Human Biomolecular Atlas Program (HuBMAP)

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dkNET Webinar Series
Oct 14, 2022

Vision

Catalyze the development of an open, global framework for comprehensively mapping the human body at cellular resolution.

HuBMAP
The Human BioMolecular Atlas Program

https://commonfund.nih.gov/HuBMAP

Accelerate Tools and Technique Development

Accelerating the development of the next generation of tools and techniques for constructing high resolution spatial tissue maps that quantify multiple types of biomolecules either sequentially or simultaneously

Generate 3D Human Tissue Maps

Generating foundational 3D human tissue maps using validated high-content, high-throughput imaging and omics assays

Establish Open Data Platform

Establishing an open data platform that will develop novel approaches to integrating, visualizing and modelling imaging and omics data to build multi-dimensional tissue maps, and making data rapidly findable, accessible, interoperable, and reusable by the global research community

Collaborate with the Research Community

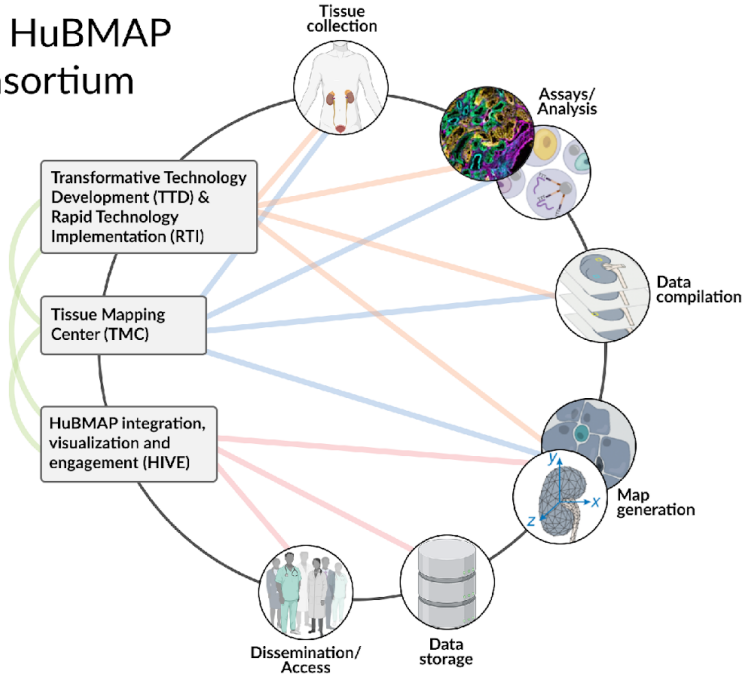
Coordinating and collaborating with other funding agencies, programs, and the biomedical research community to build the framework and tools for mapping the human body at single cell resolution

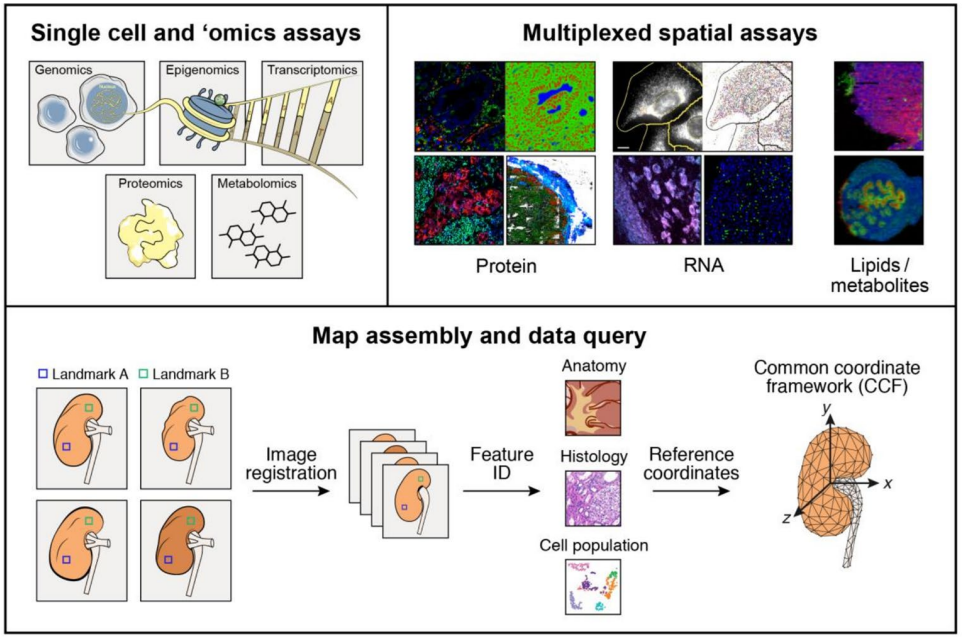
Support Pilot Projects

Supporting pilot projects that demonstrate the value of the resources developed by the program to study normal individual variations and tissue changes across the lifespan and the health-disease continuum

The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program
Snyder et al. *Nature*. 574, p. 187-192.

The HuBMAP Consortium





HuBMAP Funded Groups 2022

Rapid Technology Implementation

Transformative Technolgy Development

Tissue Mapping Centers

HuBMAP Integration Visualization Engagement

27 RTI Members
4 funded groups

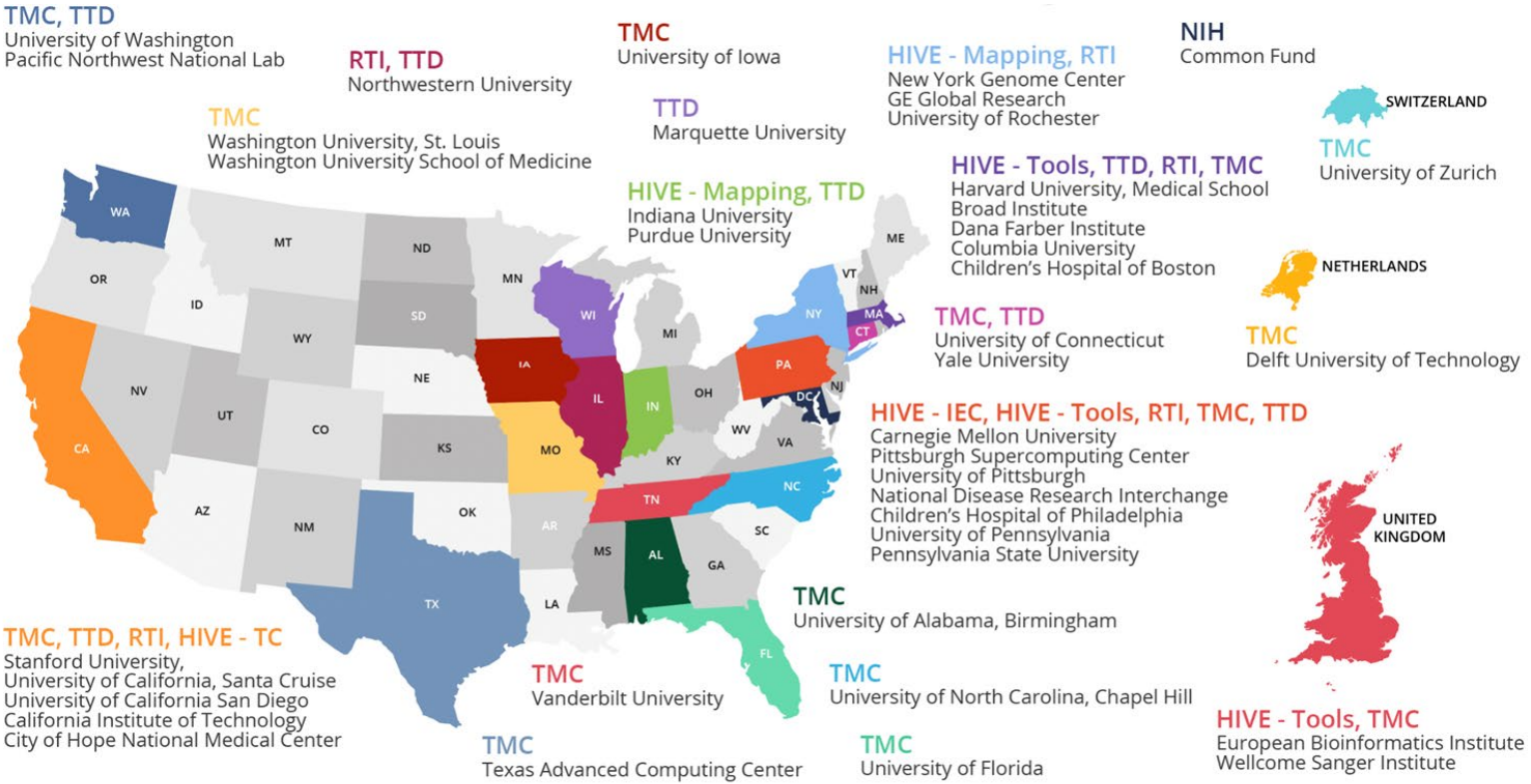
60 TTD Members
8 funded groups

160 TMC Members
11 funded groups

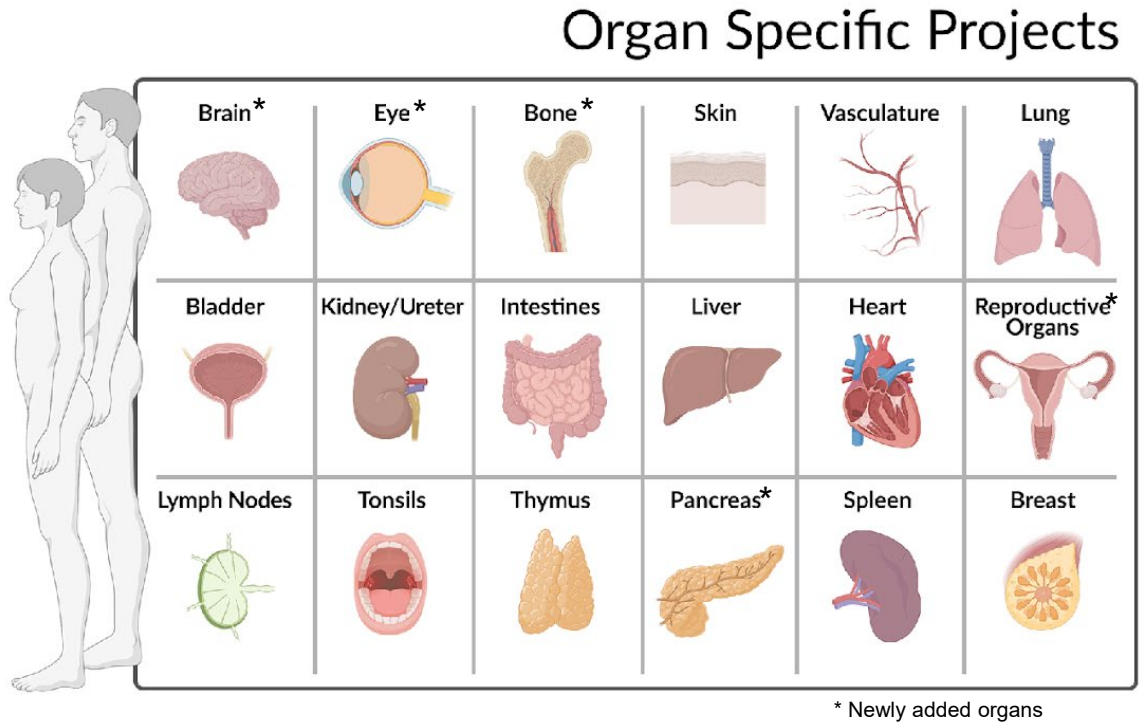
111 HIVE Members
5 funded groups

358 Members in
28 funded groups

HuBMAP Contributing Sites



HuBMAP Overview



The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program.
Snyder et al. *Nature*. 574, p. 187-192.

Setup and Scale Up Phase (2018-2022)

Tool Development

- Standardized Analytical Workflows, Metadata, Protocols
- Multimodal/Multi-scale data generation

3D Maps and Reference Datasets

- HRA Common Coordinate Framework
- ASCT+B & 3D Reference Object Library
- Azimuth

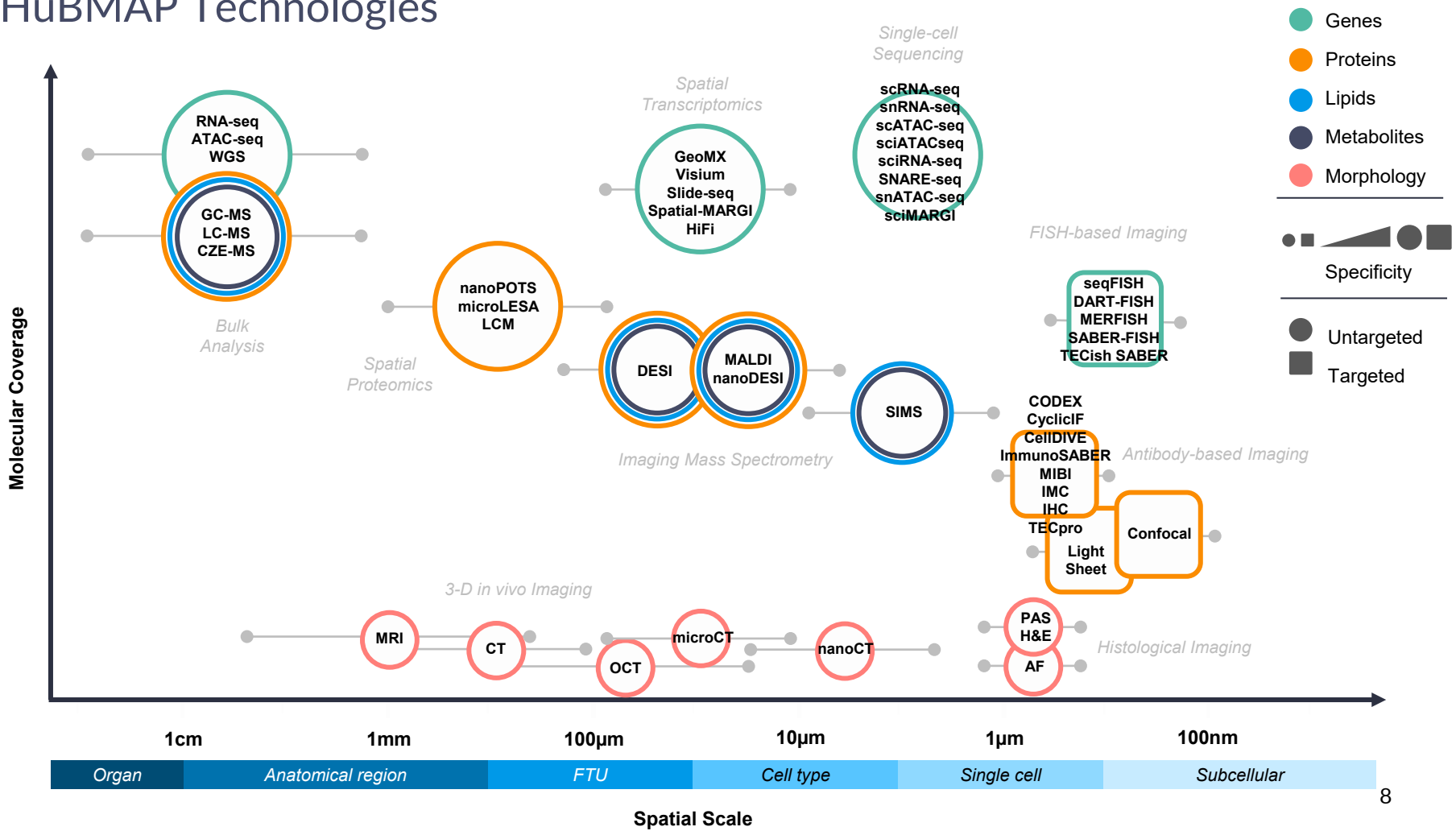
Open Data Platform

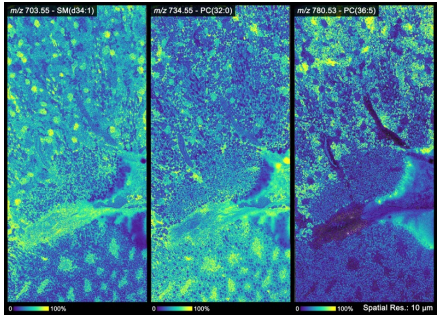
- HuBMAP Portal

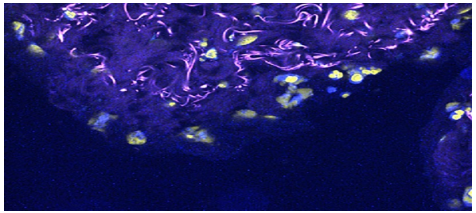
Outreach and Collaboration

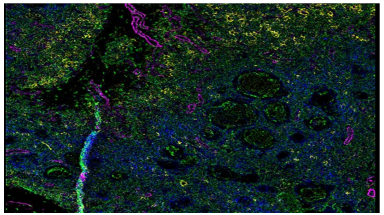
- Summer Internship Program, Jumpstart Program, Kaggle Competition

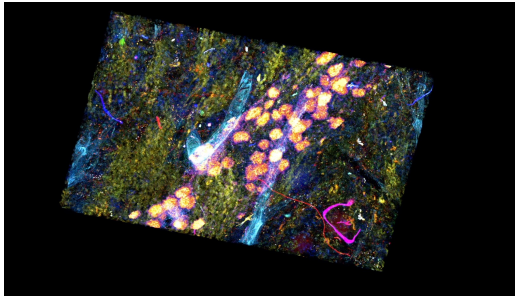
HuBMAP Technologies

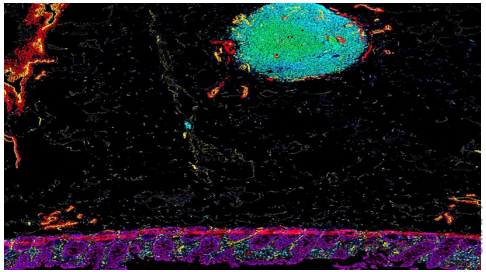


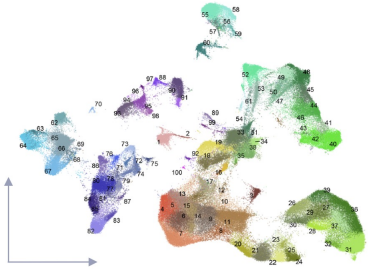

m/z 703.55 - SM(d34:1)
m/z 734.55 - PC(32:0)
m/z 780.53 - PC(36:5)
Spatial Res.: 10 µm

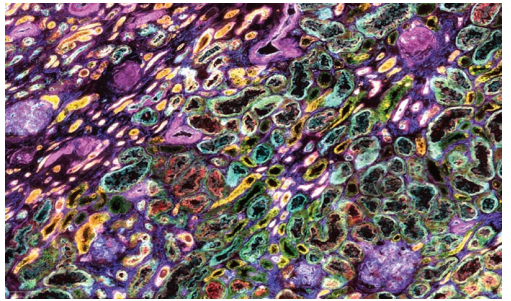


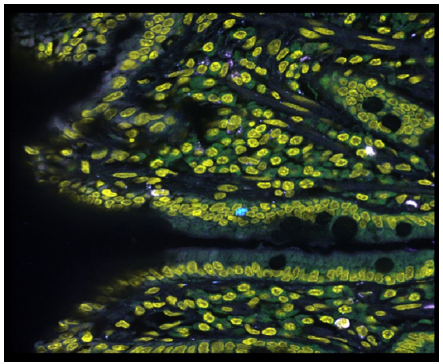


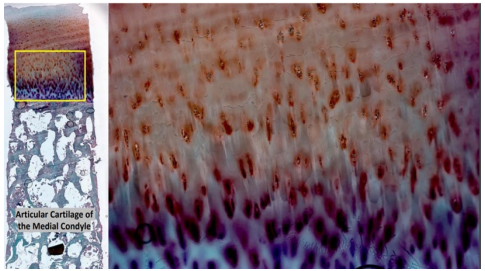


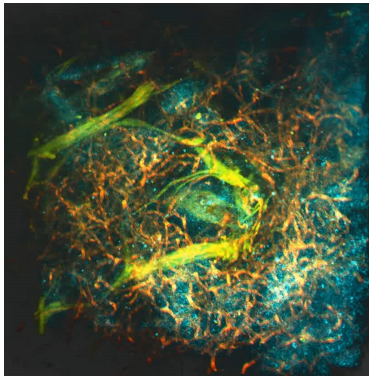


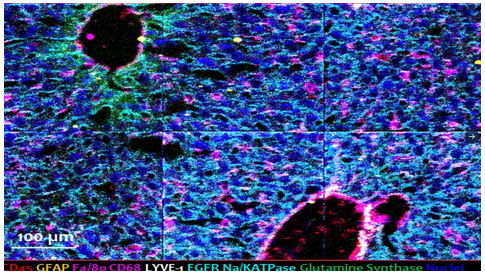

UMAP2

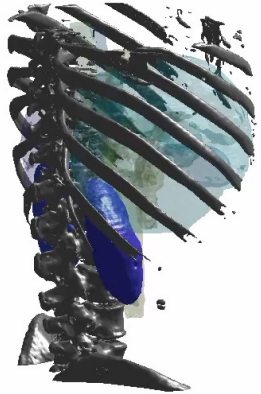


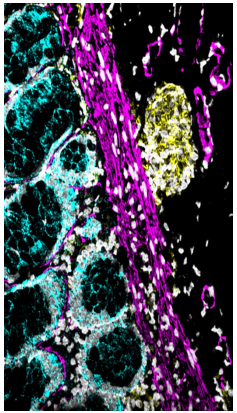


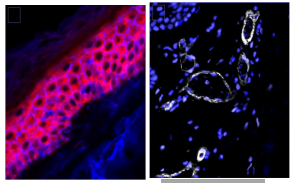

Articular Cartilage of the Medial Condyle

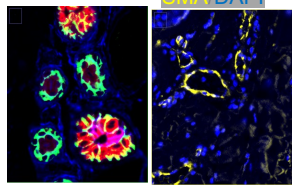



100 µm
DAPI GFAP F4/80 CD68 LYVE-1 EGFR Na/KATPase Glutamine Synthase Nuclei

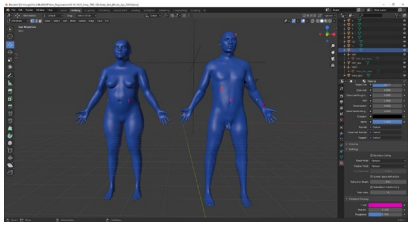




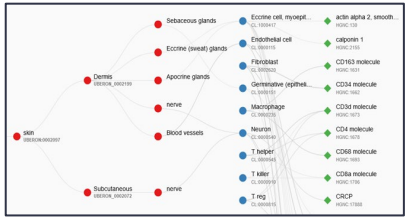

SMA/DAPI


CD31/DAPI

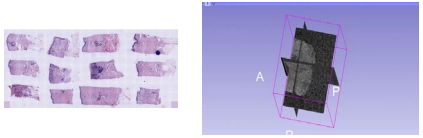
GE Research and U. Pittsburgh RTI: 3D reconstruction of multiplexed skin samples and spatial cell analysis



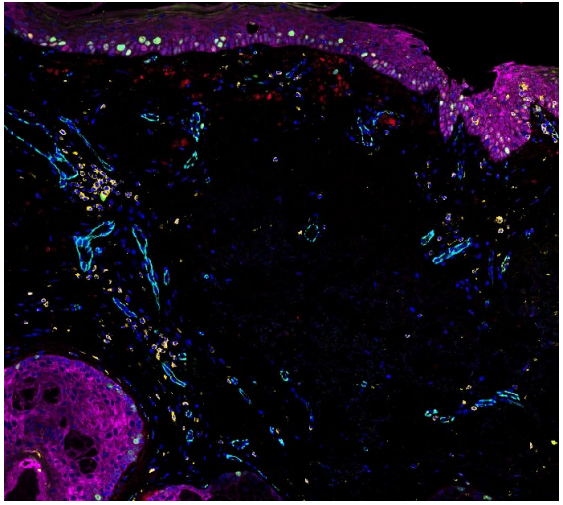
Registration of Skin Biopsy location using RUI



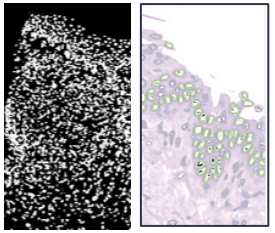
Registration of Skin Biomarkers in ASCT+B & OMAP



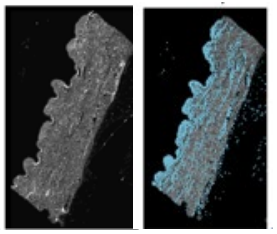
Tissue data collection: microCT imaging of skin FFPE blocks for multiplexed image 3D reconstruction



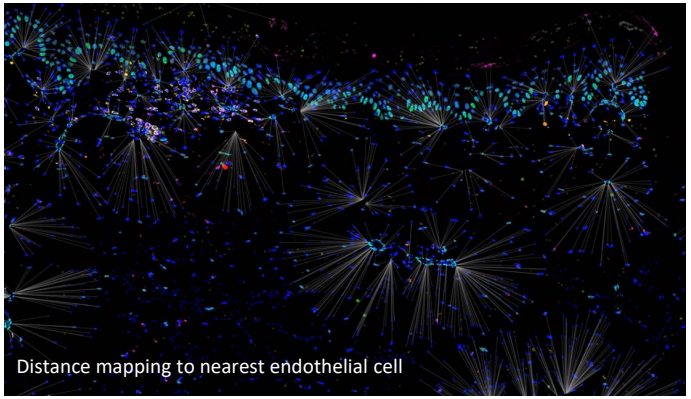
Multiplexed imaging of 18 skin biomarkers rom 40 patients (Caucasian and African American)

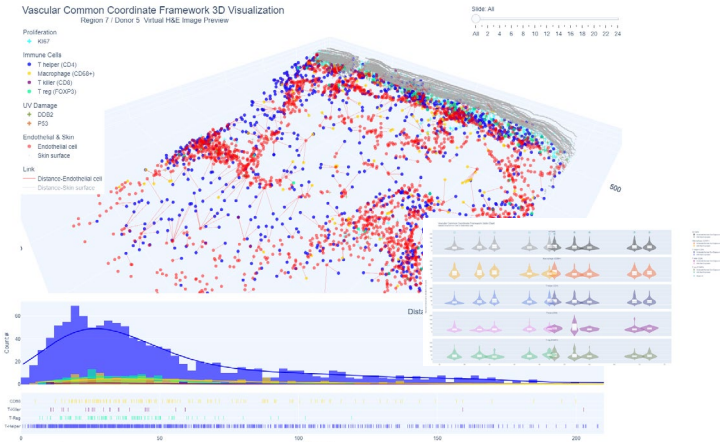


Cell type classification (epithelial, immune, endothelial…)



3D Volume Reconstruction of 24 serial sections with micro CT as reference



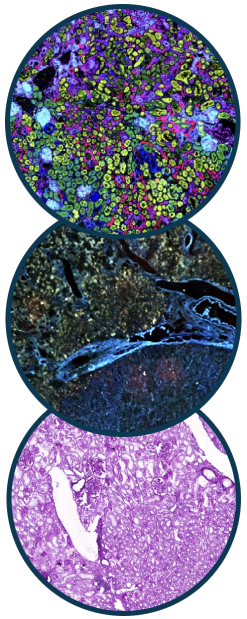


3D "Digital Twin" of skin cells and quantitative interactive spatial distances (Yingnan Ju and Katy Börner, IU)

Vanderbilt TMC Highlight

MULTIMODAL IMAGING MASS SPECTROMETRY

Discovery of important biomarkers, cell types, and tissue neighborhoods



MALDI Imaging Mass Spectrometry

- Provides molecular images of many molecular classes without the need for any stain or antibody.

Autofluorescence Microscopy

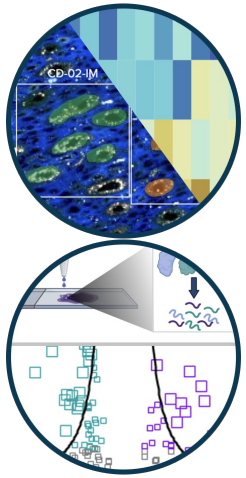
- An image type we can collect from every sample that is used for analysis and connecting data sets.

Stained Microscopy

- A common image type that can be used by pathologists to assess the tissue and identify important tissue regions.

SPATIALLY TARGETED MULTI-OMICS

Uncovers important pathways and mechanisms in regions discovered by Multimodal Imaging



Spatial Transcriptomics

- Gives a snapshot of the RNA transcript expression from defined tissue regions and cell types.

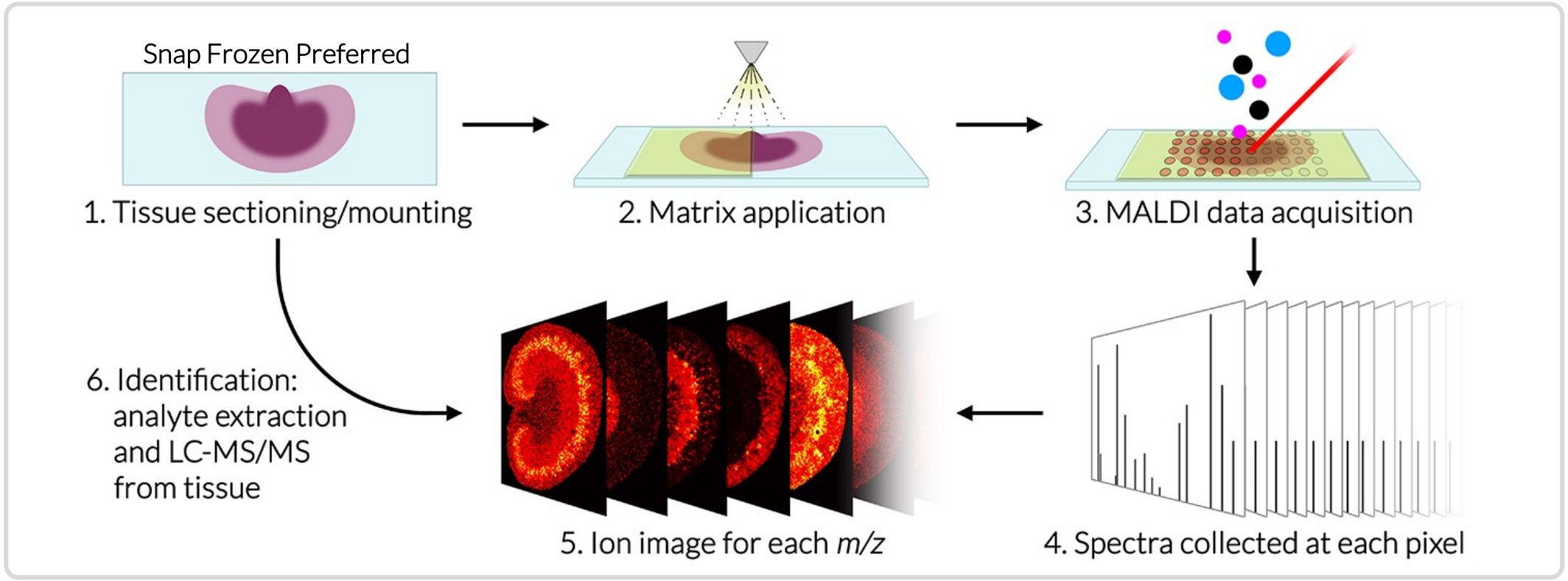
Spatial Proteomics

- Provides protein identification and abundance information from defined tissue regions and cell types.

We provide means of exploring the molecular content of human tissue in a fully open-ended way, without the need to know beforehand what we're looking for. The means for discovery we contribute to KPMP makes it possible to go look for completely new and previously unknown biochemical mechanisms behind kidney disease and can help find molecular targets for predicting, diagnosing, and mitigating disease.

Multimodal Imaging Mass Spectrometry

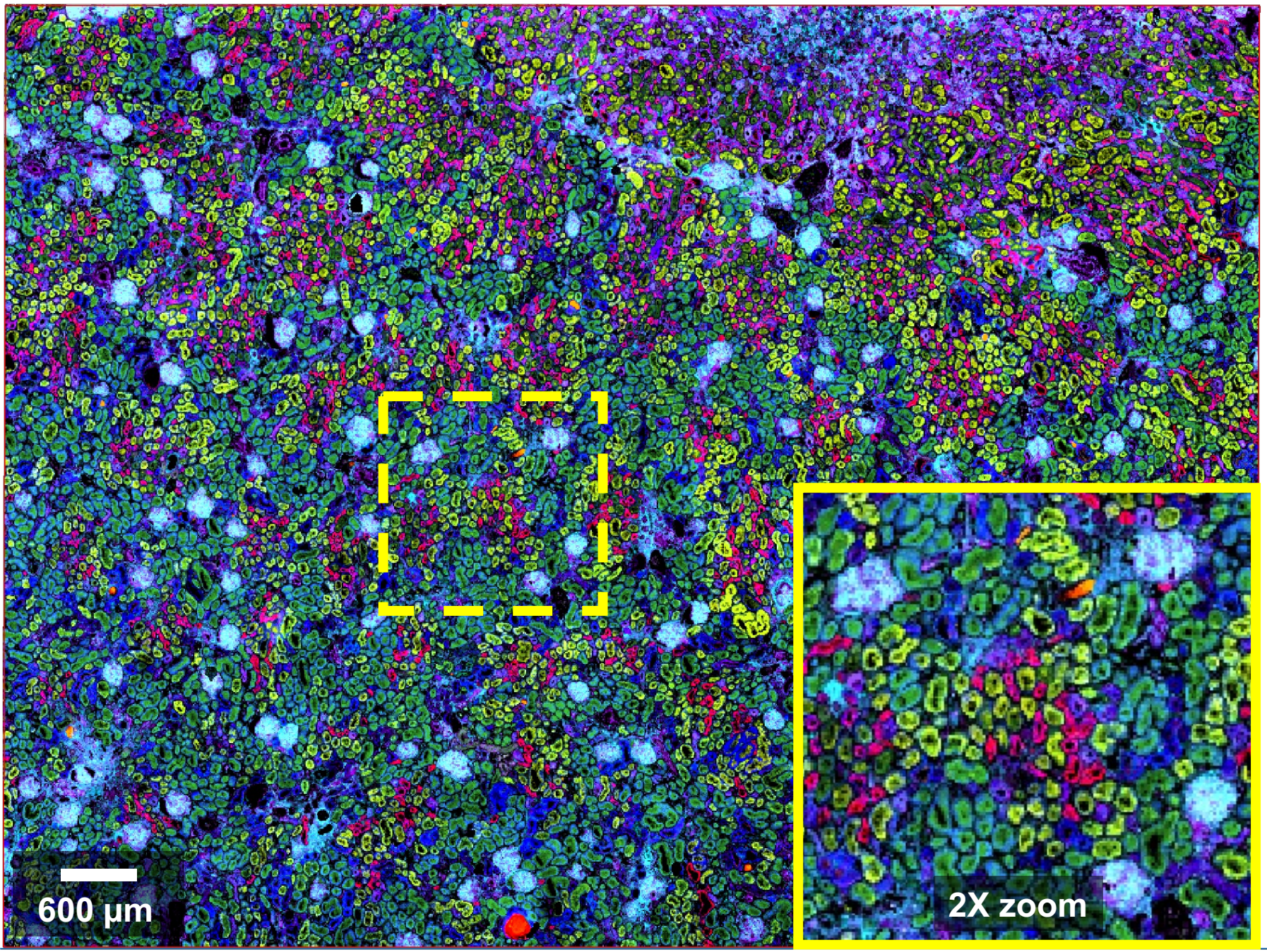
MALDI IMAGING MS / Overview



MALDI Imaging Mass Spectrometry offers untargeted, highly multiplexed molecular imaging of a wide variety of molecular classes at cellular resolution.

MALDI IMS

EXAMPLE DATA



10 µm MALDI IMS

Human kidney
MALDI timsTOF Flex
Negative Ion mode

- PE(O-38:5)
- PS(18:0_18:1)
- PS(18:0_20:4)
- SM4(d18:1_h24:0)
- SM3(d18:1_22:0)
- CL(72:8)

Kate Djambazova (VU)
Martin Dufresne (VU)

Multimodal Imaging Mass Spectrometry

EXAMPLE DATA

Modalities

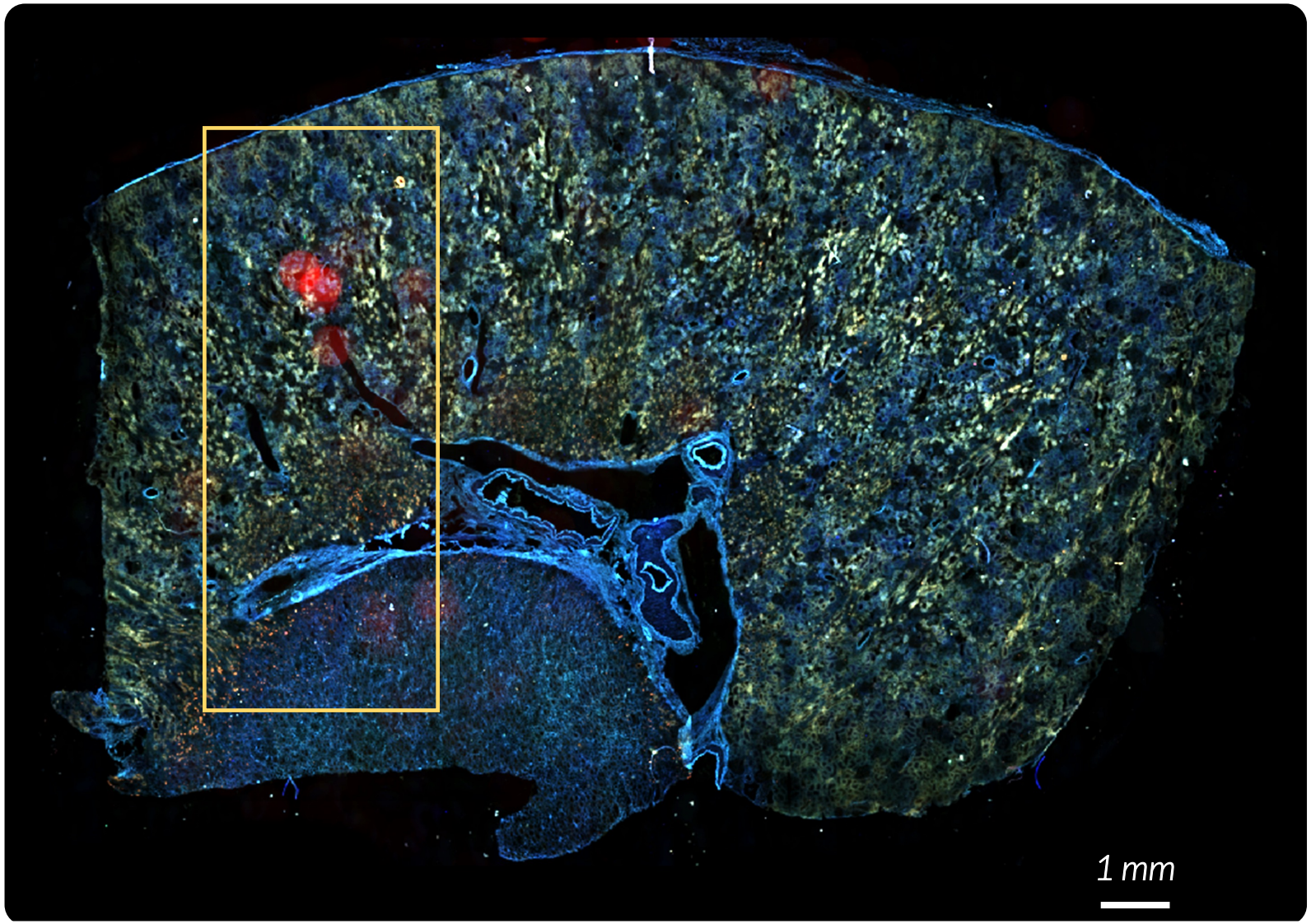
(1) Autofluorescence Microscopy
- Unstained fluorescence imaging used for image segmentation.

(2) MALDI Imaging Mass Spectrometry
- Unstained fluorescence imaging used for image segmentation.

(3) PAS-Stained Microscopy
- Tissue morphology/assessment

Sample Details

Human Kidney Tissue
38 yr Old Female
Left Kidney / Lower Pole
Cryosectioned at 10 µm
Matrix: 1,5-Diaminonaphthalene (DAN)
Matrix Application: TM-Sprayer (HTX)

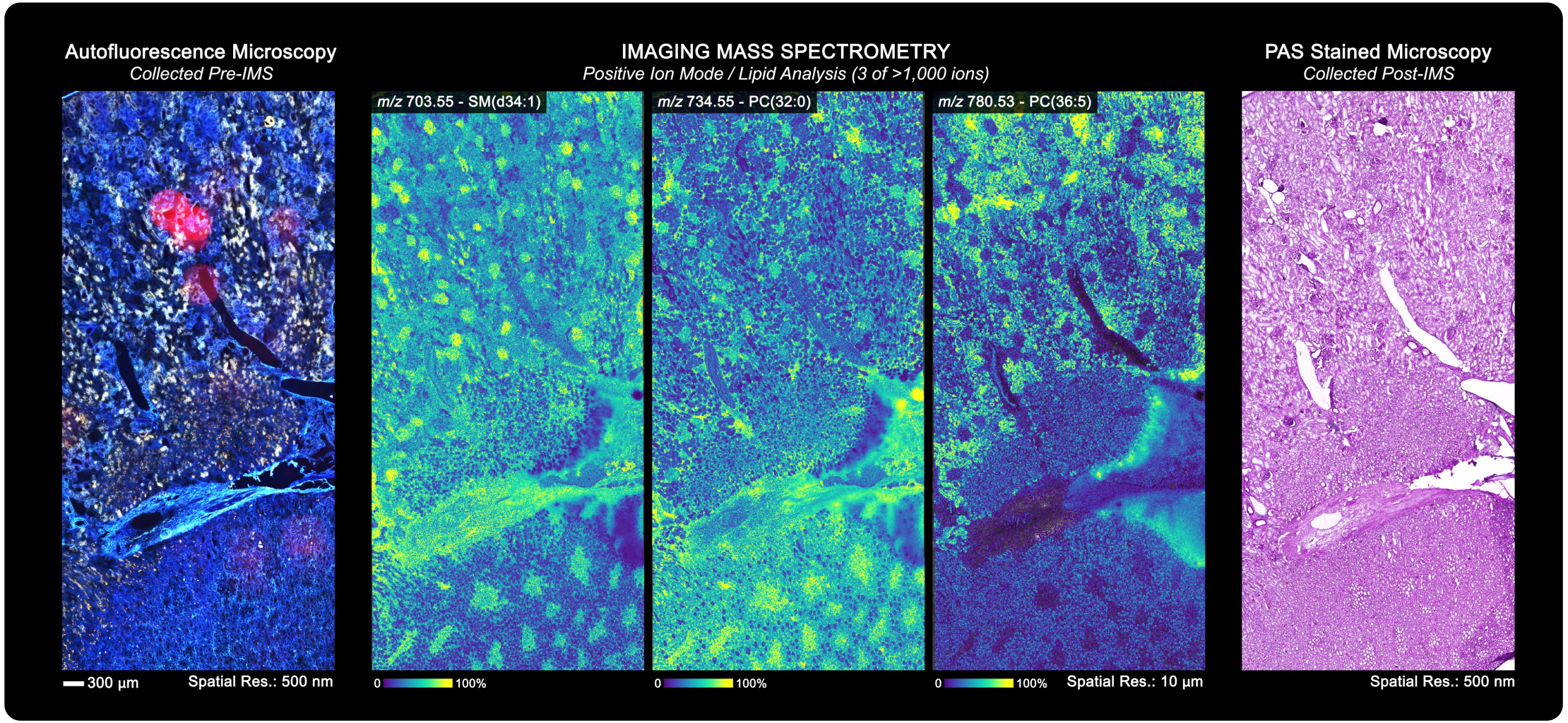


Multimodal Imaging Mass Spectrometry

EXAMPLE DATA

Kate Djambazova (VU)

Human Kidney



Multimodal Imaging Mass Spectrometry

FUNCTIONAL TISSUE UNIT SEGMENTATION

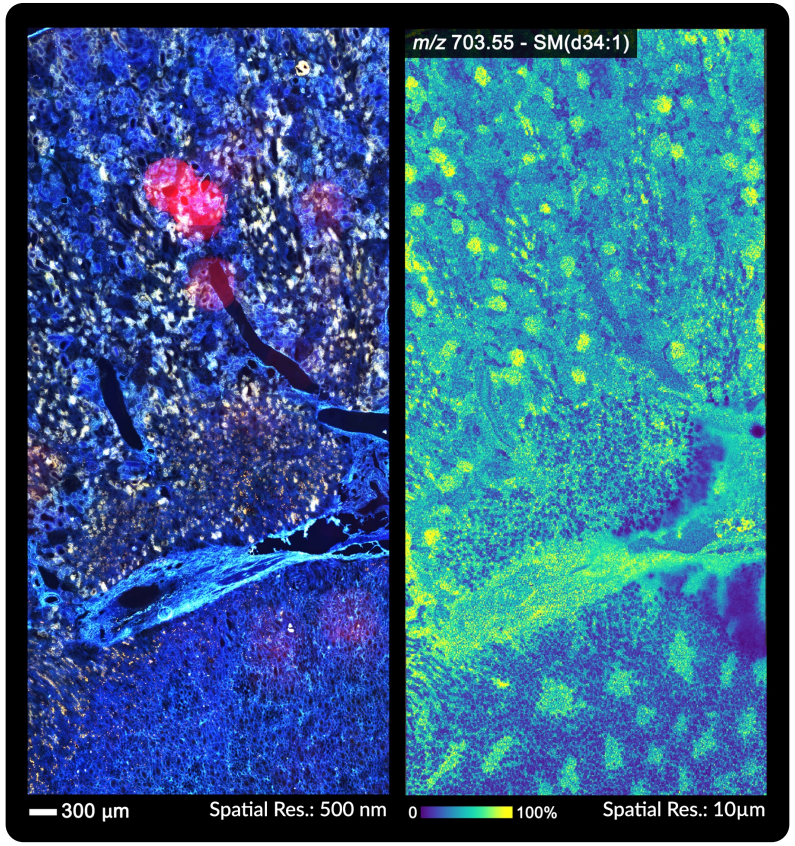
Multimodal imaging enables spatially-driven data mining and analysis of untargeted IMS data based on morphological features and functional tissue units by segmenting AF microscopy images.

MOTIVATION

- Want to segment FTUs like the glomerulus in tissue using microscopy in a reproducible way that is fully automated and compatible with any –omics technologies

SOLUTION

- Develop autofluorescence microscopy (AF) FTU segmentation
- Use co-registered stained and MxIF images to help with training data annotation
- Employ deep learning convolutional neural network approaches on whole slide images (WSIs)



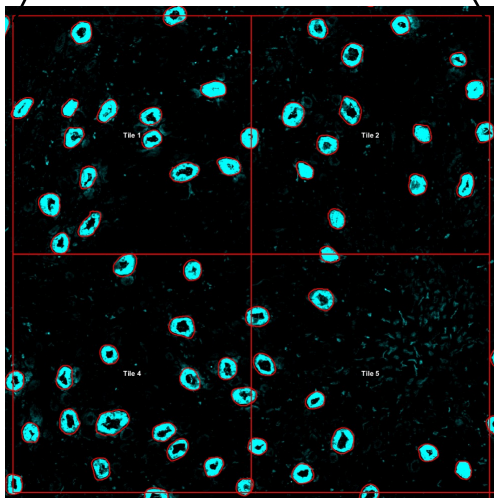
Multimodal Imaging Mass Spectrometry

FUNCTIONAL TISSUE UNIT SEGMENTATION

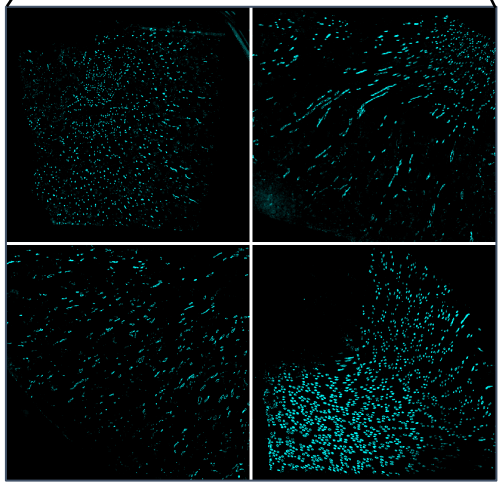
N. Heath Patterson (VU)

Rapid segmentation model development

Annotate 4-8 IF images on 4 tiles for each FTU

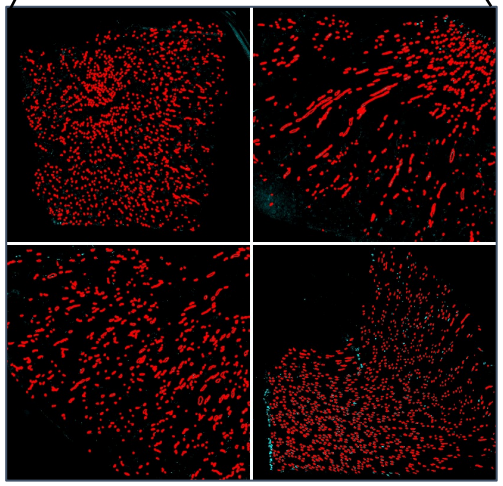


Train FTU detector using small IF dataset and segment all IF whole slide images



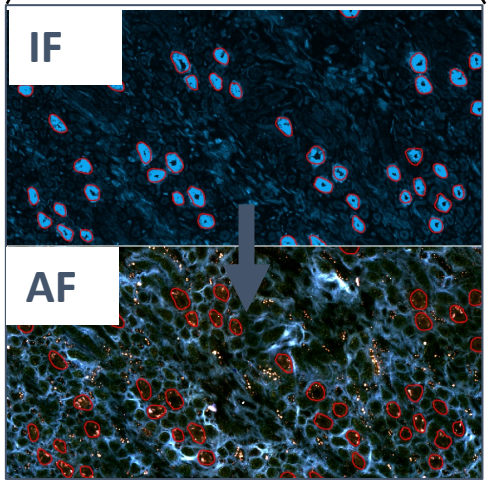
Whole slide images

Curate full dataset on **confident IF segmentations**



Whole slide images

Transfer **annotations** to AF

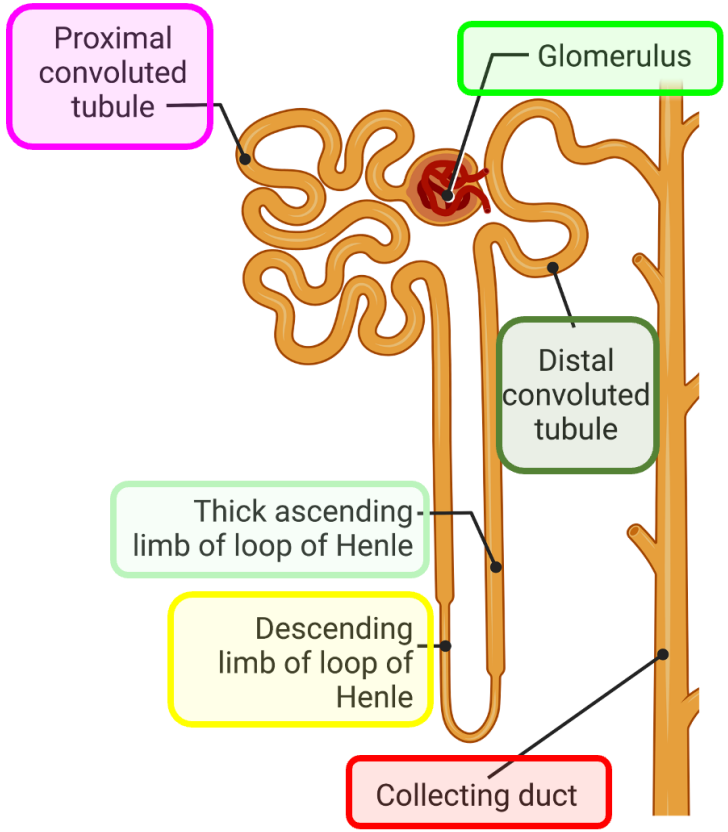


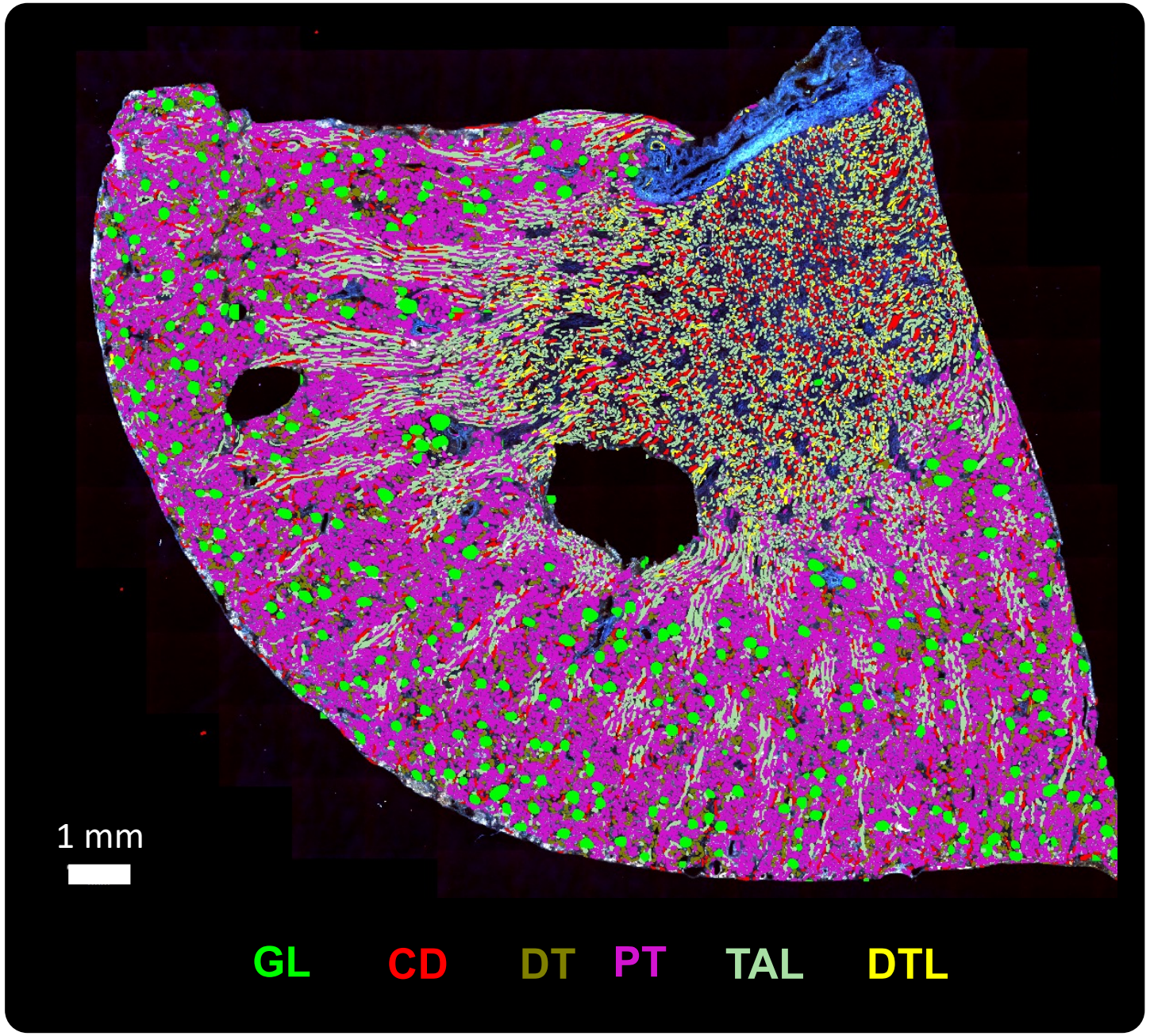
Transfer learning of CNNs models on 1000s of instances per FTU using AF data

Label-free microscopic instance segmentation of FTUs on whole slide images

FTU Segmentation Map

Unlabeled AF Microscopy



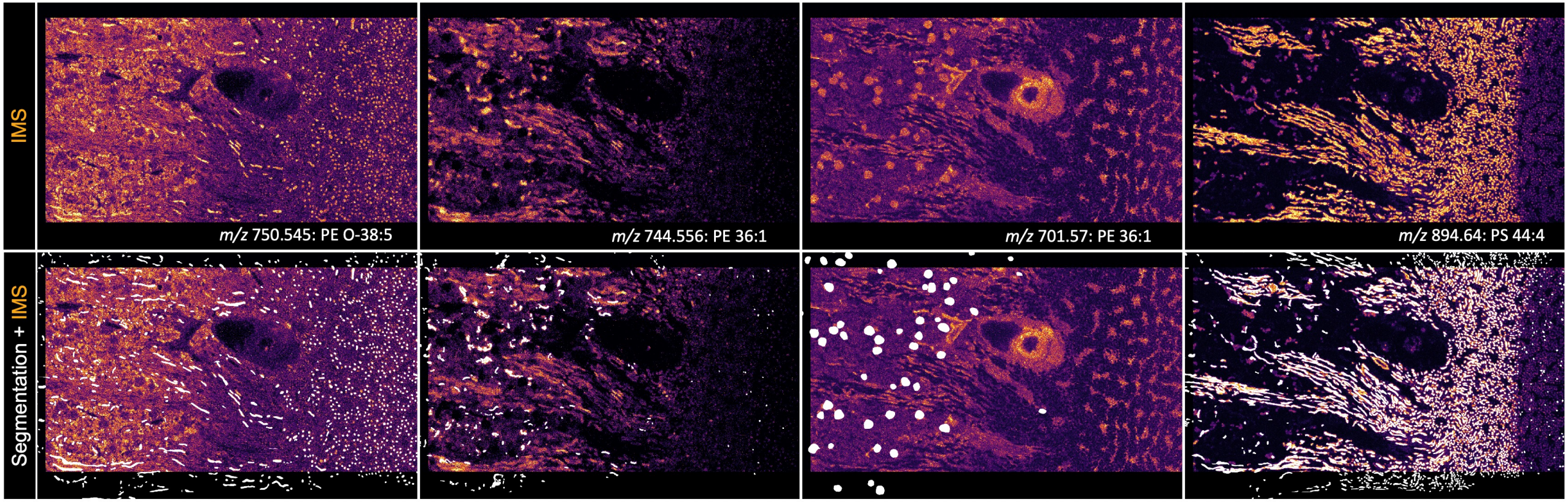


N. Heath Patterson (VU)

Multimodal Imaging Mass Spectrometry

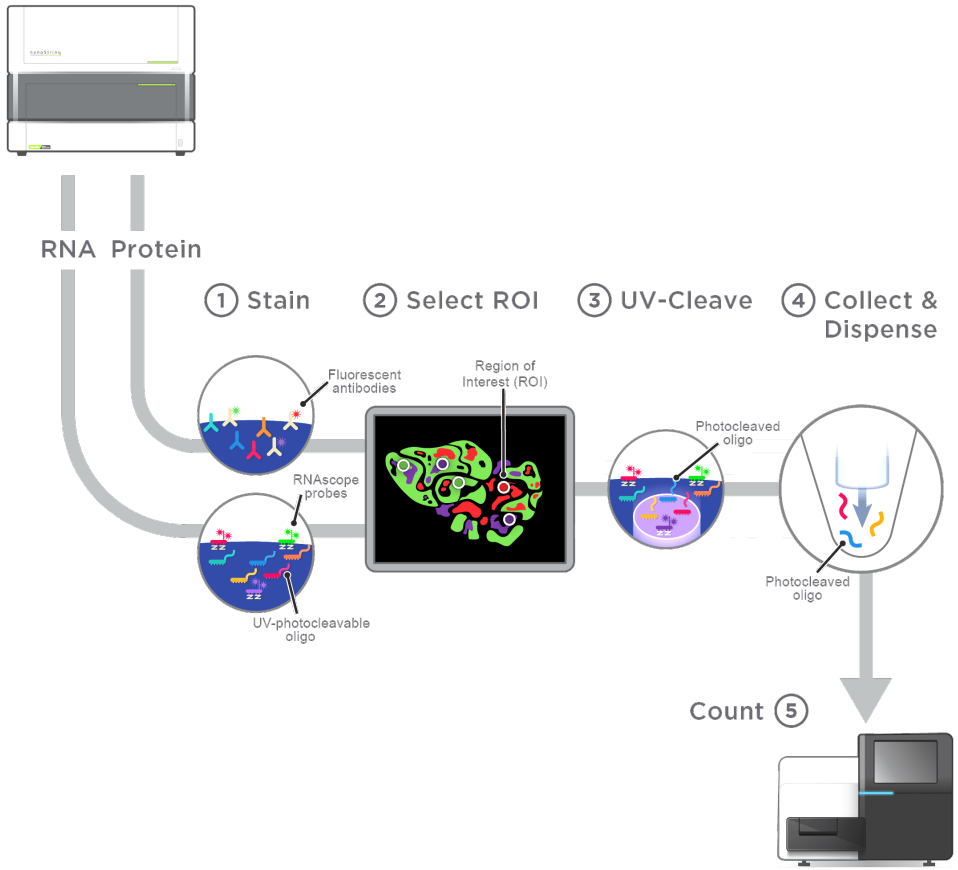
DATA INTEGRATION & MINING

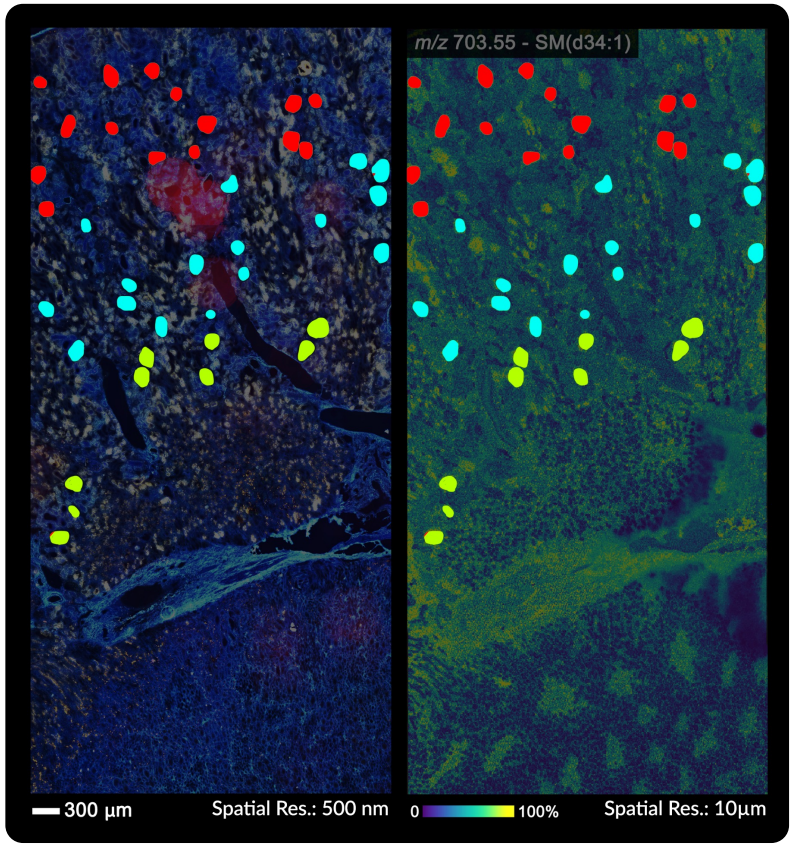
N. Heath Patterson (VU)
Martin Dufresne (VU)



nanoString GeoMx Spatial Transcriptomics

DSP Overview



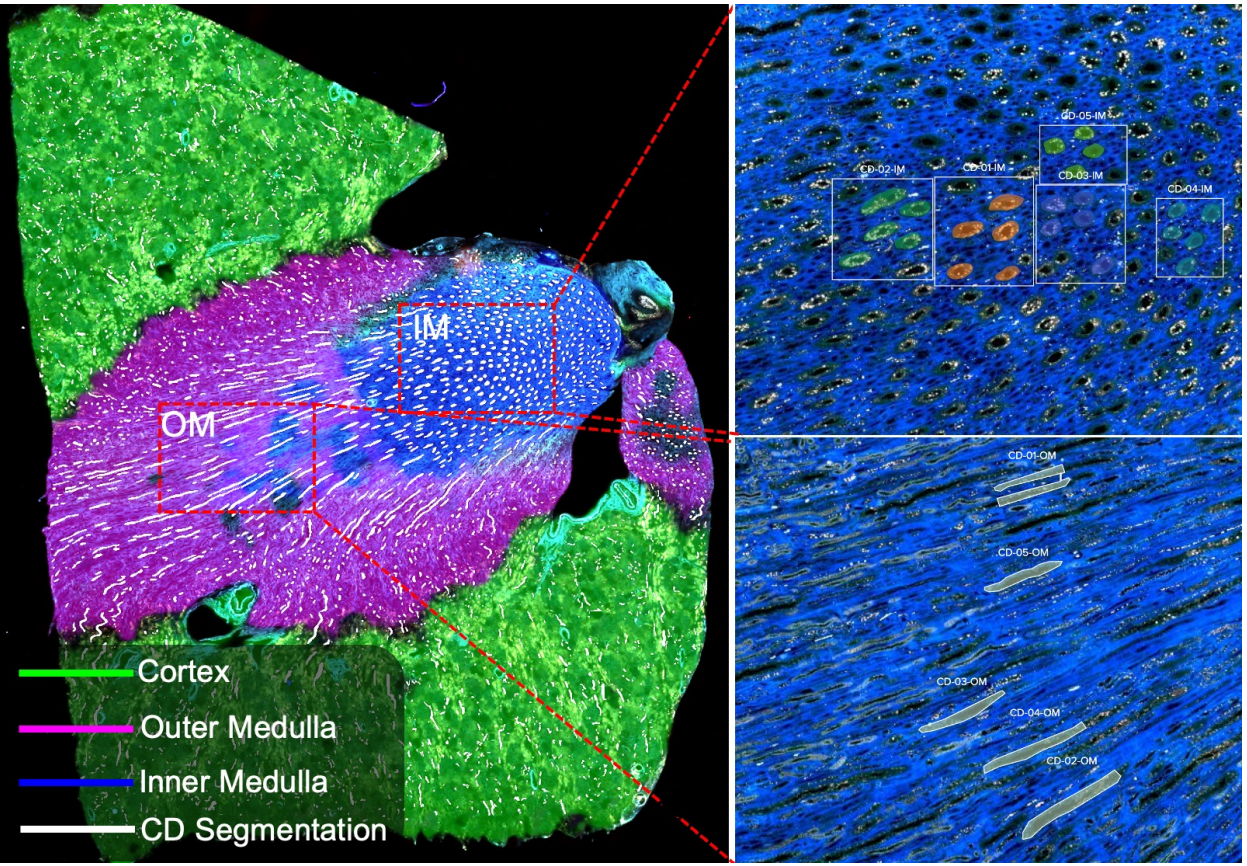


Our pipeline utilizes Multimodal Imaging Mass Spectrometry outputs to define important ROIs to drive the GeoMx Digital Spatial Profiler providing transcriptomics information for important FTUs, cell types, and neighborhoods.

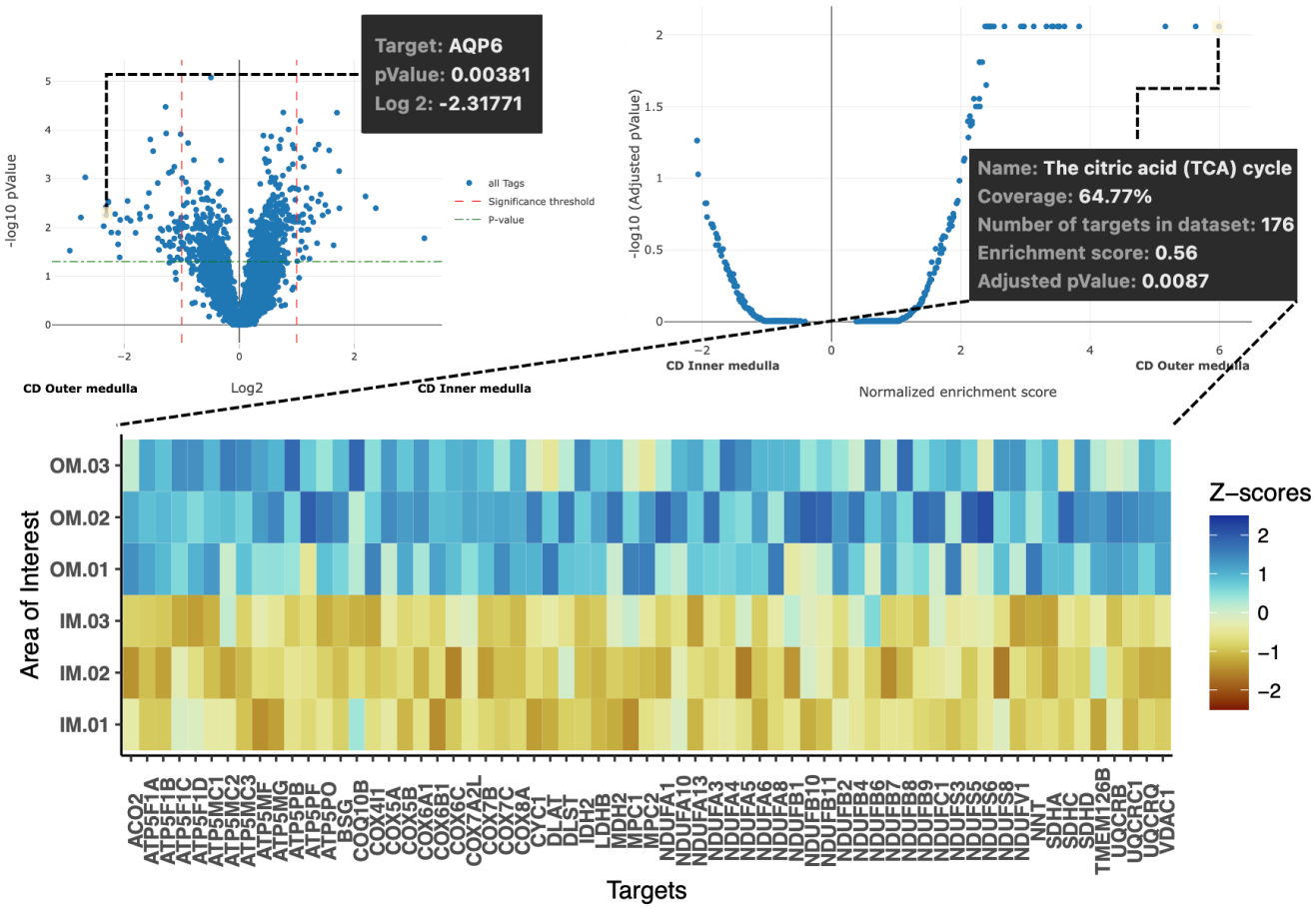
nanoString GeoMx Spatial Transcriptomics

EXAMPLE DATA

AF-Based Image Segmentation and ROI Selection

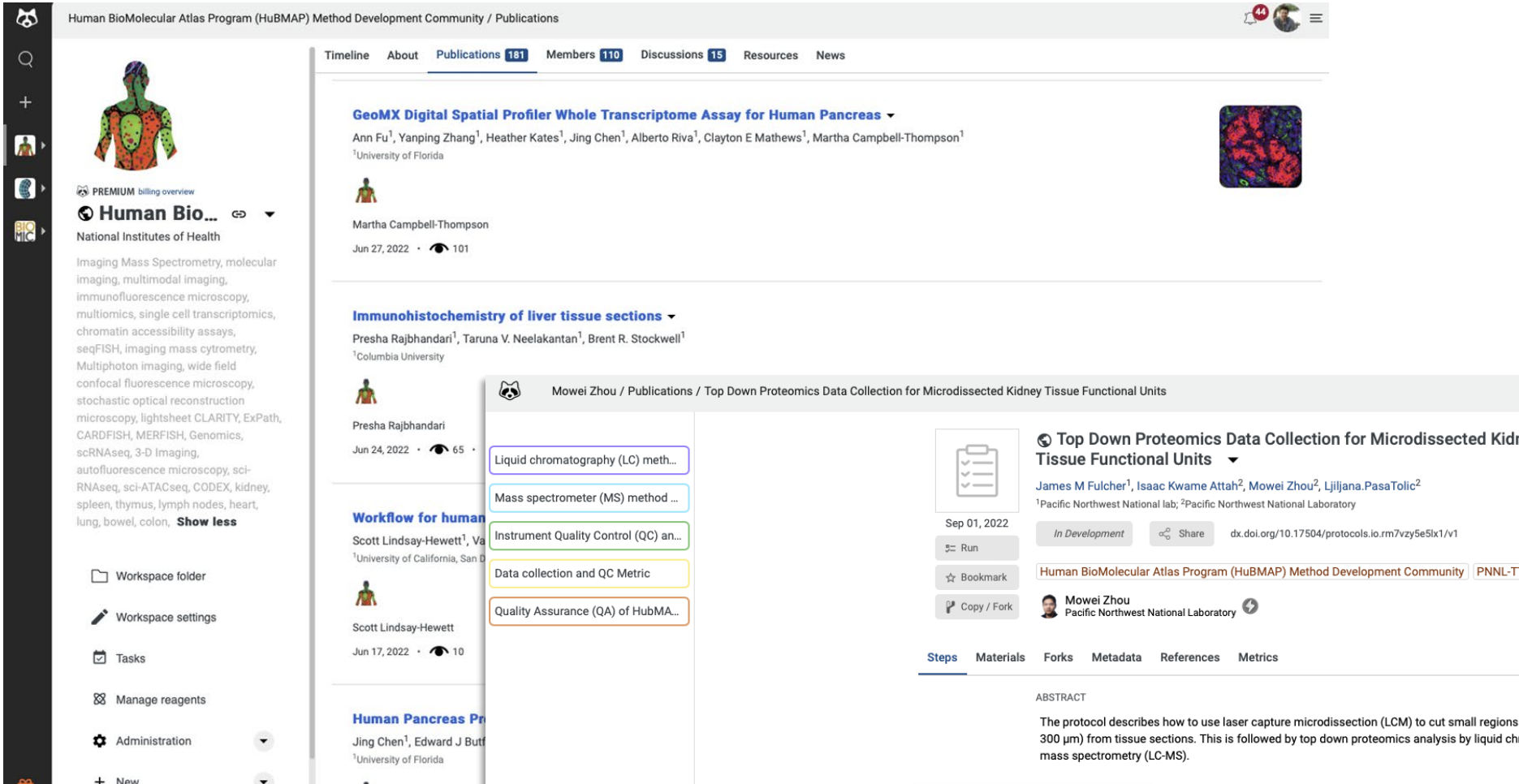


Comparison of Collecting Ducts from Inner and Outer Medulla

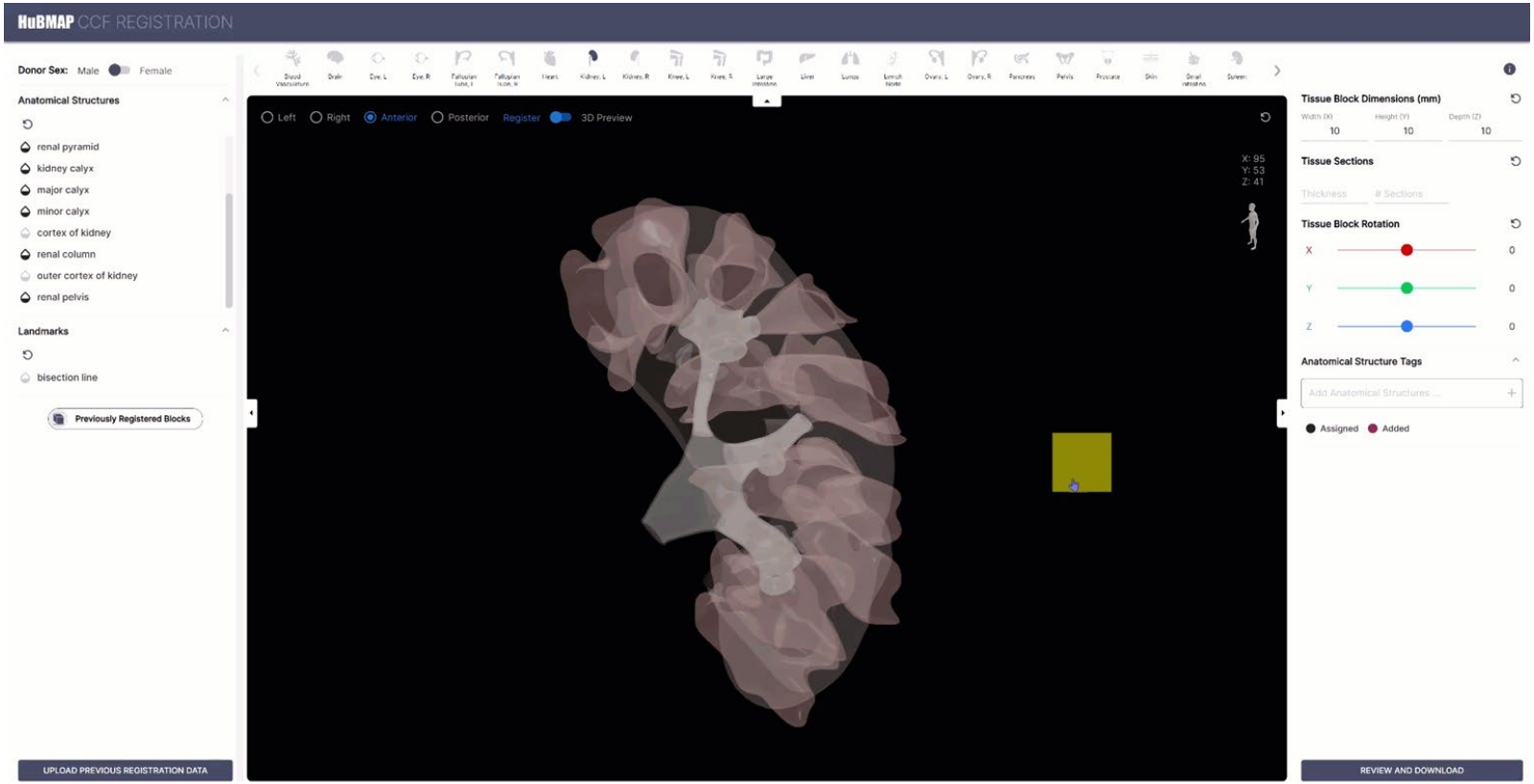


HuBMAP Protocols

Protocols.io / 181 published protocols as of Sept. 2022

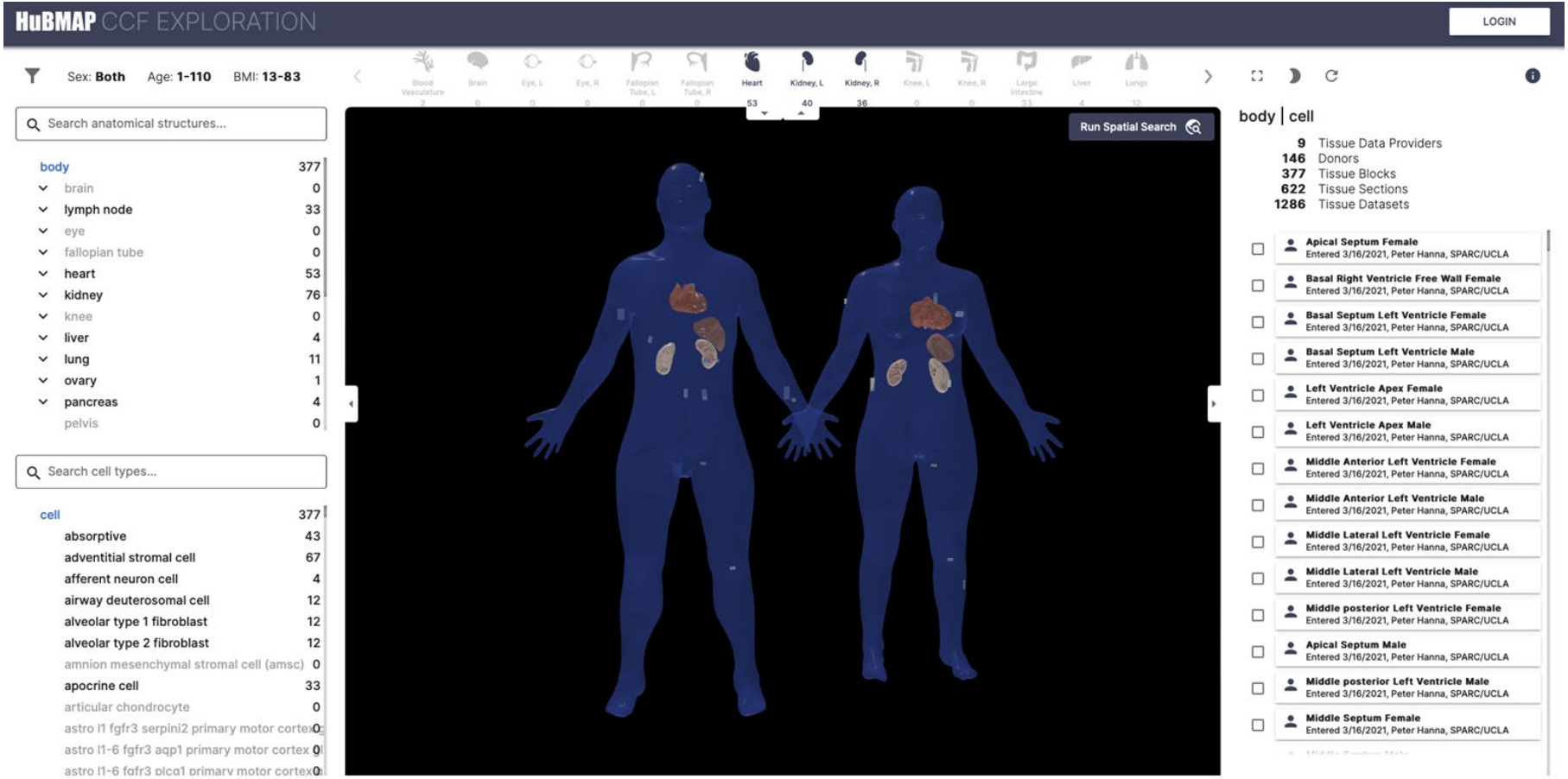


CCF Registration User Interface (RUI)



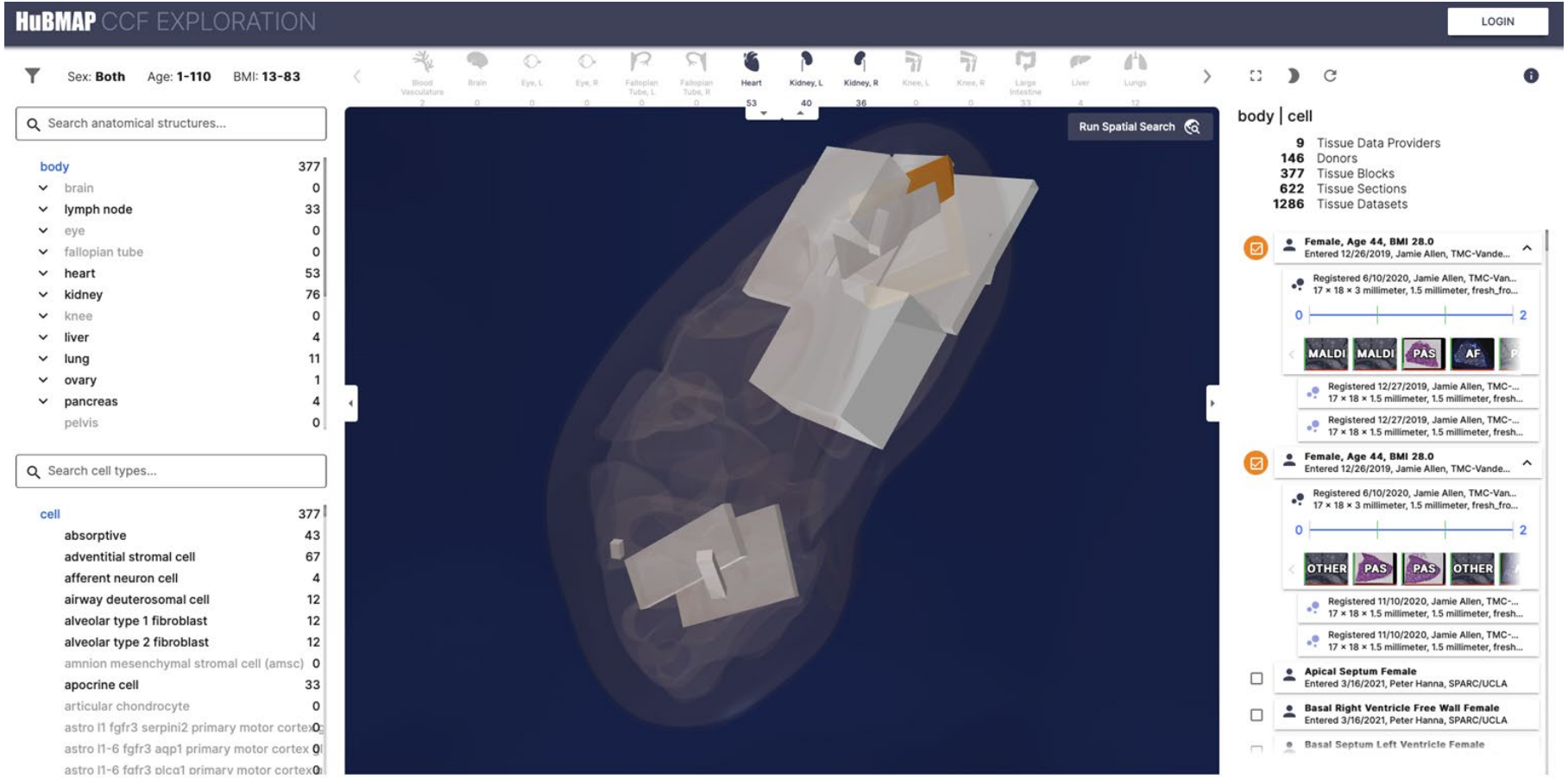
https://hubmapconsortium.github.io/ccf-ui/rui/

CCF Exploration User Interface (EUI)



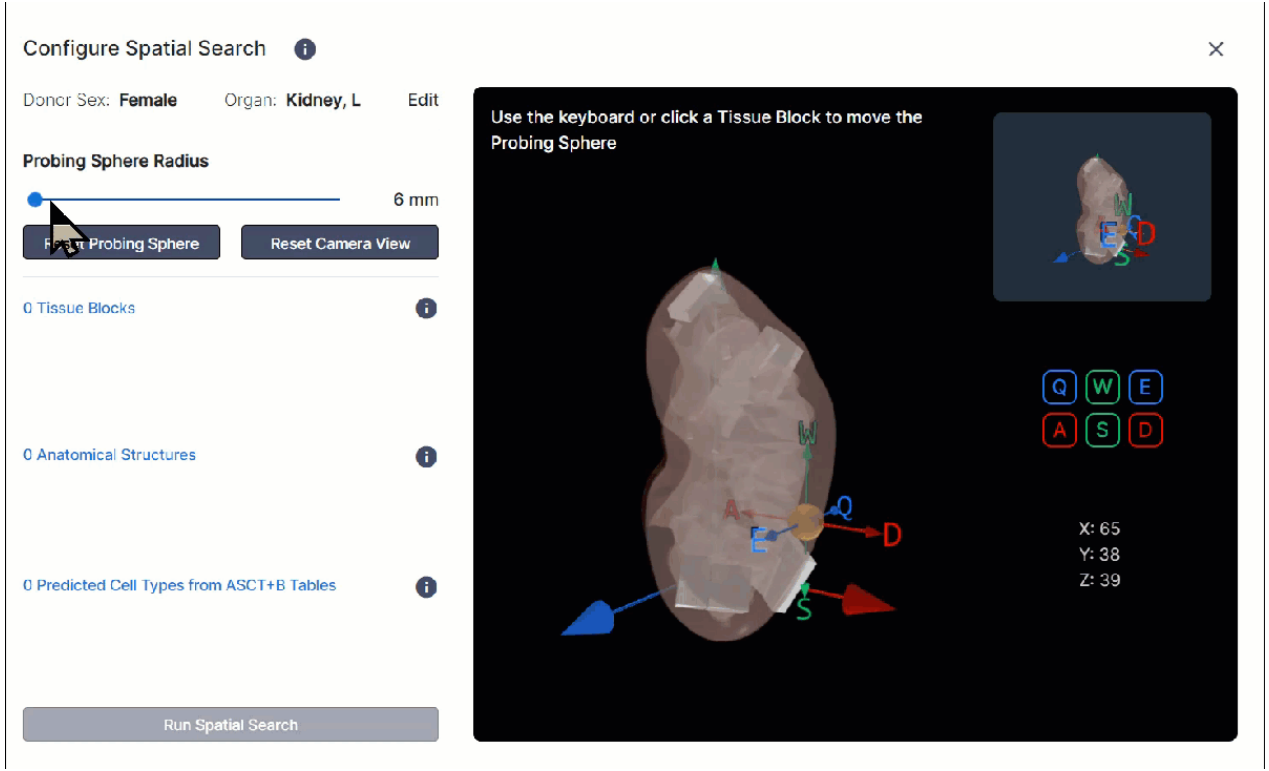
https://portal.hubmapconsortium.org/ccf-eui

CCF Exploration User Interface (EUI)



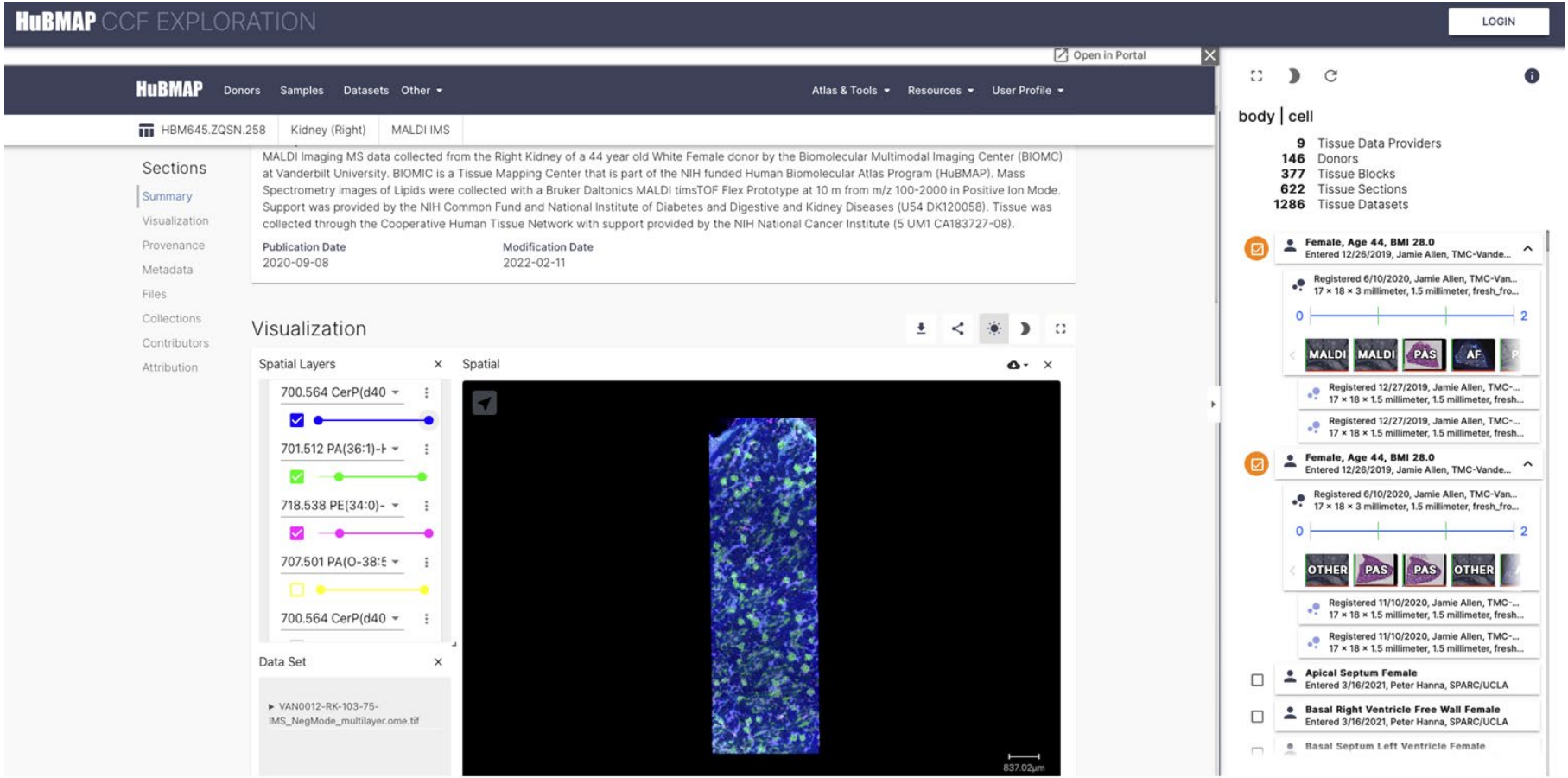
https://portal.hubmapconsortium.org/ccf-eui

CCF Exploration User Interface (EUI) - Spatial Search



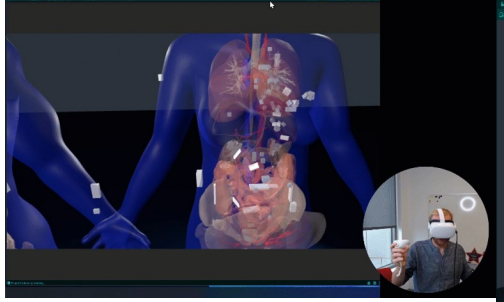
https://portal.hubmapconsortium.org/ccf-eui

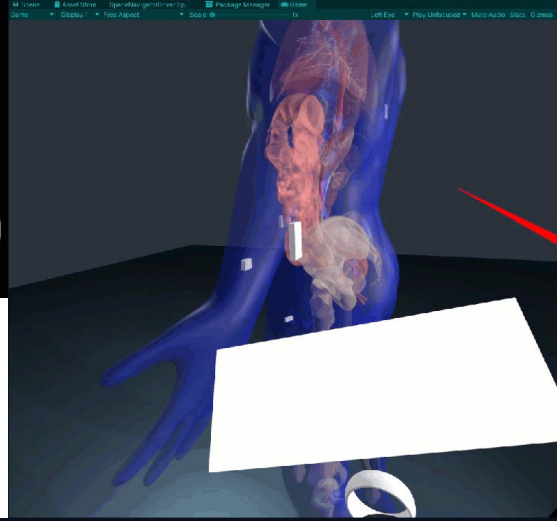
CCF Exploration User Interface (EUI) & Vitessce



https://portal.hubmapconsortium.org/ccf-eui

CCF VR Organ Gallery





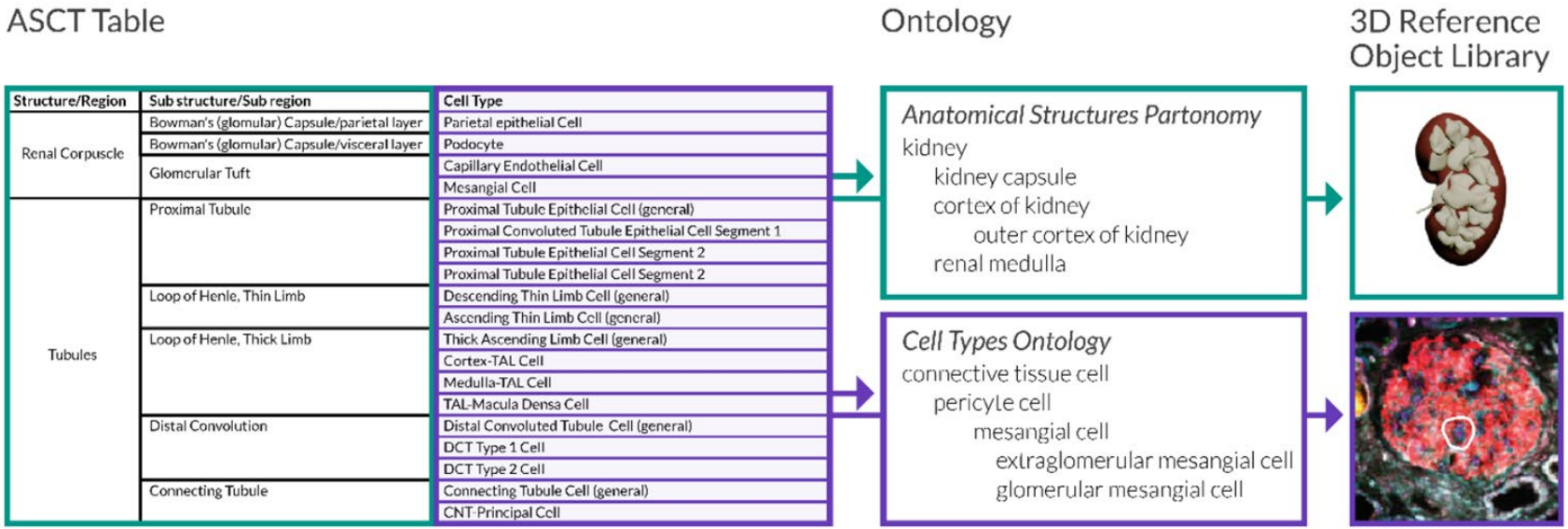
- Immersive application to view, explore, and analyze 3D reference organs, anatomical structures, and cell types
- Preserves spatiality when displaying registered tissue blocks
- Embeds biological structure in 3D space
- Allows user to subset tissue blocks and cell type counts by clinical metadata (age, sex, BMI)
- Uses CCF API to retrieve up-to-date 3D organs and tissue blocks
- Interested in becoming a tester? Contact Andreas Bueckle at abueckle@iu.edu
- More info:
  - Preprint: 10.31219/osf.io/z9gm3
  - Research demo: https://youtu.be/S9pBOlSfsnc

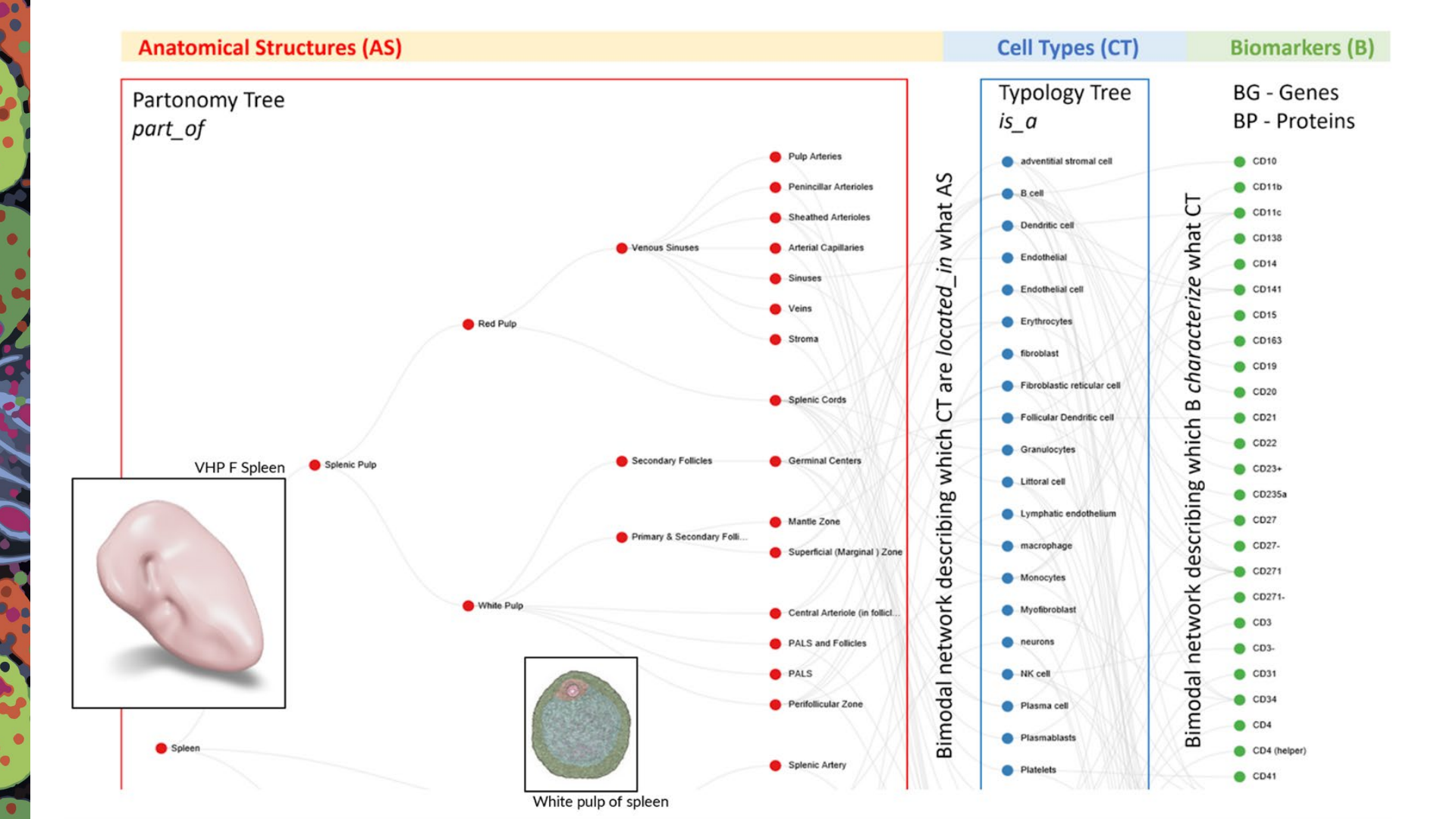
https://hubmapconsortium.github.io/ccf/pages/ccf-gallery.html

ASCT+B Tables

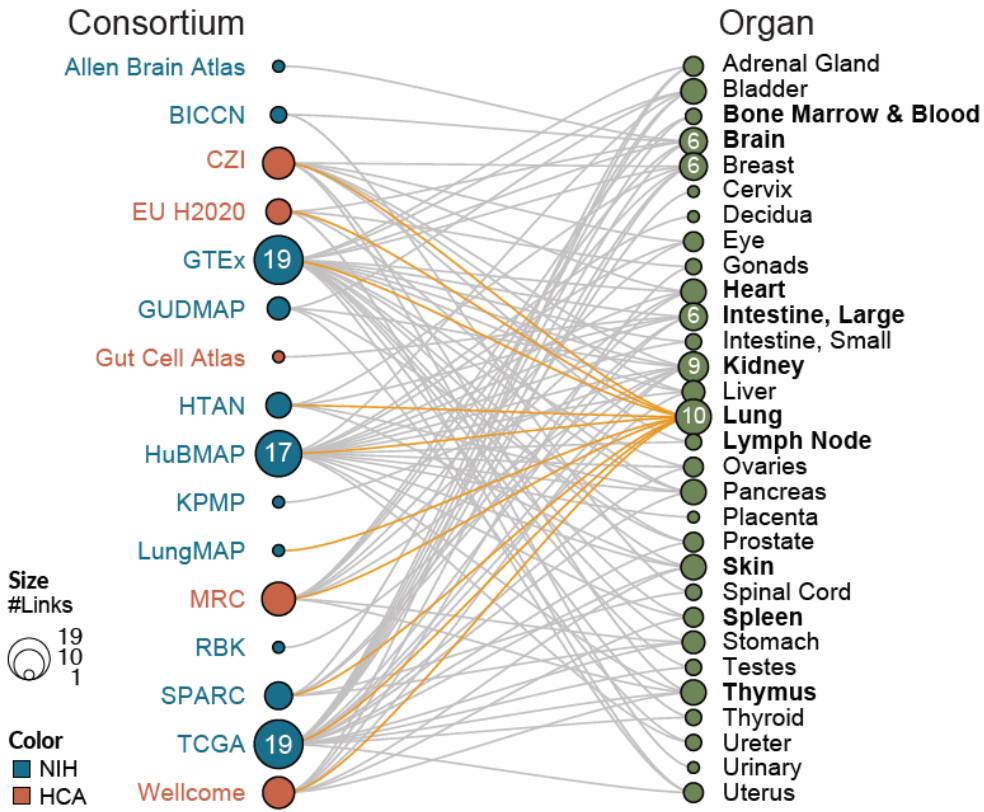
Anatomical Structures (AS), Cell Types (CT), and Biomarkers (B) or ASCT+B tables aim to capture the partonomy of anatomical structures, cell types, and major biomarkers (e.g., gene, protein, lipid or metabolic markers).

They are ESSENTIAL for developing AS partonomies, CT typologies, and 3D reference objects across scales -- from body to functional tissue unit (FTU) to cell.




Anatomical Structures (AS)
Cell Types (CT)
Biomarkers (B)
Partonomy Tree
part_of
Typology Tree
is_a
BG - Genes
BP - Proteins
Spleen
Splenic Pulp
Red Pulp
White Pulp
Venous Sinuses
Secondary Follicles
Primary & Secondary Folli...
Pulp Arteries
Penicillar Arterioles
Sheathed Arterioles
Arterial Capillaries
Sinuses
Veins
Stroma
Splenic Cords
Germinal Centers
Mantle Zone
Superficial (Marginal) Zone
Central Arteriole (in follicl...
PALS and Follicles
PALS
Perifollicular Zone
Splenic Artery
VHP F Spleen
White pulp of spleen
Bimodal network describing which CT are located_in what AS
adventitial stromal cell
B cell
Dendritic cell
Endothelial
Endothelial cell
Erythrocytes
fibroblast
Fibroblastic reticular cell
Follicular Dendritic cell
Granulocytes
Littoral cell
Lymphatic endothelium
macrophage
Monocytes
Myofibroblast
neurons
NK cell
Plasma cell
Plasmablasts
Platelets
Bimodal network describing which B characterize what CT
CD10
CD11b
CD11c
CD138
CD14
CD141
CD15
CD163
CD19
CD20
CD21
CD22
CD23+
CD235a
CD27
CD27-
CD271
CD271-
CD3
CD3-
CD31
CD34
CD4
CD4 (helper)
CD41

Constructing a Human Reference Atlas - Together!



Azimuth

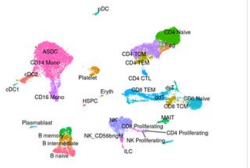
https://azimuth.hubmapconsortium.org

9 references and 1,036 cell types

> 12,000 datasets uploaded and mapped from the community

> 187,000,000 cells uploaded and mapped from the community

Human - PBMC

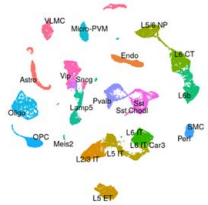


Learn more | Go to App

Human - Motor Cortex

Learn more | Go to App

Mouse - Motor Cortex

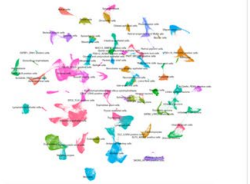


Learn more | Go to App

Human - Pancreas

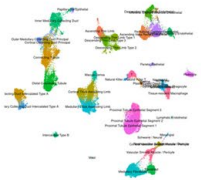
Learn more | Go to App

Human - Fetal Development



Learn more | Go to App

Human - Kidney



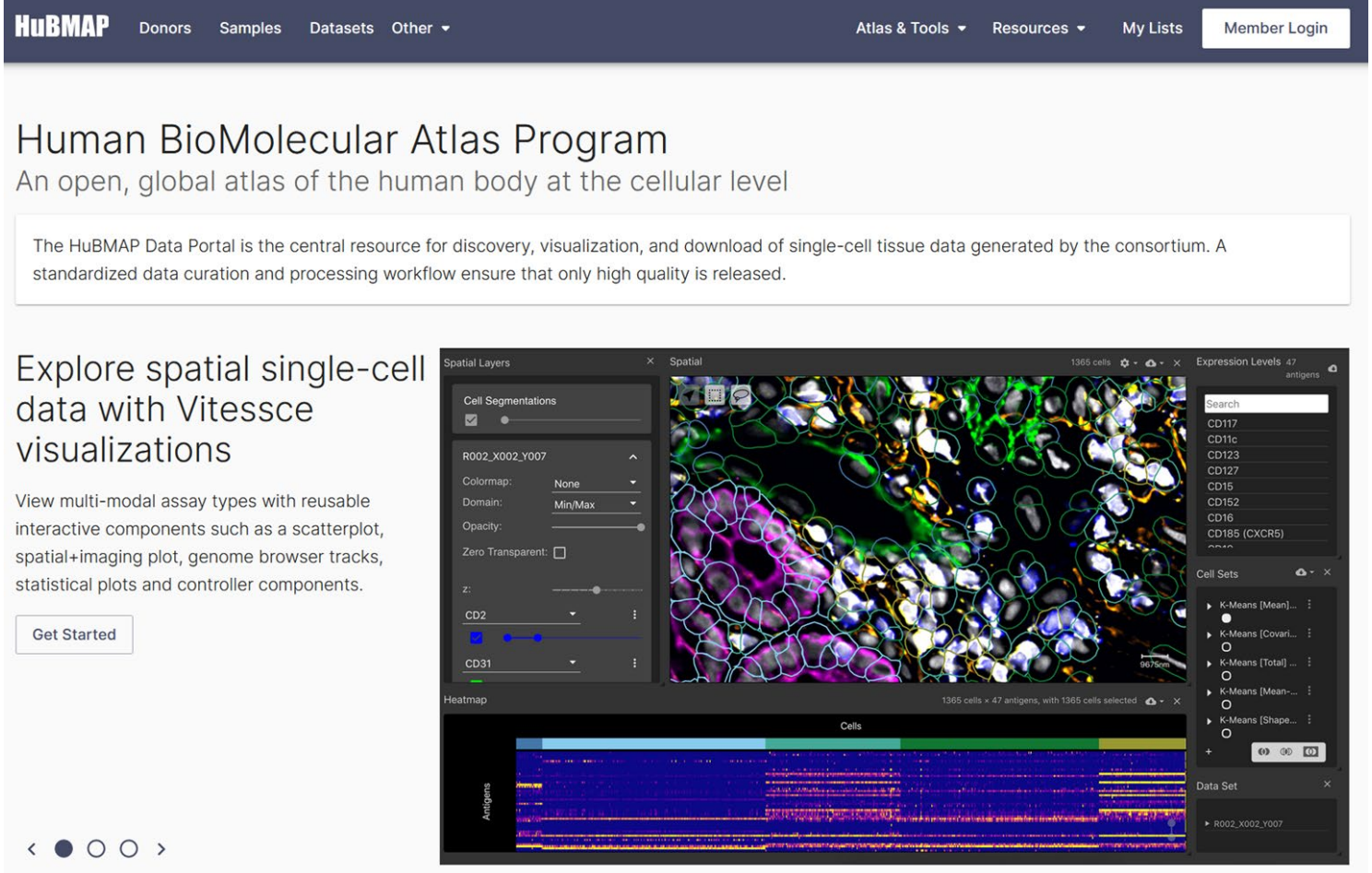
Learn more | Go to App

Human - Bone Marrow

Learn more | Go to App

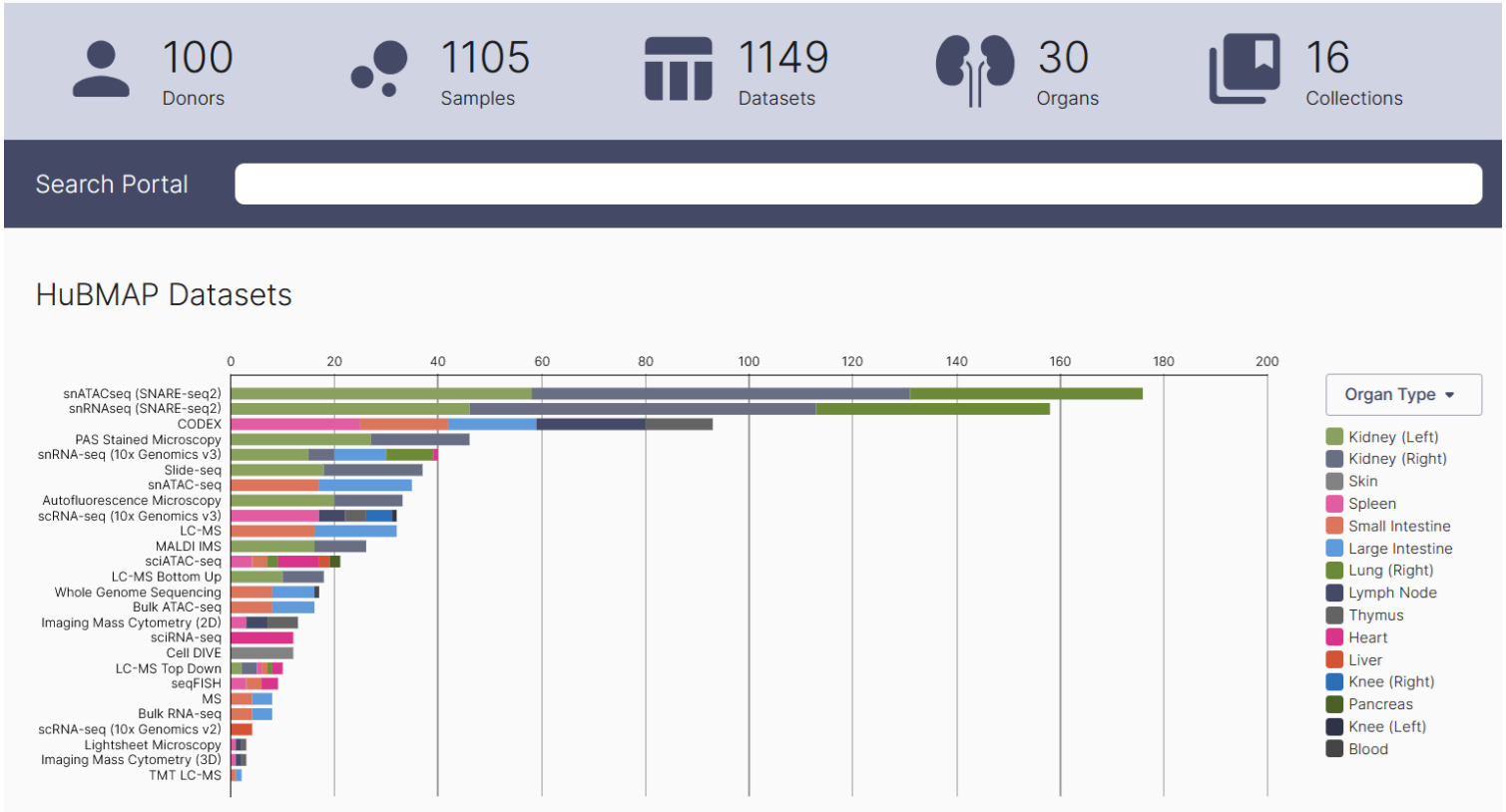
Human - Lung v2 (HLCA)

Learn more | Go to App



https://portal.hubmapconsortium.org

In October 2022



https://portal.hubmapconsortium.org

30 organs / 24 assay types

HuBMAP Training

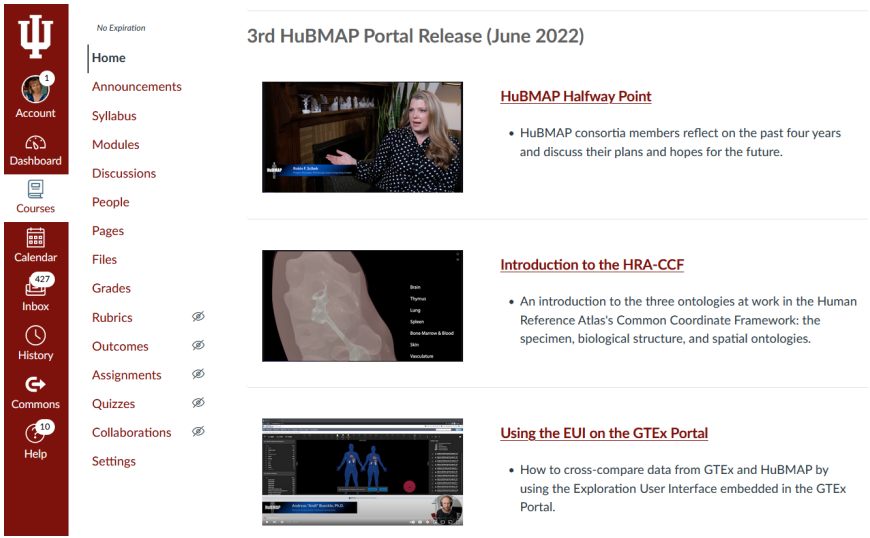
https://expand.iu.edu/browse/sice/cns/courses/hubmap-visible-human-mooc

HuBMAP Visible Human MOOC (VHMOOC)

Started Aug 4, 2020

GO TO CANVAS COURSE

You are enrolled.



INDIANA UNIVERSITY

Course Introduction

This 10h course introduces the HuBMAP project which aims to create an open, global reference atlas of the human body at the cellular level. Among others, the course describes the compilation and coverage of HuBMAP data, demonstrates new single-cell analysis and mapping techniques, and introduces major features of the HuBMAP portal.

Delivered entirely online, all coursework can be completed asynchronously to fit busy schedules. If you have questions or experience issues during registration, please email cnscntr@indiana.edu.

Learning Outcomes

- Theoretical and practical understanding of different single-cell tissue analysis techniques.
- Expertise in single-cell data harmonization used to federate data from different individuals analyzed using different technologies in diverse labs.
- Hands-on skills in the design and usage of semantic ontologies that describe human anatomy, cell types, and biomarkers (e.g., marker genes or proteins).
- Knowledge on the design and usage of a semantically annotated three-dimensional reference system for the healthy human body.
- An understanding of how the HuBMAP reference atlas might be used to understand human health but also to diagnose and treat disease.

Module Topics Include

- HuBMAP Overview: Project Goals, Setup, and Ambitions
- Tissue Data Acquisition and Analysis
- Biomolecular Data Harmonization
- Ontology, 3D Reference Objects, and User Interfaces
- HuBMAP Portal Design and Usage

Meet the Instructors

Katy Börner, Victor H. Yngve Distinguished Professor of Engineering and Information Science. Founding Director of the Cyberinfrastructure for Network Science Center at Indiana University.

Ellen M. Quardokus, staff in the Chemistry Department and research scientist, Cyberinfrastructure for Network Science Center, SICE with expertise in molecular biology, microscopy, anatomy, and interdisciplinary communication.

Andreas Bueckle, PhD Candidate in Information Science, performing research on information visualization, specifically virtual and augmented reality.

Length: 10 hours

Department: Cyberinfrastructure Network Science

Credit: None

Audience: Biomedical students and professionals interested in single-cell tissue analysis and visualization

HuBMAP Training

Undergraduate Summer Internships 2022

Awarded interns and placements

Fransiskus Agapa | Blood Lab - Pittsburgh Supercomputing Center
Gabrielle Lenoir | Kim Lab - University of Pennsylvania
Mohamed El Sadec | Gregory Lab - University of Pennsylvania
Marielena Grijalva | O'Neill Lab - University of Pennsylvania
Camryn Pettinger-Willey | Pasa-Tolic Lab - Pacific Northwest National Laboratory
Karli Prather | Pouch/Gee Lab - University of Pennsylvania
Li Xu | Spraggins Lab - Vanderbilt University
MJ Hopkins | Hagood Lab - University of North Carolina
Tran Nguyen | Gehlenborg Lab - Harvard Medical School
Anusha Thaniana | Pei Lab - Children's Hospital of Philadelphia
Lesley Aguilar Salceda | Satija Lab - New York Genome Center
Genna Mahabeer | Liu Lab - Northwestern University
Sangmyung Lee | Borner Lab - Indiana University, Bloomington

Undergraduate Summer Internships 2021

Awarded interns and placements

Roselkis Morla Adames | Gehlenborg Lab - Harvard Medical School
Oluwafolajinmi Olugbodi | Kim Lab - University of Pennsylvania
Kate da Silva | Kim Lab - University of Pennsylvania
Lester Casey Henson | PICSL - University of Pennsylvania
Injyil Gates | Nolan Lab - Stanford University
Ogechukwu Etuazim | O'Neill Lab - University of Pennsylvania
Stephanie Bobadilla-Regalado | Gregory Lab - University of Pennsylvania
Tatiana Gonzalez | Gregory Lab - University of Pennsylvania

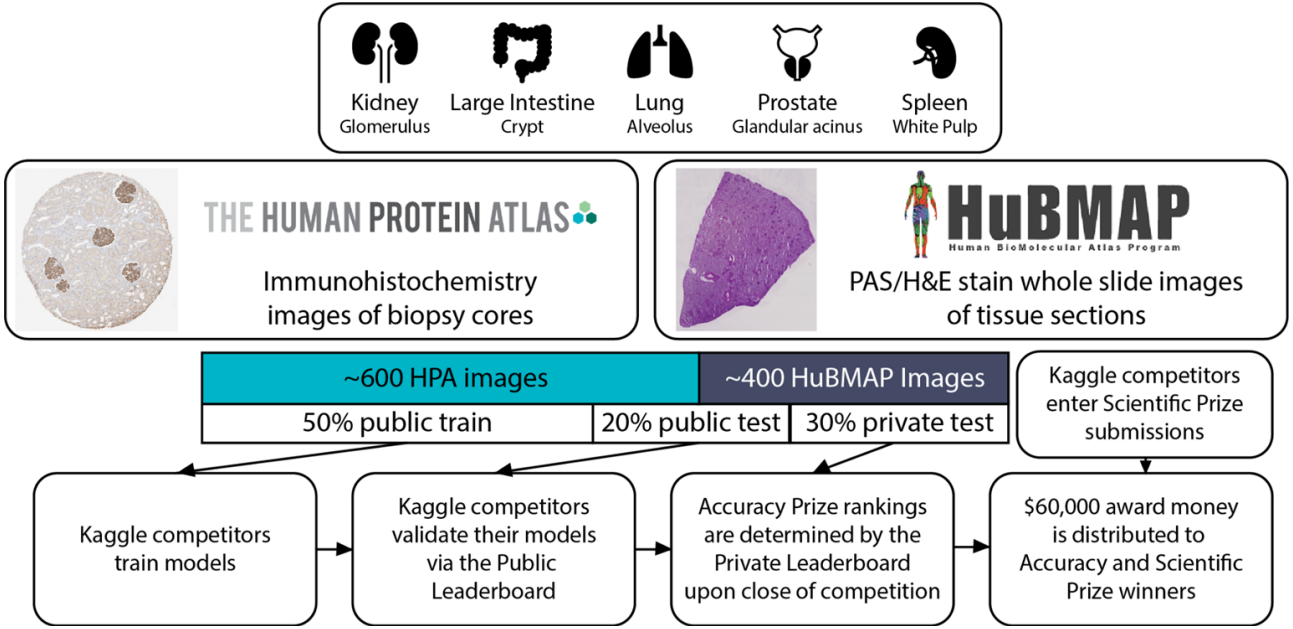
JumpStart Awardees 2021

Yang Liu	**Project Title:** Spatial multi-omics profiling of human kidney tissue using DBiT-seq **HuMAP Lab:** Yale TMC
Angela Kruse	**Project Title:** 3 D Multimodal Analysis of Eye and Pancreas Blocks Using Light Sheet Microscopy and Imaging Mass Spectrometry **HuMAP Lab:** Vanderbilt TMC
Hang Hu	**Project Title:** Self-supervised Mass Spectrometry Imaging Clustering with Convolutional Neural Network and Contrastive Learning **HuMAP Lab:** Purdue TTD

NIH Junior Investigator Meeting 2023

- **Goal**: The meeting will conduct several workshops with potential topics ranging from career development to equity in science to the academic vs. industrial world. For this meeting, we are planning to have several inter-consortia networking sessions with activities, expert subgroup meetings, and freeform discussions based on abstract topics from the attendees. Multiple plenary talks are being planned at the moment.
- **Dates**: March 1-3, 2023
- **Venue**: Cornell Graduate Hotel in NYC, and virtually
- **Who can attend**: For the purposes of this meeting, a ‘junior investigator’ is defined as a graduate student, postdoc, staff scientist, or early-career faculty.
- **More information**: A website with more details as well as registration will become available later this year.

HuBMAP-HPA Kaggle Competition



Accuracy Prizes:

- First Place: $15,000
- Second Place: $10,000
- Third Place: $5,000

Judges Prizes:

- Scientific Prizes: 2 x $10,000
- Diversity Prize: $10,000

The challenge asked teams from around the globe to develop robust and generalizable machine learning algorithms that correctly segment FTUs of different shapes and sizes across five organs (large intestine, kidney, lung, prostate, and spleen), see https://www.kaggle.com/competitions/hubmap-organ-segmentation

Two more competitions are planned with a focus on Vasculature CCF, see https://doi.org/10.3389/fcvm.2020.00029

Production Phase (2022 - 2026)

3D Maps and Reference Datasets

- Common data types: RNAseq, multiplexed IF, histology datasets
- Build bridging datasets to link data types
    - Continue work on generalization of cell x gene data
- Azimuth maps for: kidney (Jain, Spraggins), lung (Pryhuber), colon (Snyder), bone marrow (Bendall, Tan), female reproductive system (Kim, Laurent), pancreas (Qian, Spraggins), heart (Tan), eye (Spraggins), skin (Ginty, Wirtz), bone (Rowe), and lymphatics (Singhal)
- Identify and generate exemplary 2D maps of FTUs
- Cross-walk experimental data to the Human Reference Atlas
- Build out Antibody Characterization / Validation Reports (AvRs) & Organ Mapping Antibody Panels (OMAPs)

Production Phase (2022 - 2026)

Demo and Collaborative Projects

- Integration with MatrisomeDB (Naba)
- Identification of Organotypic Vasculature (Gupta)
- Reverse Engineering Ovarian Organization (Laronda)
- Identification of mitochondria variants (Pei)
- Multi-tissue analysis from single donors (Pryhuber)

Outreach and Collaboration

- Continue Junior Investigators meetings, Jumpstart, Summer Internships, Kaggles…
- Organization joint workshops / meetings (e.g., HPAP)
- Plans for Enhancing Diverse Perspectives (PEDPs)
- Open Working Groups - ASCT+B, Affinity Reagents, Data Visualization [new]

Thank you!