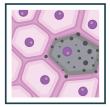

SenNet

Why + How We Construct the Human Reference Atlas

Katy Börner
(CODCC, Indiana University)

February 22, 2023

MC-IU HuBMAP+SenNet Team in Bloomington, IN

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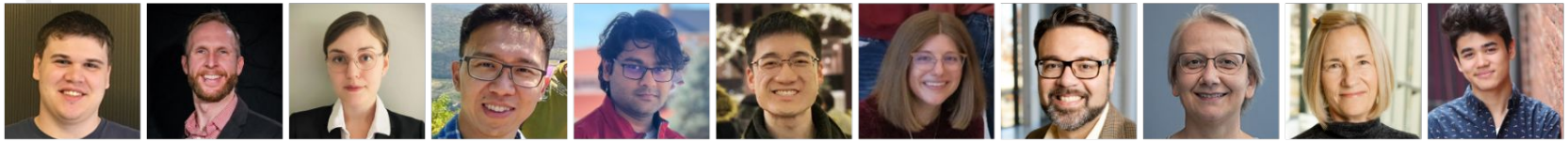
CNS Associate Director

David Van Valen
Assistant Professor of Biology and Biological Engineering & Investigator

Fusheng Wang
Associate Professor of Biomedical Informatics and Computer Science

Griffin Weber
Associate Professor of Medicine

Full Time Staff



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Research Software Engineer (Machine Learning)

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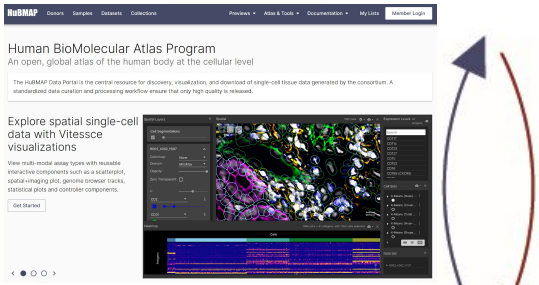
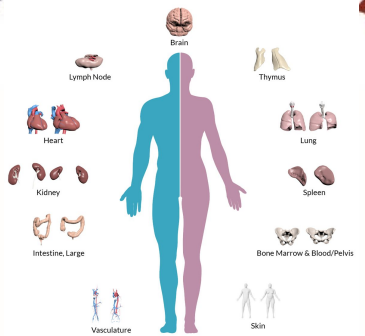
Funded by HuBMAP and SenNet and the ATLAS efforts within KPMP, GUDMAP4, CFDE.

NATIONAL INSTITUTES OF HEALTH

Why construct a Human Reference Atlas (HRA)?



Data Generation, Harmonization and Integration



Human Reference Atlas (HRA)

Advance Research Improve Human Health

https://doi.org/10.1038/s43587-022-00326-5

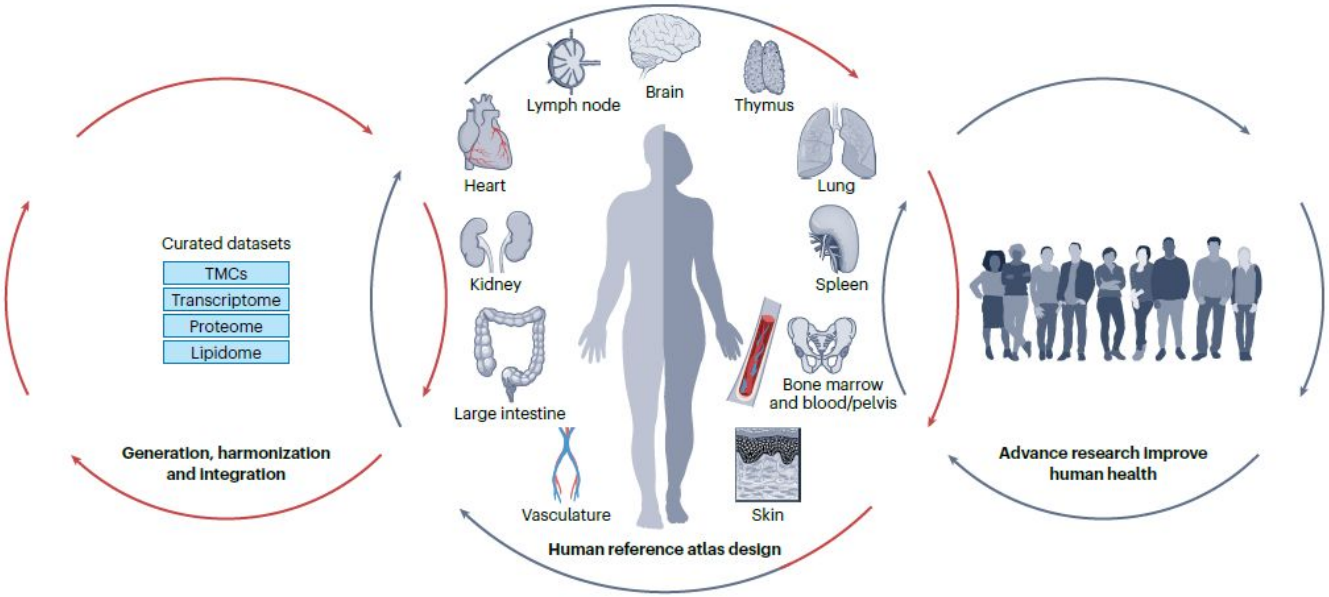
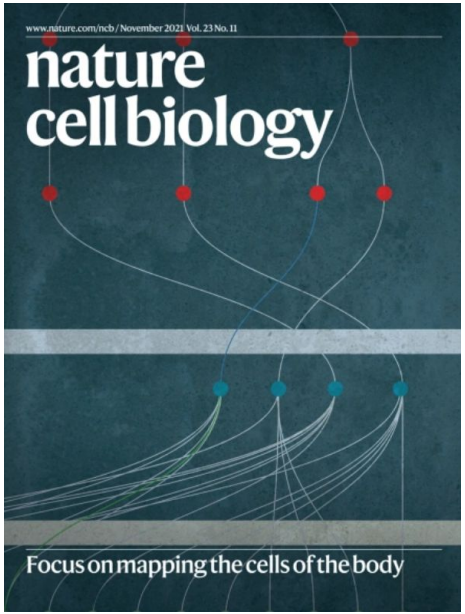


Fig. 5 | Schematic of the SenNet Consortium goals. SnC atlas building requires a framework for layering data. Data generated by the TMCs and TDA sites are input into the CODCC along with associated metadata. The datasets are organized and de-identified (curation), then analyzed and integrated. The goal is to create an atlas and public database of curated data that can be searched, analyzed and visualized as 3D images of organs using unified annotations. High-quality experimental data are needed to create a human reference atlas. The evolving reference atlas supports data standardization and federation, making it possible to integrate data from different specimens, laboratories and assay types. The atlas characterizes the healthy human—from the whole body down to the single-cell level; it can be compared across ages and diseases to understand differences, advance research and improve human health. Use case scenarios for different stakeholders (researchers, practitioners and students) guide atlas construction and usage but also experimental data acquisition and analysis. Of note, diversity in terms of human participant gender, race and socioeconomic status is emphasized in SenNet. However, these variables may impact SnC heterogeneity even further, meaning that, in the timeframe of the initial grants, statistically meaningful characterization of SnCs across diverse populations might not be achieved.

Defining the Human Reference Atlas (HRA)

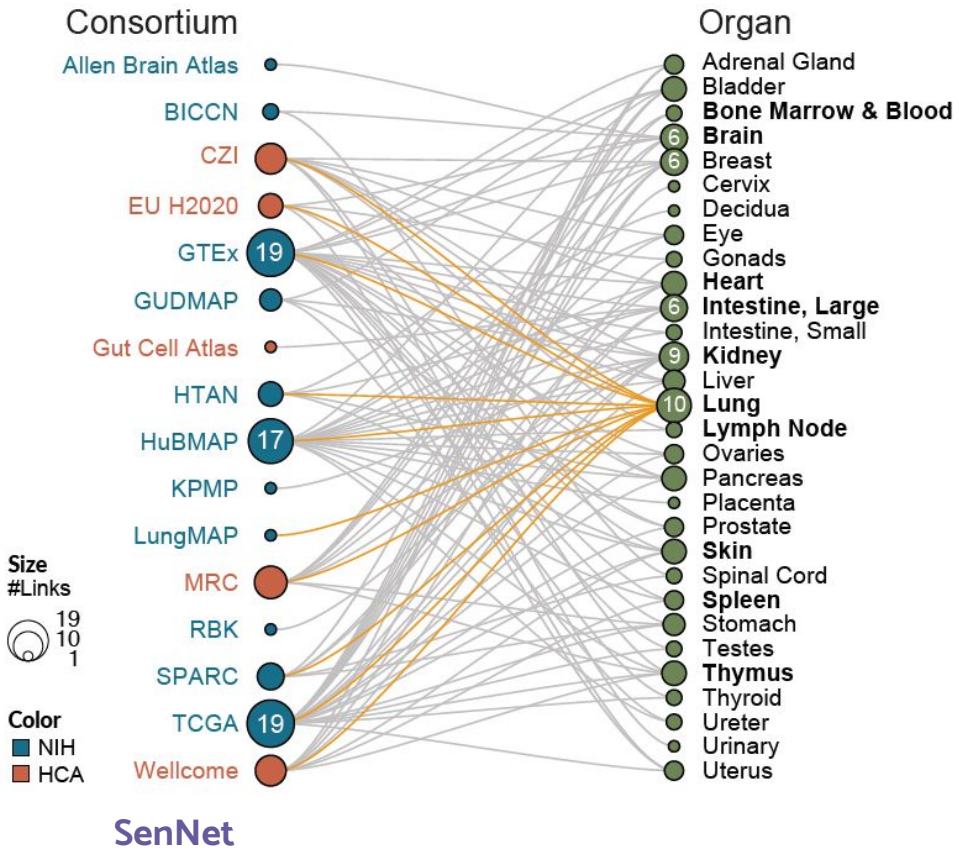
The Human Reference Atlas (HRA)

1. defines the 3D space and shape of anatomical structures and cell types that are of biomedical relevance plus the biomarkers used to characterize them. Anatomical structures, cell types and biomarkers are validated and represented in/added to ontologies (Uberon/FMA, CL, HGNC).
2. defines how new datasets can be mapped to the HRA, e.g., spatially using the Visible Human CCF or Vasculature CCF, via ASCT+B ontology terms/IDs, or via gene expression data as in Azimuth.
3. it is
    - authoritative (there exists expert agreement and it was validated by data),
    - computable (supports API queries, UIs),
    - published as LOD (connected to gene, disease, and other ontologies and data),
    - open (anyone can use the HRA data and code), and
    - continuously evolving (e.g., as new technologies become available).



https://www.nature.com/articles/s41556-021-00788-6

Constructing the Human Reference Atlas – Together!



SenNet

https://doi.org/10.1038/s43587-022-00326-5

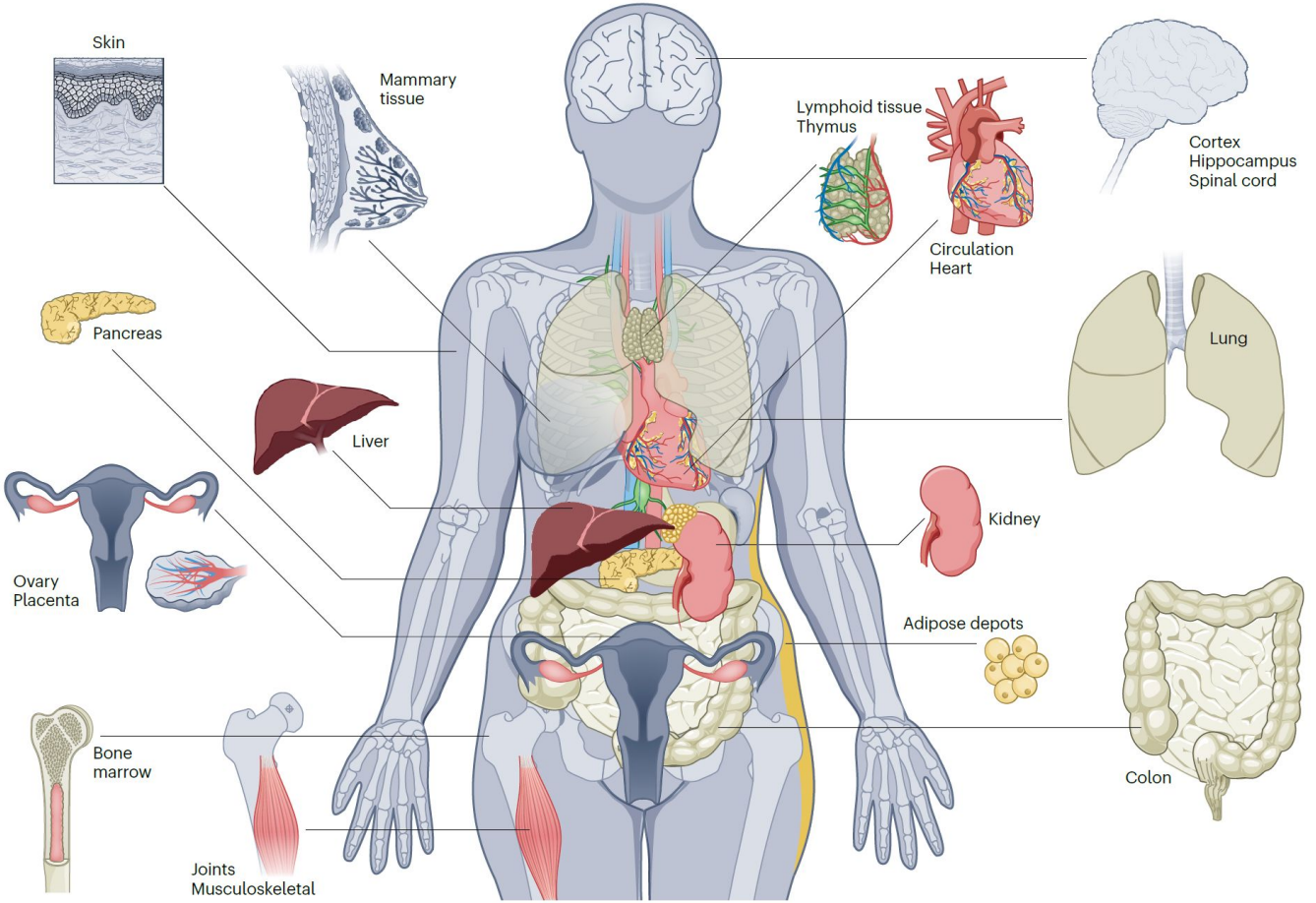


Fig. 2 | Organs in which SnCs will be mapped by SenNet. Human tissues in which SnCs will be identified and characterized by the SenNet Consortium to produce 4D atlases of senescence across the lifespan of humans.

Assay Types

https://doi.org/10.1038/s43587-022-00326-5

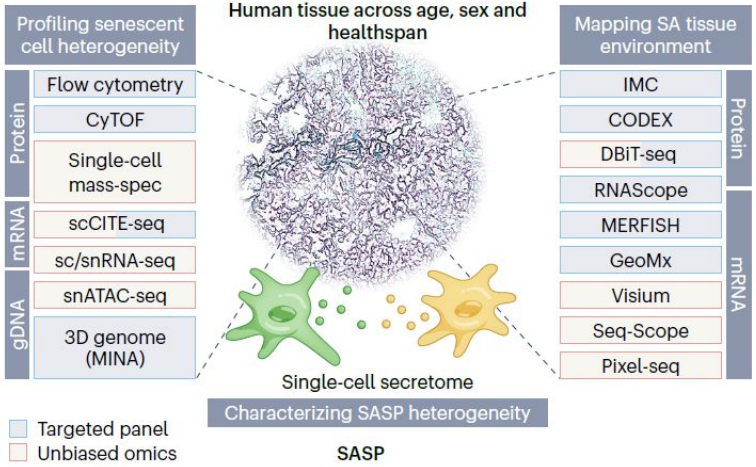


Fig. 3 | Overview of technologies that will be implemented and developed by SenNet Consortium scientists to detect, characterize and spatially map the location of SnCs. CyTOF, cytometry by time-of-flight; scCITE-seq, cellular indexing of transcriptomes and epitopes by sequencing; sc/snRNA-seq, single-cell or single-nucleus RNA sequencing; snATAC-seq, single-nucleus assay for transposase-accessible chromatin using sequencing; MINA, multiplexed imaging of nucleome architectures; IMC, imaging mass cytometry; CODEX, co-detection by indexing immunofluorescence; DBiT-seq, deterministic barcoding in tissue for spatial-omics sequencing for co-mapping mRNAs and proteins; RNAScope, RNA in situ hybridization visualization of single molecules; MERFISH, multiplexed error-robust fluorescence in situ hybridization; GeoMx, NanoString GeoMx digital spatial profiling; Visium, Visium 10x Genomics molecular profiling; Seq-Scope, a spatial barcoding technology with spatial resolution comparable to optical microscopy; Pixel-seq, polony-indexed library sequencing.

Anatomical Structures (AS)

Cell Types (CT)

Biomarkers (B)

Partonomy Tree
part_of

SenNet Organs

Spleen
Splenic Pulp
Red Pulp
Venous Sinuses
Pulp Arteries
Penicillar Arterioles
Sheathed Arterioles
Arterial Capillaries
Sinuses
Veins
Stroma
Splenic Cords
White Pulp
Secondary Follicles
Germinal Centers
Primary & Secondary Folli...
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

Typology Tree
is_a

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

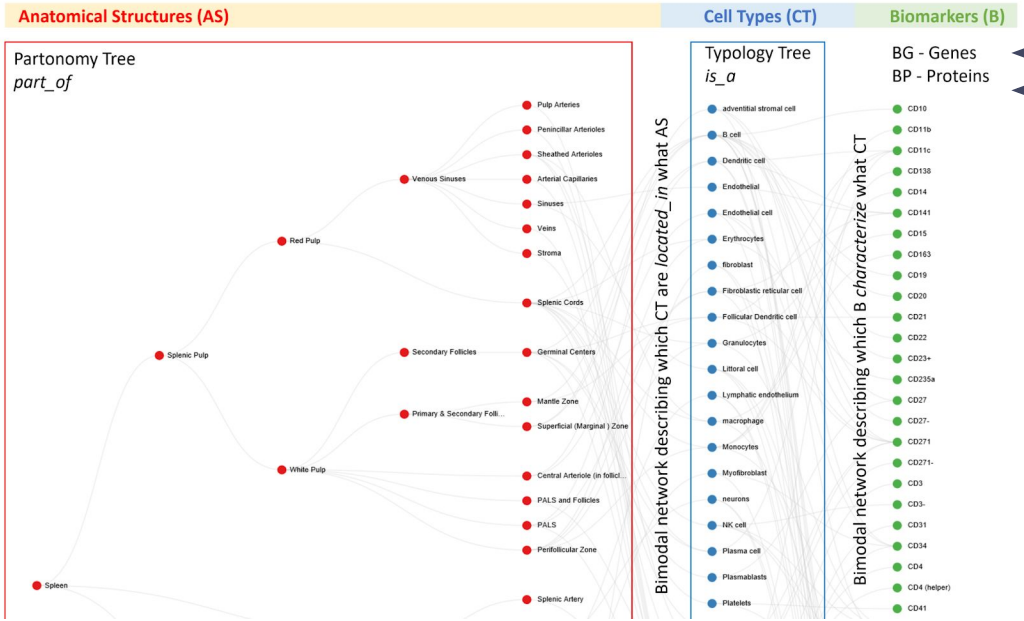
BG - Genes
BP - Proteins

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

SenNet Biomarkers

HRA Validation/ Expansion

New ATLAS publications



2D/3D Maps & Ontology Crosswalks

Azimuth Maps

Validated Antibody Panels (OMAPs)

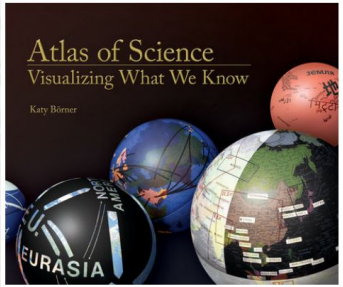
New ATLAS datasets

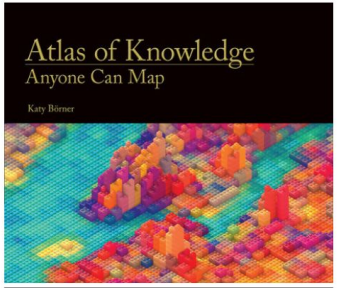
BF – Proteoforms
BL – Lipids
BM – Metabolites

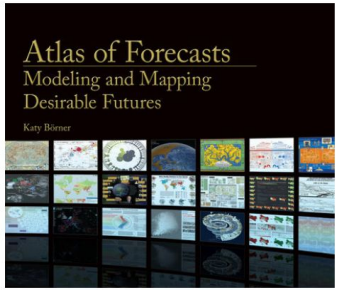
Atlas Construction

Atlas Construction

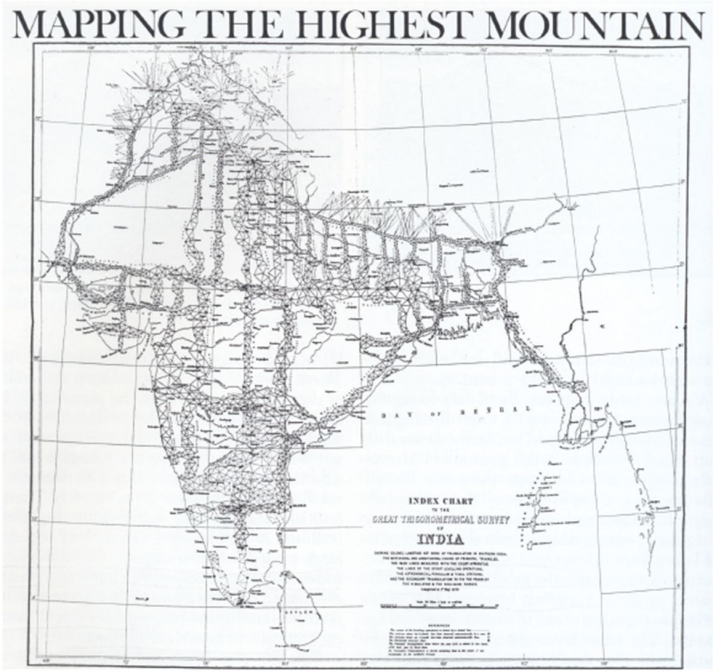
Requires careful data collection and processing, 100% provenance so all results can be reproduced.







https://mitpress.mit.edu/60-off-the-atlas-trilogy-from-katy-borner/



History of Map Mapmaking in *Atlas of Science*

For generations, a vast network of repeating sightline triangles was meticulously measured and recorded. What resembles a pattern of eyelashes on the northern border represents the sightlines to stations built above treetops. While analyzing the triangles in the calculating offices of Calcutta, the mapmakers discovered the highest peak in the world: Mount Everest.

Atlas Construction

Requires careful data collection and processing, 100% provenance so all results can be reproduced.

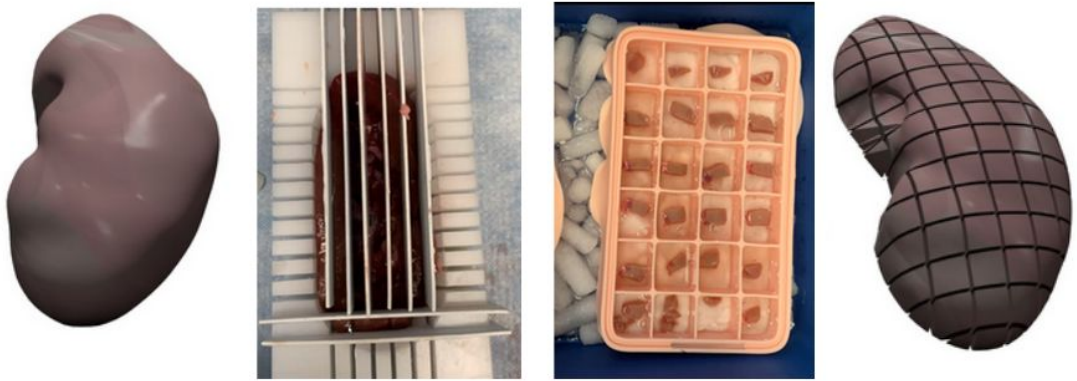
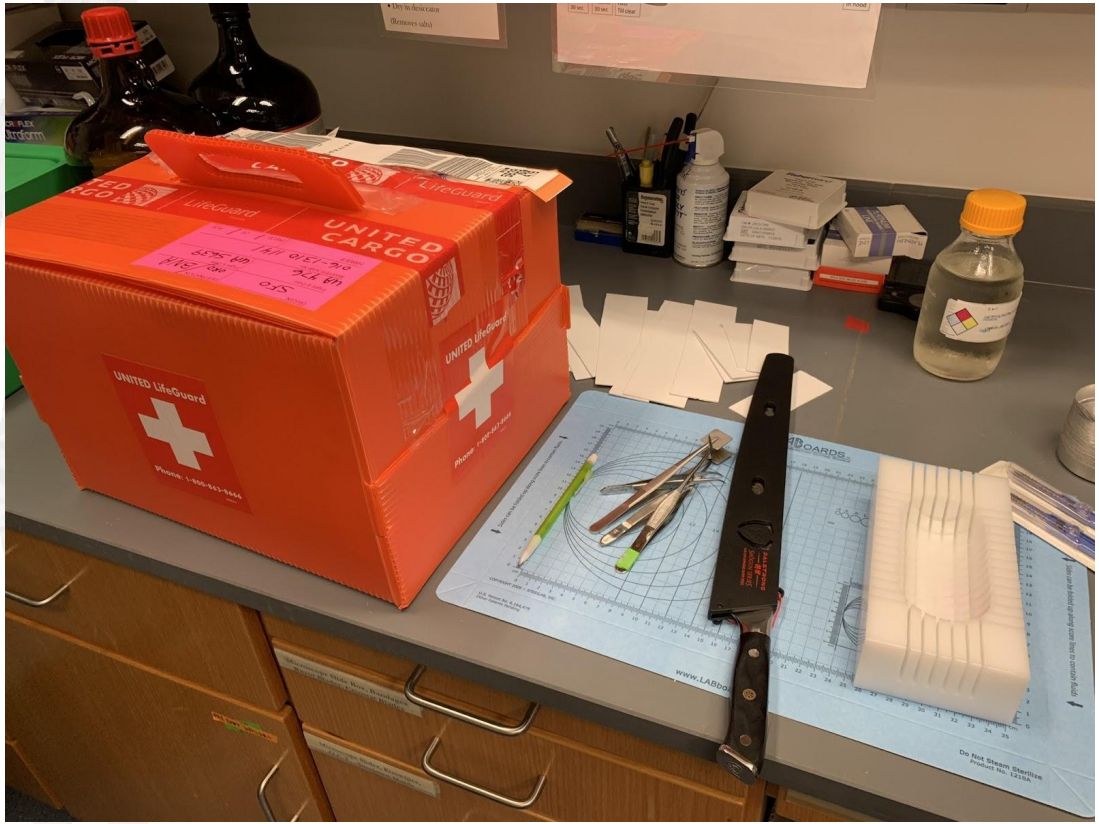
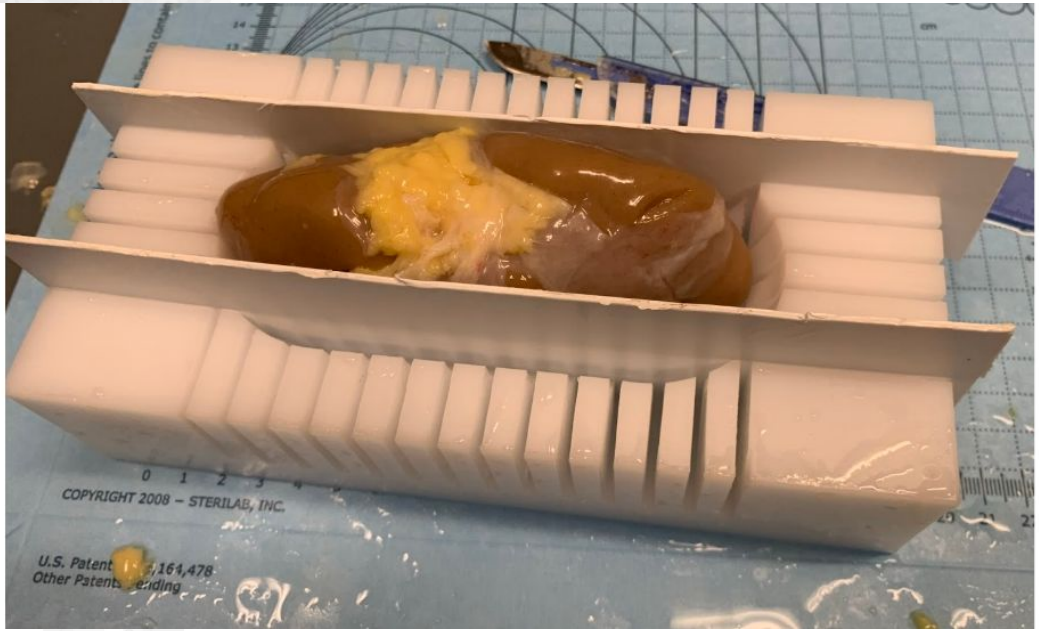


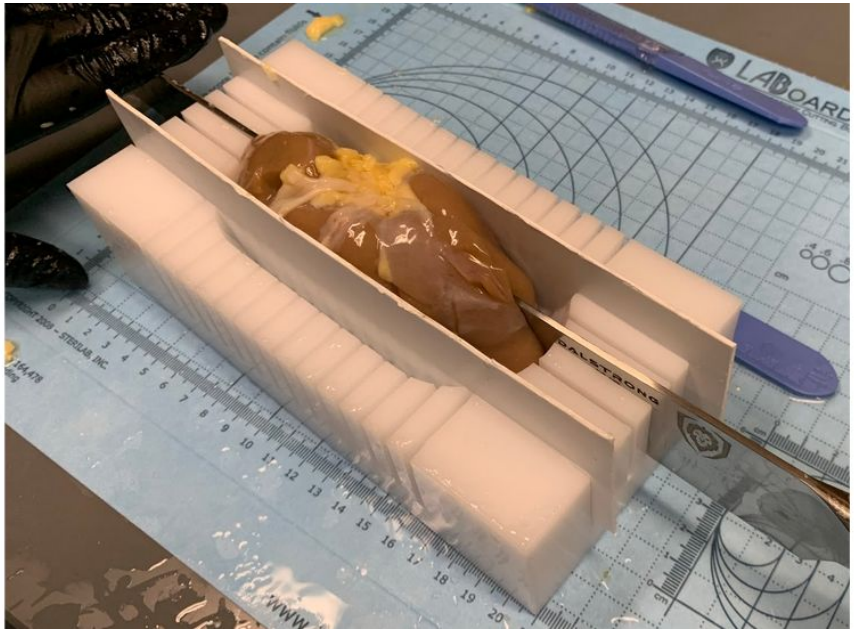
Fig 2. Millitome process for the kidney (from left to right): Digital 3D model of left male kidney, millitome for the lower half of the kidney with 7 x 14 blocks, ice cube tray holding a subset of the tissue blocks, a screenshot showing 98 blocks registered in the EUI.

https://zenodo.org/record/7382704#.Y5Zy7BzMIuU



VU presented process in ASCT+B WG Meeting #22 on Jan 12, 2022, 11a ET





VU presented process in ASCT+B WG Meeting #22 on Jan 12, 2022, 11a ET

VU presented process in ASCT+B WG Meeting #22 on Jan 12, 2022, 11a ET

Atlas Construction

Requires careful data collection and processing, 100% provenance so all results can be reproduced.

Please make sure to generate/share for each tissue block/section/suspension

- All essential donor, organ, sample, and assay metadata
- Spatial RUI registration data
- High-resolution histopathology images--used for AS and FTU segmentation
- scRNAseq data--to generate cell type annotations via Azimuth
- CODEX/CellDive/MxIF--use/contribute to OMAPs, see next slide

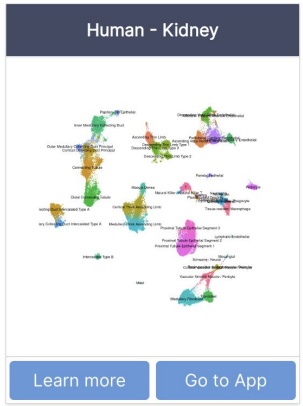
In addition, please consider

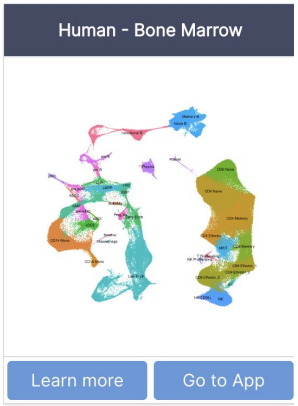
- Running the assays on the same or adjacent tissue sections
- Utilization of biomarkers mapped to ASCT+B via Azimuth references and OMAPs

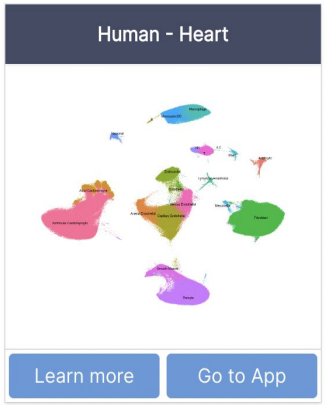
Azimuth Reference Mapping

Mapping to Azimuth Single-cell References:

- Enables integration, re-use, and comparison of data across labs and consortia
- Encourages community adoption of ontologies and standards
- Projects HuBMAP data into consistent cell labels







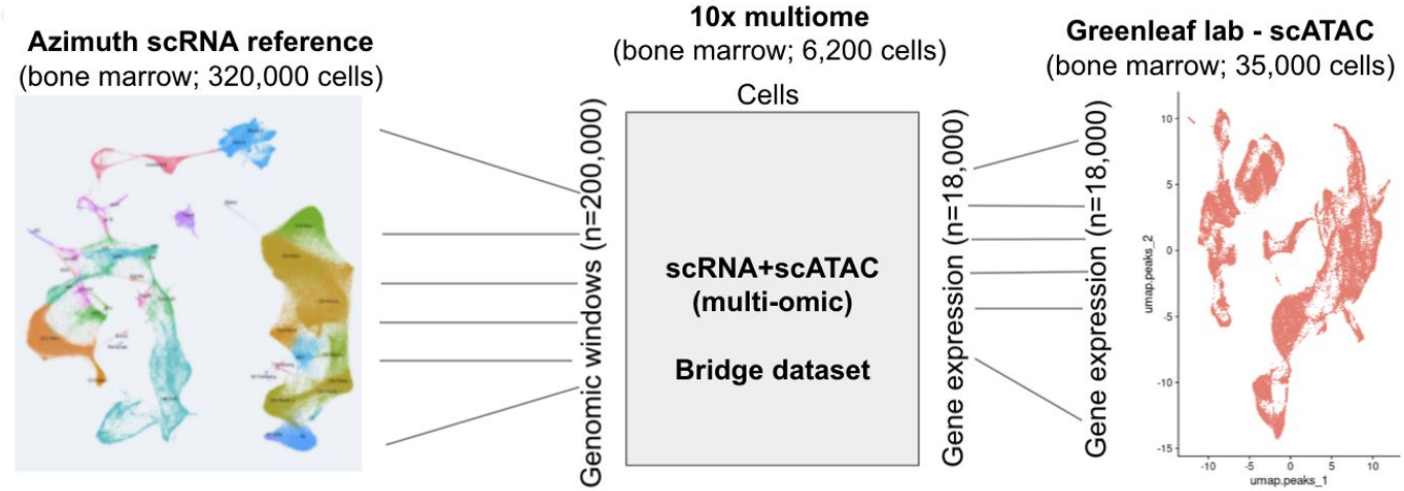
Azimuth: Bridge Integration to Annotate/Map scATAC-seq Data to HRA

scATAC-seq measures DNA accessibility per cell

- Data is sparse and difficult to annotate

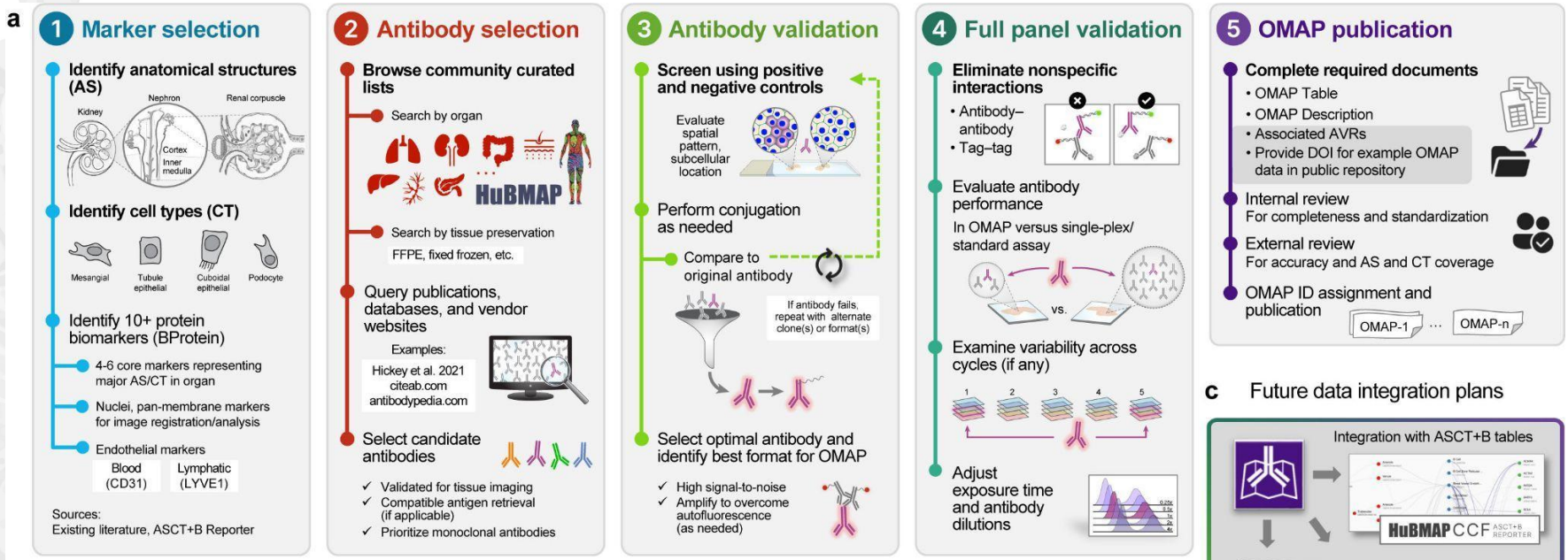
Goal: Use bridge integration (Hao et al., 2022) to map scATAC-seq query to scRNA-seq reference

- Learn dictionary representation of RNA reference and ATAC query to transfer annotations



https://satijalab.org/seurat/articles/bridge_integration_vignette.html

Organ Mapping Antibody Panels (OMAPs)



Created by Diane Saunders, Vanderbilt University. Now accepted for *Nature Methods.*

OMAPs How to Contribute (Andrea Radtke, NIAID, NIH)

Goals for OMAPs:

- Offset the considerable time (6-8 months) and cost (~$30-60,000 in 2022 USD) associated with creating such resources de novo
- Standardize data acquisition for multiplexed tissue imaging studies
- Empower construction of atlases from healthy and diseased human tissues
- Support the spatial biology community by aggregating highly cited antibody clones
- Identify essential markers for anatomical structures and cell types in diverse human organs

- SOP: Construction of Organ Mapping Antibody Panels for Multiplexed Antibody-Based Imaging of Human Tissues
- Frequently Asked Questions (FAQs) for OMAPs
- OMAP table template
- OMAP description document template

Interested in contributing to OMAPs?

Contact:
Andrea Radtke andrea.radtke@nih.gov
Ellen Quardokus ellenmq@indiana.edu
Michael Caldwell michael.caldwell@northwestern.edu

Existing OMAPs

Choose CCF-HRA Release **version:** 3rd HRA Release (v1.2), June 2022

OMAP ID	Organ	Tissue Preservation Method	Multiplexed antibody-based imaging method	#AS	#CT	#BP
OMAP-1	Lymph Node	Fixed Frozen	IBEX	29	31	40
OMAP-2	Intestines	Fresh Frozen	CODEX	42	29	51
OMAP-3	Kidney	Fresh Frozen	CODEX	30	37	26
OMAP-4	Skin	FFPE	Cell DIVE	16	15	18
OMAP-5	Liver	Fresh Frozen	SIMS	17	16	20
OMAP-6	Pancreas	FFPE	CODEX	3	9	12
OMAP-7	Lung	FFPE	Cell DIVE	50	42	30
			Totals:	**187**	**179**	**197**

https://hubmapconsortium.github.io/ccf/pages/omap.html

Human Reference Atlas Standard Operating Procedures

Table of Contents

https://humanatlas.io

Planned Changes in HRA Digital Objects for 5th Release (April 1, 2023 Deadline)

Organ	Replied to email inquiry	ASCT+B Table (Authors)	2D FTU	3D Obj	OMAP
Blood	☐	☐	☐	☐	☐
Blood Vasculature	☑	☑	☐	☐	☐
Bone Marrow	☐	☐	☐	☐	☐
Brain	☑	☑	☐	☐	☐
Breast	☑	☑	☐	☐	☐
Eye	☐	☐	☐	☑	☐
Fallopian Tube	☐	☐	☐	☐	☐
Heart	☐	☐	☐	☐	☐
Kidney	☐	☐	☑	☐	☑
Knee	☐	☐	☐	☑	☐
Large Intestine	☐	☐	☐	☐	☑
Liver	☐	☐	☐	☐	☑
Lung	☑	☑	☐	☐	☑
Lymph Node	☐	☐	☐	☐	☑
Lymph Vasculature	☐	☐	☐	☐	☐
Pancreas	☐	☐	☐	☐	☑
Peripheral Nervous System	☐	☐	☐	☐	☐
Placenta Full Term	☑	☑	☐	☐	☐
Prostate	☐	☐	☐	☐	☐
Skin	☐	☐	☐	☐	☑
Small Intestine	☐	☐	☑	☐	☑
Spinal Cord	☑	☑	☐	☐	☐
Spleen	☐	☐	☑	☐	☐
Thymus	☐	☐	☐	☐	☐
Uterus	☐	☐	☐	☐	☐
Ovary	☐	☐	☐	☐	☐
Tonsil	☑	☐	☐	☐	☐
Nasal Passage	☐	☐	☐	☑	☐

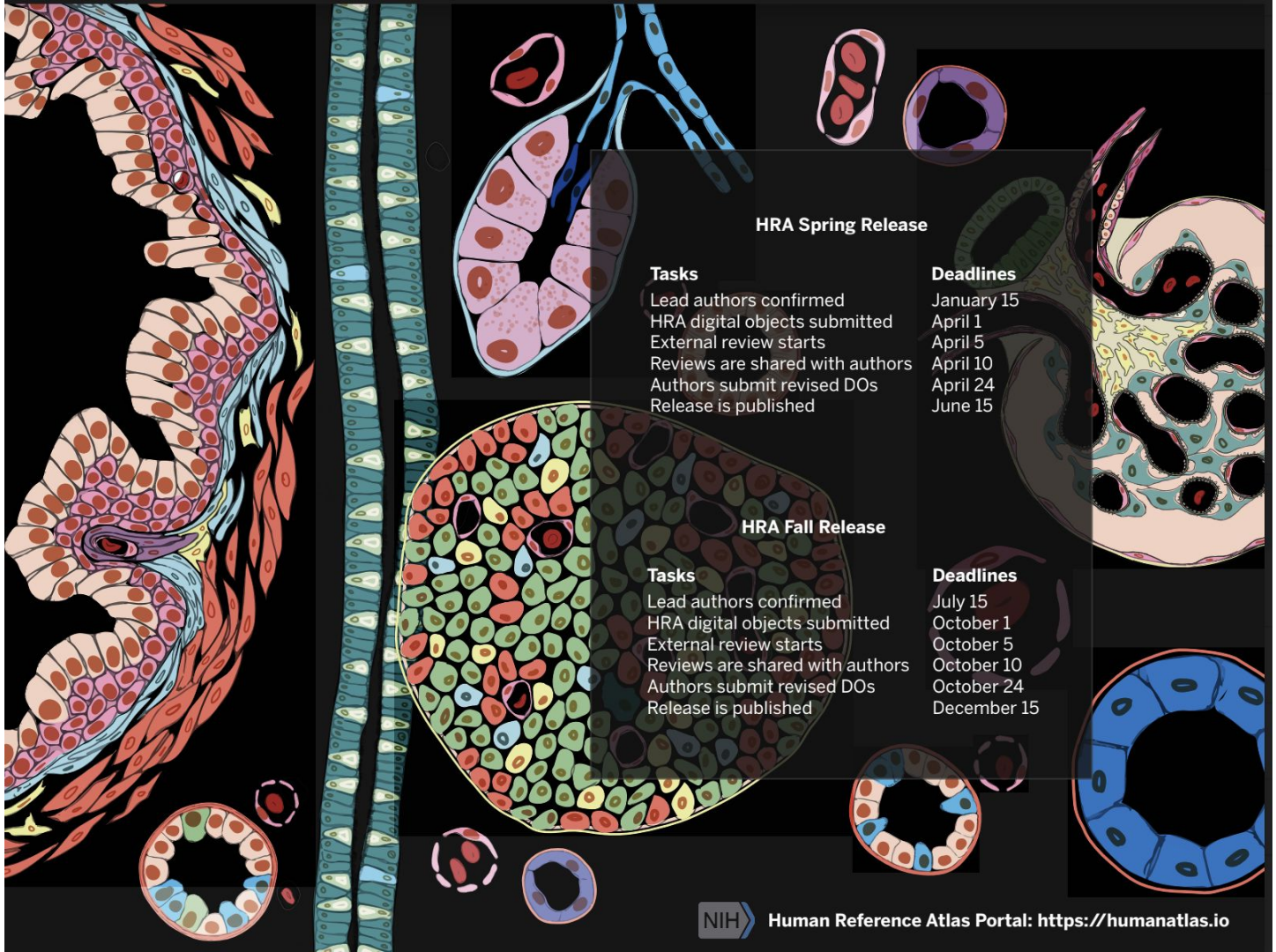
Azimuth

Organs in work:

- Liver
- Small and large intestine
- Skin
- Retina

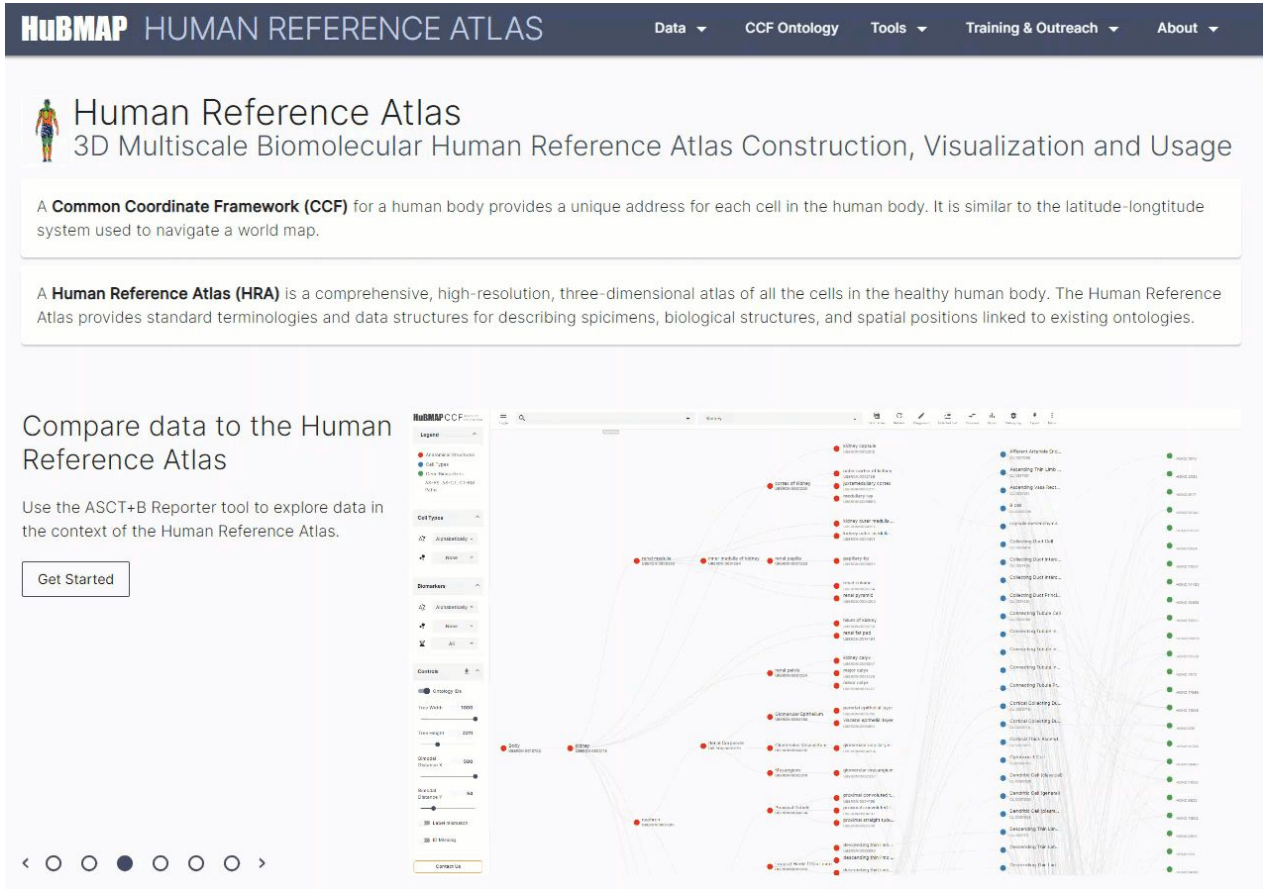
HRA

29 Organs total
57 3D reference organs (L/R, M/F)


HRA Spring Release
Tasks
Lead authors confirmed
HRA digital objects submitted
External review starts
Reviews are shared with authors
Authors submit revised DOs
Release is published
Deadlines
January 15
April 1
April 5
April 10
April 24
June 15
HRA Fall Release
Tasks
Lead authors confirmed
HRA digital objects submitted
External review starts
Reviews are shared with authors
Authors submit revised DOs
Release is published
Deadlines
July 15
October 1
October 5
October 10
October 24
December 15
NIH
Human Reference Atlas Portal: https://humanatlas.io

Human Reference Atlas

Human Reference Atlas (HRA) Portal



https://humanatlas.io

HRA Use Cases: Three key use cases have been identified, discussed with experts, and help prioritize HRA construction and usage:

US#1 API to HRA, e.g, to improve CT annotation

US#2 API to HRA to predict spatial location of tissue

US#3 Exploration of CTs, Bs to understand what changes with age or during disease

Human Reference Atlas data and APIs

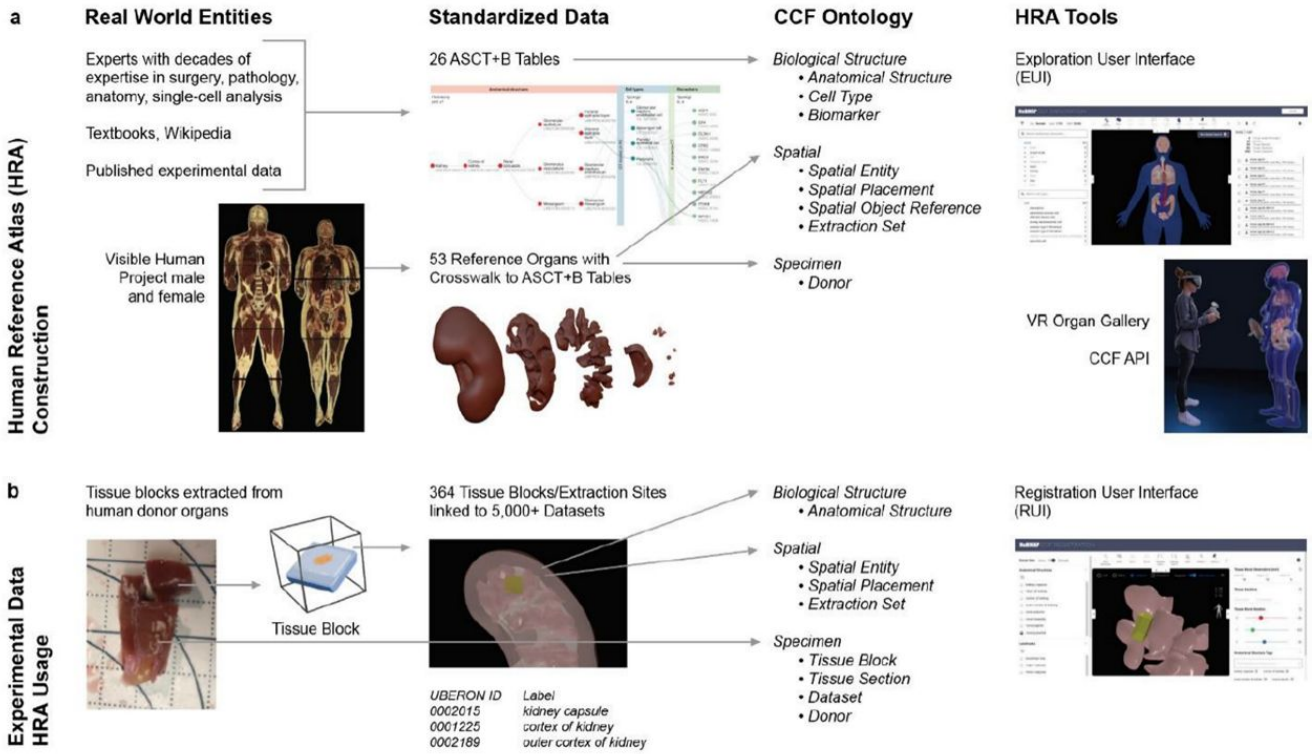


Figure 1. From real-world entities, to standardized data, to ontology. a. Human Reference Atlas construction takes real-world data and represents it in standardized data structures that are defined by the interlinked Biological Structure, Spatial, and Specimen ontologies.

Specimen, Biological Structure, and Spatial Ontologies in Support of a Human Reference Atlas https://biorxiv.org/cgi/content/short/2022.09.08.507220v1

Human Reference Atlas (HRA)

Anatomical Structures, Cell Types, and Biomarkers 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). 3D and 2D reference object capture the shape, size, and spatial composition of ASCT.

ASCT Table

Structure/Region	Sub structure/Sub region	Cell Type
Renal Corpuscle	Bowman's (glomular) Capsule/parietal layer	Parietal epithelial Cell
	Bowman's (glomular) Capsule/visceral layer	Podocyte
	Glomerular Tuft	Capillary Endothelial Cell
		Mesangial Cell
Tubules	Proximal Tubule	Proximal Tubule Epithelial Cell (general)
		Proximal Convoluted Tubule Epithelial Cell Segment 1
		Proximal Tubule Epithelial Cell Segment 2
		Proximal Tubule Epithelial Cell Segment 2
	Loop of Henle, Thin Limb	Descending Thin Limb Cell (general)
		Ascending Thin Limb Cell (general)
	Loop of Henle, Thick Limb	Thick Ascending Limb Cell (general)
		Cortex-TAL Cell
		Medulla-TAL Cell
		TAL-Macula Densa Cell
	Distal Convolution	Distal Convoluted Tubule Cell (general)
		DCT Type 1 Cell
		DCT Type 2 Cell
	Connecting Tubule	Connecting Tubule Cell (general)
		CNT-Principal Cell

Ontology

Anatomical Structures Partonomy

kidney
- kidney capsule
- cortex of kidney
  - outer cortex of kidney
- renal medulla

Cell Types Ontology

connective tissue cell
- pericyle cell
  - mesangial cell
    - extraglomerular mesangial cell
    - glomerular mesangial cell

3D Reference Object Library

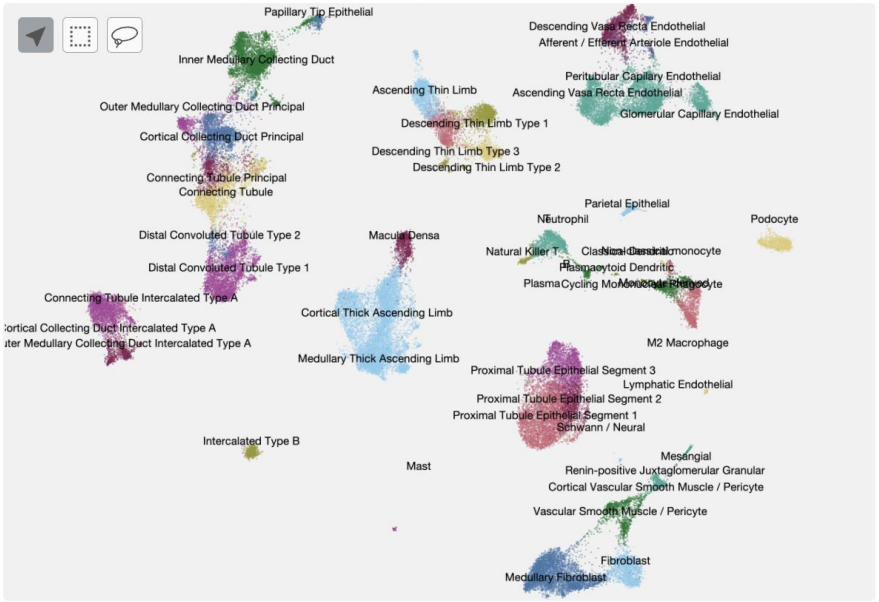
Sections

- Description
- Organ
- info
- Azimuth
- Search

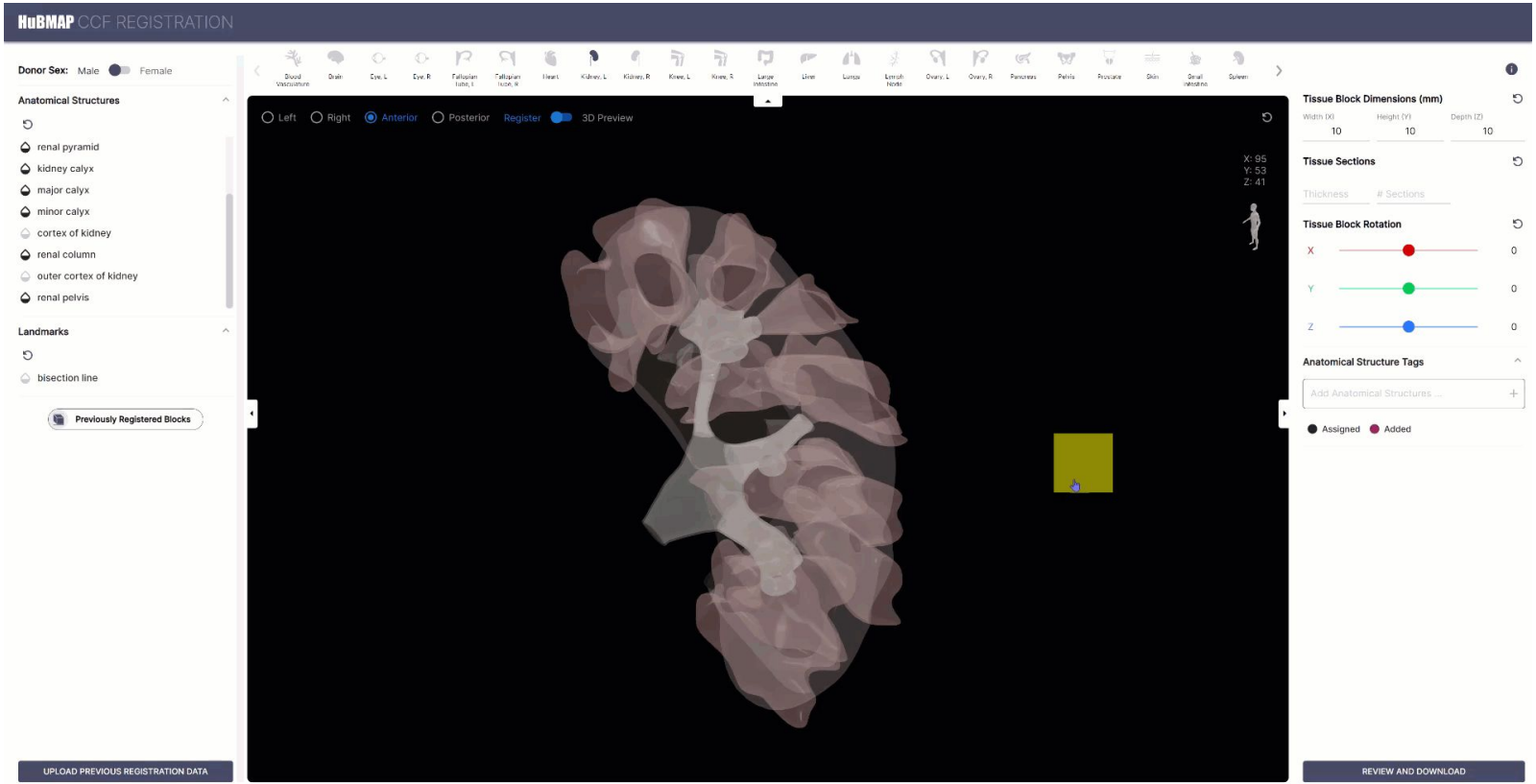
Reference-Based Analysis

Open Azimuth App

Modalities
RNA
Nuclei in reference
64,693
Reference dataset
Lake et al, bioRxiv 2021

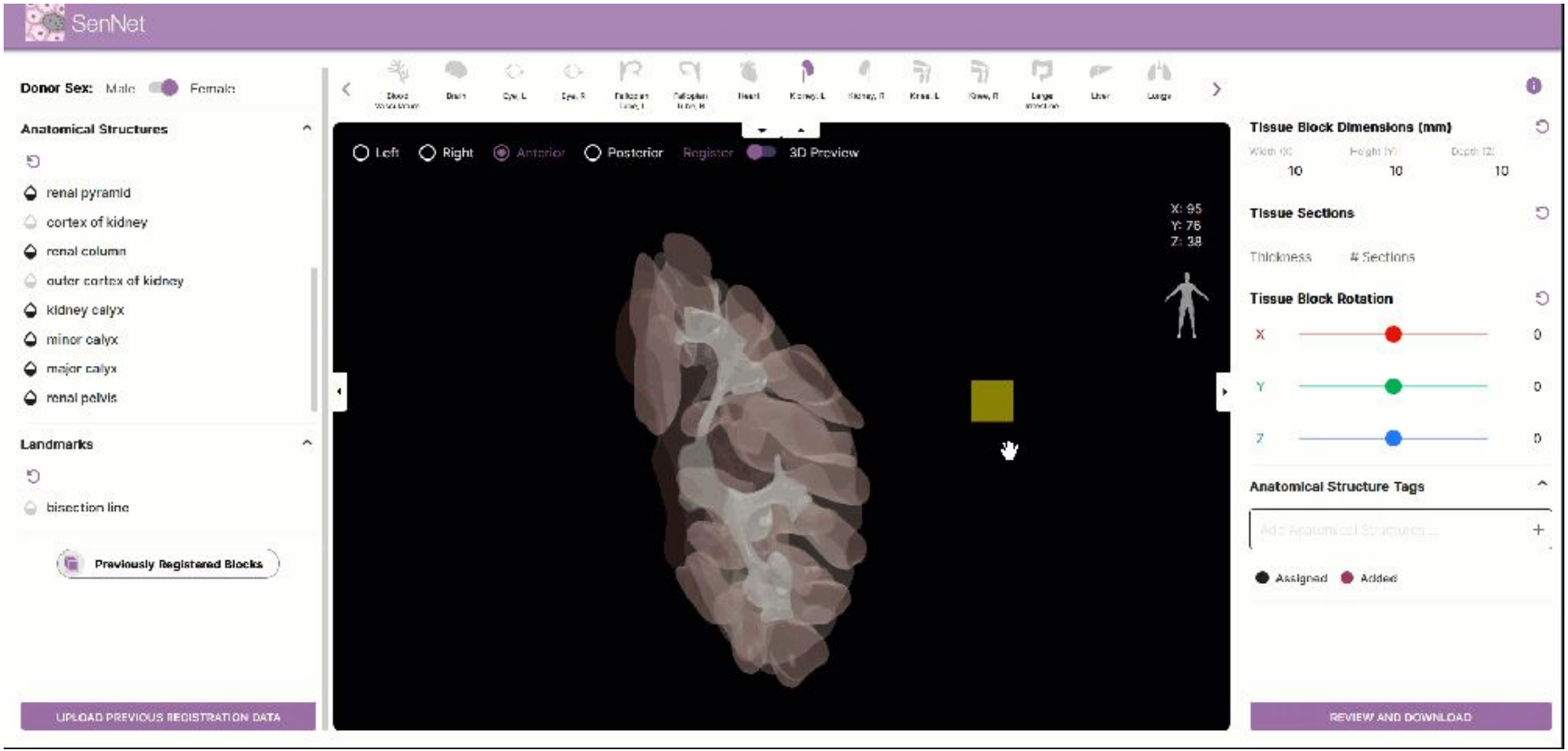


Registration User Interface (RUI)

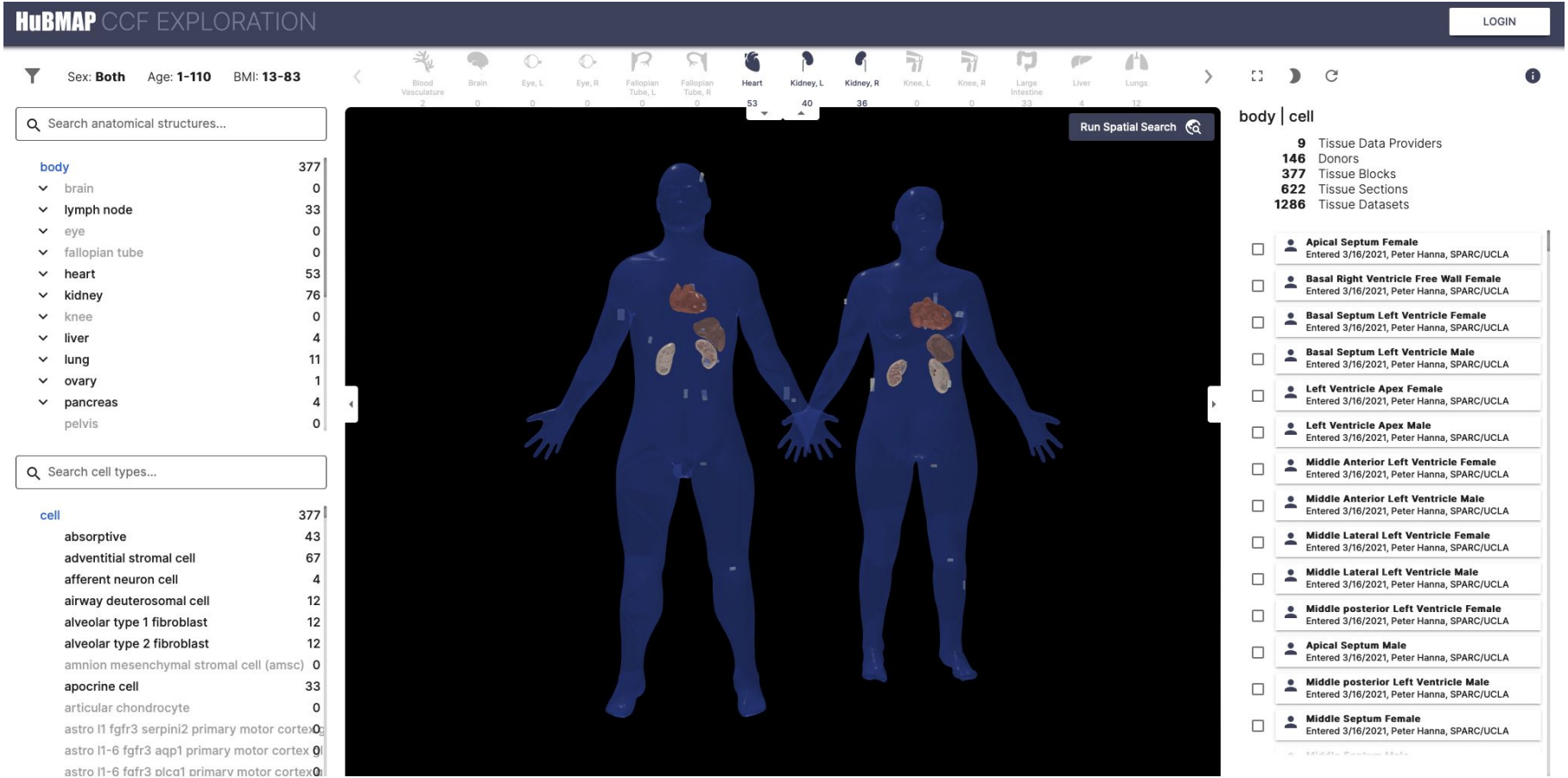


https://hubmapconsortium.github.io/ccf-ui/rui

RUI supports 57 organs (L/R, M/F) with 1,542 anatomically correct 3D anatomical structures.

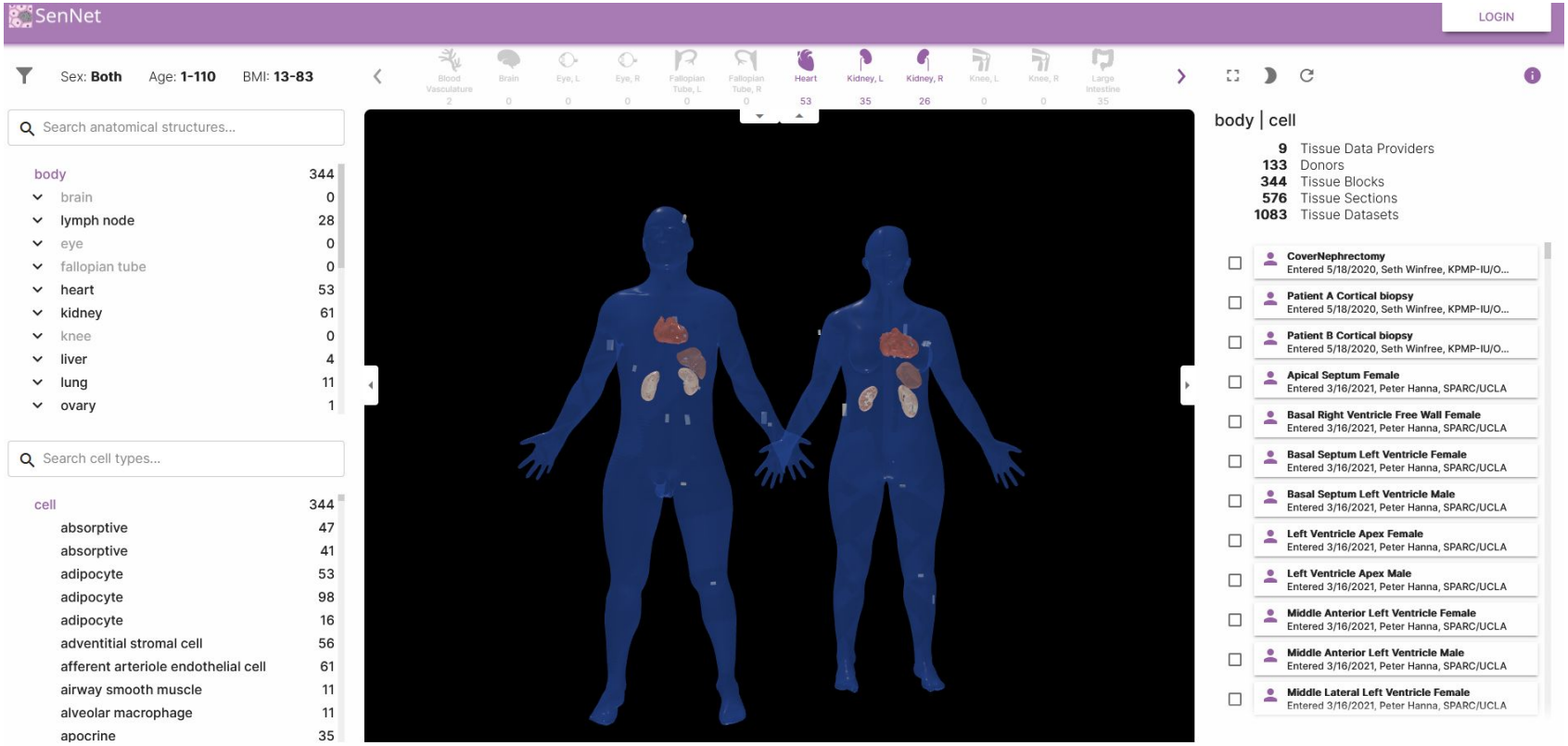

SenNet
Donor Sex: Male Female
Anatomical Structures
renal pyramid
cortex of kidney
renal column
outer cortex of kidney
kidney calyx
minor calyx
major calyx
renal pelvis
Landmarks
bisection line
Previously Registered Blocks
UPLOAD PREVIOUS REGISTRATION DATA
Left
Right
Anterior
Posterior
Register
3D Preview
X: 95
Y: 76
Z: 38
Tissue Block Dimensions (mm)
10
10
10
Tissue Sections
Thickness
Sections
Tissue Block Rotation
X
Y
Z
0
0
0
Anatomical Structure Tags
Assigned
Added
REVIEW AND DOWNLOAD

Exploration User Interface (EUI)



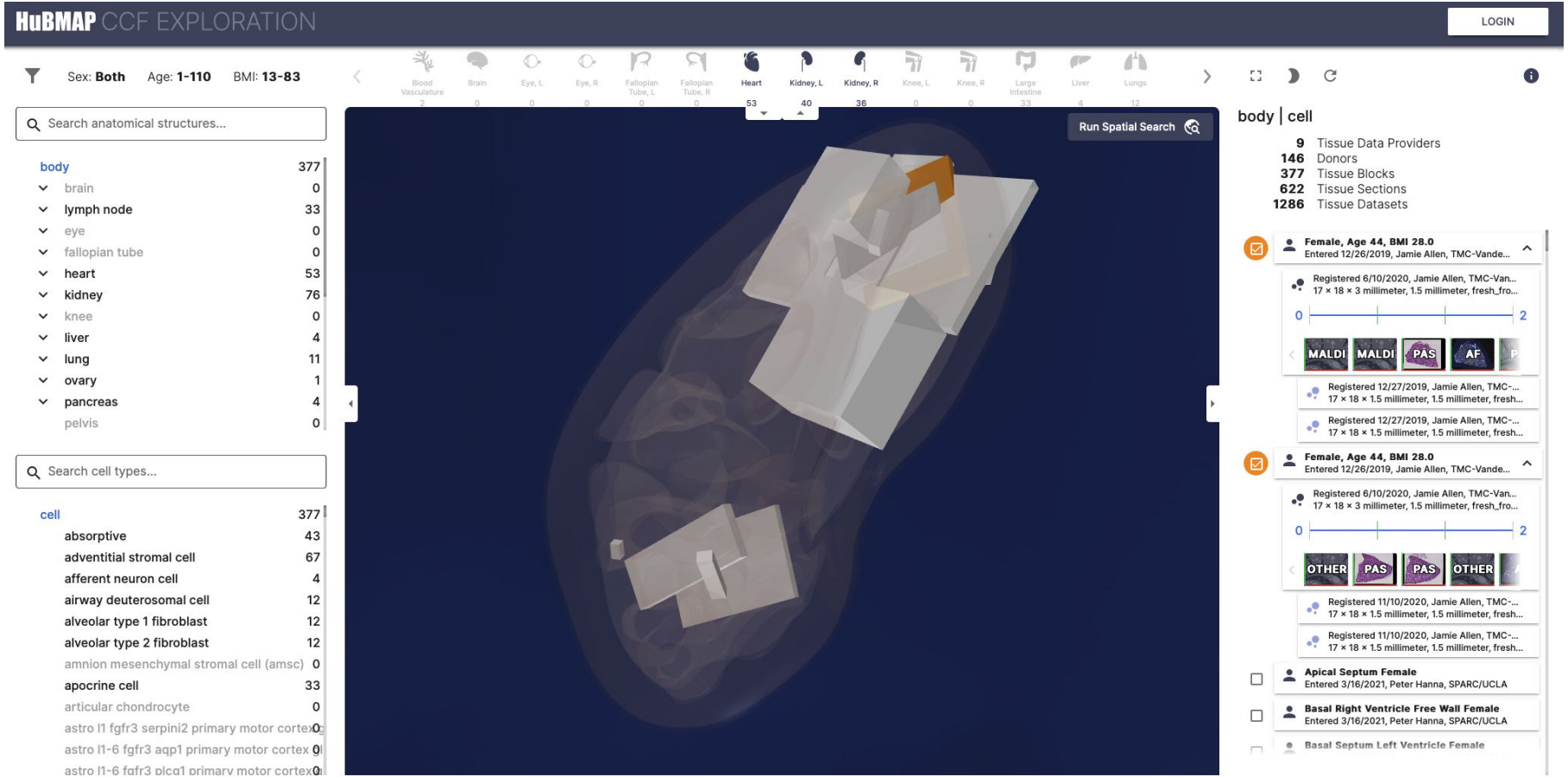
https://portal.hubmapconsortium.org/ccf-eui

EUI supports search for 1,542 AS and 953 cell types. Will soon add search for biomarkers.



Note: The screenshot shows HuBMAP data

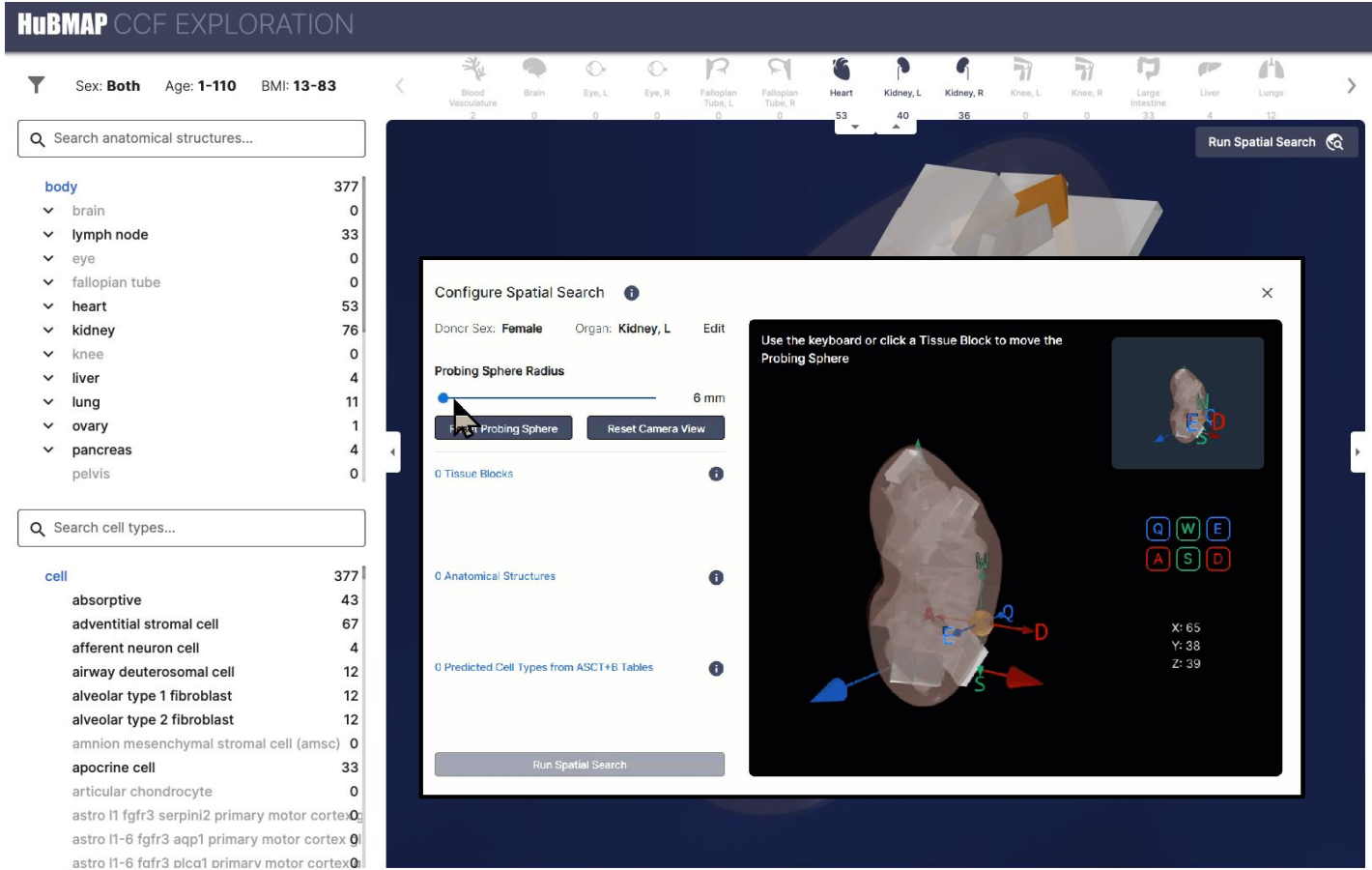
Exploration User Interface (EUI)



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

More than 5,000 tissue datasets from 4 consortia have been RUI registered.

Exploration User Interface (EUI) - Spatial Search



See demo of spatial search at https://www.youtube.com/watch?v=UfxMpzatowE

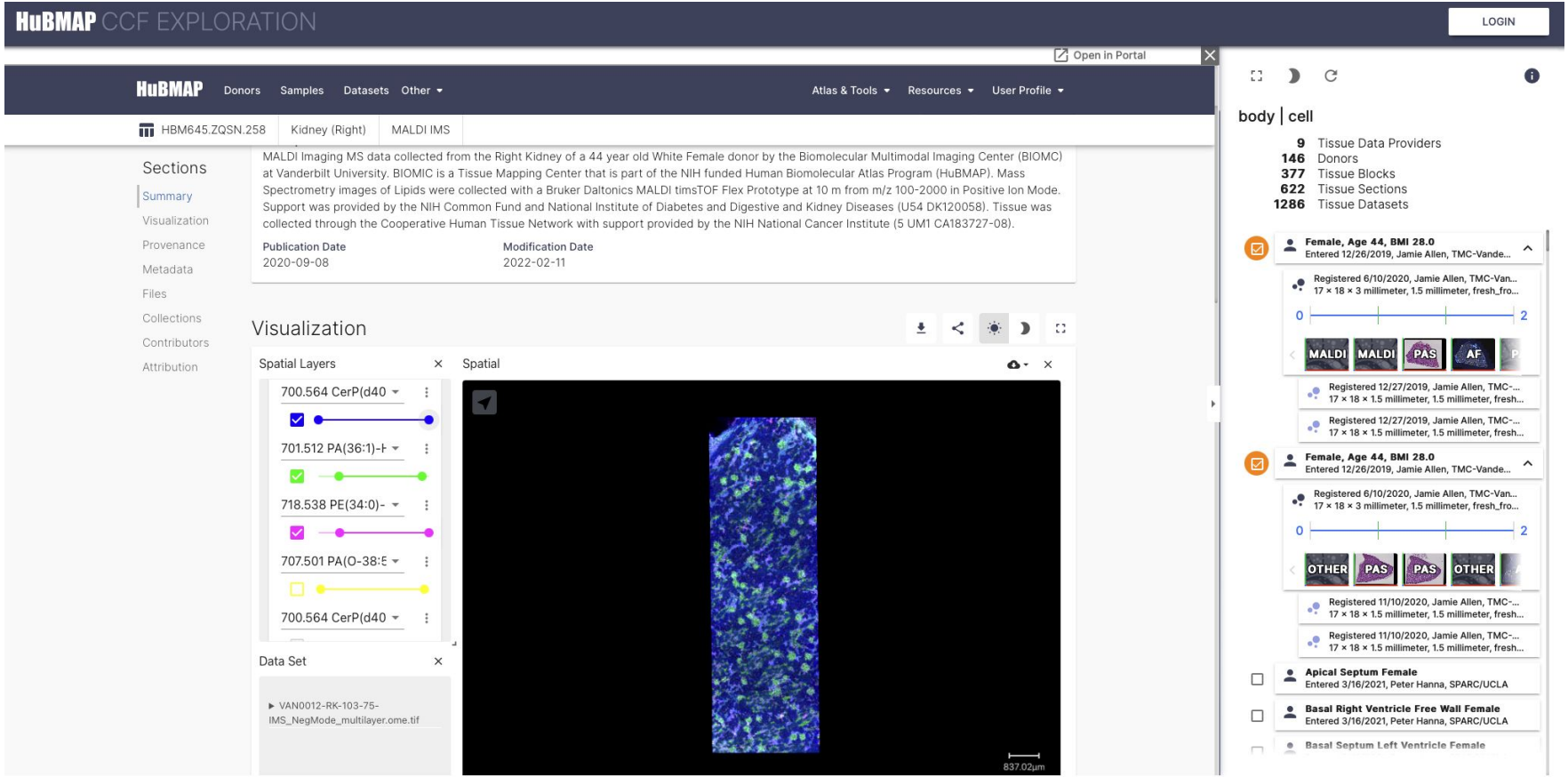
Cell types in lower left are from ASCT+B Table data.

Explore spatial search at https://portal.hubmapconsortium.org/ccf-eui and https://gtexportal.org/home/eui

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

Spatial search API is ready for HuBMAP portal wide usage.

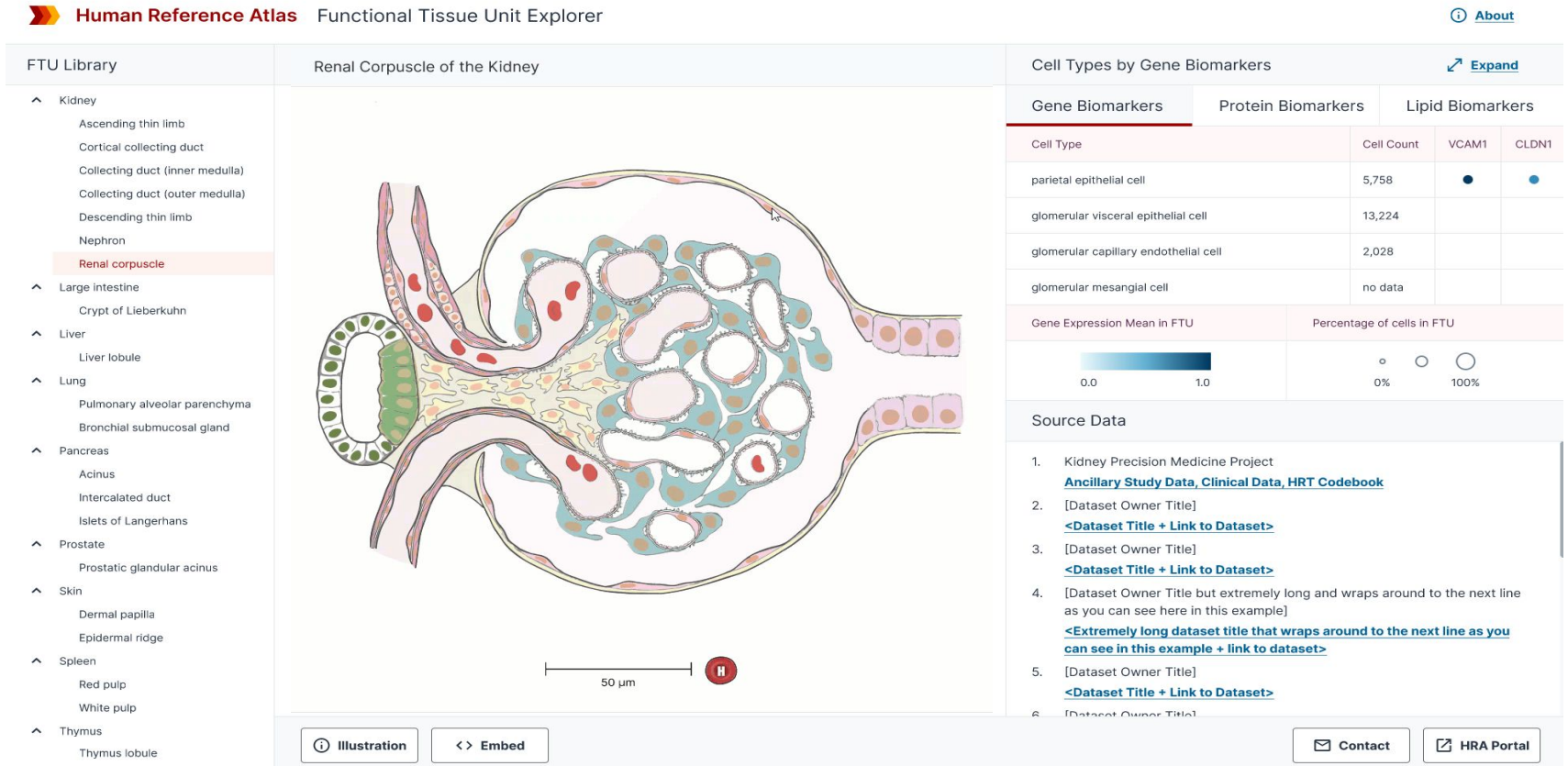
Exploration User Interface (EUI) & Vitessce



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

Works. Need to connect OMAP data to 'Spatial Layers' image channels. TMCs have this info.

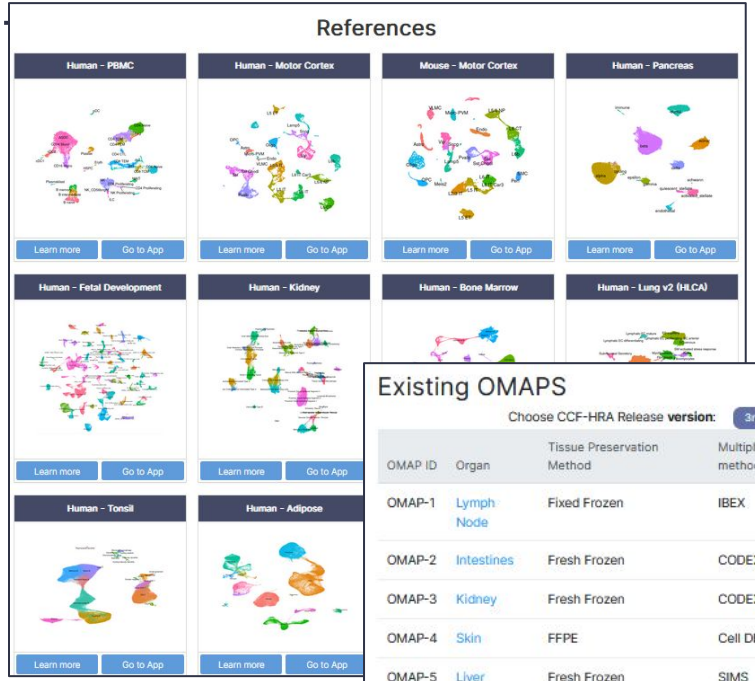
Interactive FTUs: Explore CT x B matrices for 19 FTUs across organs--what changes as we age, change BMI?

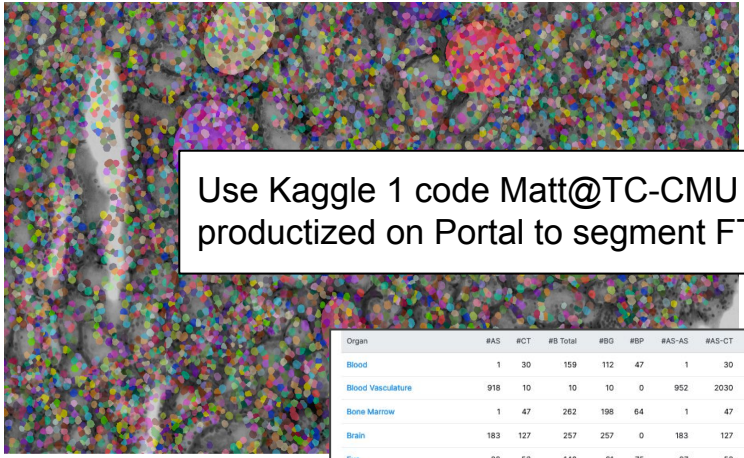


UI Specification done and tested. Will be implemented for 19 FTUs by June 2023. Need Kaggle 2 code + Azimuth/OMAP references to compile cell x gene, cell x protein data at FTU level.

Interactive FTUs: Data

Use Azimuth references + OMAPs to assign ontology aligned CT / B names to bulk or spatially explicit experimental data.





Use Kaggle 1 code Matt@TC-CMU productized on Portal to segment FTUs.

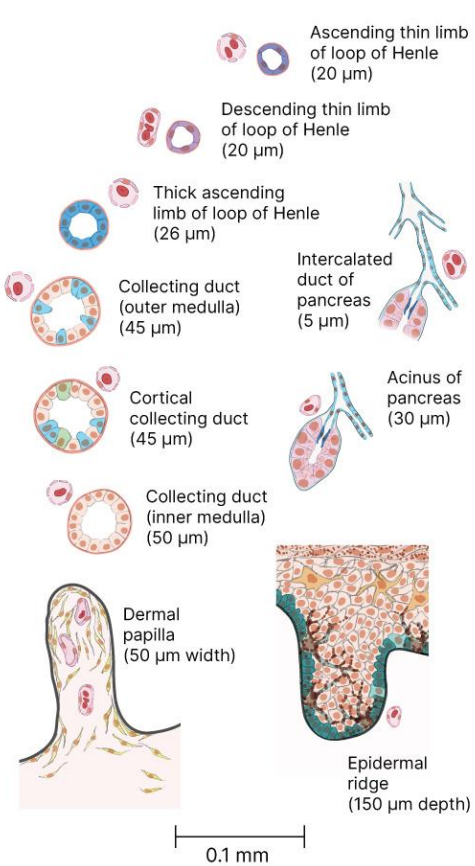
Existing OMAPS

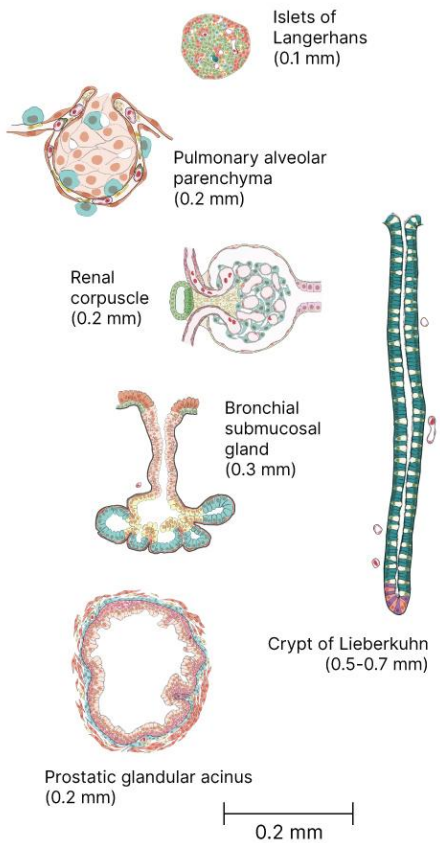
Choose CCF-HRA Release **version:** 3rd HRA Release (v1.2), June 2022

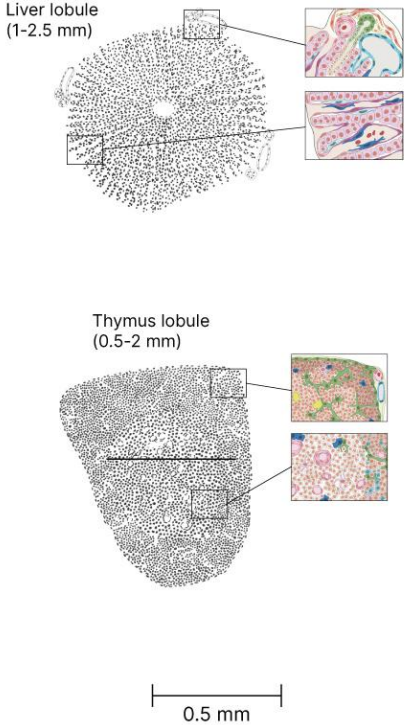
OMAP ID	Organ	Tissue Preservation Method	Multiplexed antibody-based imaging method	#AS	#CT	#BP
OMAP-1	Lymph Node	Fixed Frozen	IBEX	29	31	40
OMAP-2	Intestines	Fresh Frozen	CODEX	42	29	51
OMAP-3	Kidney	Fresh Frozen	CODEX	30	37	26
OMAP-4	Skin	FFPE	Cell DIVE	16	15	18
OMAP-5	Liver	Fresh Frozen	SIMS	17	16	20
OMAP-6	Pancreas	FFPE	CODEX	3	9	12
OMAP-7	Lung	FFPE	Cell DIVE	50	42	30

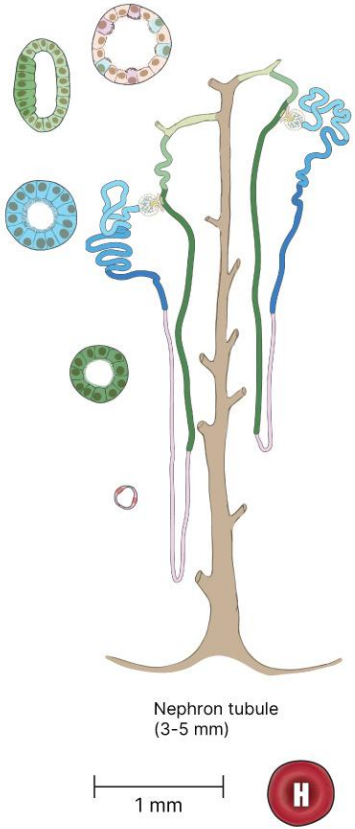
ASCT+B tables record what CTs are found in which FTUs.

Organ	#AS	#CT	#B Total	#BG	#BP	#AS-AS	#AS-CT	#CT-B
Blood	1	30	159	112	47	1	30	506
Blood Vasculature	918	10	10	10	0	952	2030	11
Bone Marrow	1	47	262	198	64	1	47	838
Brain	183	127	257	257	0	183	127	346
Eye	26	53	140	61	75	27	58	404
Fallopian Tube	72	18	26	13	13	84	81	27
Heart	50	23	45	45	0	60	183	74
Kidney	57	67	184	184	0	72	75	300
Knee	33	41	12	0	12	33	21	47
Large Intestine	54	57	166	83	83	287	1156	360
Liver	17	31	85	29	56	17	32	116
Lung	76	76	280	191	89	121	168	456
							86	499
							19	1
							30	11
							228	126
							609	2
							44	74
Prostate	4	12	31	31	0	4	12	36
Skin	15	36	70	0	70	17	19	100
Small Intestine	39	48	89	43	46	69	178	131
Spleen	37	60	194	85	109	50	129	421
Thymus	17	51	394	318	76	28	39	603
Ureter	7	14	30	30	0	7	14	61
Urinary Bladder	16	15	30	30	0	16	16	63
Uterus	61	18	45	39	6	89	34	65
Totals:	2,665	953	2,842	1,959	878	3,306	5,465	5,678

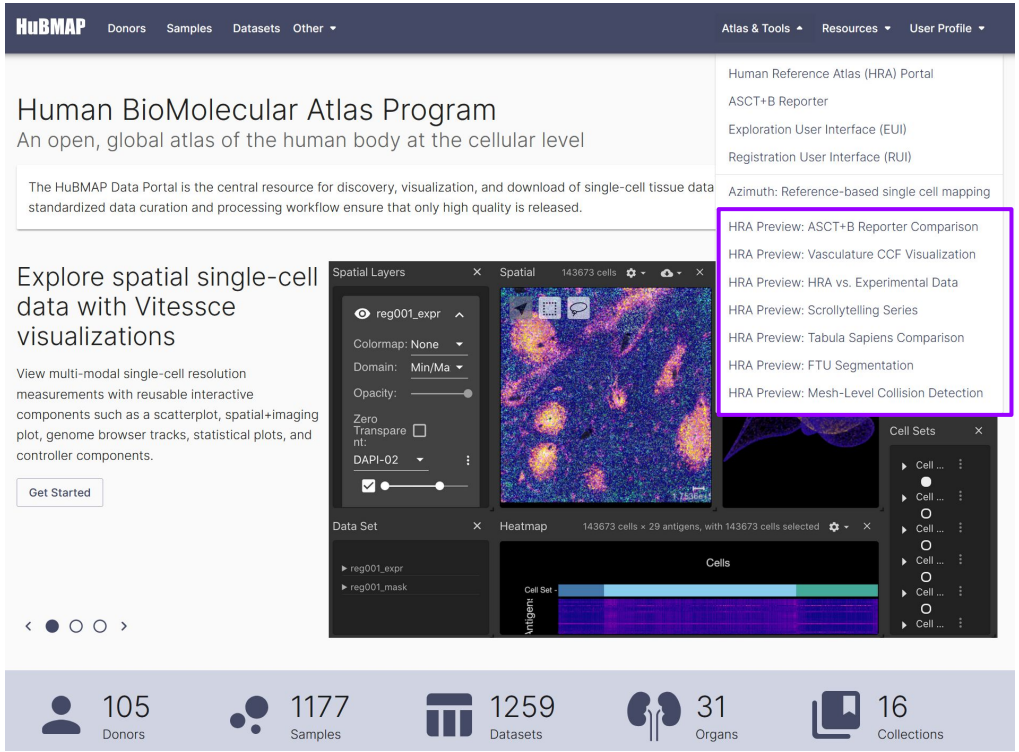

Ascending thin limb of loop of Henle (20 µm)
Descending thin limb of loop of Henle (20 µm)
Thick ascending limb of loop of Henle (26 µm)
Collecting duct (outer medulla) (45 µm)
Intercalated duct of pancreas (5 µm)
Cortical collecting duct (45 µm)
Acinus of pancreas (30 µm)
Collecting duct (inner medulla) (50 µm)
Dermal papilla (50 µm width)
Epidermal ridge (150 µm depth)
0.1 mm


Islets of Langerhans (0.1 mm)
Pulmonary alveolar parenchyma (0.2 mm)
Renal corpuscle (0.2 mm)
Bronchial submucosal gland (0.3 mm)
Crypt of Lieberkuhn (0.5-0.7 mm)
Prostatic glandular acinus (0.2 mm)
0.2 mm


Liver lobule (1-2.5 mm)
Thymus lobule (0.5-2 mm)
0.5 mm

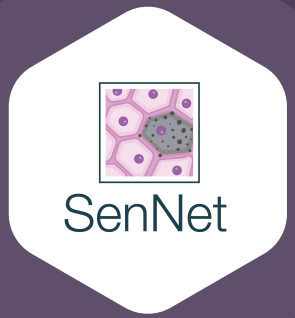

Nephron tubule (3-5 mm)
1 mm
H

Scientific Map/Atlas construction requires data/code that is documented/shared so others can reproduce results



Previews explain new data, code, functionality.

https://portal.hubmapconsortium.org



SenNet Talks on HRA construction and usage:

- 2022.06.01 **SenNet-Biomarkers** Slides, Recording (at 35 min mark)
- 2022.04.27 **Onboarding SenNet TMCs** Slides, Recording

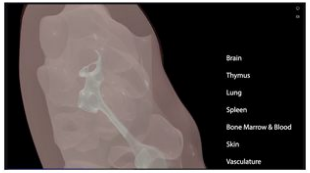
Visible Human MOOC

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

3rd HuBMAP Portal Release (June 2022)

HuBMAP Halfway Point

- HuBMAP consortia members reflect on the past four years and discuss their plans and hopes for the future.



Introduction to the HRA-CCF

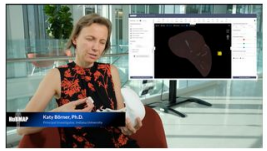
- An introduction to the three ontologies at work in the Human Reference Atlas's Common Coordinate Framework: the specimen, biological structure, and spatial ontologies.

Using the EUI on the GTEx Portal

- How to cross-compare data from GTEx and HuBMAP by using the Exploration User Interface embedded in the GTEx Portal.

The Great VHMOOC Blooper Reel

Not everything goes according to plan when we make our VHMOOC videos. These outtakes give a humorous look behind the scenes!



Katy Börner—Atlas Construction and Usage

Also featuring a demonstration of tissue registration with 3D models.

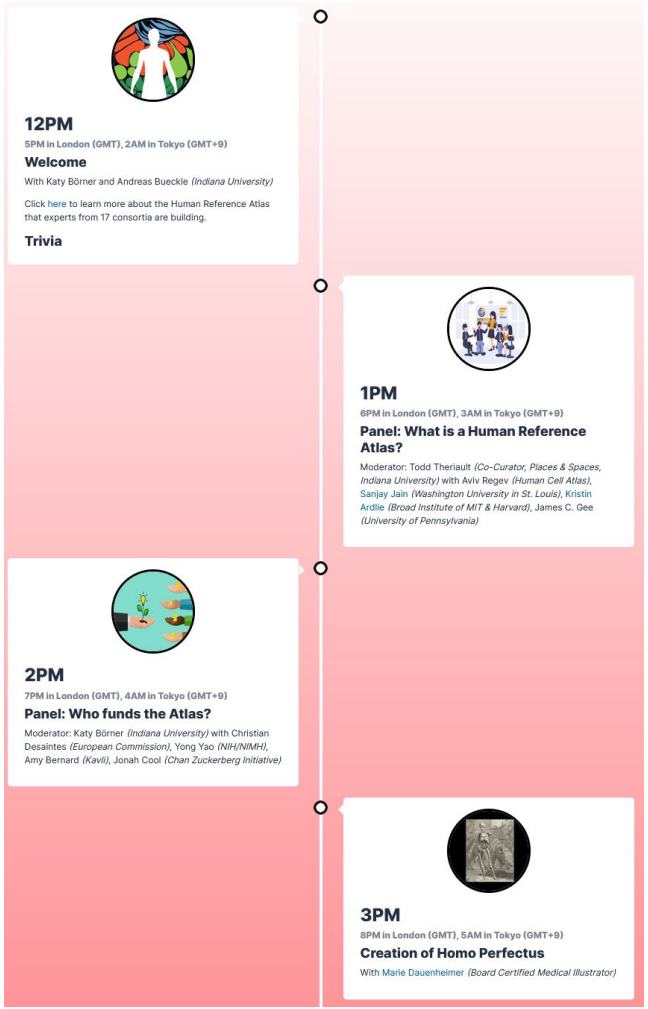
Mike Snyder Explains How to Map Human Intestines

A lively demonstration of the crucial role the intestines play in human health, and what we can learn by mapping them at the single-cell level.

Richard Conroy—How HuBMAP Works

A big-picture overview of the first four years of HuBMAP.

https://humanatlas.io/events/2022-24h



Conclusions

Human Reference Atlas construction requires high-quality data

We understand that all TMCs are expected to generate and submit the following for their relevant tissue:

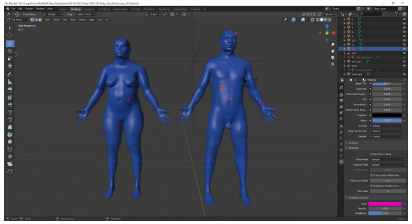
1. Histopathology images
2. scRNAseq data
3. CODEX/CellDive/MxIF

In addition to basic expectations on types of data generated per tissue, there are other important considerations such as:

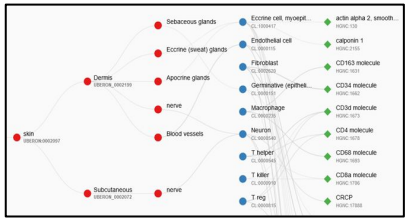
1. Running the assays above on the same or adjacent tissue sections
2. Including all essential donor, organ, sample, and assay metadata
3. RUI registration of all tissues
4. Utilization of biomarkers mapped to ASCT+B via Azimuth references and OMAPs

Plus, 3D data will be critically important to understand cell structure and function in their native 3D context. We would like to collaborate with teams that (will) generate 3D data.

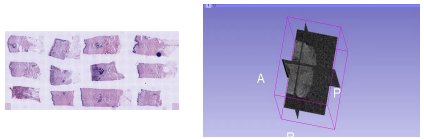
GE Research and U. Pittsburgh RTI: 3D reconstruction of multiplexed skin samples and spatial cell analysis



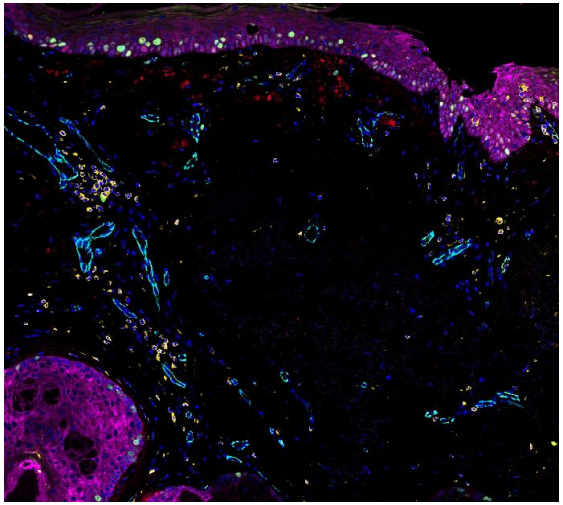
Registration of Skin Biopsy location using RUI



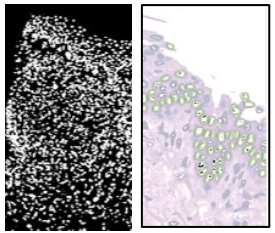
Registration of Skin Biomarkers in ASCT+B & OMAP



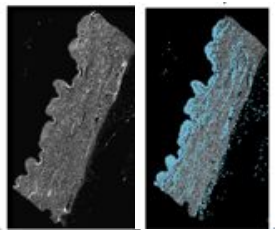
Tissue data collection: microCT imaging of skin FFPE blocks for multiplexed image 3D reconstruction



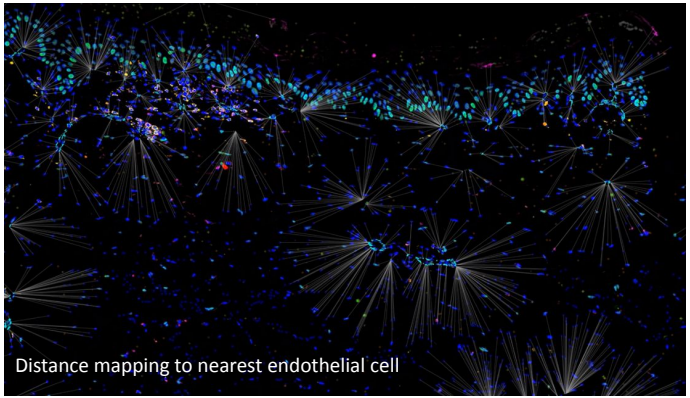
Multiplexed imaging of 18 skin biomarkers from 40 patients (Caucasian and African American)

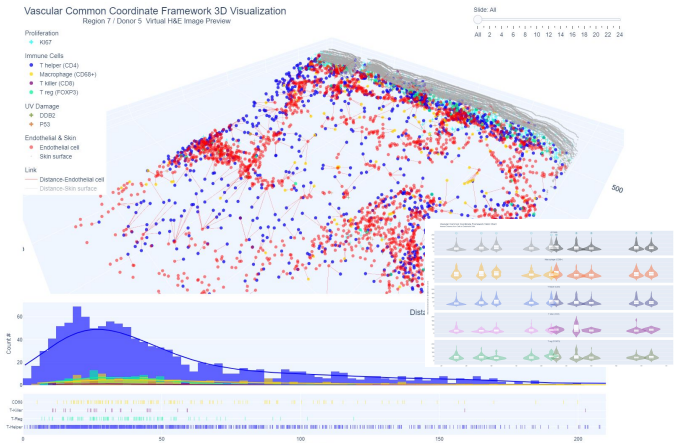


Cell type classification (epithelial, immune, endothelial…)



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)

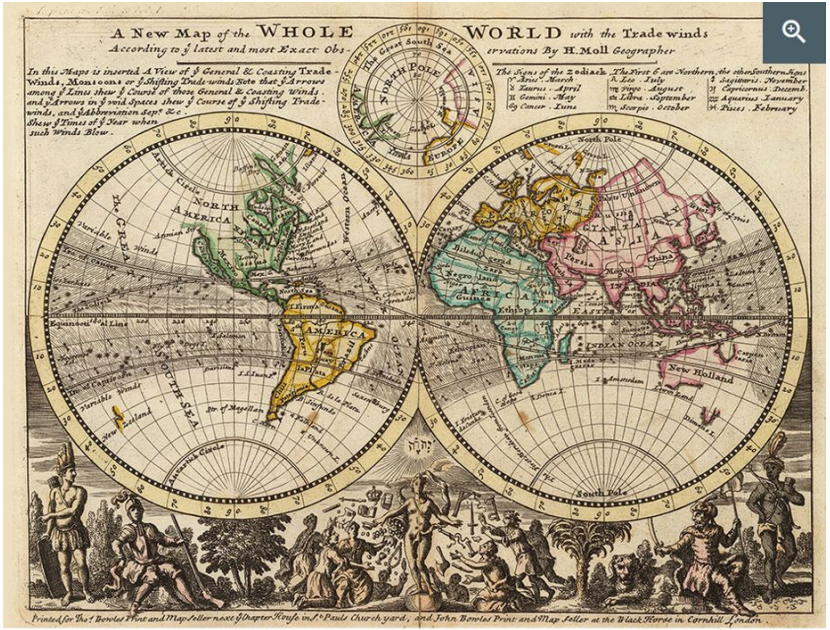
Early Maps are NOT perfect or complete

A New Map of the Whole World with the Trade Winds According to the Latest and Most Exact Observations

Makers: Herman Moll

Languages: English | Español | 汉语 | Deutsch

At the turn of the 17th century, Herman Moll was the most famous map publisher in England. He was also the first cartographer to create an elegant map of England that correctly portrayed its shape. His style combined time-consuming embellishment with bold, clear lettering to highlight important information. Moll prided himself on his work and publicly rebuked mapmakers who republished preexisting maps under new titles without having investigated their accuracy or completion—as this could prove fatal in cases where known depths of water and sands were omitted. This map is a hand-colored, engraved double-hemisphere of the whole world, featuring California as an island, a popular misconception at the time. The continents are represented by 12 allegorical figures surrounded by plants native to these lands. The long note at the top left discusses the trade winds indicated by arrows throughout the map.



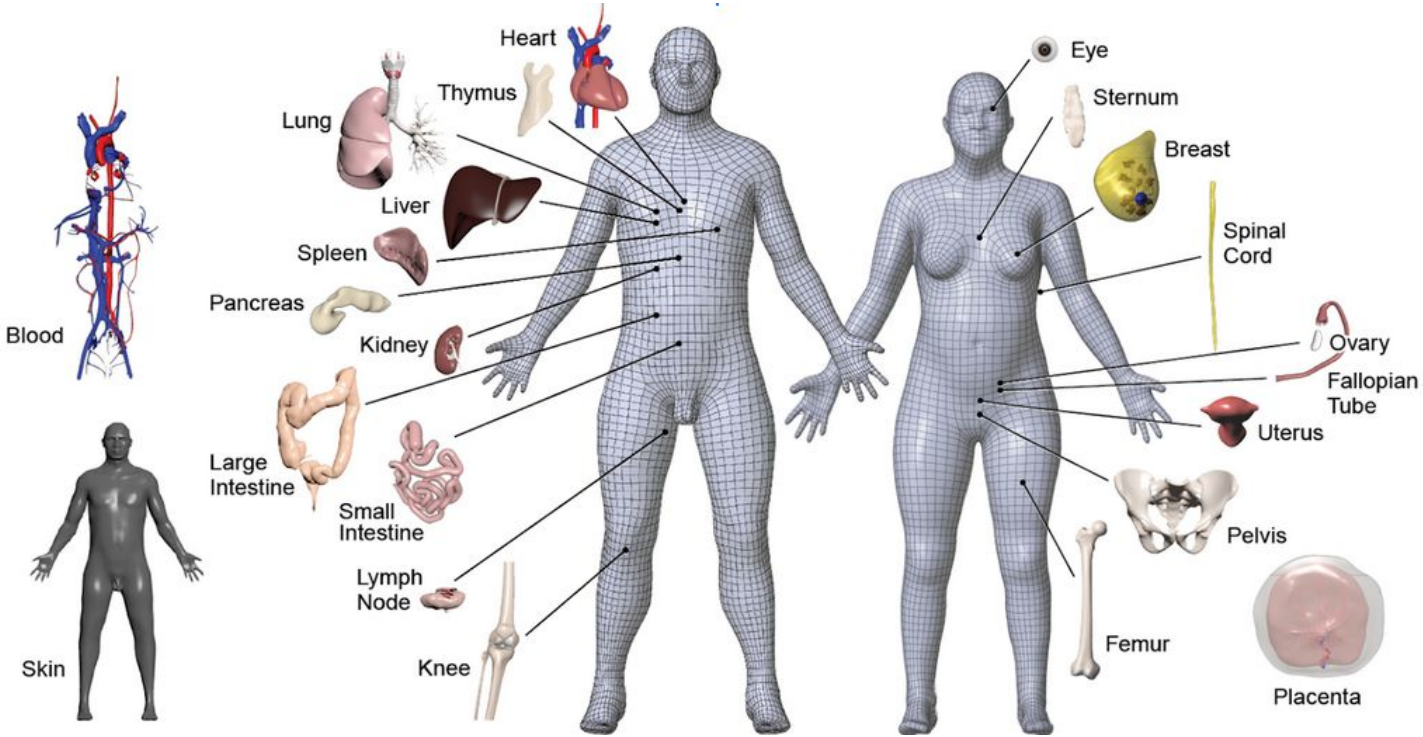
References
Moll, Herman. 1736. Atlas Minor. *Or a New and Curious Set of Sixty-Two Maps*. . . . London: Thos. Bowles and John Bowles.

Places & Spaces: Mapping Science exhibit: https://scimaps.org/map/1/3

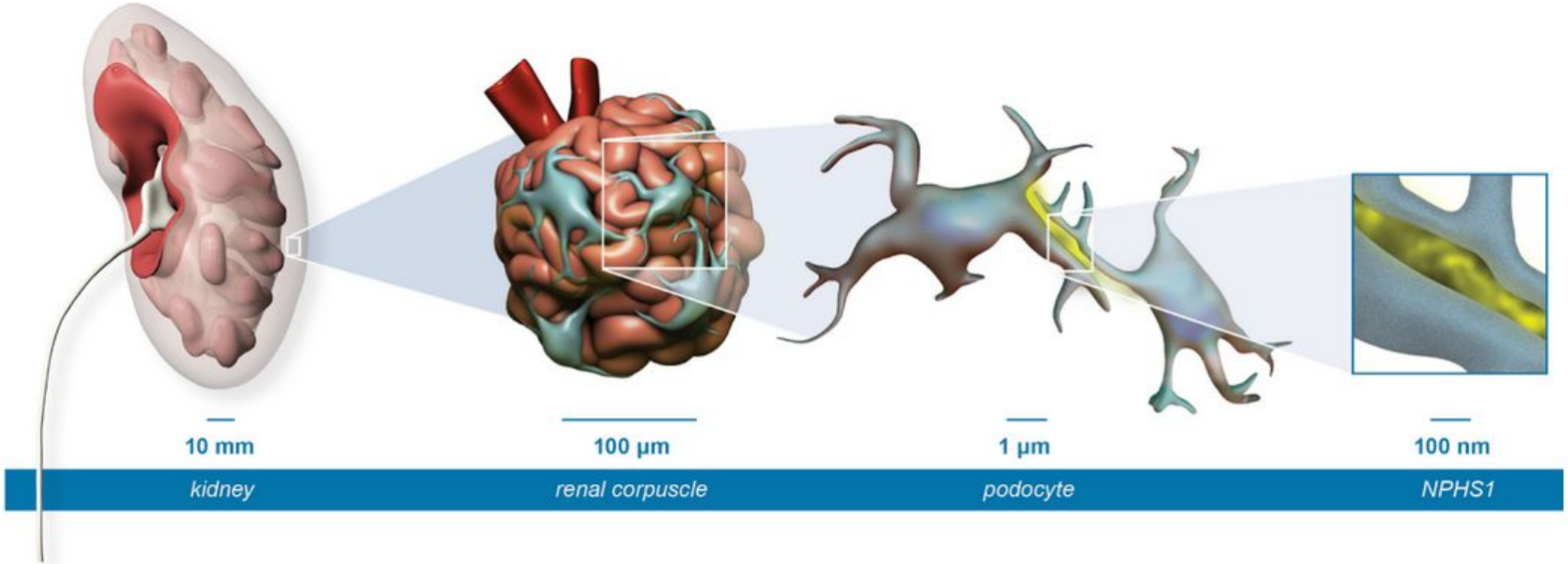
Early HRA will show organs that are funded.
It will NOT be perfect or complete.

First Phase

Organs added in **Production Phase**



HRA will be multiscale!



The multi-scale HRA covers more than 1,500 anatomical structures in the male and female body. A zoom into the kidney (10 mm level) reveals a representative view of a renal corpuscle (200 µm level), a subsegment of one of the ca. 1 million FTUs (nephron) of the kidney that is important in filtration. Podocytes, one of the cells important in filtration (µm level) with nucleus (in blue) and a protein NPHS1 that maintains the structural integrity of the filtration barrier (yellow) is illustrated.

Questions