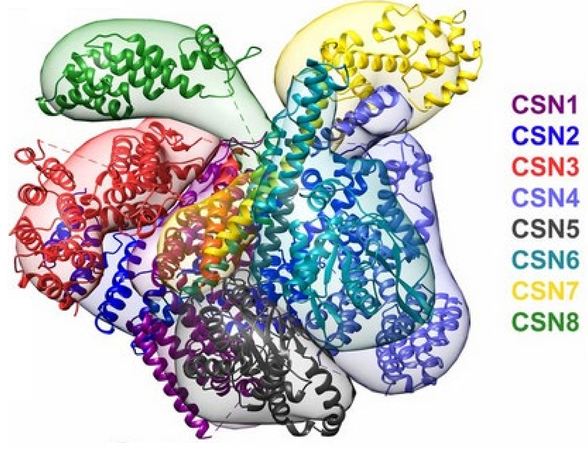
Durairaj, et al., 2022. Cell Chem Biol. 2022 29(9):1381-1395.e13

Protein-protein interactions



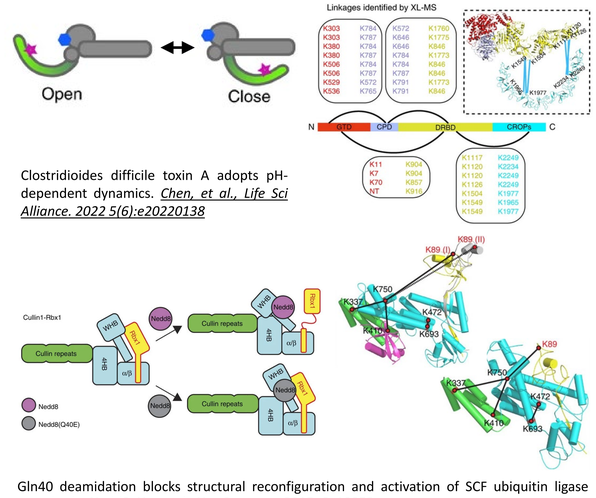
XL-MS-derived protein-protein interaction networks of the ubiquitin-proteasome (UPS) system determined. *Wheat, et al., 2021. PNAS 118(32).e2023360118*

Protein structure / Integrative modeling



XL-MS directed integrative model of the CSN (COP9 signalosome) complex *Gutierrez, et al., 2020. PNAS 117 (8) 4088-4098*

Protein dynamics / Conformational changes



Clostridioides difficile toxin A adopts pH-dependent dynamics. *Chen, et al., Life Sci Alliance. 2022 5(6):e20220138*

Gln40 deamidation blocks structural reconfiguration and activation of SCF ubiquitin ligase complex by Nedd8. *Yu, et al., Nat Commun. 2015; 6: 10053.*

Mass Spectrometry: Metabolomics

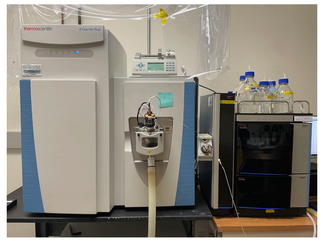
UCI Chao Family Comprehensive Cancer Center

Cholsoon Jang, PhD
Director, Metabolomics MS

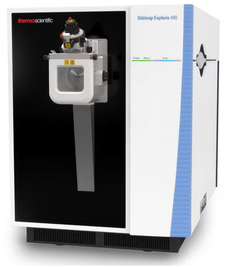
Sunhee Jung, PhD
Manager

Instrumentation (Liquid Chromatography Mass Spectrometers)

Q-Exactive Plus Hybrid Quadrupole-Orbitrap Mass Spectrometer coupled Vanquish HPLC and UHPLC Systems



Orbitrap Exploris 480 Mass Spectrometer coupled Vanquish HPLC and UHPLC Systems (Installation ongoing)

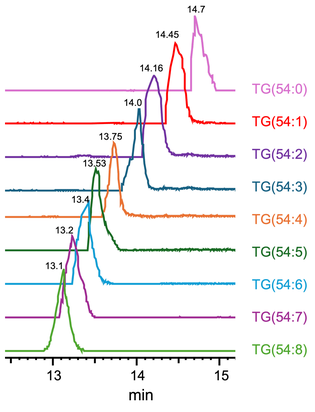


These state-of-the-art LC-MS instruments provide exceptional **sensitivity** and **resolution**, which enable detailed analysis of metabolites, lipids, and stable isotope tracing in biological samples. These capabilities are critical for both metabolic profiling and quantitative analyses in diverse research areas.

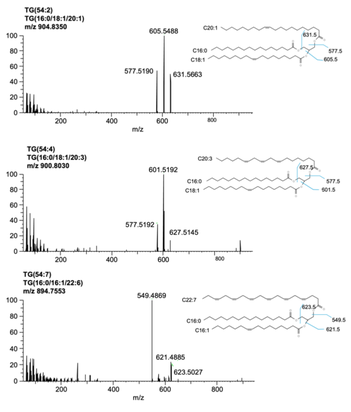
- **QE Plus**: Features ultra-high resolution and sensitivity, suitable for intricate metabolomics and lipidomics profiling.
- **Exploris 480**: Enhanced speed and sensitivity for high-throughput applications, provides accurate and robust data.

Lipidomics: lipid metabolite changes & biomarkers

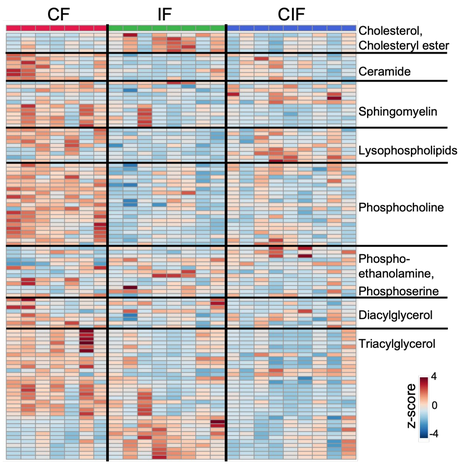
Lipid separation using reversed-phase LC



MS² for identification



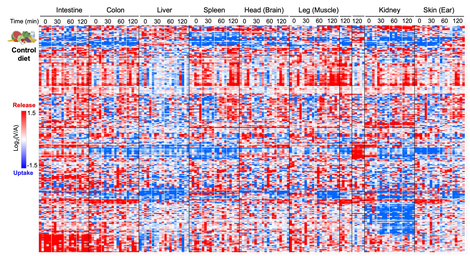
Lipid profiling : bile acid, acyl carnitine, cholesterol, cholesterol ester, ceramide, sphingomyelin, phospholipid, and mono-, di- and tri-glycerides



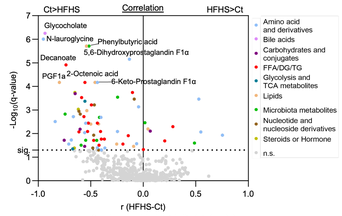
Metabolomics: soluble metabolite changes & biomarkers

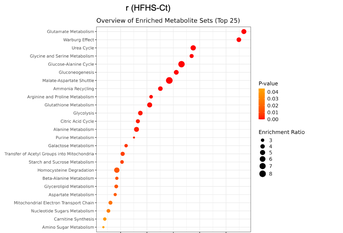
Hydrophilic Interaction Liquid Chromatography (HILIC) analysis

- Detected 20,000~ molecules in multiple biological samples
- Identified 2000~ metabolites based on in-house-library and MS² analysis

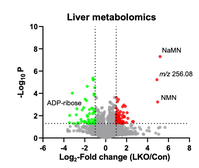


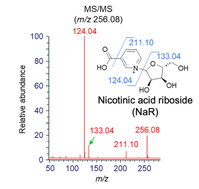
Metabolomics and pathway analysis





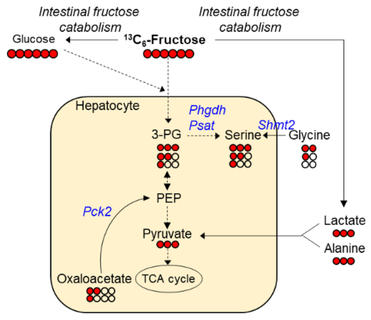
Identification of interesting molecule using MS²

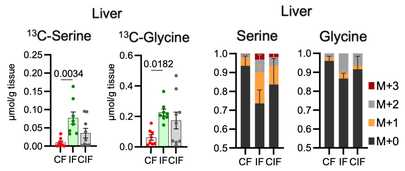




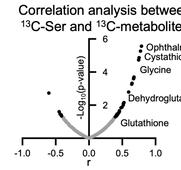
Non-radioactive Stable Isotope Tracing: metabolic flux analysis

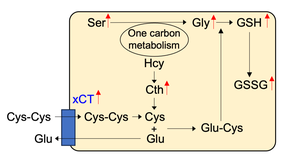
Metabolic pathway tracing (metabolic fates, pathway activities)



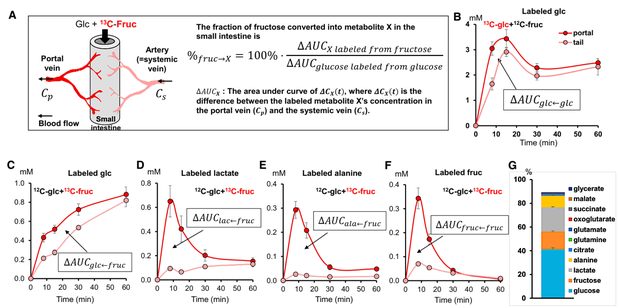


Integrated analysis of metabolic networks





Quantifying organ-specific metabolic flux



The Mass Spectrometry Core provides comprehensive services, supporting a wide range of applications in metabolomics, lipidomics, and stable isotope tracing. Our expertise allows researchers to gain in-depth insights into metabolic processes, paving the way for advances in metabolic health and disease research.

Contact Information: For more information about our services or to collaborate with the Mass Spec analysis, please reach out to us at **choljang@uci.edu**

In Vivo Functional Onco-Imaging

UCI Chao Family Comprehensive Cancer Center

Leadership & Team

Gultekin Gulsen, PhD
Co-Director

Zhuoli Zhang, MD, PhD
Co-Director

Farouk Nouizi, PhD
Facility Manager

Lena Qin
Animal Tech

Mission

Enhance and support basic and clinical cancer researchers by providing them with the necessary expertise, imaging instrumentation, and image analysis techniques.

To fulfill this mission, **IVFOI**:

- provide high-quality image acquisition and data analysis services for translational clinical studies;
- establish several multi-modality imaging systems to support innovative imaging studies; and
- develop several cutting-edge technologies for quantitatively accurate high-resolution small animal imaging and translate them to clinical settings

Services

Existing systems (on Irvine campus):

- MR: 3.0 T (human & animal) | MR: 9.4 T (animal)
- Combined MRI & Optical Tomography (animal)
- Combined X-ray micro CT & Fluorescence Tomography (animal)
- Hybrid MRI & SPECT (animal)

Existing Systems (located at UCI Medical Center):

- PET/CT & PECT/CT (clinical scanners available at UCIMC)
- MR (1.5 & 3 T - clinical scanner available at UCIMC)

Systems currently under development or under acquisition:

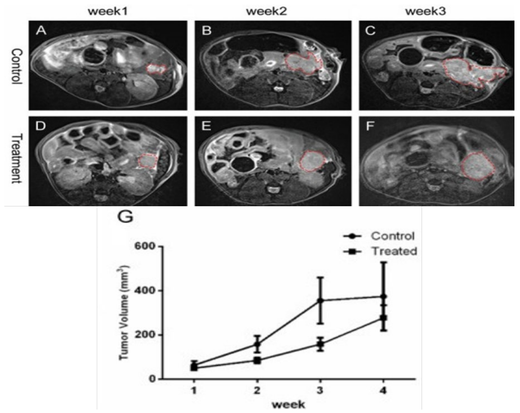
- Micro SPECT/CT (Hitachi, animal)
- Micro PET/CT (Siemens, animal)
- MRI Sodium Imaging (brain cancer)
- Hybrid MRI/Scintimammography (breast cancer)
- Hybrid MRI/Positron Emission Mammography (PEM)
- Temperature-modulated Fluorescence Tomography (animal)
- Photo-magnetic Imaging (animal)

Further information regarding all offered services can be found at the website:
https://cancer.uci.edu/ivfoi

Research Highlights

1 | Image-guided Interventional Combination Liver Cancer Immunotherapy

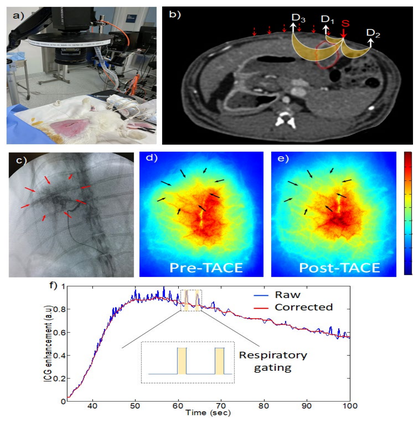
Z. Zhang (BIDD)



- The purpose of the study is to improve therapeutic response in HCC as combining FDA-approved sorafenib drug therapy with natural killer cell immunotherapy.
- In collaboration with IVFOI, an animal model of HCC was monitored using MRI scanner following different treatment strategies e.g. sorafenib, memory-like NK cell immunotherapy response and sorafenib plus NK cell immunochemotherapy.
- During the first of the studies, significantly advanced therapeutic response were observed in different HCC animal models.
- By integrating FDA approved drug and immune therapy approach, translational value of the recent study was obtained.

2 | Development of an optical molecular imaging system for TACE

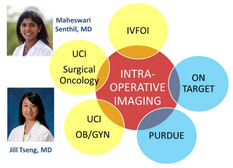
G. Gulsen (BIDD), N. Abi-Jaoudeh (BIDD)

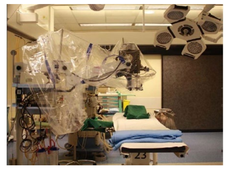


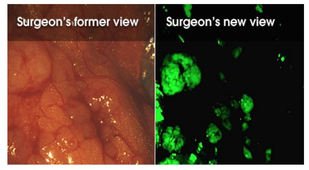
50% of patients with HCC will be treated with trans-arterial chemoembolization using Lipiodol conventional TACE (cTACE). Complete lipiodol coverage of the tumor is associated with improved outcomes. This project is geared towards developing and optical molecular imaging system to evaluate the effect of. Figure shows the preliminary results obtained on a rabbit bearing VX2 tumor undergoing the TACE procedure. Dynamic Florescence Images were acquired before and after the TACE with the injection of Indo-cyanine Green (ICG)).

a) Experimental setup. b) CT axial slice showing the positioning of the source points (S) and representative three detector pixels (D1-3) positioned at different distances from the source, which allows probing different depths. The sensitivity of the optical measurement is presented using the banana shapes that allow separation between superficial and deep tissue. c) X-ray fluoroscopy image showing the position of the tumor (red arrows). The planar DynFI image at the maximum enhancement: c) Pre-TACE and d) Post-TACE. e) Representative kinetics profile: raw (blue) and the corrected (red) using a respiratory gating

3 | Folate Targeting Optical Probes for Fluorescence Imaging Guided Ovarian Cancer Debunking Surgery: Cytalux



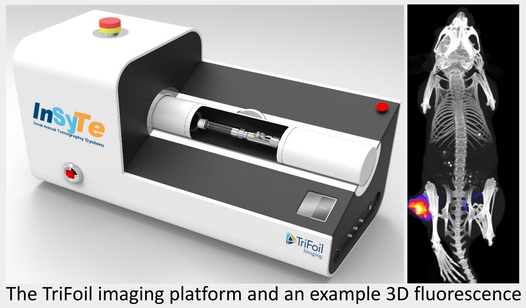




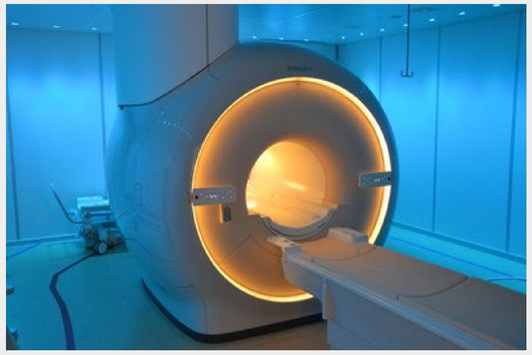
- Folate Receptor is highly expressed in ovarian cancer. A fluorescent folate analog (Cytalux) binds to the receptor with high affinity (1nM).
- Cytalux fluorescence can be excited by near-infrared light during surgery to identify and illuminate ovarian cancer lesions
- IVFOI played a key role in making UCI a site for Phase II and III clinical trials of Cytalux for ovarian cancer surgery
- FDA Approval of this first-of-kind novel optical molecular probe was announced Nov. 29, 2021
- IVFOI is now helping Dr. Senthil to apply Fluorescence Intraoperative Imaging with Cytalyx for Colon Cancer Surgery
- IVFOI is now working with PI Dr. Phil Low (faculty member of Purdue University (NCI) Center for Cancer Research) to develop a swept-wavelength laser based intra-operative surgery camera

Key Equipment & Technologies

Our LA based industrial collaborator, TriFoil, Inc, installed one of their commercial X-ray CT/Fluorescence Tomography machine into IVFOI, which is now open to any cancer member user **for free.**



The TriFoil imaging platform and an example 3D fluorescence image of a 4T1 tumor bearing mice



Our 3T and 9.4T MRIs can provide unprecedented anatomic and functional MR images for preclinical and clinical research studies. Please do not hesitate to contact us for **free pilot study** imaging opportunities.

Future Plans

- We are helping our industry collaborator Endocyclic Therapeutics , an Orange-County based company by MR Imaging of Endometriosis for their novel therapeutic agent ENDO-210.
- We established a service contract with San Diego-based industrial collaborator ClearPoint, Inc. to test their MR guided therapy platform in our 3T MRI system.
- We are expanding our service area by helping/encouraging CFCCC members to utilize Artificial Intelligence (AI) in their research by collaborating with the UCI Center for Artificial Intelligence in Diagnostic Medicine (CAIDM).
- Our 3- year STTR grant ($1.5 M) with TriFoil Inc. (PI Gulsen), to improve their photodiode-based Fluorescence Tomography imaging system by adding an integrated CCD camera is being funded by NIH.

Experimental Tissue Resource

UCI Chao Family Comprehensive Cancer Center

Leadership

Robert Edwards, MD, PhD
Director

Wendy Cozen, DO, MPH
Co-Director

Delia Tifrea, PhD, MBA
Manager

Mission

To support the research mission across UC Irvine and the campus research community

To fulfill this mission **ETR** assists investigators with tissue procurement, processing, and histopathology interpretation.

Services

- Fresh and FFPE Tissue Procurement and Interpretive Histopathology Consultation
- Tissue Histology and IHC services
- Mouse Pathology services/consultation on mouse models of human disease
- Biorepository/tissue banking services, including a user-searchable de-identified database of archival tissue

Inventory (Available Samples)

TISSUE	SURGICAL RESECTIONS FFPE (# 5 years)	BIOPSIES FFPE (# 5 years)	FROZEN tissue
brain	589 (326)	3,006 (1297)	644
colon	2,204 (956)	23,352 (13,546)	259
pancreas	875 (266)	398 (211)	98
breast	5,808 (2,505)	1,211 (354)	118
uterus	899 (547)	237 (99)	219
ovary, adnexa	1,671 (713)	206 (77)	280
prostate	1,858 (602)	377 (239)	735
kidney	1,180 (422)	169 (78)	295
bladder	535 (288)	1,308 (513)	29
lung	285 (130)	177 (133)	36
TOTAL	328,987		5,682

Support Provided (Annual) 65% cancer related

- Clinical trials..... **97**
- Individual patients..... **1,348**
- Investigator-initiated trials..... **8**
- Basic research projects..... **43**
- ETR consultation for database, IRB, sample collection, protocol review..... **84**
- TMA..... **10**

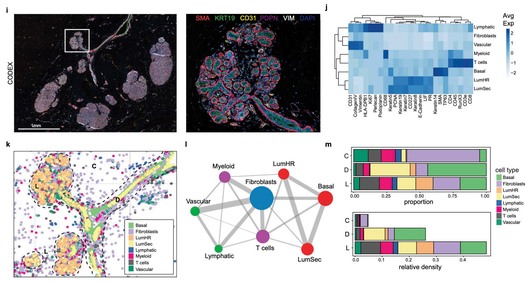
Research Highlights

1 | A spatially resolved single cell genomic atlas of the adult human breast

Kessenbrock K (SPT), Lawson DA (SPT), Edwards R (SPT), Lin E (SPT), Parajuli R (SPT)

Nature 2023; 620 (7972): 181-191. 5966421

A comprehensive Human Breast Cell Atlas (HBCA) at single-cell and spatial resolution, with focus on non-epithelial cell types was detailed. This single-cell transcriptomics study profiled 714,331 cells from 126 women, and 117,346 nuclei from 20 women, identifying 12 major cell types and 58 biological cell states. These data reveal abundant perivascular, endothelial and immune cell populations, and highly diverse luminal epithelial cell states. Spatial mapping using four different technologies revealed an unexpectedly rich ecosystem of tissue-resident immune cells, as well as distinct molecular differences between ductal and lobular regions.



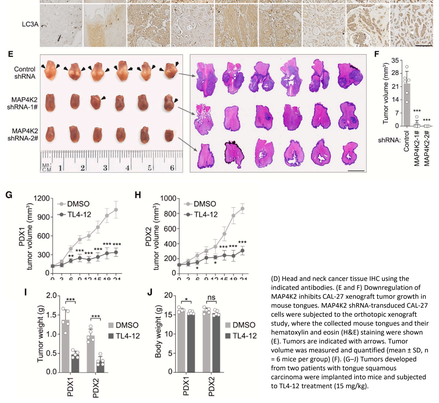
j, Heatmap showing protein levels for markers that were used to identify different cell types. **k**, Cell segmentation using combinations of markers to identify cell types in the CODEX data from one tissue sample, with topographic areas annotated. **l**, Spatial colocalization graph of segmented cell types in the CODEX data from 4 tissues. **m**, Cell type and cell density frequencies from the CODEX data summarized across 4 tissue samples.

2 | The Hippo pathway noncanonically drives autophagy and cell survival in response to energy stress

Wang W (SPT), Edwards R (SPT), Huang L (BIDD)

Molecular Cell 2023; 83 (17):3155-3170.e8

The Hippo pathway is known for its crucial involvement in development, regeneration, organ size control, and cancer. While energy stress is known to activate the Hippo pathway and inhibit its effector YAP, the precise role of the Hippo pathway in energy stress response remains unclear. Here, we report a YAP-independent function of the Hippo pathway in facilitating autophagy and cell survival in response to energy stress, a process mediated by its upstream components MAP4K2 and STRIPAK. Mechanistically, energy stress disrupts the MAP4K2-STRIPAK association, leading to the activation of MAP4K2. Subsequently, MAP4K2 phosphorylates ATG8-family member LC3, thereby facilitating autophagic flux. MAP4K2 is highly expressed in head and neck cancer, and its mediated autophagy is required for head and neck tumor growth in mice. Altogether, our study unveils a noncanonical role of the Hippo pathway in energy stress response, shedding light on this key growth-related pathway in tissue homeostasis and cancer.



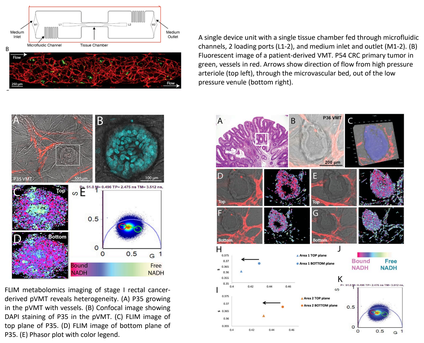
(D) Head and neck cancer tissue IHC using the indicated antibodies. (E and F) Downregulation of MAP4K2 inhibits CAL-27 xenograft tumor growth in mouse tongues. MAP4K2 shRNA-transduced CAL-27 cells were subjected to the orthotopic xenograft study, where the collected mouse tongues and their hematoxylin and eosin (H&E) staining were shown (E). Tumors are indicated with arrows. Tumor volume was measured and quantified (mean ± SD, n = 6 mice per group) (F). (G–J) Tumors developed from two patients with tongue squamous carcinoma were implanted into mice and subjected to TL4-12 treatment (15 mg/kg).

3 | A human vascularized microtumor model of patient-derived colorectal cancer recapitulates clinical disease

Hughes CCW (BIDD), Edwards RA (SPT), Lowengrub JS (SPT), Waterman ML (SPT), Zell JA (CC)

Translational research: the journal of laboratory and clinical medicine 2023; 255:97-108.

Accurately modeling tumor biology and testing novel therapies on patient-derived cells is critically important to developing therapeutic regimens personalized to a patient's specific disease. The vascularized microtumor (VMT), or "tumor-on-a-chip," is a physiologic preclinical cancer model that incorporates key features of the native human tumor microenvironment within a transparent microfluidic platform, allowing rapid drug screening in vitro. This study is optimizing the methods for generating patient-derived VMT (pVMT) using fresh colorectal cancer (CRC) biopsies and surgical resections to test drug sensitivities at the individual patient level. In response to standard chemotherapy and TGF-βR1 inhibition, the study reports heterogeneous responses between pVMT derived from 6 patient biopsies, with the pVMT recapitulating tumor growth, histological features, metabolic heterogeneity, and drug responses of actual CRC tumors. This results suggest that a translational infrastructure providing rapid information from patient-derived tumor cells in the pVMT can be used support efforts to improve patient outcomes.



A single device unit with a single tissue chamber fed through microfluidic channels, 2 loading ports (L1-2), and medium inlet and outlet (M1-2). (B) Fluorescent image of a patient-derived VMT. P54 CRC primary tumor in green, vessels in red. Arrows show direction of flow from high pressure arteriole (top left), through the microvascular bed, out of the low pressure venule (bottom right).

FLIM metabolomics imaging of stage I rectal cancer-derived pVMT reveals heterogeneity. (A) P35 growing in the pVMT with vessels. (B) Confocal image showing DAPI staining of P35 in the pVMT. (C) FLIM image of top plane of P35. (D) FLIM image of bottom plane of P35. (E) Phasor plot with color legend.

Key Equipment & Technologies

We acquired additional space and added the second histotechnologist with complementary skills

- Whole Slide Ventana Scanners

- Automated tissue microarray (TMA Grand Master)

# core/block	core diameter
558	0.6 mm
286	1 mm
135	1.5 mm
84	2 mm

Feasible for proteomics ***nanoString***- GeoMx DSP

Future Plans

- To continue to expand procurement of fresh specimens for clinical trialists and integration into clinical trials workflow.
- To increase utilization of basic histology services and expand the utilization of current Discovery Automated Ventana stainer to immunofluorescence and custom IHC
- To advertise and increase utilization of the new services: **automated tissue microarrays (TMA) and specialized histology services for special transcriptomics**
- To complete the build-out of new, dedicated **ETR** facility space for processing, annotation, and storage of high quality solid organ and hematopoietic malignancy specimens, **with the goal of meeting CAP accreditation requirements for Biorepositories**
- To enhance the EMR-LIS integration platforms utilization to link surgical pathology specimen data with patient data to facilitate outcomes research
- To establish regular Open house- Training sessions for FFPE and frozen tissue sectioning

Publications

CFCCC Investigator	Program	Published Journal	Year
Robert Edwards, MD, PhD Erin Lin, DO Ritesh Parajuli, MD Qing Nie, PhD Kai Kessenbrock, PhD	SPT SPT SPT SPT SPT	*Nature genetics*	2023
Mei Kong, PhD	SPT	*Nature communications*	2023
Matthew Inlay, PhD	SPT	*EMBO molecular medicine*	2023
Edward Uchio, MD Xiaolin Zi, PhD	CC CC	*Biomolecules*	2023
Jogeshwar Mukherjee, PhD	BIDD	*International journal of molecular sciences*	2023

Biostatistics Shared Resource

UCI Chao Family Comprehensive Cancer Center

Leadership

Min Zhang, MD, PhD[2]
Director

Wen-Pin Chen, MS
Facility Manager

Mission

The BSR provides a centralized resource of biostatistical expertise for the experimental design and analysis of basic, translational, clinical and population-based cancer research.

To fulfill this mission, BSR:

- Initiates active participation during grant preparation in the areas of cancer etiology, genetics, detection, and prevention
- Partners on research design, qualitative and quantitative protocol features
- Incorporates existing and develops new statistical methods
- Provides guidance on sample size requirements

Services

Basic Statistical Analysis
- Statistical analysis for manuscript/grant preparation

Omics Data Analysis
- Genomic (SNP, WGS, WES) including GWAS, PheWAS
- Transcriptomic (microarray data, bulk RNA-seq) including eQTL analysis
- Epigenetics (ChIP-seq; ATAC-seq)
- Single-cell omics
- Functional analysis (pathway, GO)
- Metabolomics
- Microbiome
- Radiomics and radiogenomics

Advanced Statistical Analysis
- Project-oriented special study design and data analysis

Research Computing
- Project planning with HIPAA-compliant computational needs, and best practices on cloud computing technologies
- Database design, creation and management (e.g., linking EHR and omics data for PheWAS)
- Programming assistance
- Setting up and running intensive jobs on Cloud

Training and Education
- Annual NCI "*Big Data Training for Cancer Research*"
- Offer regular need-based workshops

Consulting
- Bioinformatics | Biostatistics | Database | Machine learning | Research computing | Statistical/computational genetics and genomics

Research Highlights

1 | Hereditary Cancer Clinics Improve Adherence to NCCN Germline Testing Guidelines for Pancreatic Cancer

Claudia Rosso, Naomie Devico Marciano, Deepika Nathan, Wen-Pin Chen, Christine E McLaren (CC), Kathryn E Osann, Pamela L Flodman, May T Cho, Fa-Chyi Lee (BIDD), Farshid Dayyani (SPT), Jason A Zell (CC), Jennifer B Valerin(SPT)

Publication: *J Natl Compr Canc Netw. 2024 ; 22(5):299-305 PMID: 38889755.*

Background: Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis, with a 5-year overall survival rate of 10%. In November 2018, NCCN recommended that all patients with PDAC receive genetic counseling (GC) and germline testing regardless of family history. We hypothesized that patients with PDAC were more likely to be referred for testing after this change to the guidelines, regardless of presumed predictive factors, and that compliance would be further improved following the implementation of a hereditary cancer clinic (HCC).

Methods: We conducted a retrospective analysis of patients diagnosed with PDAC from June 2017 through December 2021 at University of California, Irvine. We compared rates of genetics referral among patients in different diagnostic eras: (a) pre-NCCN era: June 2017 through November 2018), (b) post-NCCN era: December 2018 through January 2020, and (c) HCC (HCC era: June 2020 through December 2021). Data were compared using chi-square, Fisher exact, and multivariate analyses.

Results:
- Prior to the guideline changes, 30% were referred to GC compared with 54.7% in the post-NCCN era. After the implementation of the HCC, 77.4% were referred to GC (Table 1, *P*<.0001).
- The odds ratio (OR) for referral to GC among patients with a positive family history of cancer progressively decreased following the change (pre-NCCN era: OR, 11.90 [95% CI, 3.00–80.14]; post-NCCN era: OR, 3.39 [95% CI, 1.13–10.76]; HCC era: OR, 3.11 [95% CI, 0.95–10.16]).

Conclusions: The 2018 changes to the NCCN Guidelines recommending germline testing for all patients with PDAC significantly increased GC referral rates at this academic medical center. The implementation of an HCC further boosted compliance.

Table 1. Genetic Counseling Referral Patterns

	All (n=368)	Pre- NCCN (N=125)	Post-NCCN (N=140)	HCC (N=103)	P-value
Referred to GC	124	24/80 (30.0%)	35/64 (54.7%)	65/84 (77.4%)	<0.0001*
Attended GC	84	15/24 (83.3%)	26/35 (96.3%)	43/65 (74.1%)	0.0362
Completed Testing	74	13/15 (100%)	22/26 (91.7%)	39 /42 (92.9%)	0.8411
Deleterious Mutation Positive	15	3/9 (33.3%)	6/22 (27.3%)	6/38 (15.8%)	0.3818

2 | Interventions to mitigate cancer-related medical financial hardship: A systematic review and meta-analysis

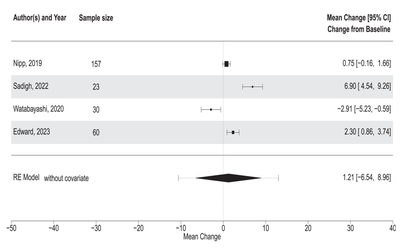
Ali Rashidi, Jinho Jung, Raymond Kao, Emily Lan Nguyen, Theresa Le, Brandon Ton, Wen-Pin Chen, Argyrios Ziogas (CC), Gelareh Sadigh (CC)

Publication: *Cancer.* 2024 Sep 15;130(18):3198-3209. PMC11347103
Funding: National Cancer Institute of the National Institutes of Health (P30CA062203)

Background: This study systematically reviewed interventions mitigating financial hardship in patients with cancer and assessed effectiveness using a meta-analytic method.

Methods: PubMed, Cochrane, Scopus, CINAHL, and Web of Science were searched for articles published in English during January 2000–April 2023. Two independent reviewers selected prospective clinical trials with an intervention targeting and an outcome measuring financial hardship. Quality appraisal and data extraction were performed independently by two reviewers using a quality assessment tool. A random-effects model meta-analysis was performed. Reporting followed the preferred reporting items for systematic review and meta-analyses guidelines.

Results:
- Eleven studies (2211 participants; 55% male; mean age, 59.29 years) testing interventions including financial navigation, financial education, and cost discussion were included.
- Financial worry improved in only 27.3% of 11 studies.
- Four studies (373 participants; 37% male, mean age, 55.88 years) assessed the impact of financial navigation on financial worry using the comprehensive score of financial toxicity (COST) measure (score range, 0–44; higher score = lower financial worry). Adjusting for pre-intervention COST, mean change of COST significantly decreased by 0.88 with every 1-unit increase in pre-intervention COST (p = .02). The intervention significantly changed COST score when pre-intervention COST was ≤14.5.



Conclusion
A variety of interventions have been tested to mitigate financial hardship. Financial navigation can mitigate financial worry among high-risk patients.

Key Equipment & Technologies

- SAS® software Version of 9.4
- R package
- StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.
- PASS 2023 Power Analysis and Sample Size Software. NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass.
- nQuery 8. Sample Size and Power Calculation. "Statsols" (Statistical Solutions Ltd), Cork, Ireland.
- QIAGEN Ingenuity Pathway Analysis (IPA)

Future Plans

Community Engagement / Catchment Area
- Continue to support the development of grant applications / manuscripts that focus on the catchment area and result from partnerships developed through CE efforts;
- Continue to provide consulting services on bioinformatics, biostatistics, database access, data integration;
- Expand new services on machine learning, statistical genetics and genomics, research computing to facilitate interdisciplinary collaborations in catchment area.

Enhancing Diversity, Equity and Inclusion
- Offer scholarships for underrepresented trainees to attend the NCI-funded big data workshop;
- Develop new machine learning methods to improve the analysis of data from minority populations.

Education and Training
- Organize the annual NCI-funded summer workshop on "*Big Data Training for Cancer Research*";
- Offer regular need-based workshops on basic statistical analysis, workflow for sequencing data analysis, FAIR computational workflows on the cloud;
- Organize regular seminar series to provide education opportunities for trainees.

Publications

CFCCC Investigator	Program	Published Journal	Year
Christine McLaren, PhD Fa-Chyi Lee, MD Farshid Dayyani, MD, PhD Jason Zell, DO, MPH Jennifer B Valerin, MD, PhD	CC BIDD SPT CC SPT	J Natl Compr Canc Netw	2024
Daniela Bota, MD, PhD	BIDD	Neuro-oncology	2024
Christine McLaren, PhD Xiaolin Zi, PhD	CC CC	Clin Transl Med.	2024
Argyrios Ziogas, PhD Gelareh Sadigh, MD	CC CC	Cancer	2024
Farshid Dayyani, MD, PhD Fa-Chyi Lee, MD	SPT BIDD	Oncologist	2024
Helen Ma, PhD Pankaj Gupta, MD Wendy Cozen, PhD	CC SPT CC	Blood Adv.	2024

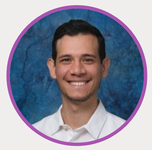
Biobehavioral Shared Resource

UCI Chao Family Comprehensive Cancer Center

Leadership

Michael Hoyt, PhD
Director

Michelle Fortier, PhD
Assistant Director



Jose Lechuga, MS
Facility Manager

Mission

To support Cancer Center members and cancer researchers with expertise and services in planning, conducting, and dissemination of translational biobehavioral research.

- Assists in the conduct and communication of high quality biobehavioral research.
- Provides consultation on behavioral and/or quality-of-life patient-reported outcome measures, research design, data collection, interpretation of self-report data, manuscript preparation, and behavioral interventions.
- Participates in translational research in psychoneuroimmunology and examination of behavioral issues that enhance recruitment and development of behavioral and quality-of-life outcomes.
- Offers expertise on instrument selection and development, as well as consideration for data collection assessment intervals and strategies to obtain valid and reliable data.

Services

- Selection of Patient Reported Outcomes and Measures (PROs)
- Participant Recruitment and Retention Strategy Assistance
- Qualitative and Quantitative Data Collection and Management
- Intervention Design and Implementation
- Training and Education in biobehavioral research
- Consultation and support in best practices for the collection of biomarkers in behavioral studies
- Advanced project-oriented special study design and analysis

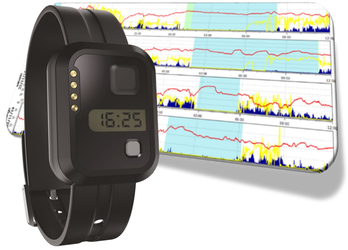
Research Highlights

1 | Standardizing the Fertility Preservation Discussion Amongst Reproductive Age Women Diagnosed with Cancer

PI: Holly Yong, MD (Assistant Clinical Professor, Surgery)

The BBSR is assisting in the development of a comprehensive patient-report tool regarding oncofertility and fertility preservation. The tool focuses on the utility of conversations with healthcare providers and factors influencing fertility decision making. This project aims to gain deeper insights into how patients can make informed choices about reproductive health after cancer.

2 | Addressing Financial and Social Needs Among Patients with Cancer

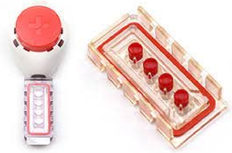


PI: Gelareh Sadigh, M.D. (Associate Professor In Residence, Radiological Sciences, School of Medicine)

The BBSR is engaged in the assessment of objective sleep quality monitoring through the use of wrist actigraphy to examine the potential impact of a financial needs intervention among Latinx patients. In addition, the BBSR will collect and analyze qualitative interview data about participation.

3 | Stress & Well-being in Asian Americans with Advanced/Metastatic Cancer

PI: Jacqueline H. J. Kim, PhD (Assistant Professor In Residence, Medicine/HemOnc)



The BBSR is supporting with participant coordination and tracking, in additional to processing and storage of biosample devices collected from participants throughout the study. Through this project, the BBSR developed and tested a protocol for the collection of dried blood spot sample through a TASSO collection device. This involved coordination of the manufacturer, investigator, and the Institute for Interdisciplinary Salivary Bioscience.

Key Equipment & Technologies

- Patient Reported Outcomes and Measures (PROs)
- Participant Recruitment and Retention
- Data Collection and Management
- Intervention Design and Implementation
- Training and Education
- Biosample Collection for Behavioral Research

Future Plans

Enhancing Equity, Diversity, and Inclusion, Community Engagement & Catchment Area

- The BBSR is in discussion with the COE and ICTS to develop a training program for multi-lingual community members who would like to participate in the research process and learning research interviewing skills
- Continued expansion of focus on Asian American and Latino survivorship populations

Education and Training

- Continued involvement in the Cancer Clinical Trials training program
- Planned trainings on biobehavioral research methods and biomarker use (workshops)

Planned and Continued Activities

- Continue to explore the formation of a workgroup for inclusion of PROs in EPIC
- Continued expansion of project portfolio

Contact Information