UC Irvine 趙 Chao Family Comprehensive Cancer Center

Multiphoton Microscopy as a Tool to Monitor Immune Activation Induced by Checkpoint Inhibitors

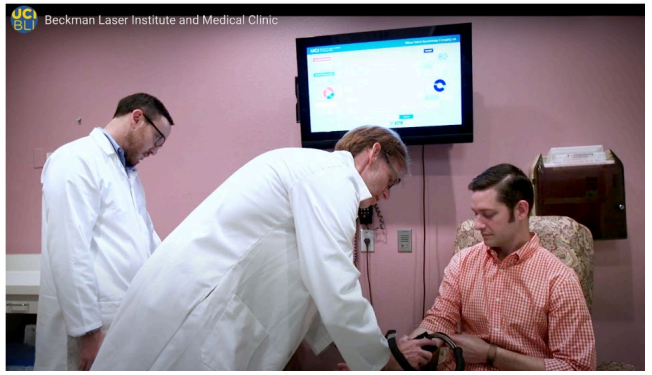
Mihaela Balu, PhD

2026 Scientific Retreat

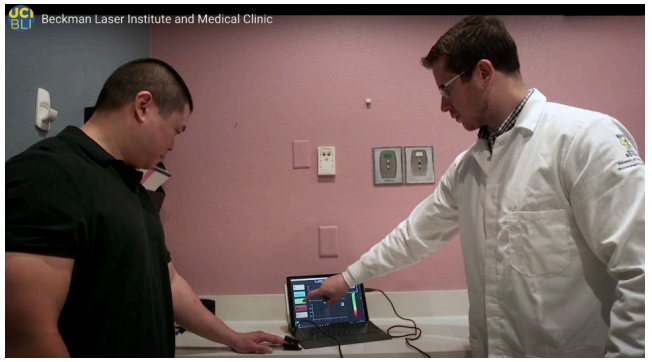
November 5, 2026

Beckman Laser Institute and Medical Clinic









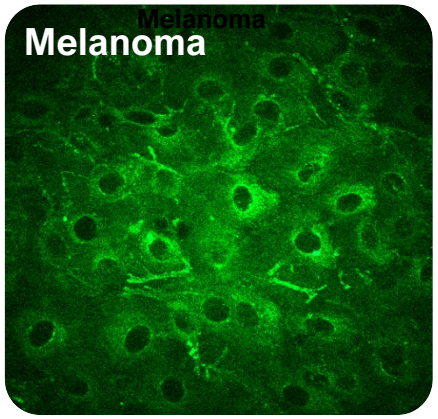
Advanced Technology Suites (ATS) for clinical testing of new technologies

Clinical Multiphoton Imaging: >350 Patients (2012–2019)

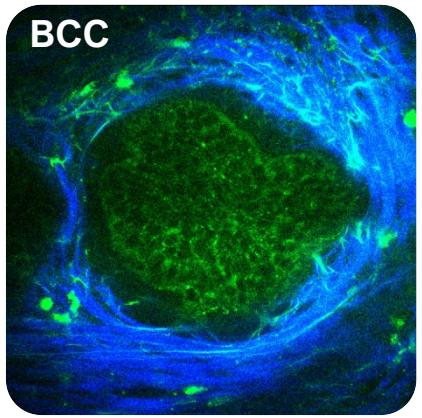
From skin cancer detection to tissue biology and treatment monitoring

DIAGNOSIS / LESION CHARACTERIZATION:

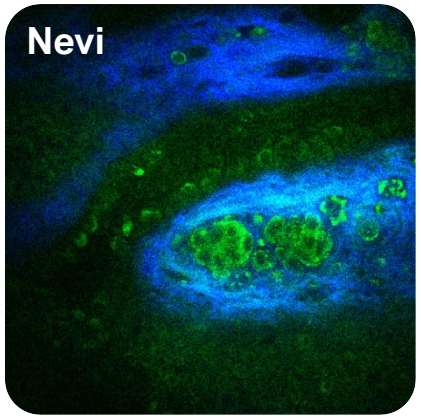
Melanoma · Basal Cell Carcinoma · Melanocytic Nevi



Balu *et. al* Cancer Research (2014)
Pouli *et. al,* Sc. Trans. Med. (2016)



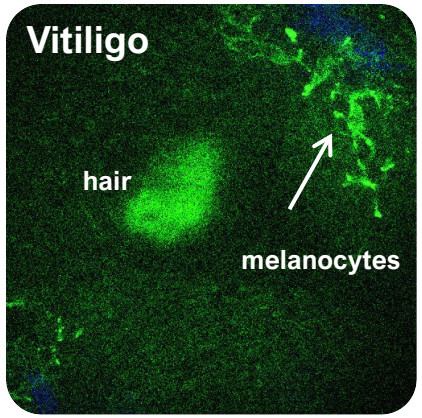
Balu *et. al,* JAMA Derm (2015)



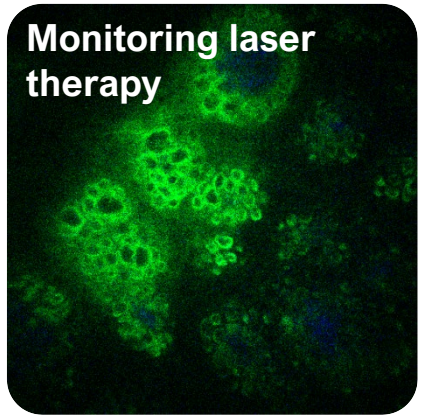
Lentsch *et. al,* PCMR (2020)

TREATMENT MONITORING:

Laser Treatment · Vitiligo Treatment

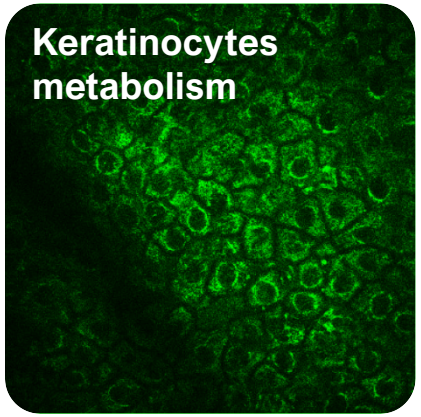


Shiu *et. Al JCI (2022)*

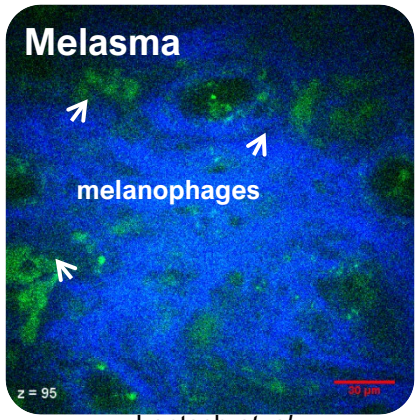


Balu *et. al* Laser Surg Med, (2017)

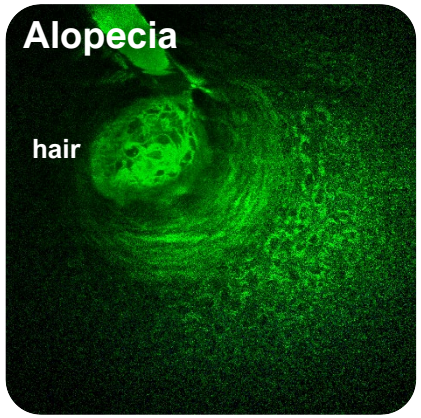
SKIN BIOLOGY: Keratinocyte Metabolism · Melasma · Alopecia



Balu *et. al,* Biophys J (2013)

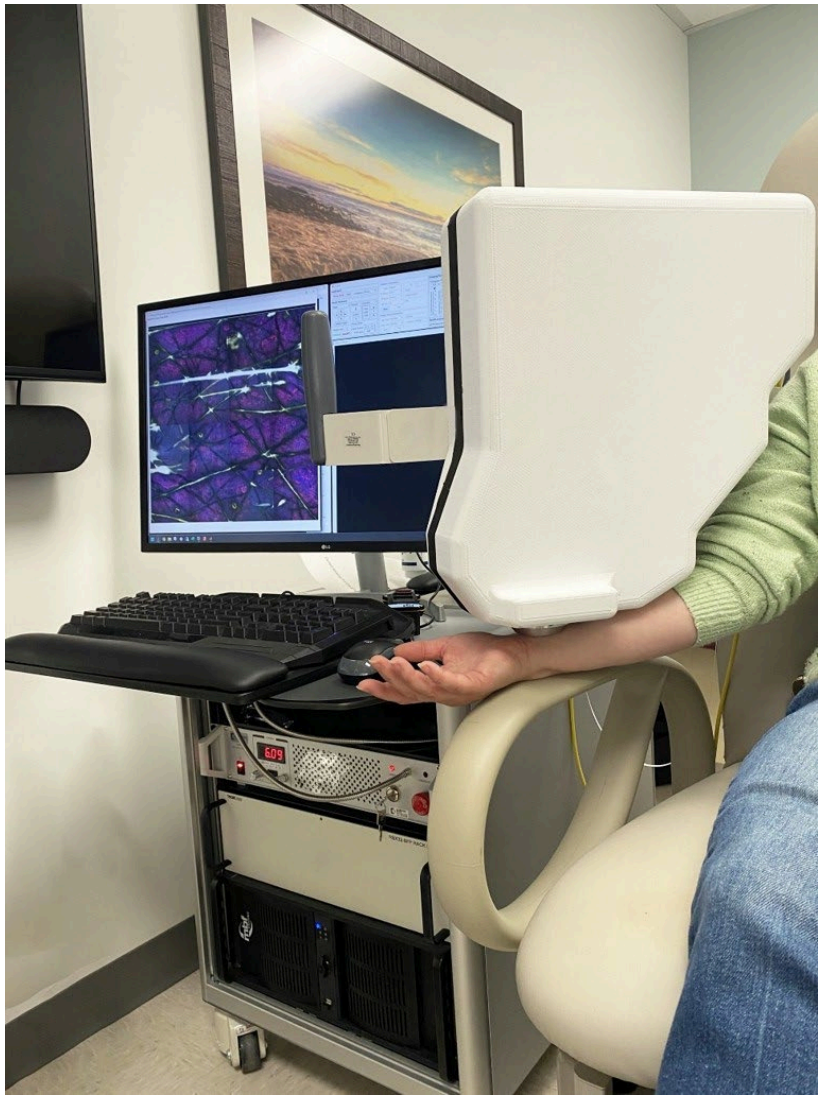


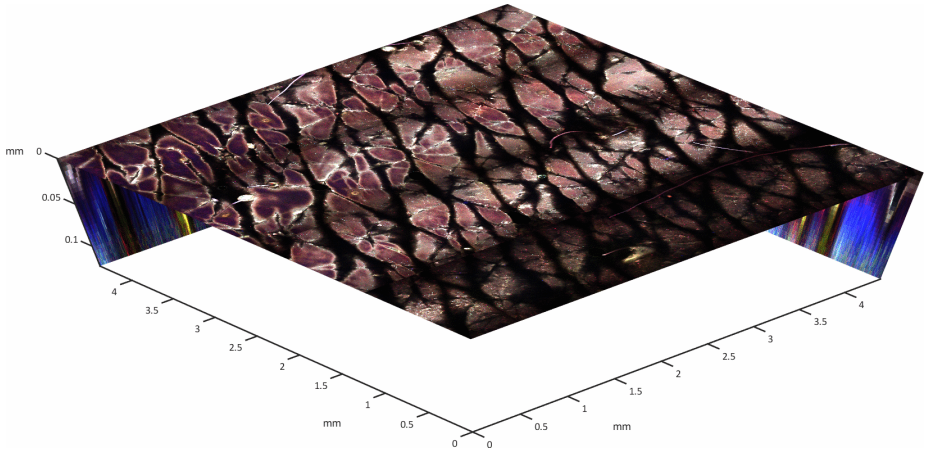
Lentsch *et. al,*
Pigm. Cell &Melanoma Res (2018)



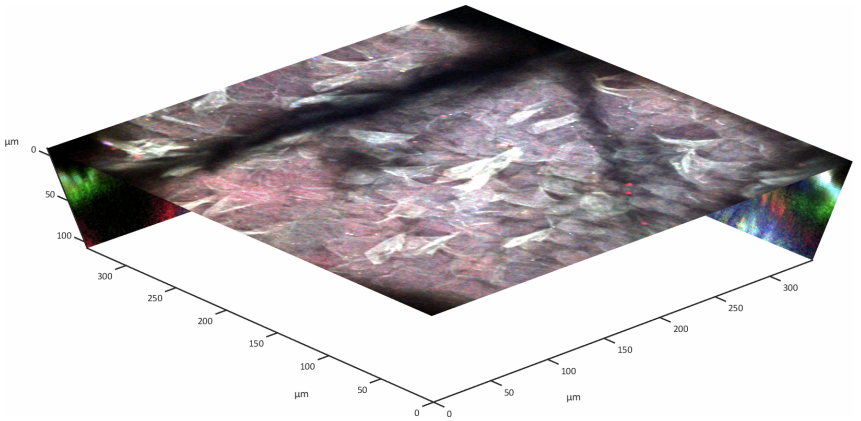
Lin *et. al,* Lasers Surg Med (2019)

FLAME: Large-Area Multiphoton Imaging at Cellular Resolution



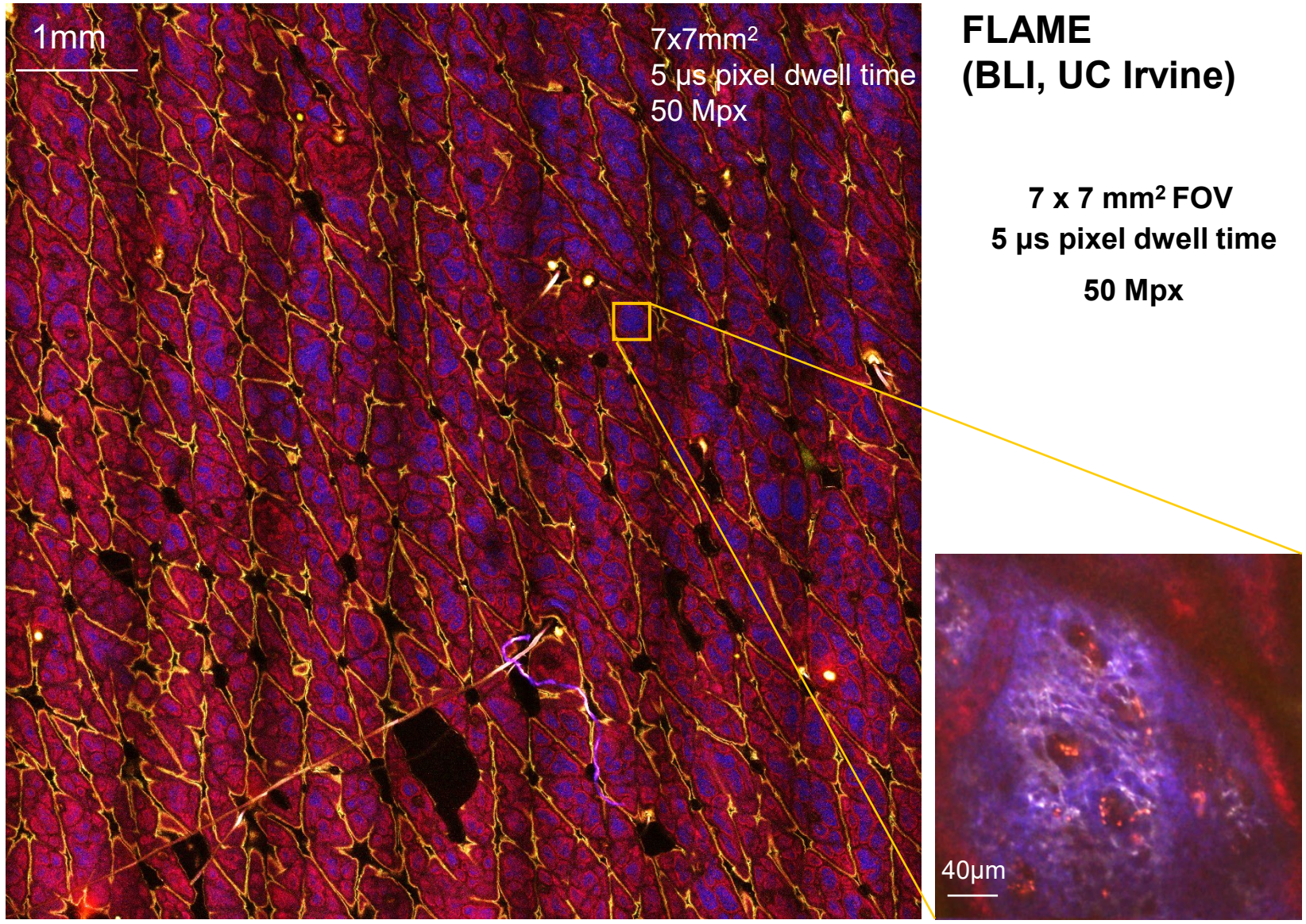


~ 5 x 5 mm^2



~ 300 x 300 µm^2

FLAME: Large-Area Multiphoton Imaging at Cellular Resolution



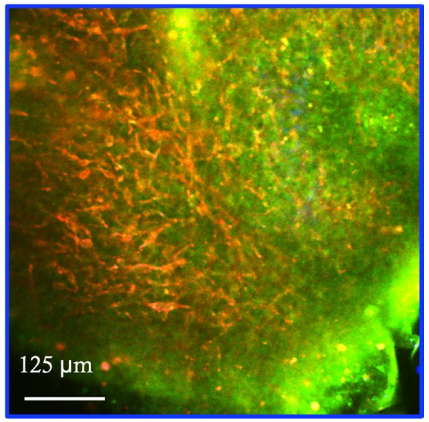
FLAME
(BLI, UC Irvine)

7 x 7 mm² FOV
5 µs pixel dwell time
50 Mpx

Clinical Multiphoton Microscopy: From Diagnosis to Treatment Monitoring

EARLY DETECTION

Melanoma



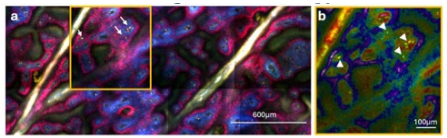
Non-invasive cellular-scale assessment of suspicious lesions

Large-area imaging links tissue architecture with sub-cellular detail.

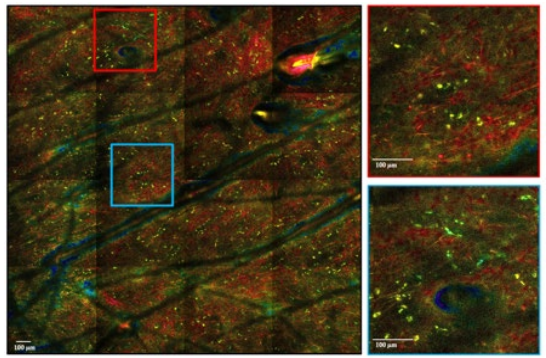
TREATMENT MONITORING

Melanoma + Vitiligo

Melanoma immunotherapy



Vitiligo therapy



Track tissue response longitudinally

Repeat imaging can reveal cellular changes before they are obvious clinically.

CELL DYNAMICS

Wound healing

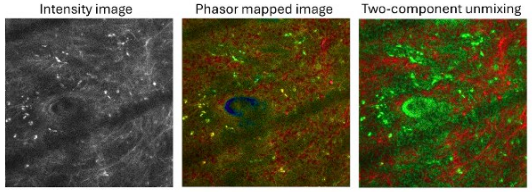


Visualize immune-cell behavior

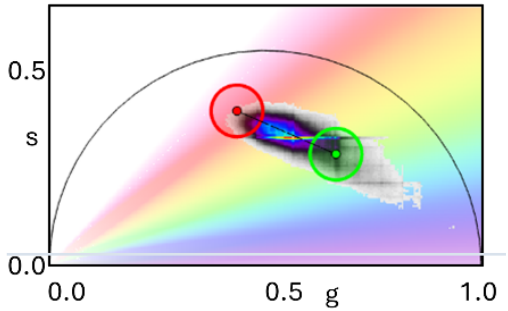
Label-free imaging captures cell migration and tissue remodeling during healing.

CELLULAR PHENOTYPING

Inflammatory skin disease



Intensity → lifetime / phasor → unmixing



Detect + characterize cellular infiltrates

Fluorescence lifetime adds a biochemical dimension beyond morphology alone.

Vallmitjana *et. al. Biomed Opt. Express* (2025) · Ranjit *et. al. Comm. Biology* (2025) · Torrado *et. al* J. of Investigative Dermatology (2025) · Vallmitjana *et. al. Bioinformatics* (2025)

Monitoring Immune Responses to Checkpoint Inhibitors in Melanoma

Study Design and Enrollment Progress

Enrollment

8/15

53% of target enrolled

Patient characteristics

52-85 years

6 male · 2 female

Recruited from the UCI Health Chao Family Comprehensive Cancer Cente

Neoadjuvant/adjuvant treatment
IPI/NIVO most common

All patients received immunotherapy before definitive surgery
Typically 2–4 cycles; one patient discontinued after 1 cycle due to side effects

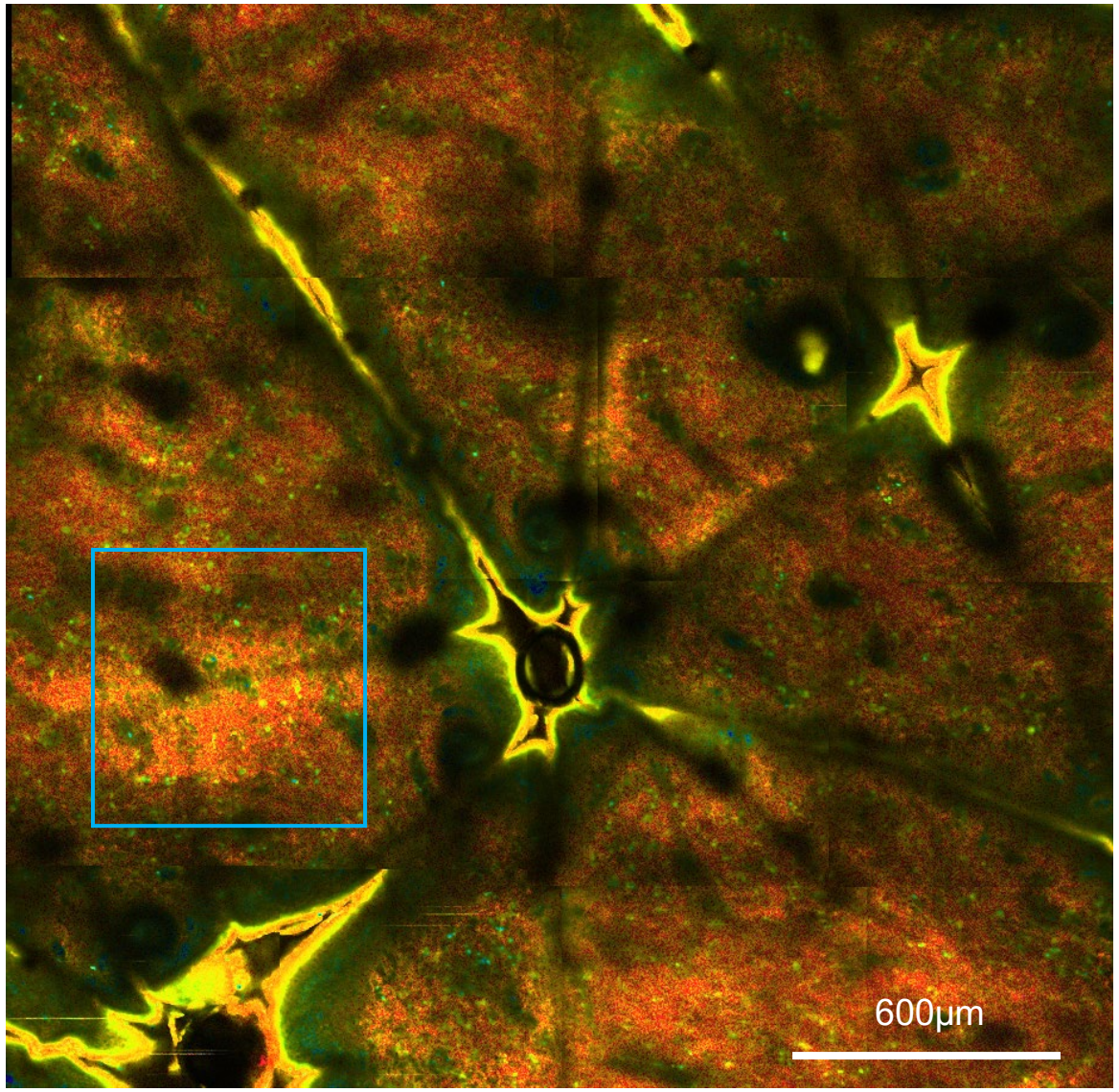
Imaging follow-up
4/8 completed

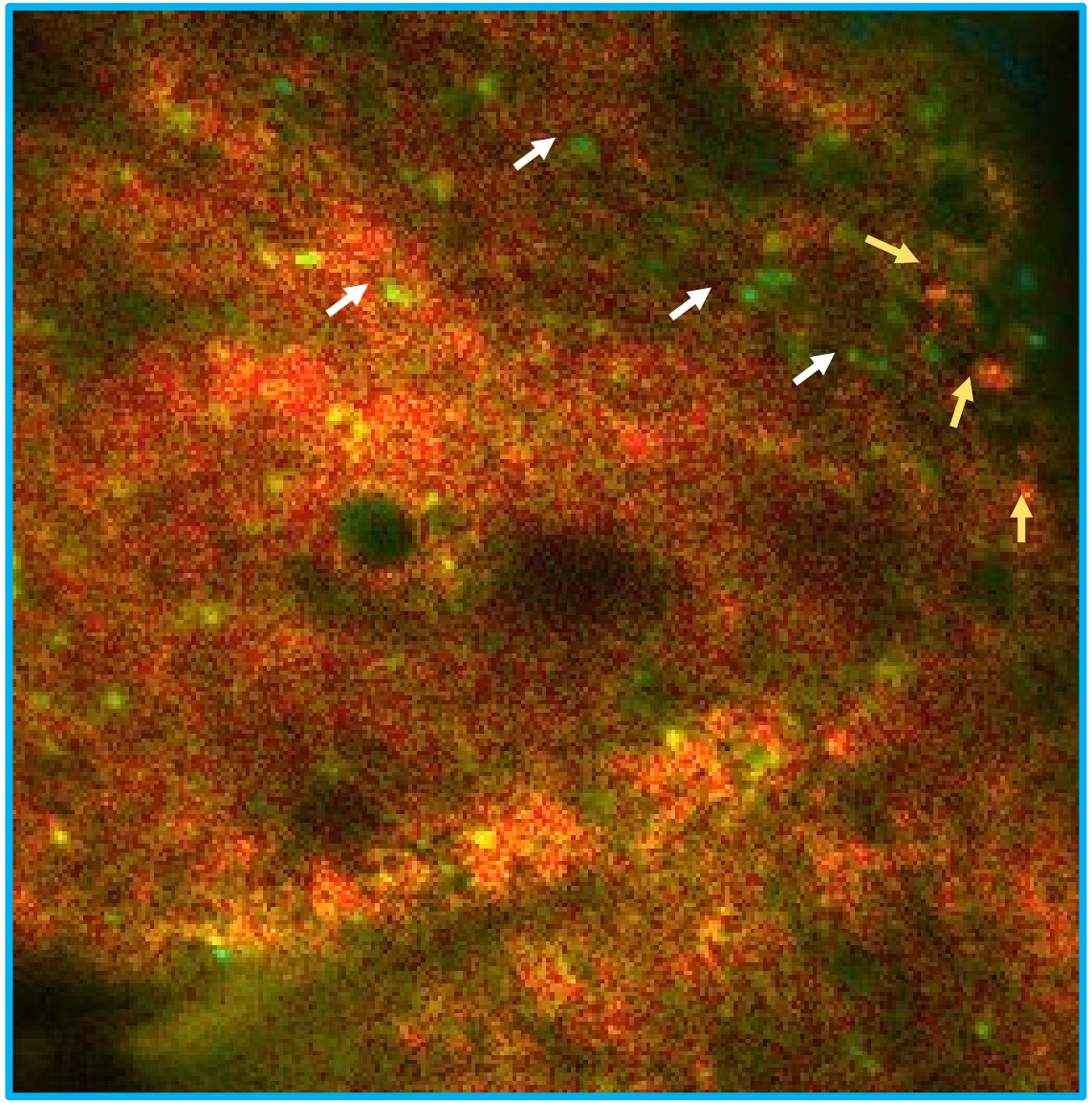
4 visits: 4 patients
1-3 visits: 4 patients
One ongoing patient expects final visit in November

Study status: enrollment and longitudinal imaging are ongoing

Monitoring Immune Responses to Checkpoint Inhibitors in Melanoma

Baseline

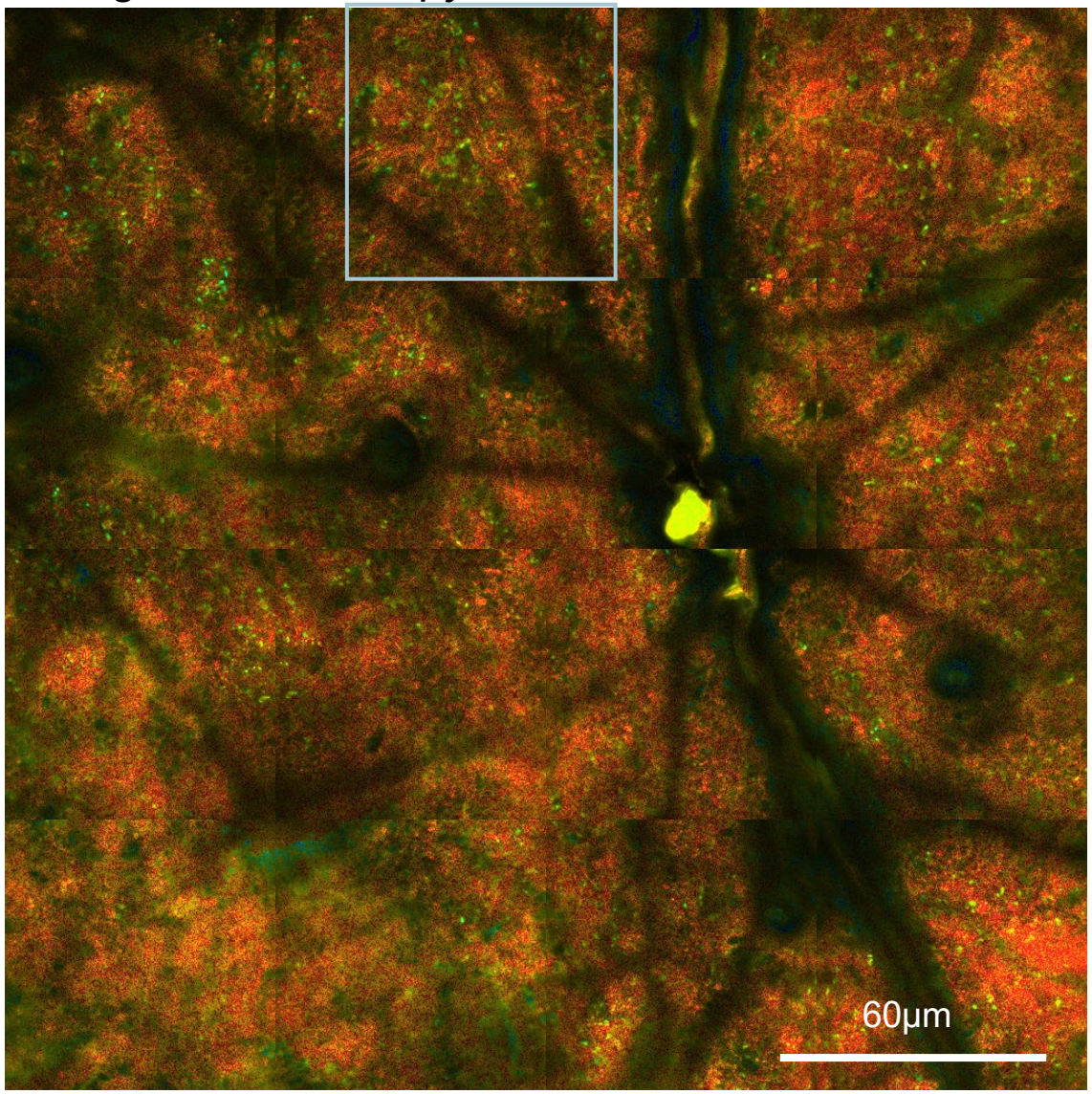


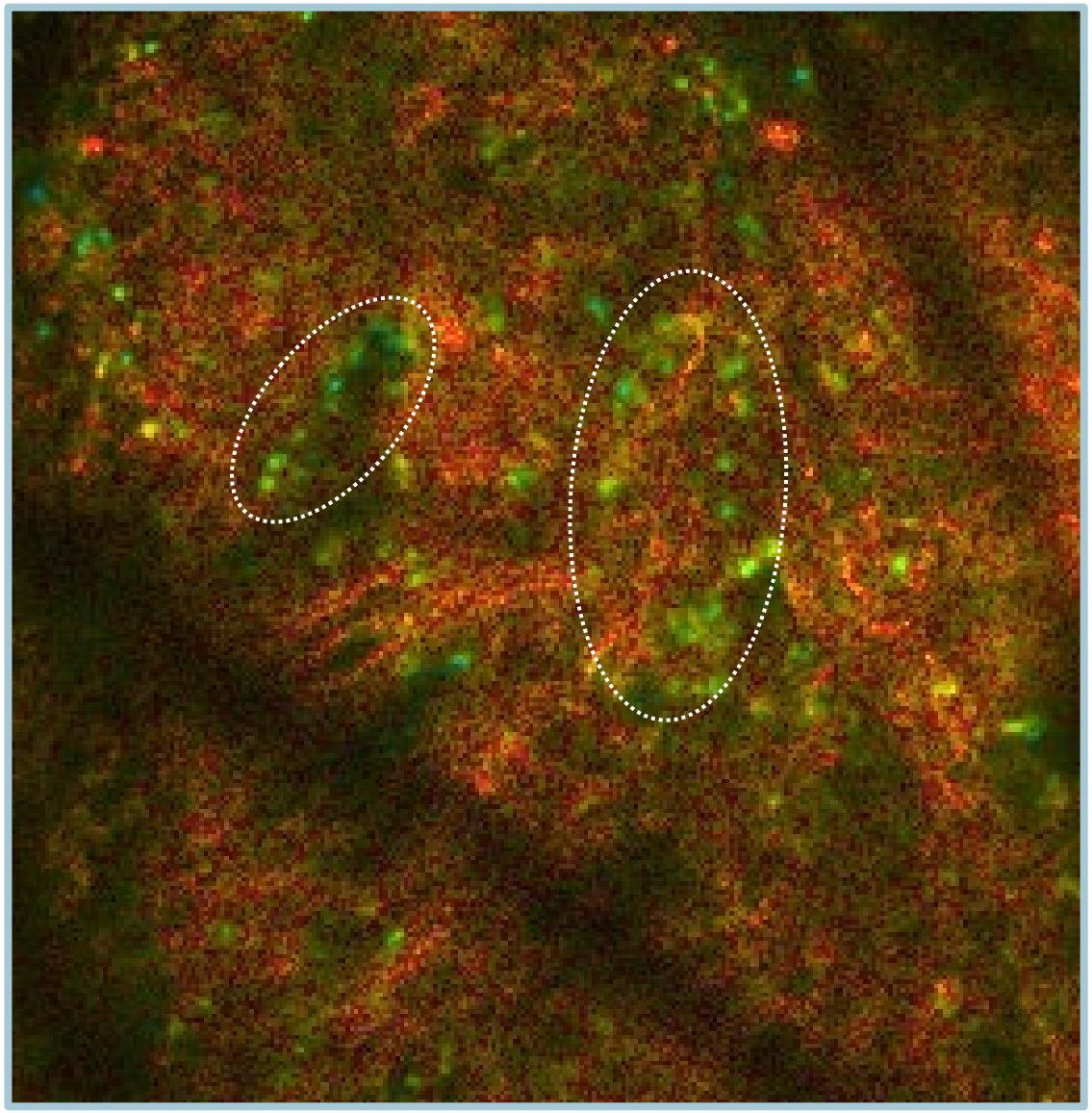


Torrado *et. al* J. of Investigative Dermatology (2025)

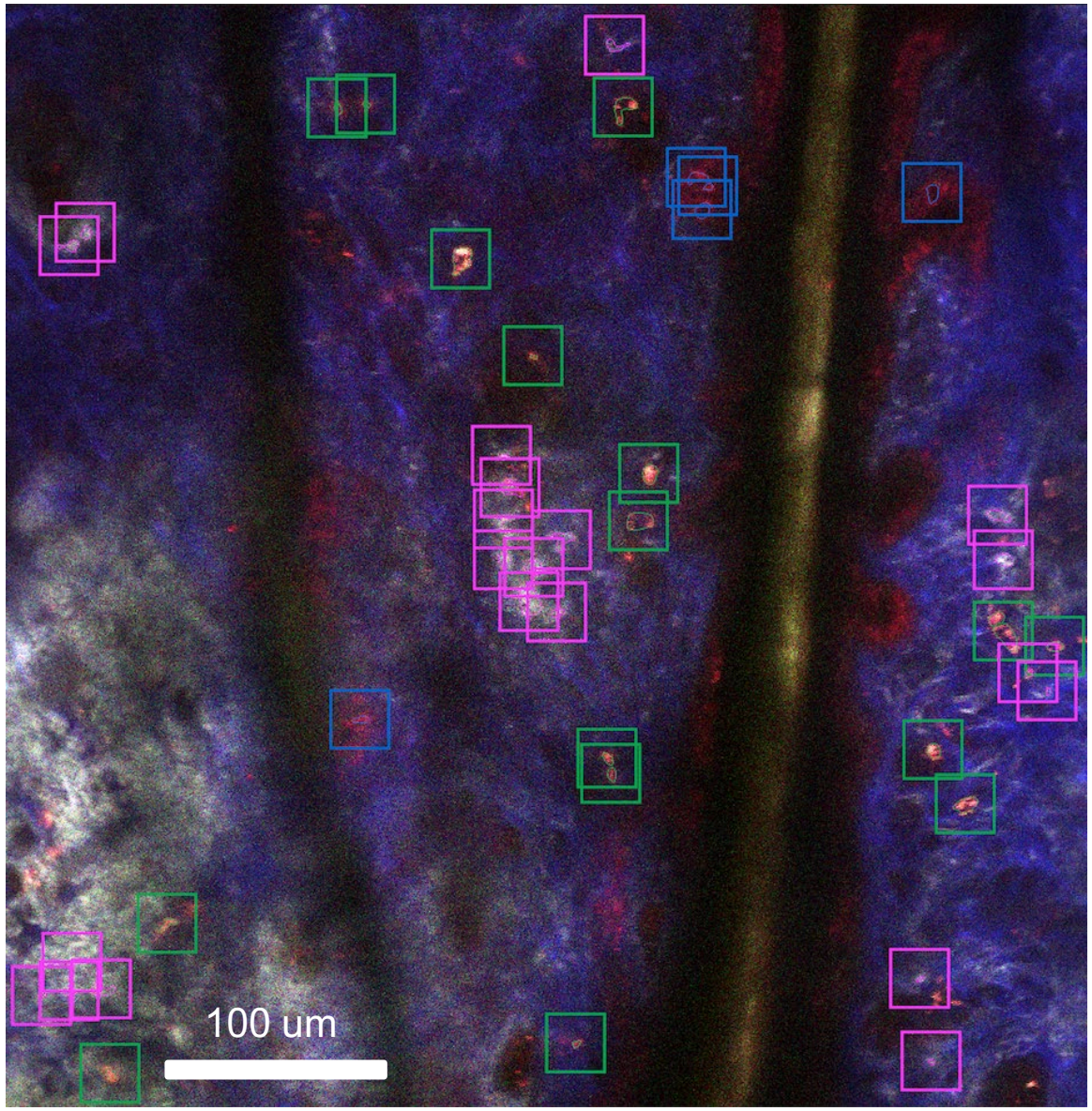
Monitoring Immune Responses to Checkpoint Inhibitors in Melanoma

During Immunotherapy





Automatic Cell Segmentation in Thick Tissue



Expert-annotated MPM images

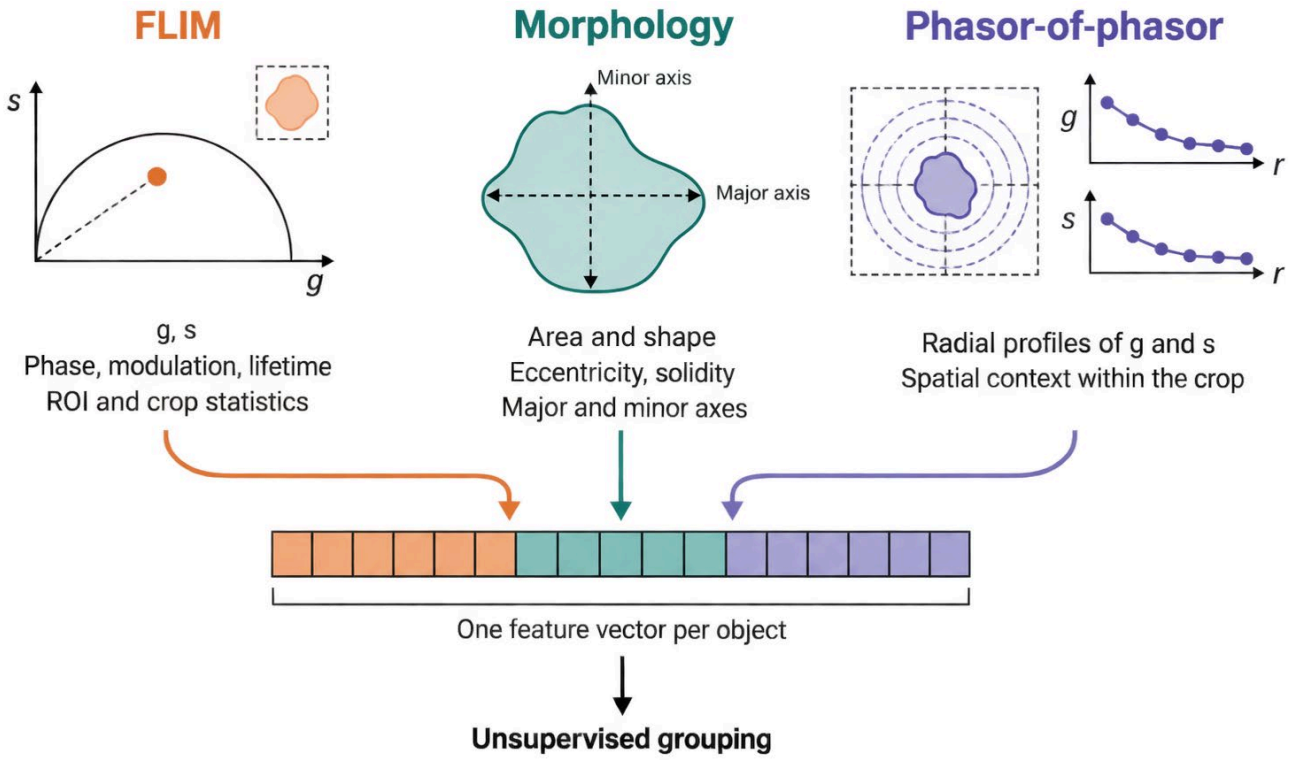
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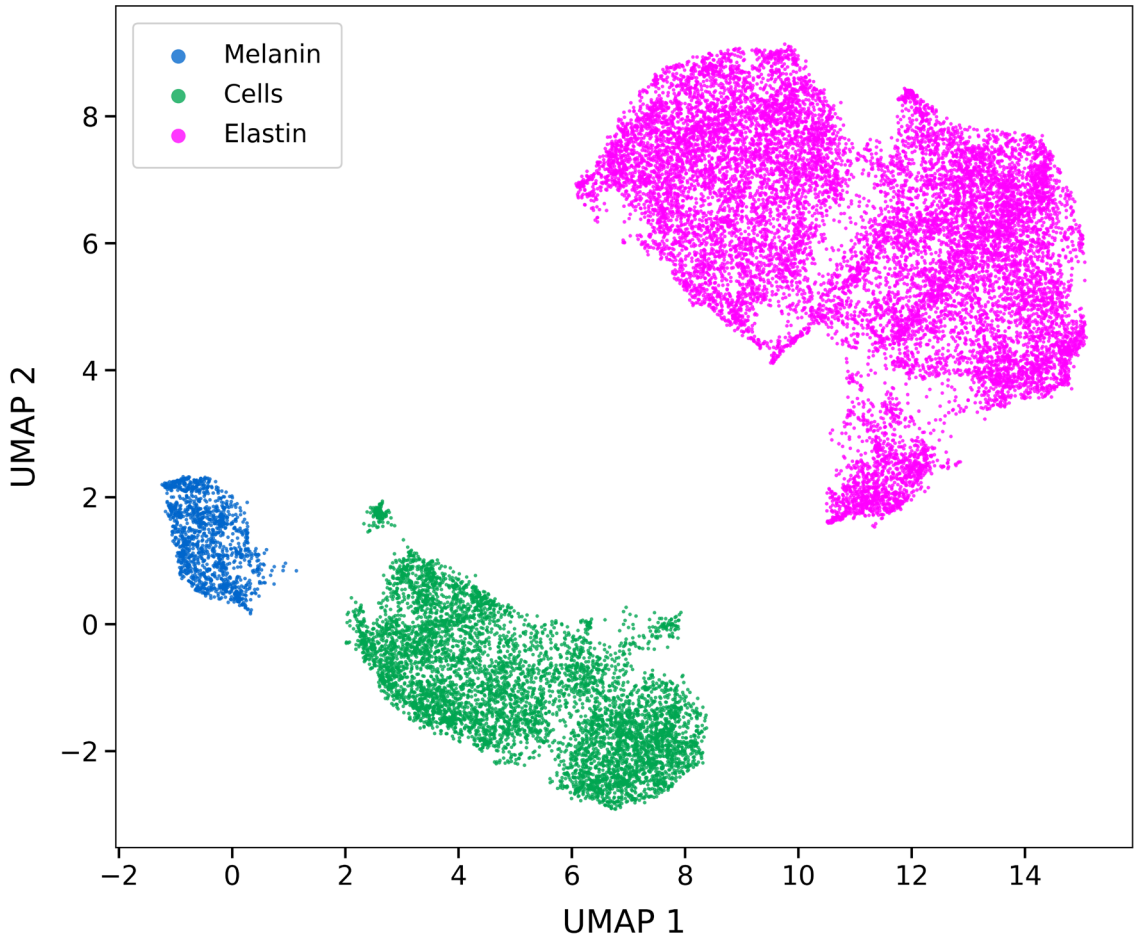
Deeply supervised U-Net trained



Peter Chang, MD
Associate Professor
Department of Radiological Sciences
Director, Institute for Precision Health

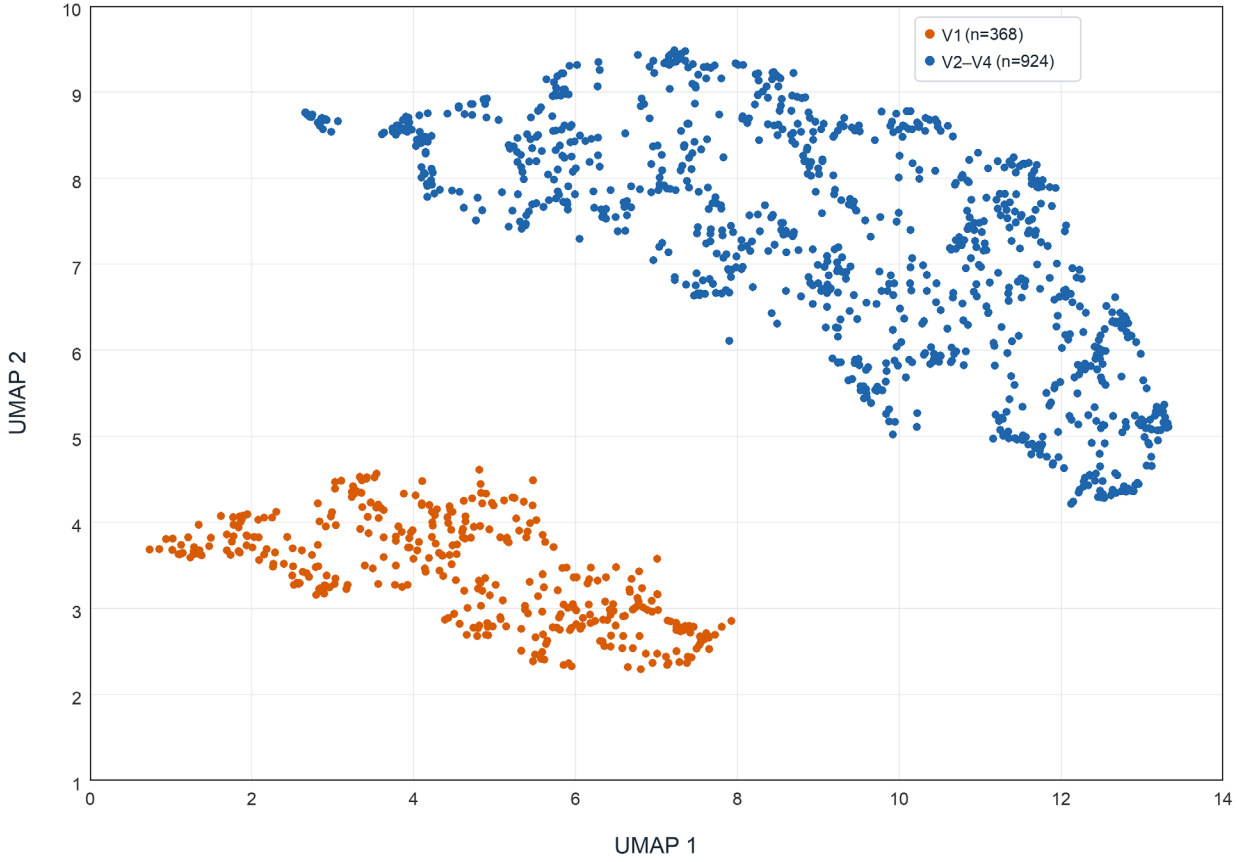
Unsupervised Classification of Dermal Structures in FLIM Images



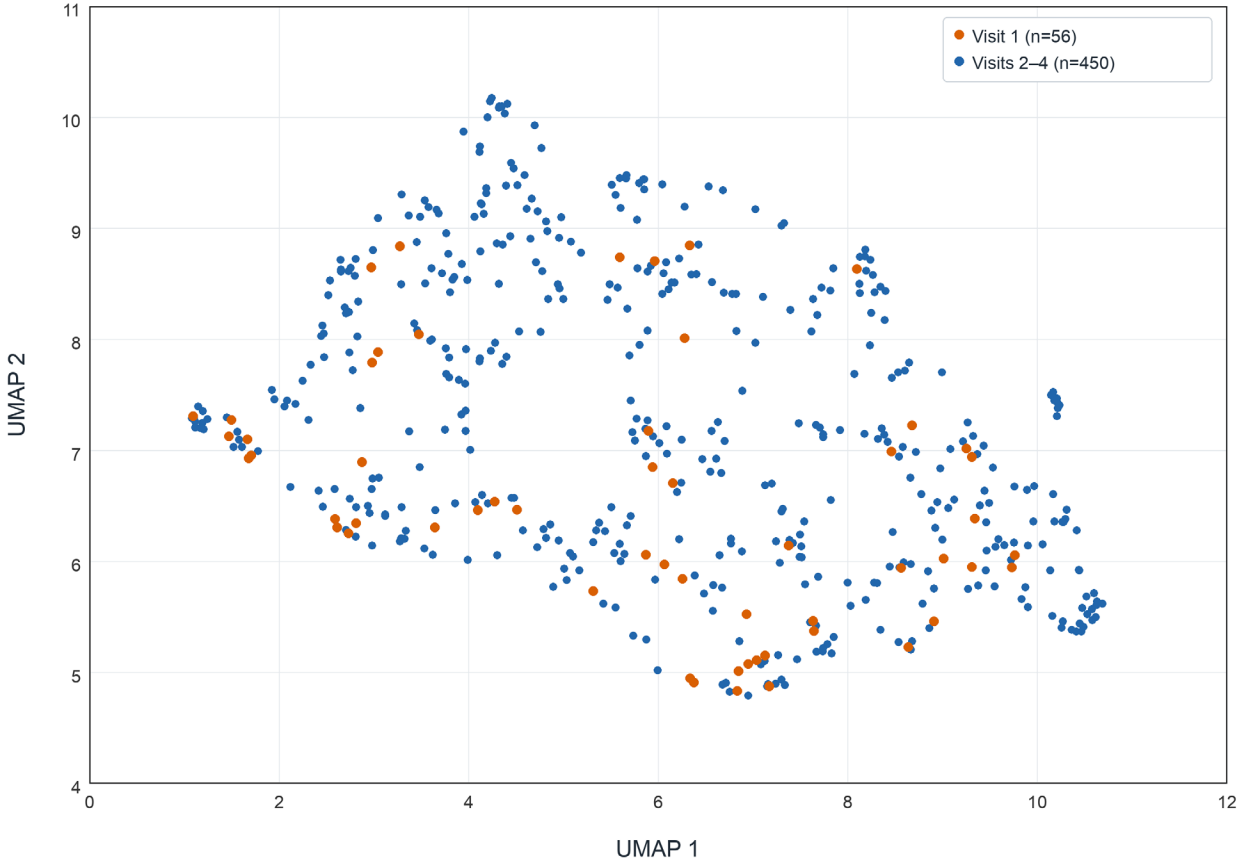


Longitudinal Cellular Analysis in Treatment Responders vs Non-Responders

Responding patient



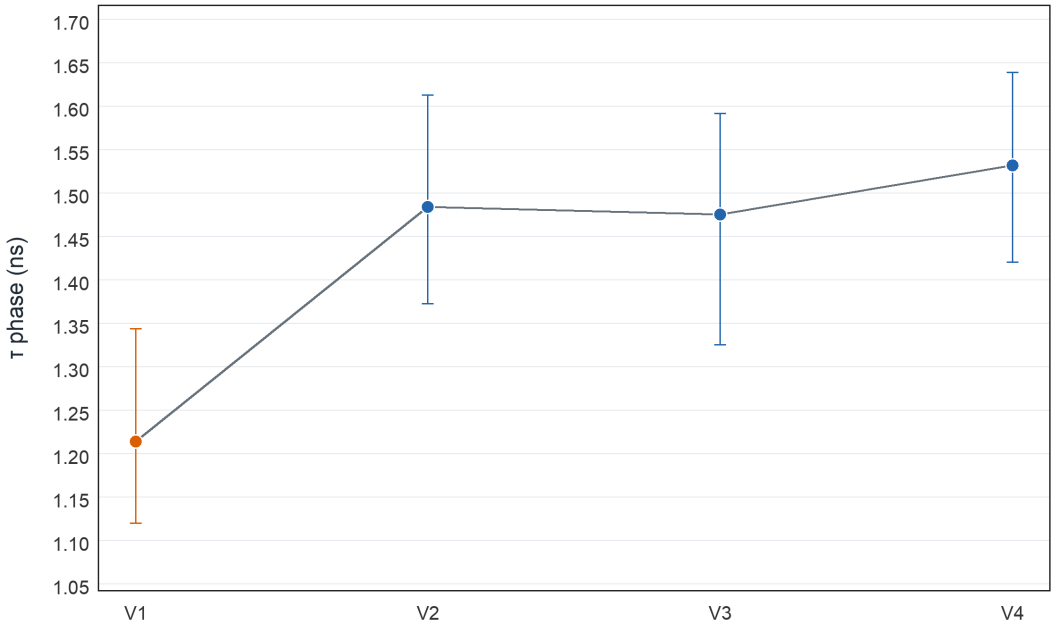
Non-responding patient



Metabolic Changes in Treatment Responders vs Non-Responders

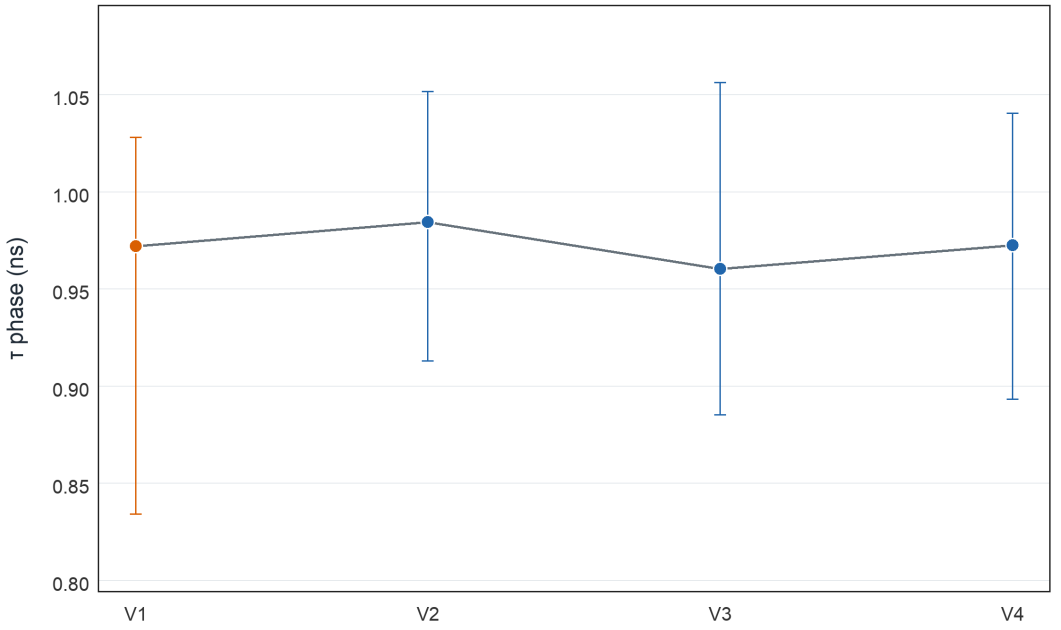
Responding patient

Tau Phase



Non-responding patient

Tau Phase



UC Irvine Chao Family Comprehensive Cancer Center

Multidisciplinary Teams Advancing Clinical Multiphoton Microscopy

Researchers and Senior Members



Alex Vallmitjana, PhD
Physics



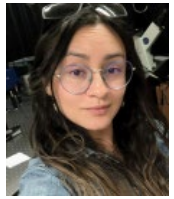
Belen Torrado, PhD
Biology



Sasha Dvornikov, PhD
Chemistry



Amanda Durkin
BME



Yryx Palacio, PhD
Physics

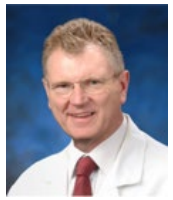
Clinical Team



K. Kelly, MD



A. Ganesan MD, PhD



C. Zachary, MD



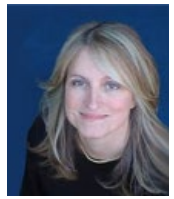
J. Shiu, MD, PhD



K. Linden, MD



H. Rizvi, MD
Clinical Research Fellow



J. Smith, MD



X. Fan, MD, PhD



T. Tran, MD



P. Vaidya, MD



Hanna Kim
Clinical Coordinator

Graduate Students



Bruno Schuty
BME



Wenyu Zhang
MCSB



Dayuan NI
Physics

Funding sources

- NIH/NIBIB (5R01EB026705)
- NIH/NCI (1R01CA259019)
- NIH/NIAMS (1R21AR082648)
- UCI Skin Biology Resource-Based Center (P30AR075047)
- CFCCC (P30CA062203)
- Department of Defense
- Abbvie

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Comprehensive Cancer Center

Questions?