2 Optical Biology Core

UCI Chao Family Comprehensive Cancer Center

LEADERSHIP & MISSION

Rahul Warrior, PhD
Director

Adeela Syed, PhD
Manager, SUF

Michelle Digman, PhD
Manager, LFD

Mihaela Balu, PhD
Manager, NLOM

Michael Hou, PhD
Manager, FCF

OBC is a matrix of 4 cores that provide access to cutting-edge imaging and sorting capabilities. **OBC** operates the:

- Self-Use Facility (SUF)
- Laboratory of Fluorescence Dynamics (LFD) – **NEW in 2024**
- Non-Linear Optical Microscopy (NLOM) Laboratory
- Flow Cytometry Facility (FCF)

SERVICES, TECHNOLOGIES & EQUIPMENT

SELF-USE FACILITY (SUF)
Offers suite of confocal, lightsheet and photon microscopes for deep tissue, whole tissue, fluorescence lifetime (FLIM) and Super Resolution imaging and analysis

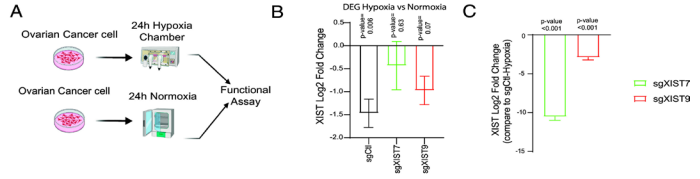
LAB OF FLUORESCENCE DYNAMICS (LFD)
Dedicated to the development and application of advanced fluorescence microscopy techniques

NON-LINEAR OPTICAL MICROSCOPY (NLOM)
Specializes in multiphoton microscopy-based imaging with large fields of view and rapid scanning for skin cancers and other skin conditions. Collaborative use

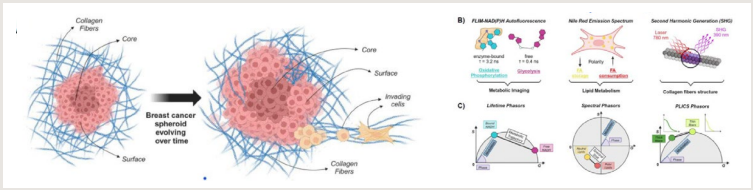
FLOW CYTOMETRY FACILITY (FCF)
Operates a suite of multi-parameter flow cytometers equipped for fluorescence activated cell sorting and/or analysis

RESEARCH HIGHLIGHTS

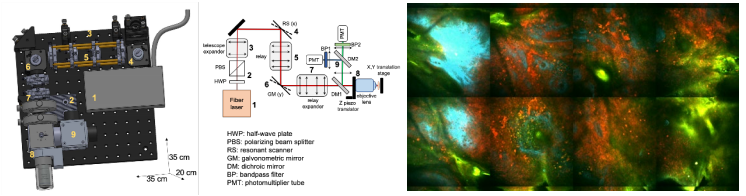
XIST Loss Drives Ovarian Cancer Stemness and Progression



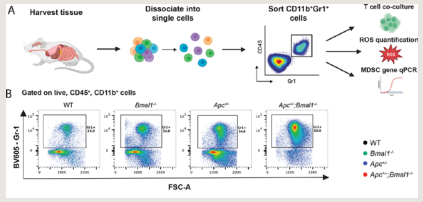
Tumor spheroids invasion and response to stressors



Non-Invasive Imaging of the Melanoma

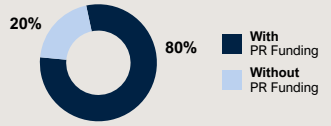


Circadian control of tumor immunosuppression



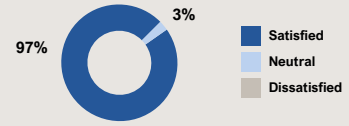
IMPACT & KEY METRICS CY2024

CFCCC MEMBER UTILIZATION



Used by **70** Unique CFCCC Member Labs
29% Overall Usage by CFCCC Members

CFCCC USER SATISFACTION

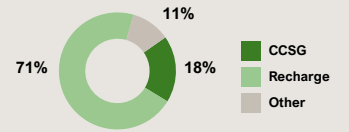


60% Response Rate

$15.8M Supported CFCCC Members Receive 24 New Cancer-relevant Grants (Total Direct Costs)

13 Support Led to New Cancer-Relevant Publications (**15%** in IF ≥ 10 Journals)

BASE SR FUNDING



$484,536 Annual Budget

TRAINING

- Workshops and hands-on trainings on hardware and image analysis software
- Demo's of newest technologies
- Annual LFD/OBC hands on workshop on Advanced Fluorescence Imaging
- GSLab phasor analysis training
- FlowJoTM Software v10 Training
- BD Biosciences flow cytometry lunch and learn

FUTURE PLANS

- Continuously adds new users on a regular basis
- Continuously provides outreach, awareness, and educational activities
- Continuously explores cutting-edge science and technology to better support research community
- Bring in new technologies/equipment based on research needs

Internal Advisory Committee

David Fruman, PhD
Associate Director
Basic Science, CFCCC

Katherine Thompson-Peer, PhD
Assistant Professor
Developmental & Cell Biology

Christopher Hughes, PhD
Professor
Molecular Biology & Biochemistry

Grant MacGregor, PhD
Director
Transgenic Mouse Facility, CFCCC

Eric Pearlman, PhD
Professor
Ophthalmology

Ian Smith, PhD
Assistant Professor
Developmental & Cell Biology

MEMBERS

- The internal advisory committee includes experts in microscopy, flow cytometry, shared resource management, and research administration
- **Member Responsibilities:** Advising on current and future financial planning, equipment acquisitions and upgrades. Attend annual meeting and provide guidance on goals
- **Selection Process:** Nominated or invited. Expertise in microscopy, flow cytometry, shared resource management, and other relevant areas
- **Appointment Terms:** 5 years

FREQUENCY
Yearly

FUNCTION
Oversees operations, pricing, budgeting, and alignment with institutional goals and user needs

AUTHORITY
Provides strategic guidance on operations, pricing, budgeting, and alignment with institutional goals and user needs

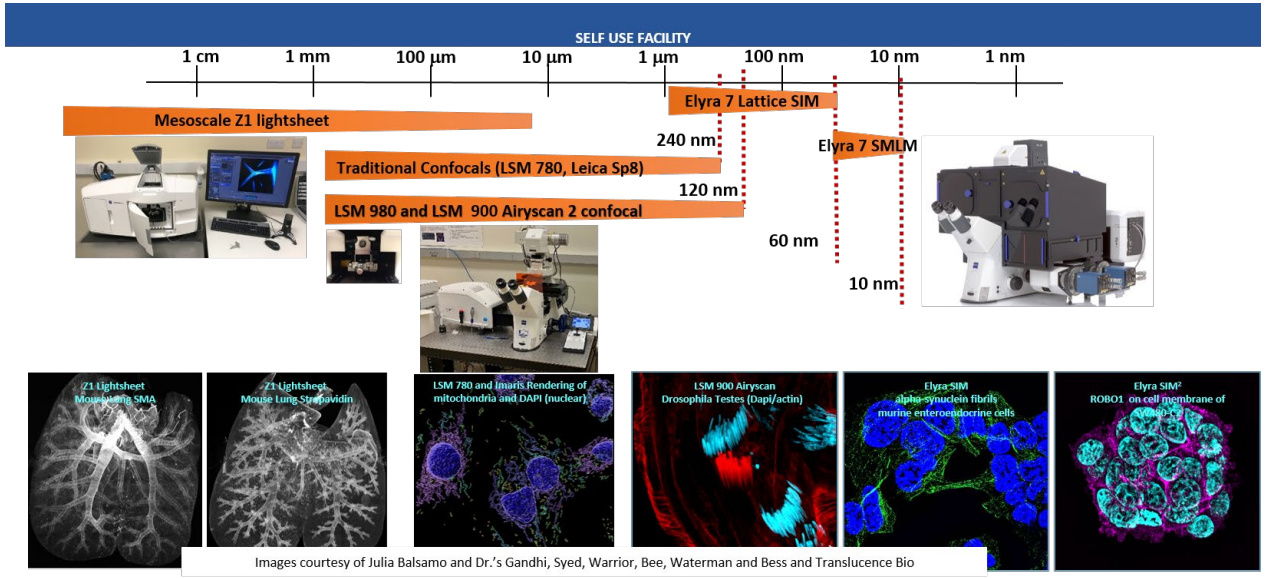
MAIN

Services, Technologies & Equipment

Self-Use Facility (SUF)

Walk-up use of suite of microscopes

- 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) with training on advanced imaging techniques such as Airyscan imaging, Spectral Imaging and 2-photon microscopy
- Single plane illumination microscope (SPIM) able to analyze both live sample and cleared tissues. The Z1 has four laser lines (405 nm, 488 nm, 561 nm, 633 nm) and a custom chamber for organically cleared samples
- Super Resolution Lattice SIM with SMLM capabilities and 60nm resolution with SIM2 for live super resolution (255fps/60nm)
- Workstations for Image Analysis – Imaris, Arivis, ZEN etc



Images courtesy of Julia Balsamo and Dr.'s Gandhi, Syed, Warrior, Bee, Waterman and Bess and Translucence Bio

NEXT

Services, Technologies & Equipment

Laboratory of Fluorescence Dynamics (LFD)

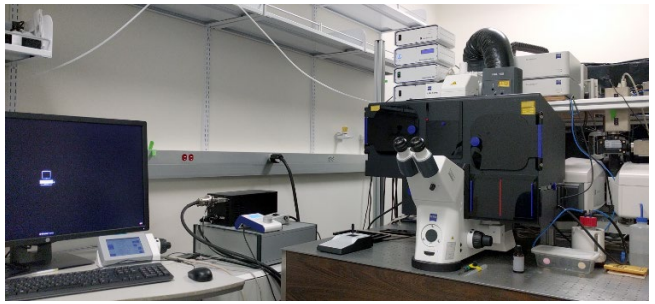
A national biomedical fluorescence spectroscopy center with over 10 instruments for dynamic imaging

- 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

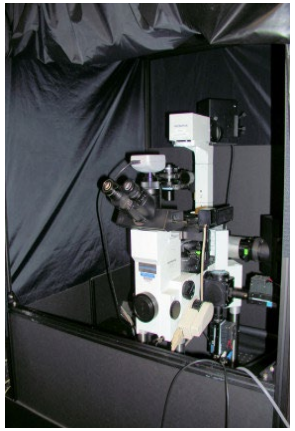
Customized 2-photon scanning
M1: Olympus IX81
M3: Zeiss Axiovert S100TV, SPC830
M5: Olympus IX70 particle tracking Number and Brightness (N&B)

Commercial 1 or 2-photon
ISS Alba **STED**
Zeiss LSM880 NLO, AiryScan
Zeiss LSM710 NLO
Olympus FV1000 , SIM scanner, DIVER, spectral imaging

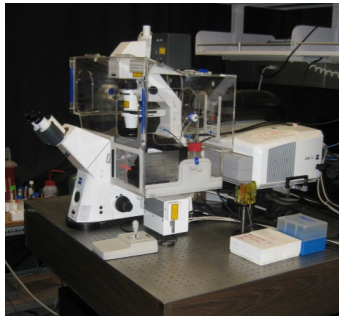
Full-field
TIRF/FLIM: Olympus IX81, TIRFM, LI2Cam, pco.flim, Evolve
New TIRF: Olympus IX83, 2x Photometrics 95B sCMOS, 4 channel
uSPIM: custom body, Andor Zyla sCMOS
SPIM: custom body, Photmetrics Prime 95B and pco.edge sCMOS



LSM880



M5



LSM710

Advanced Imaging methods at the LFD	Data output/what it measures
Fluorescence Correlation Spectroscopy (FCS)	From a laser spot: molecular diffusion, concentration, binding from Brownian motion
Image Correlation Spectroscopy: ICS, RICS, ICM	From images: molecular maps of diffusion, concentration, binding kinetics
Number and Brightness (N&B)	Maps molecular aggregates across images
Pair Correlations Spectroscopy (pCF)	Maps molecular flow and barriers
Fluorescence Lifetime Imaging Microscopy (FLIM)	Fluorescence lifetimes, environmental changes including pH, calcium, FRET, metabolic imaging
Hyperspectral Imaging	Captures the full spectrum of light. Applications: agriculture, environmental monitoring, biotechnology, airborne sensing, food analysis, metabolism
Super-Resolution imaging: STED and SIM, Lattice lightsheet, Airyscan	Increase the resolution imaging: but can also be used for RICS and N&B

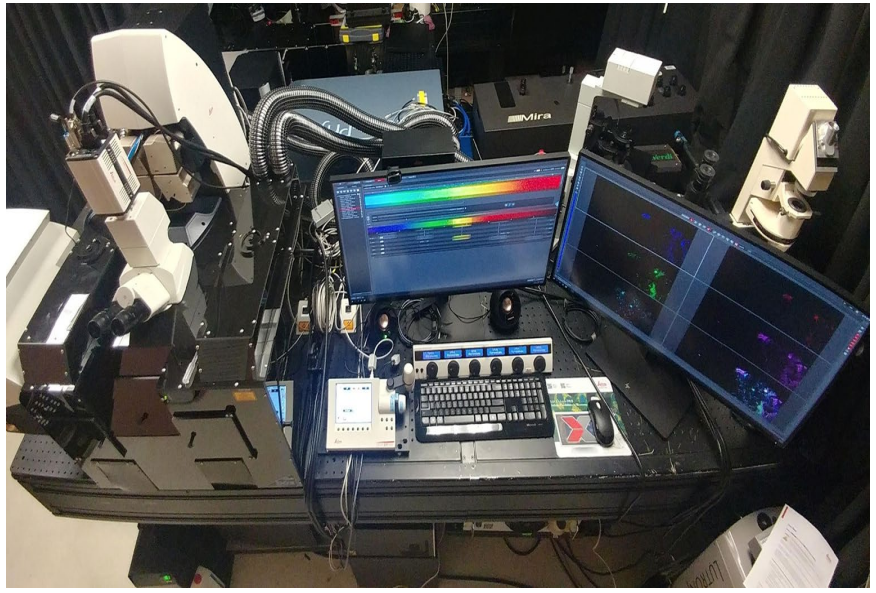
NEXT

Services, Technologies & Equipment

Non-Linear Optical Microscopy (NLOM) Laboratory

Develops biopotonics technologies for research and clinical applications via nonlinear optical microscopy

- The NLOM Lab specializes in designing and developing optical imaging devices utilizing multiphoton microscopy for clinical applications, particularly focusing on skin imaging in dermatology. These imaging platforms employ label-free molecular contrast, utilizing time-resolved two-photon excited fluorescence and second harmonic generation
- The NLOM Lab offers access to a commercial imaging platform, Leica SP8 Falcon, customized to feature the following imaging modalities: confocal fluorescence and two-photon excited fluorescence microscopy, second/third harmonic generation, coherent anti-Stokes Raman Scattering and fluorescence lifetime microscopy. This imaging platform is well-suited for basic research and preclinical imaging projects



NEXT

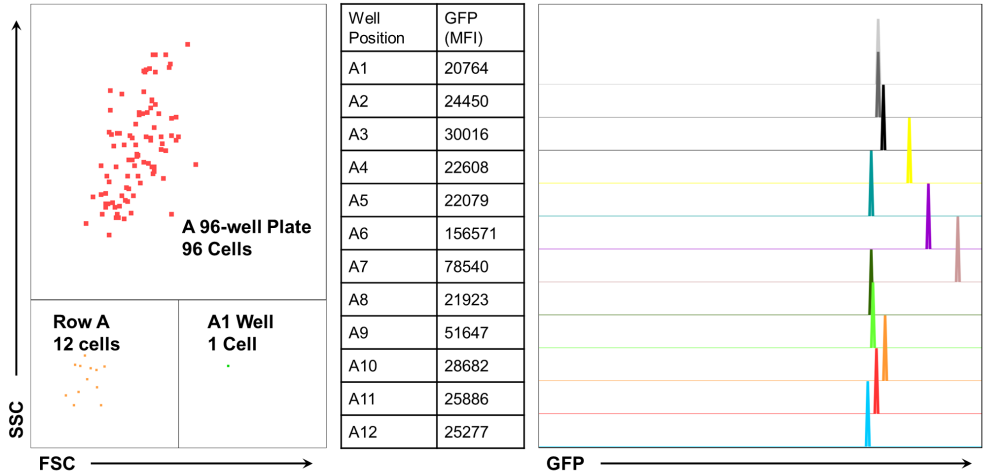
Services, Technologies & Equipment

Flow Cytometry Facility (FCF)

Self use of suite of cytometers

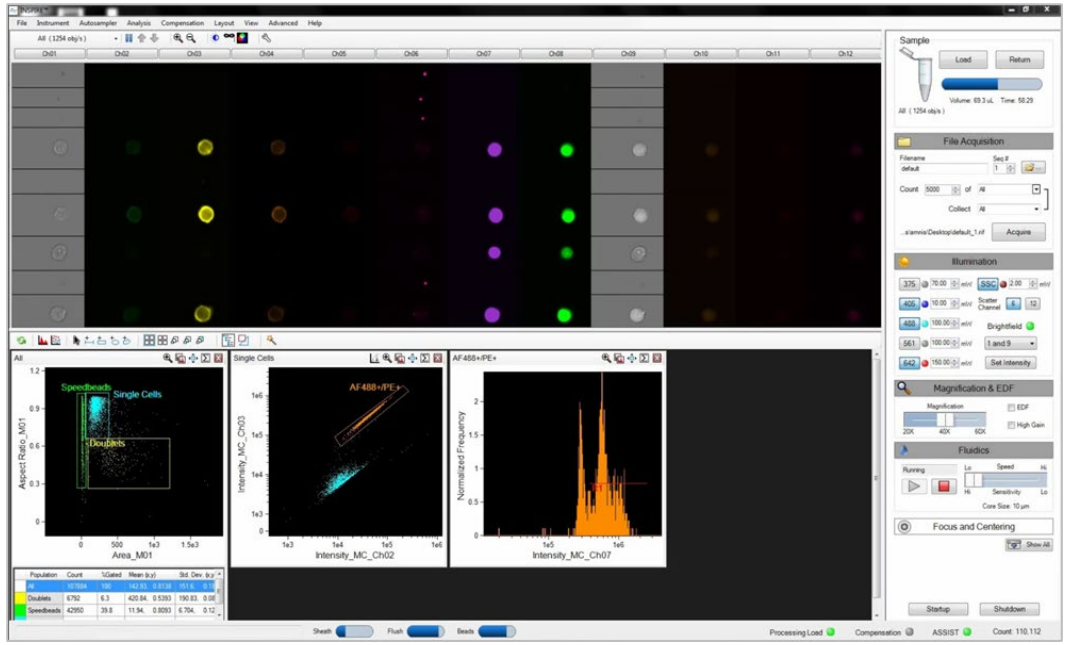
- 4 multi-parameter flow cytometers including one equipped for fluorescence activated cell in a BSL2 cabinet featuring downstream applications of single cell cloning and single cell analysis
- Access to: High-end workstations for data analysis, including advanced 3D/4D analyses and cell sorting analysis

Single cell index sorting allows the isolation of single cells for downstream applications of single cell cloning and single cell analysis



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.

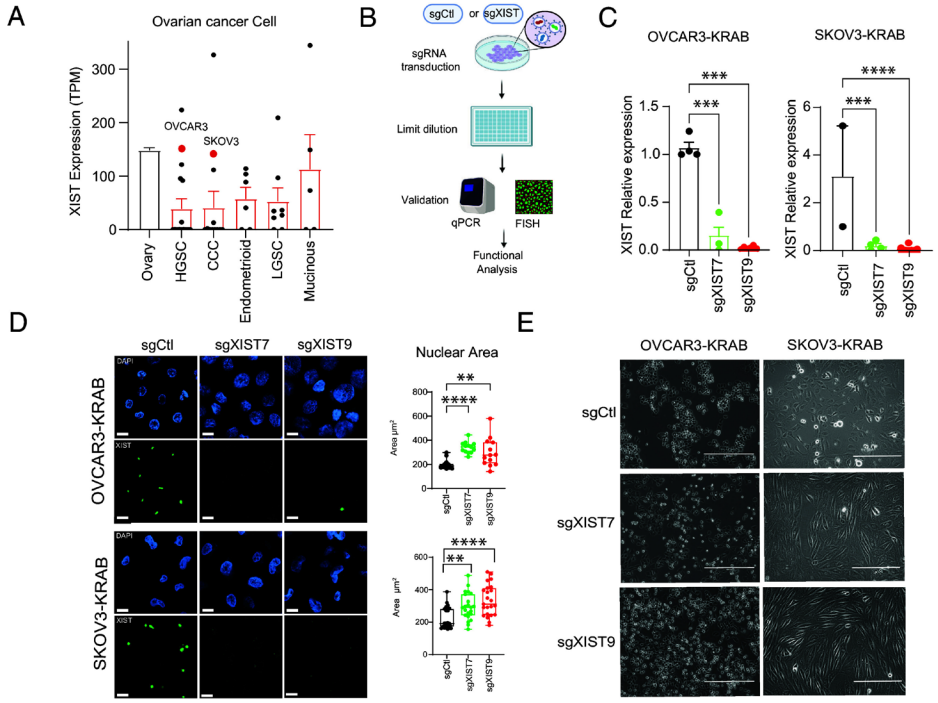


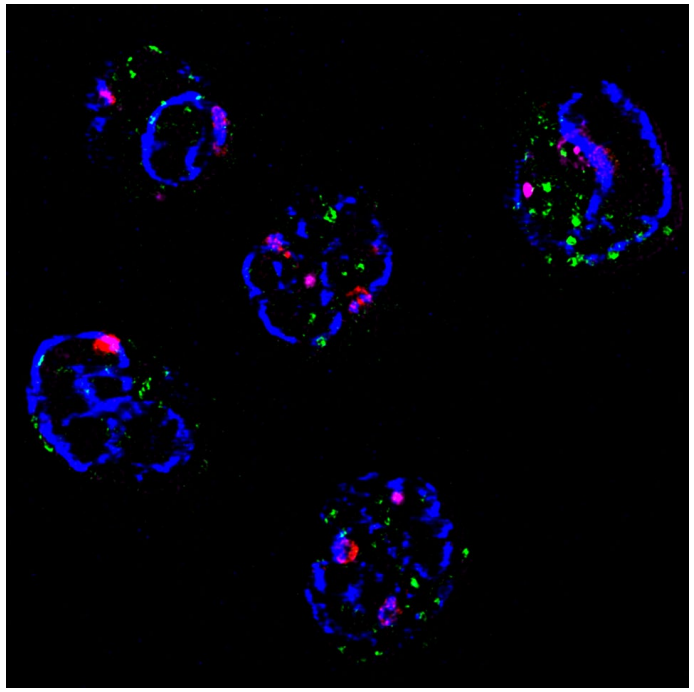
MAIN

LncRNA Linking Stemness and Cancer

X-inactive specific transcript regulates ovarian cancer cell stemness and plasticity

- Our work has shown that X-inactive specific transcript (XIST), a long noncoding RNA that controls X chromosome dosage compensation during embryo development, plays a critical role in regulating ovarian cancer cell stemness and plasticity





CATCHMENT AREA RELEVANCE

Investigators


Sun, PhD


Kong, PhD


Nicholas, PhD


Razorenova, PhD

CFCCC Investments

SHARED RESOURCE

DOT

FUNDING
2019, 2021
2023

PROGRAMS

Outcomes

PUBLICATION
Sun, Proc Natl Acad Sci, 2024
PMC11588085

GRANTS R01GM141424*

*Supported research

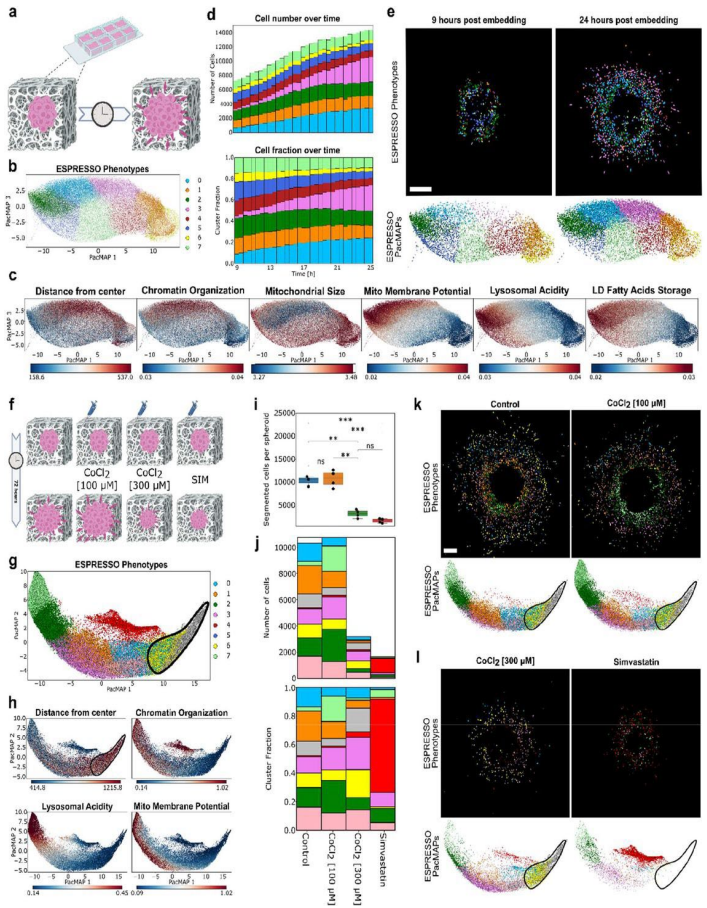
IMPACT | XIST loss leads to cancer stem cells enrichment and cellular plasticity in ovarian cancer, pointing to potential therapeutic targets for patients with low XIST expression

MAIN

ESPRESSO: Organelle Phenotyping based Spatiotemporal ‘Omics

Collagen-invading phenotypes in triple negative breast cancer (TNBC)

- This new study introduces a novel imaging approach named ESPRESSO (**E**nvironmental Sensor Phenotyping Relayed by Subcellular Structure and Organelles). ESPRESSO uses fluorescent labeling, advanced microscopy, bioimaging and data analysis to examine cellular organelle networks in living cells over time and associate those changes with cellular and disease processes
- In the inaugural example shown here, ESPRESSO used imaging of organelle networks in cells within 3D TNBC tumor spheroids. ESPRESSO identified a metastatic signature
- Tumor spheroids embedded in collagen showed TNBC cells invading the matrix. A 16-hour time-lapse revealed two new cell clusters that appear to represent collagen-invading phenotypes (i.e., metastatic phenotypes) within cells localized farther away from spheroid center
- This analysis identifies specific trains of invading cells, triggering new ideas for therapeutic strategies



CATCHMENT AREA RELEVANCE

Investigators

Digman, PhD

Atwood, PhD

Prescher, PhD

CFCCC Investments

SHARED RESOURCE

DOT

FUNDING
2017, 2019

PROGRAMS

Outcomes

PUBLICATION

Digman, bioRxiv: the preprint server for biology, 2024, PMC11195137

GRANTS U54CA217378*

*Supported research

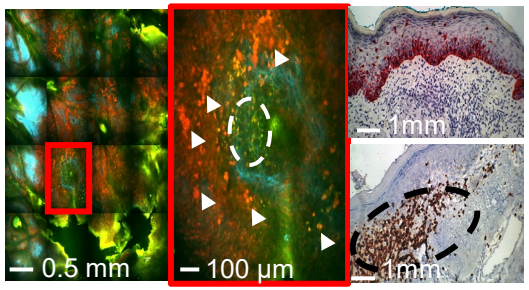
IMPACT | ESPRESSO reveals collagen-invading TNBC phenotypes in 3D spheroids, highlighting hypoxia resistance and simvastatin’s potential to target invasive cells

MAIN

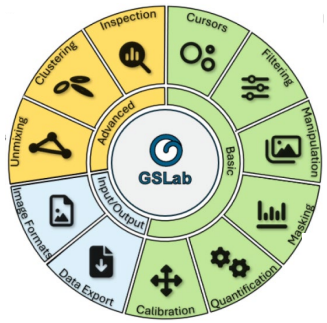
Melanoma's Immune Landscape with Cutting-Edge Imaging

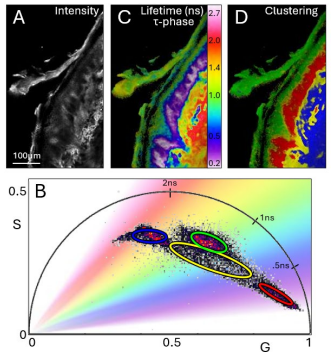
NLOM Lab: Capturing cellular immune responses with multiphoton microscopy

2022: FLAME (non-invasive multiphoton microscopy) developed to study melanoma: immune microenvironment, *in vivo*, in living skin

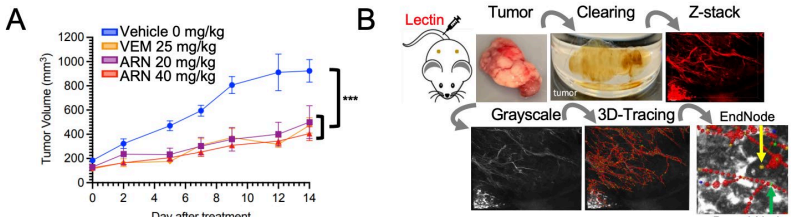


2024: FLAME goes Open Source with GS Lab

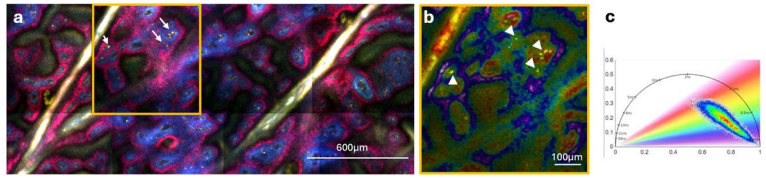




Current FLAME Projects



CDC42 inhibitors (vemurafenib, ARN22089) reduce vasculature network in tumors: L.M. Vuong … CC Hughes (BIDD), A. Ganesan (BIDD). 2024 BioRxiv



In vivo time-resolved FLAME imaging enables detection of immune cells in metastatic melanoma of patients undergoing immunotherapy. M. Balu (BIDD), A. Ganesan (BIDD), R. Tinoco (BIDD), F. Marangoni (BIDD).
DoD/CDMRP MPI: DoD/CDMRP HT94252311024

CATCHMENT AREA RELEVANCE

Investigators


Balu, PhD


Kelly, MD


Ganesan, MD, PhD

CFCCC Investments

SHARED RESOURCE GRT HUB, OBC, ETR

DOT

FUNDING 2019, 2022

PROGRAMS

Outcomes

PUBLICATION

Balu, Scientific Reports, 2022, PMC9110384

GRANTS R01CA259019*; R01EB026705*, DoD/CDMRP HT94252311024

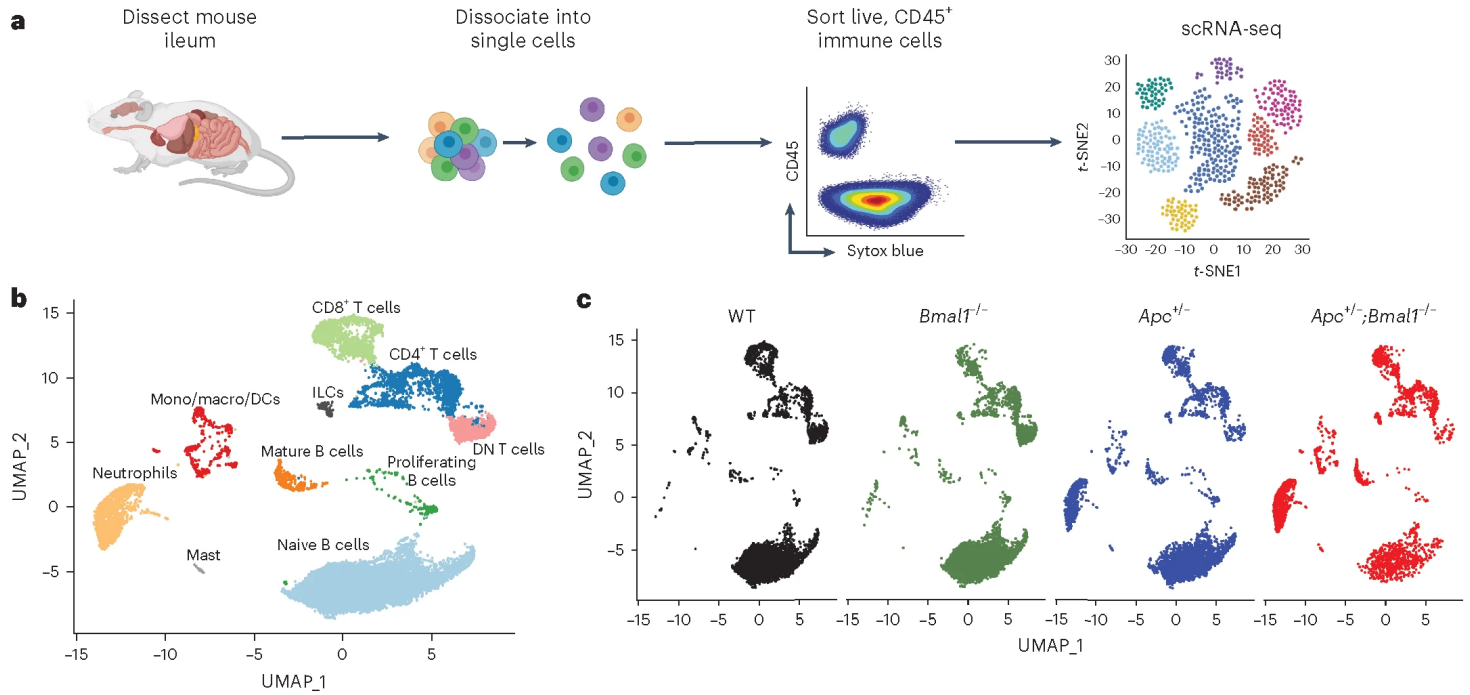
*Supported research

IMPACT | Non-invasive 3D imaging of the tumor microenvironment aids tumor pathogenesis and therapy strategies

MAIN

Circadian control of tumor immunosuppression

Understanding the immune landscape in the colon by cell sorting technology



a, Schematic depicting the workflow for scRNA-seq of live, CD45+ immune cells sorted from mouse small intestine isolated at Zeitgeber time. 4. **b**, UMAP of cell types clustered by single-cell transcriptional analysis (n = 15,234 cells, n = 3 mice per genotype). **c**, UMAP of cell types clustered by single-cell transcriptional analysis broken down by mouse genotype WT, Bmal1$^{-/-}$, Apc$^{+/-}$ and Apc$^{+/-}$;Bmal1$^{-/-}$

CATCHMENT AREA RELEVANCE

Investigators


Pannunzio, PhD


Kessenbrock, PhD


Lawson, PhD


Eng, MD


Marangoni, PhD


Marazzi, PhD


Masri, PhD

CFCCC Investments

SHARED RESOURCE

DOT

FUNDING
2017, 2019
2021

PROGRAMS

Outcomes

PUBLICATION
Masri, Nature Immunology, 2024
PMC11374317

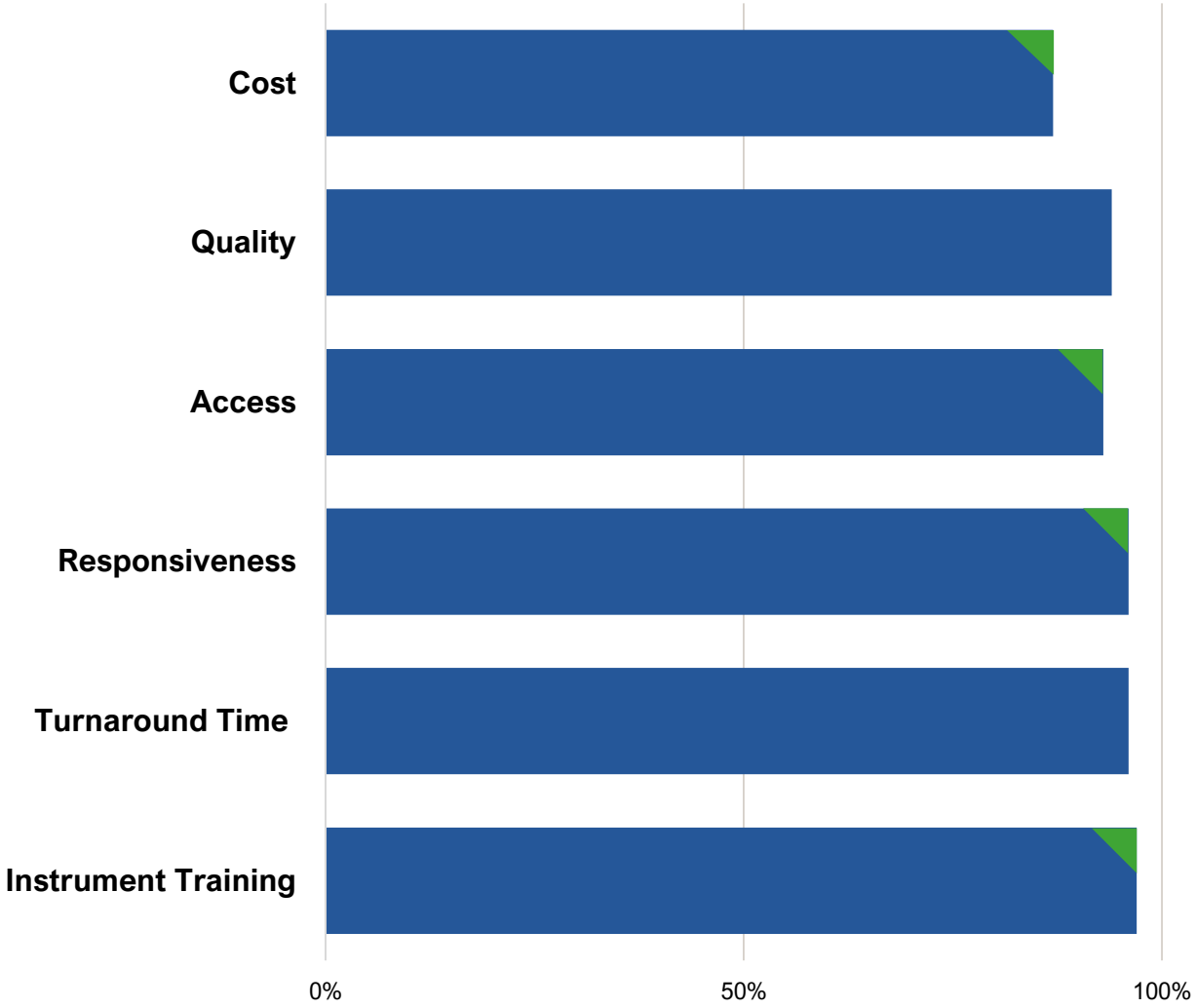
GRANTS R01CA244519
R01CA259370

IMPACT | Circadian-regulated epithelial-immune crosstalk influences immunity; disruption causes suppression. Timed anti-PD-L1 delivery improves immunotherapy

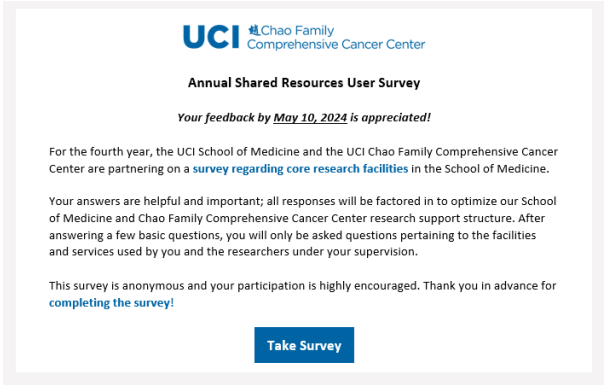
MAIN

2024 Annual Core Research Facilities Survey

Excellent + Good (No scores below average received) Improved since 2021



SURVEY PROMOTION



UCI Chao Family Comprehensive Cancer Center

Annual Shared Resources User Survey

Your feedback by May 10, 2024 is appreciated!

For the fourth year, the UCI School of Medicine and the UCI Chao Family Comprehensive Cancer Center are partnering on a **survey regarding core research facilities** in the School of Medicine.

Your answers are helpful and important; all responses will be factored in to optimize our School of Medicine and Chao Family Comprehensive Cancer Center research support structure. After answering a few basic questions, you will only be asked questions pertaining to the facilities and services used by you and the researchers under your supervision.

This survey is anonymous and your participation is highly encouraged. Thank you in advance for **completing the survey!**

Take Survey

2024 Core Facilities Survey

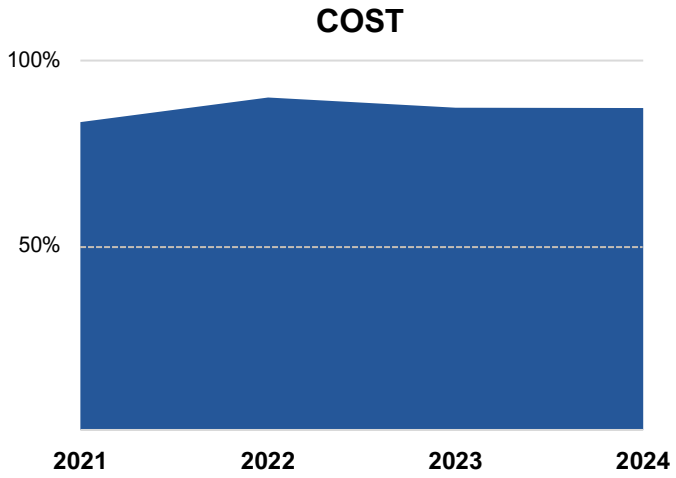
UCI School of Medicine and the UCI Chao Family Comprehensive Cancer Center are partnering on a survey regarding core research facilities in the School of Medicine. Your answers are helpful and important; all responses will be factored in to optimize our research support structure. After answering a few basic questions, you will only be asked questions pertaining to the facilities and services used by you and the researchers under your supervision. This survey is anonymous. For questions, contact **Claire Brainard Draper**. Please complete the survey by **May 10, 2024**.

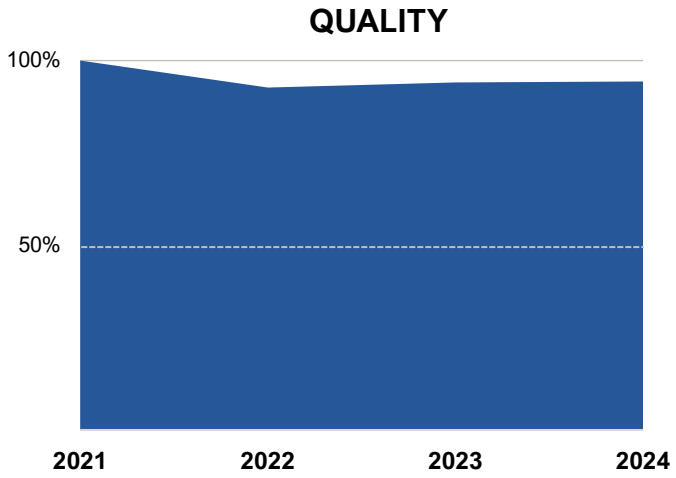
Complete Survey

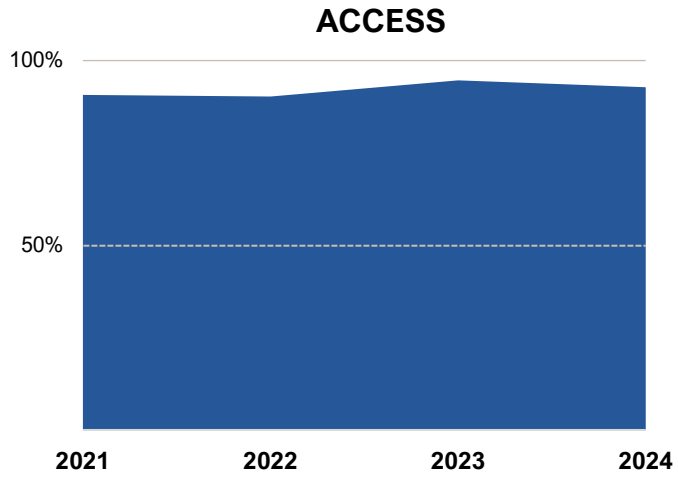
NEXT

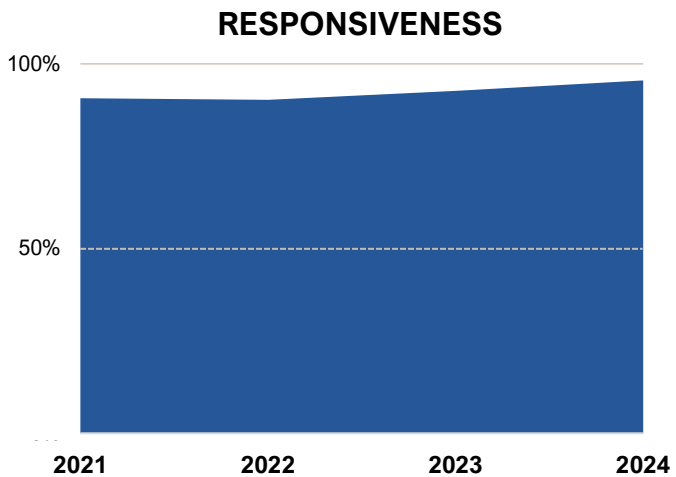
Annual Core Research Facilities Survey

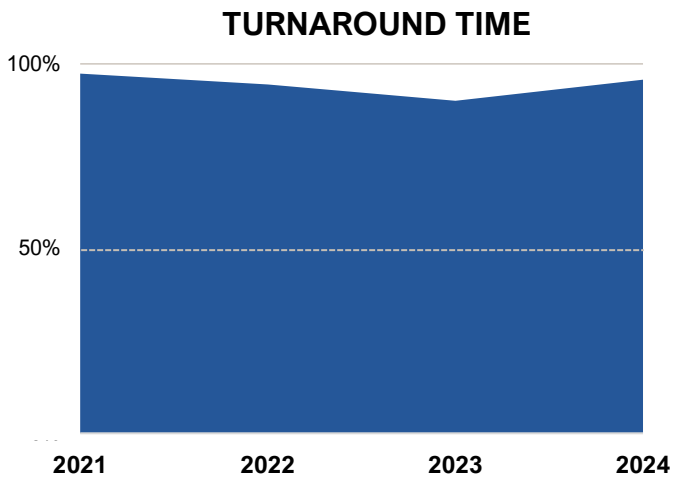
Excellent + Good

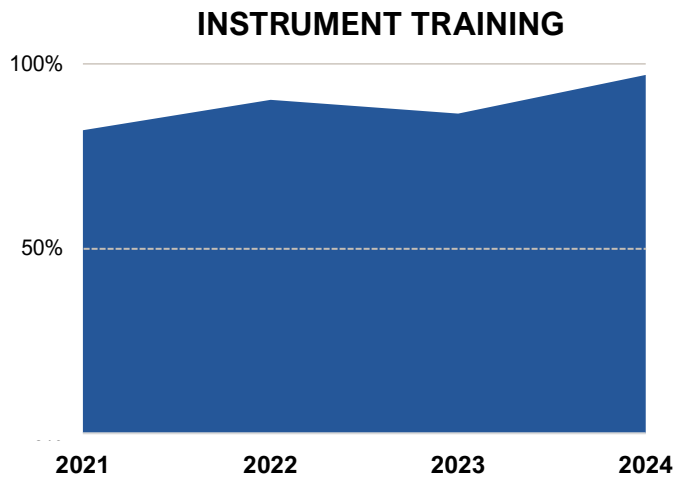












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Selected 2024 Publications

CFCCC INVESTIGATOR(S)	PROGRAM	JOURNAL	YEAR
Anand Ganesan, MD PhD Francesco Marangoni, PhD	BIDD SPT	Cancer Cell	2024
Selma Masri, PhD Francesco Marangoni, PhD Devon Lawson, PhD Kai Kessenbrock, PhD	SPT	Nat Immunol	2024
Sha Sun, PhD Olga Razorenova, PhD Mei Kong, PhD Dequina Nicholas, PhD	SPT	Proc Natl Acad Sci	2024
Anand Ganesan, MD PhD Chris Hughes, PhD	BIDD	bioRxiv	2024
Aimee Edinger, VMD, PhD Christopher Halbrook, PhD	BIDD SPT	Molecular Biology of the Cell	2024

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