Human Reference Atlas Construction and Usage

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CCB Seminar Series at HMS

May 2, 2022

HuBMAP

https://commonfund.nih.gov/HuBMAP

Vision

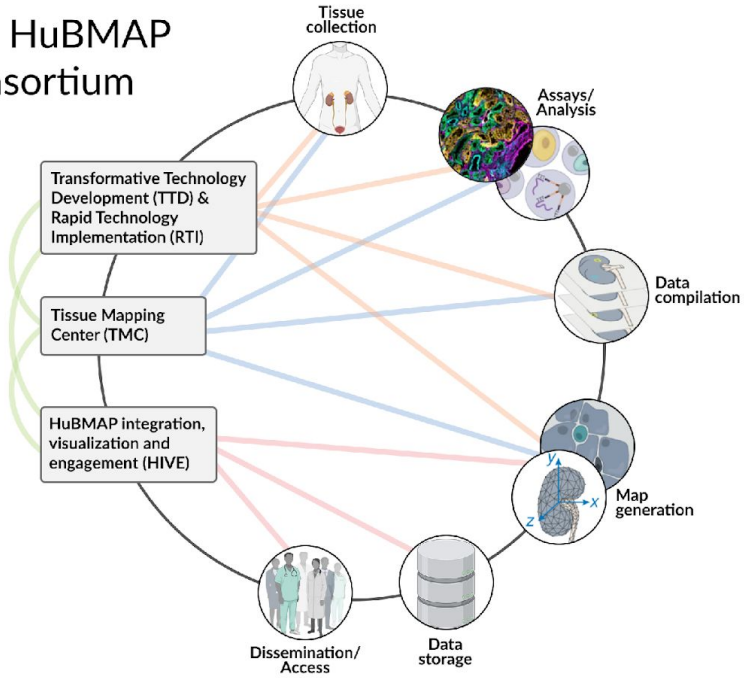
Catalyze the development of an open, global framework for comprehensively mapping the human body at cellular resolution.

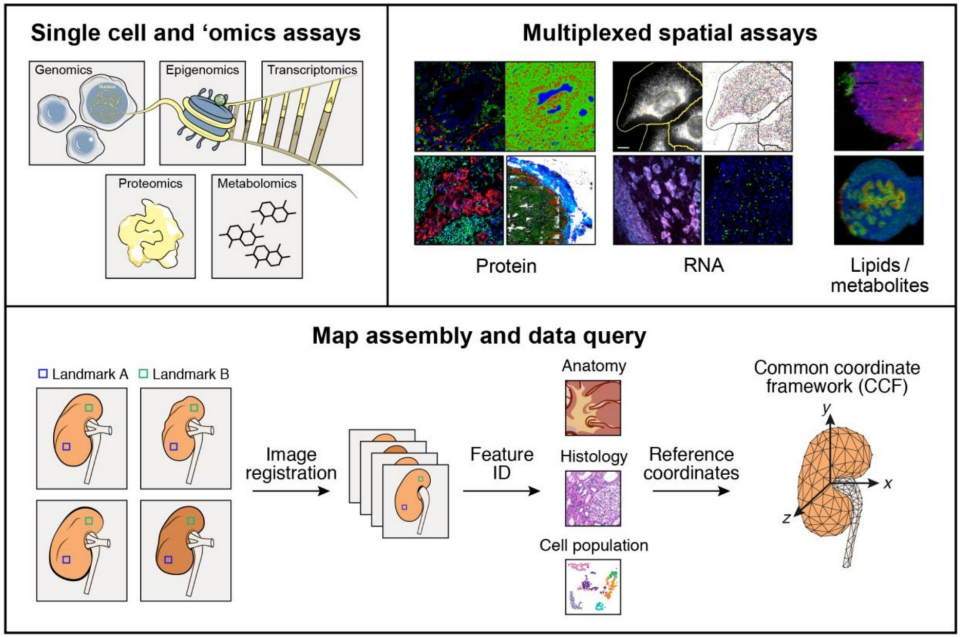
Goals

1. Accelerate the development of the next generation of tools and techniques for constructing high resolution spatial tissue maps
2. Generate foundational 3D tissue atlases
3. Establish an open data platform
4. Coordinate and collaborate with other funding agencies, programs, and the biomedical research community
5. Support projects that demonstrate the value of the resources developed by the program

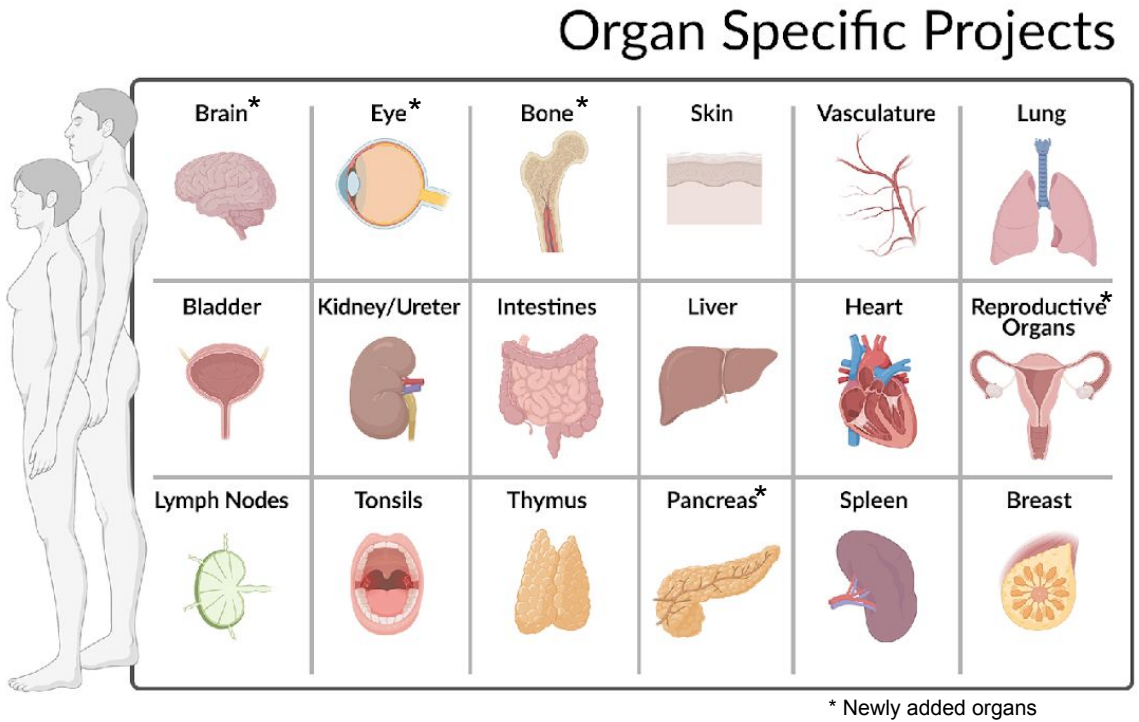
The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program
Snyder et al. *Nature*. 574, p. 187-192.

The HuBMAP Consortium



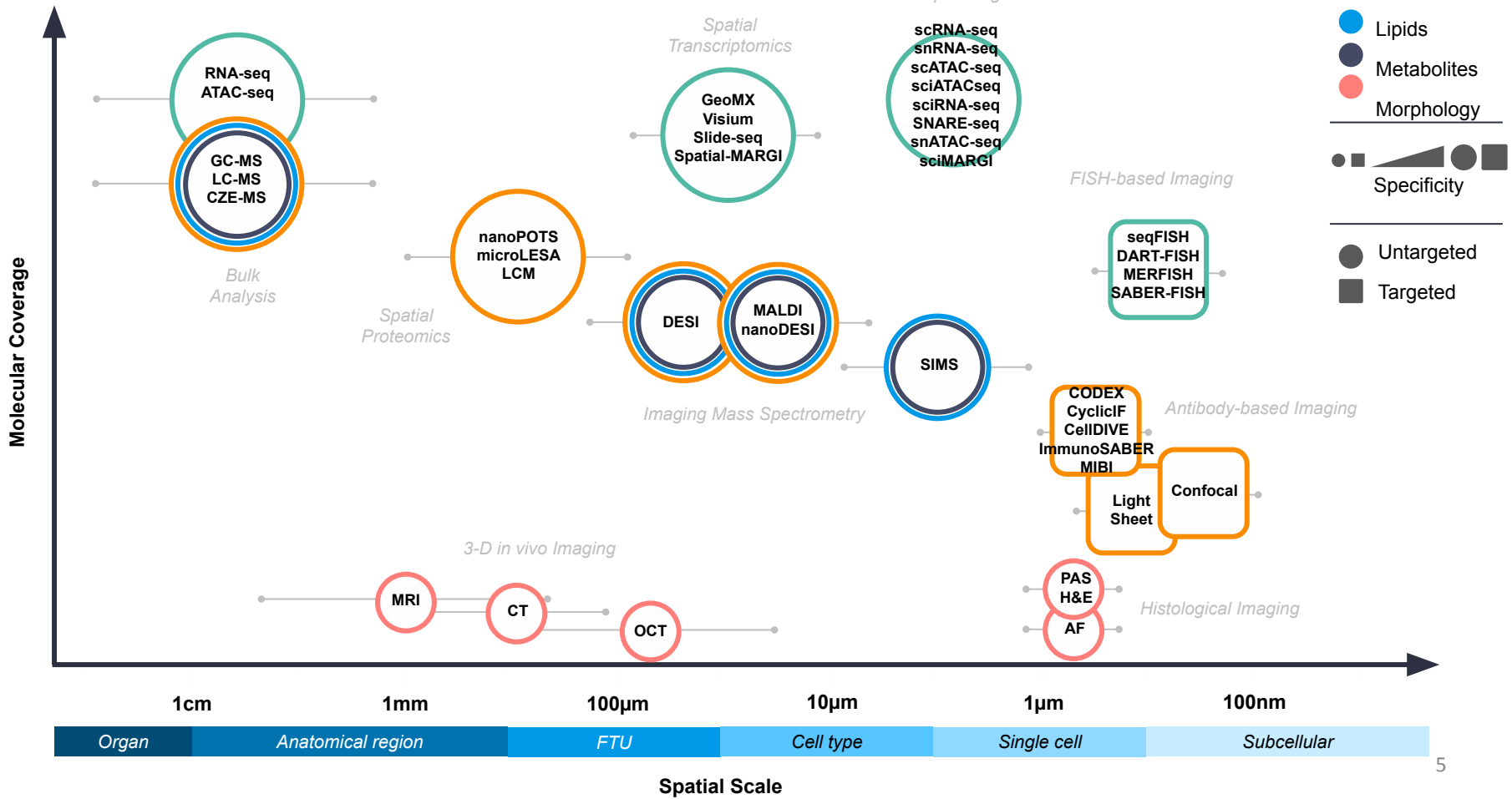


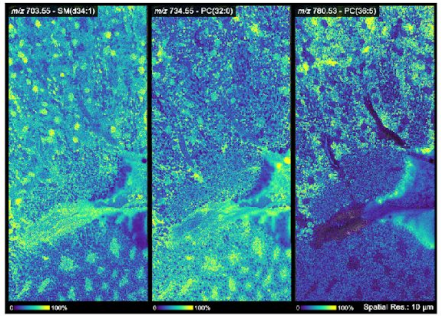
HuBMAP Overview



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

HuBMAP Technologies

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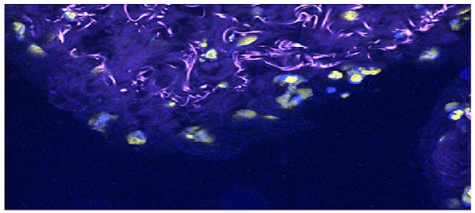
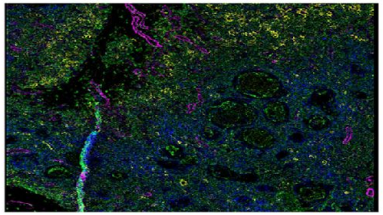
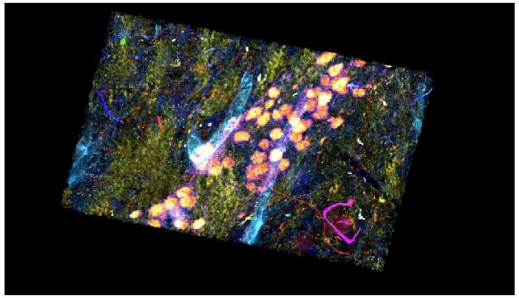
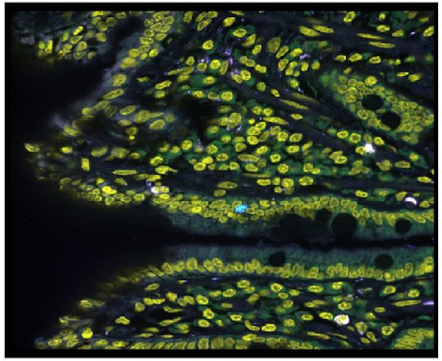
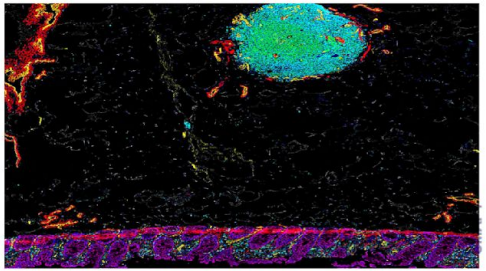
m/z 734.55 - PC(32:0)
m/z 780.59 - PC(36:5)
Spatial Res.: 10 µm

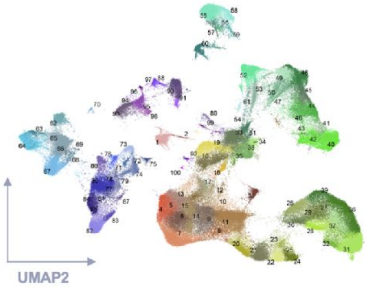


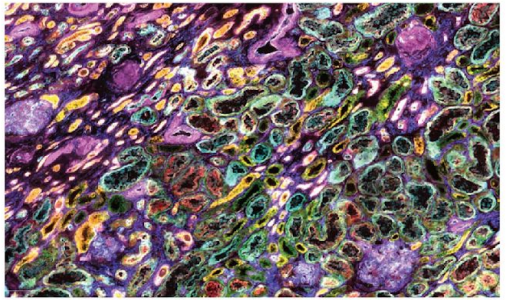


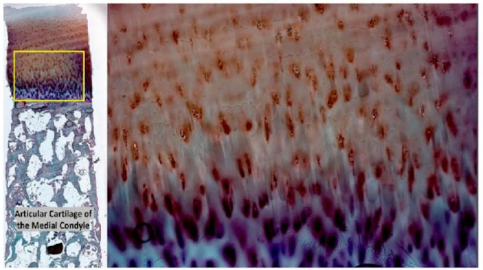


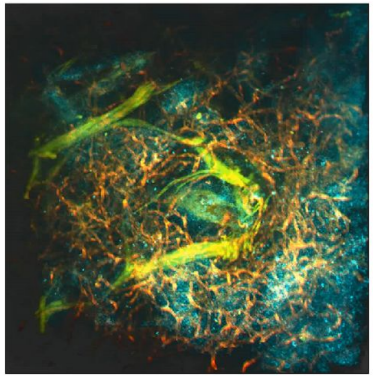


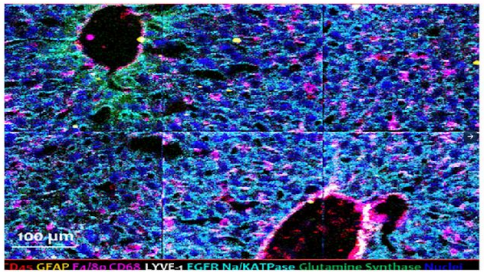


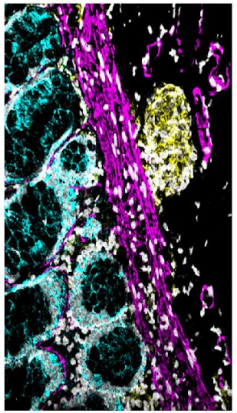

UMAP2

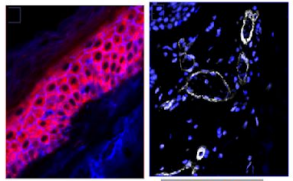


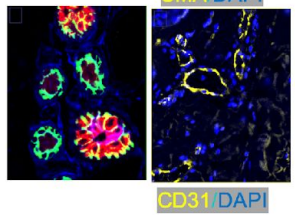

Articular Cartilage of the Medial Condyle




100 µm




SMA/DAPI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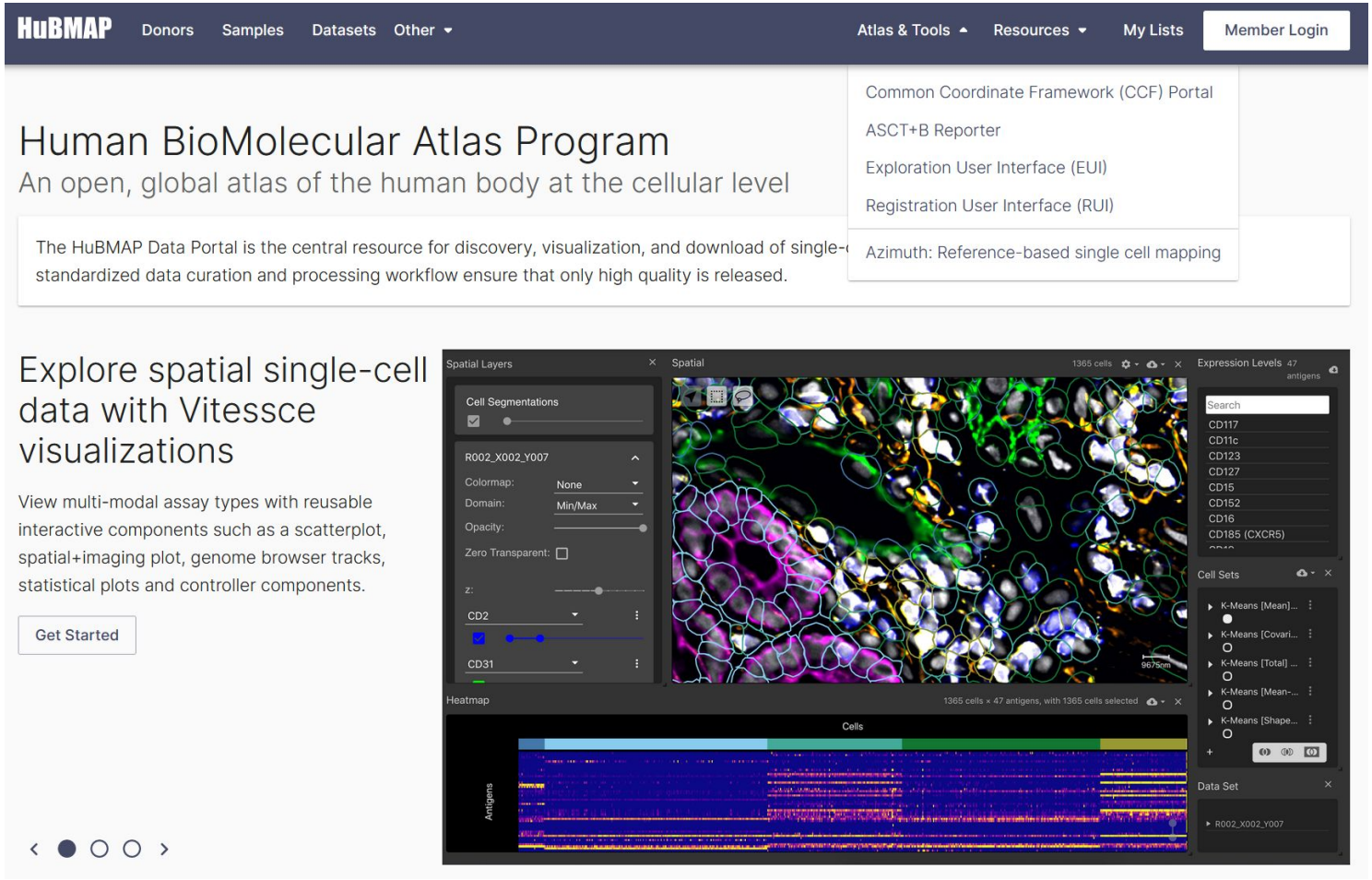
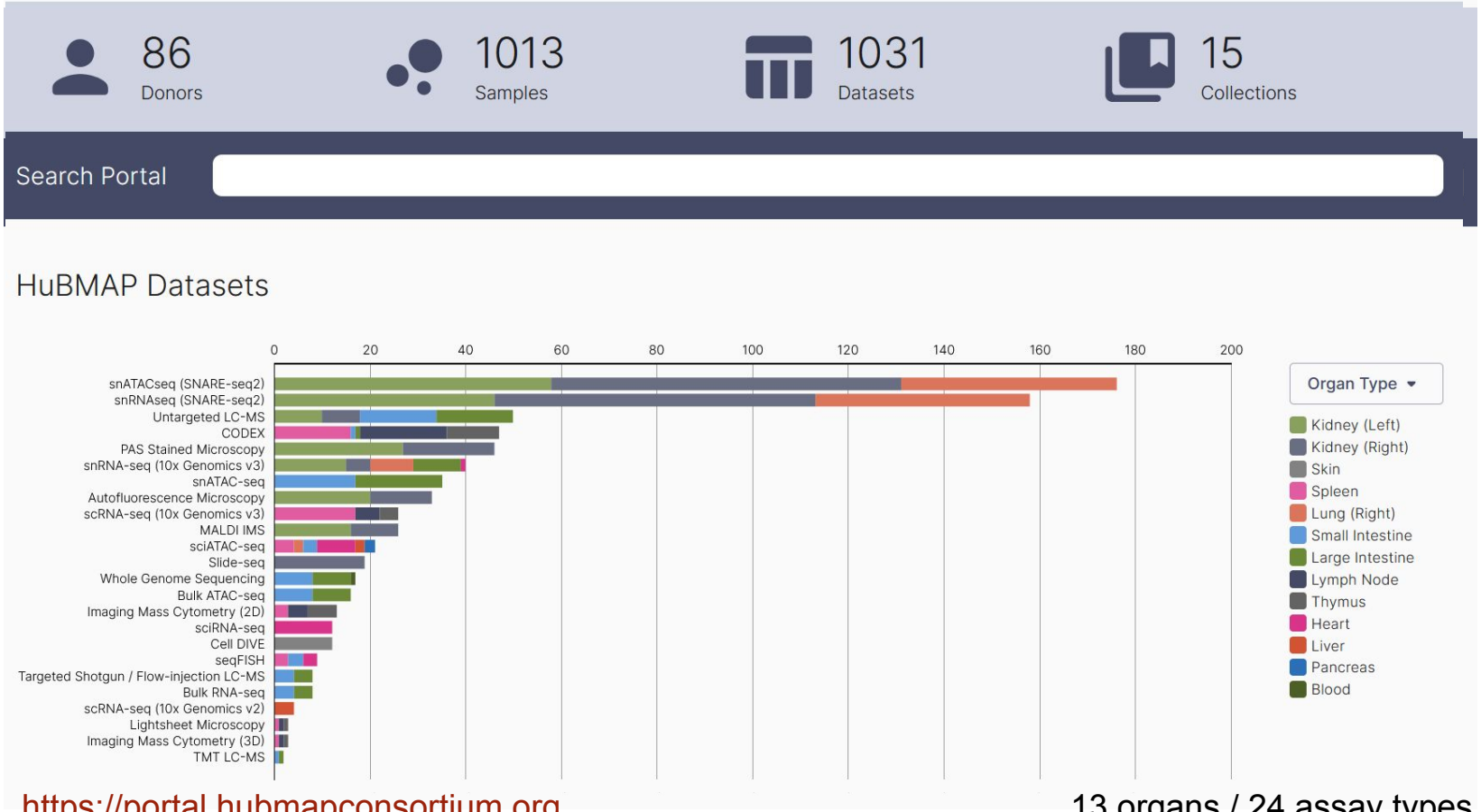


https://portal.hubmapconsortium.org

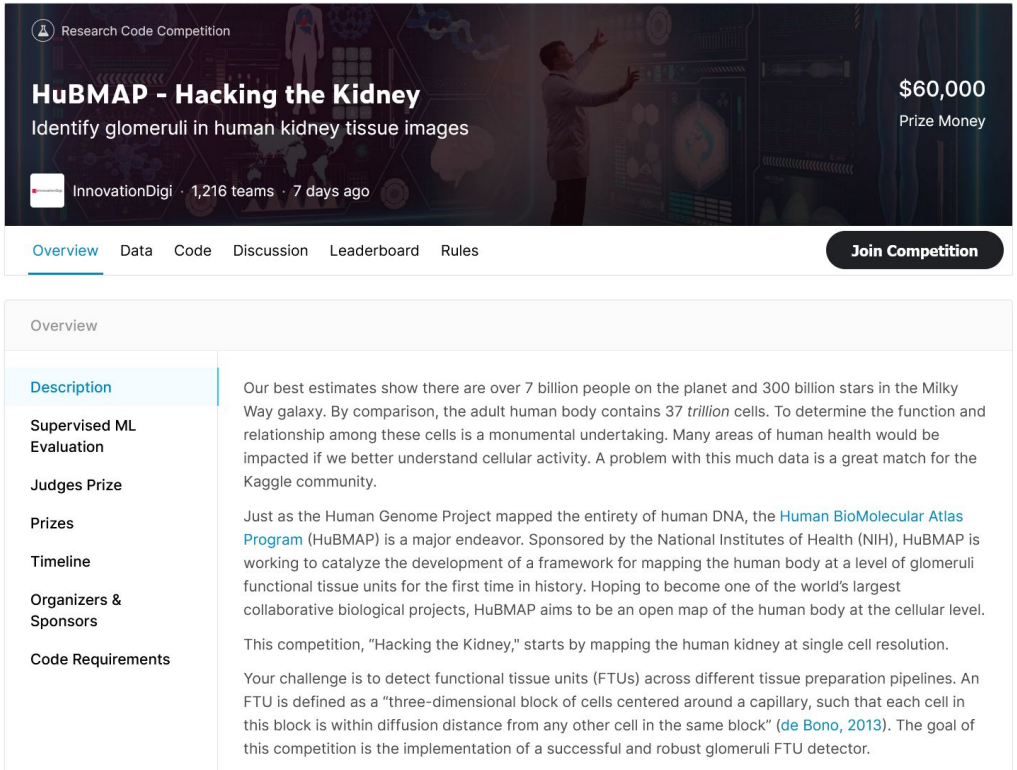
In May 2022



https://portal.hubmapconsortium.org

13 organs / 24 assay types

HuBMAP Kaggle Competition



https://www.kaggle.com/c/hubmap-kidney-segmentation

https://hubmapconsortium.github.io/ccf/pages/kaggle.html <- datasets

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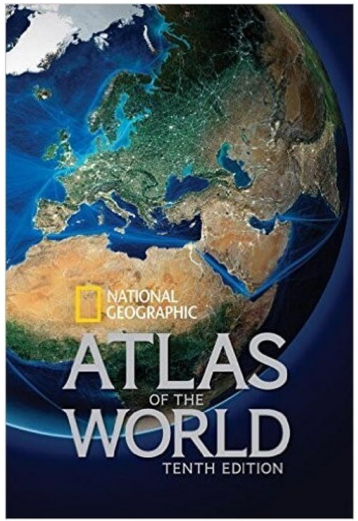
an atos company

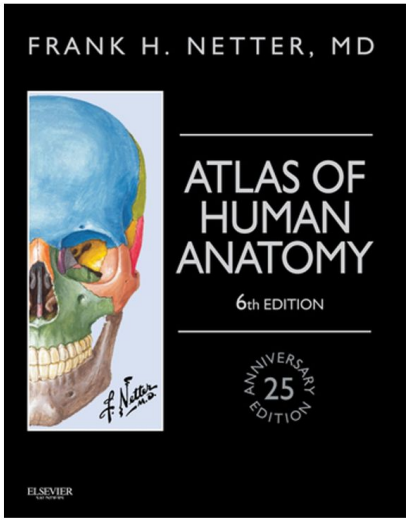
Human Reference Atlas (HRA)

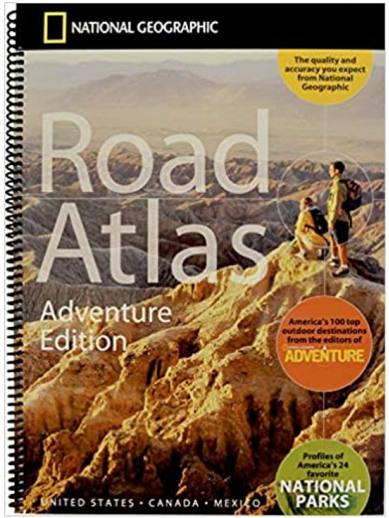
Overall Vision

An **atlas** is an oversized, bound book of maps.

It has descriptive text, an index, possibly other data visualizations.



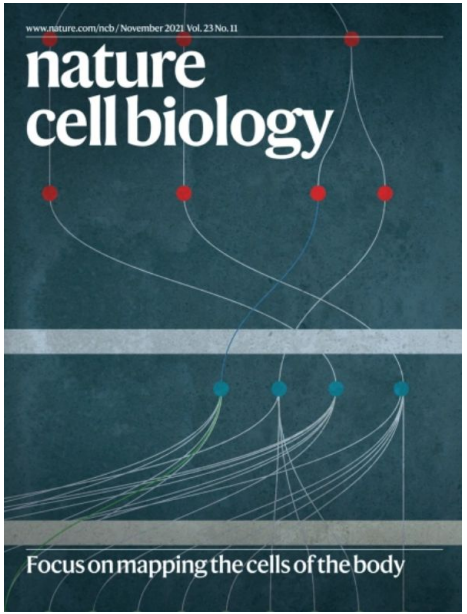




Define Human Reference Atlas

The NIH 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 (or both, see next slide), 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).

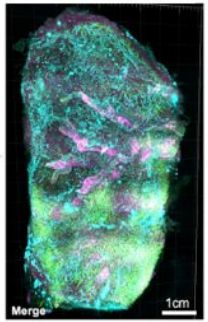


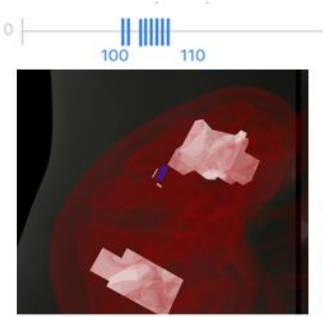
https://www.nature.com/articles/s41556-021-00788-6

Construct a Human Reference Atlas

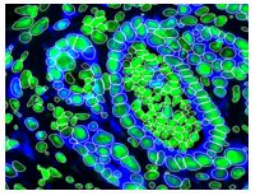
Tissue Data

Whole organ data,
e.g., light-sheet data

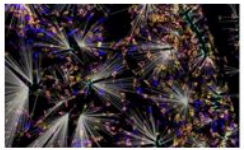




Registered tissue blocks
multiple sections per block



Cell, FTU, AS
segmentation/annotation



Cell type populations
cell distances to vessels
diverse biomarkers per cell

1 Human

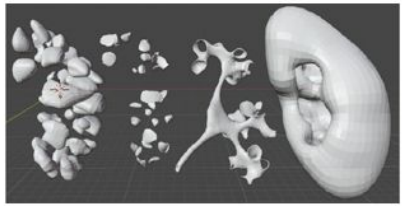
Organs
(kidney shown here)

10,000+
Anatomical
Structures

37T Cells

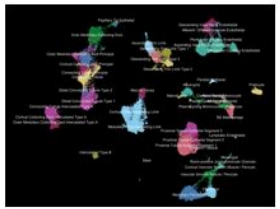
Reference Atlas

3D coordinate system,
geometric mapping process



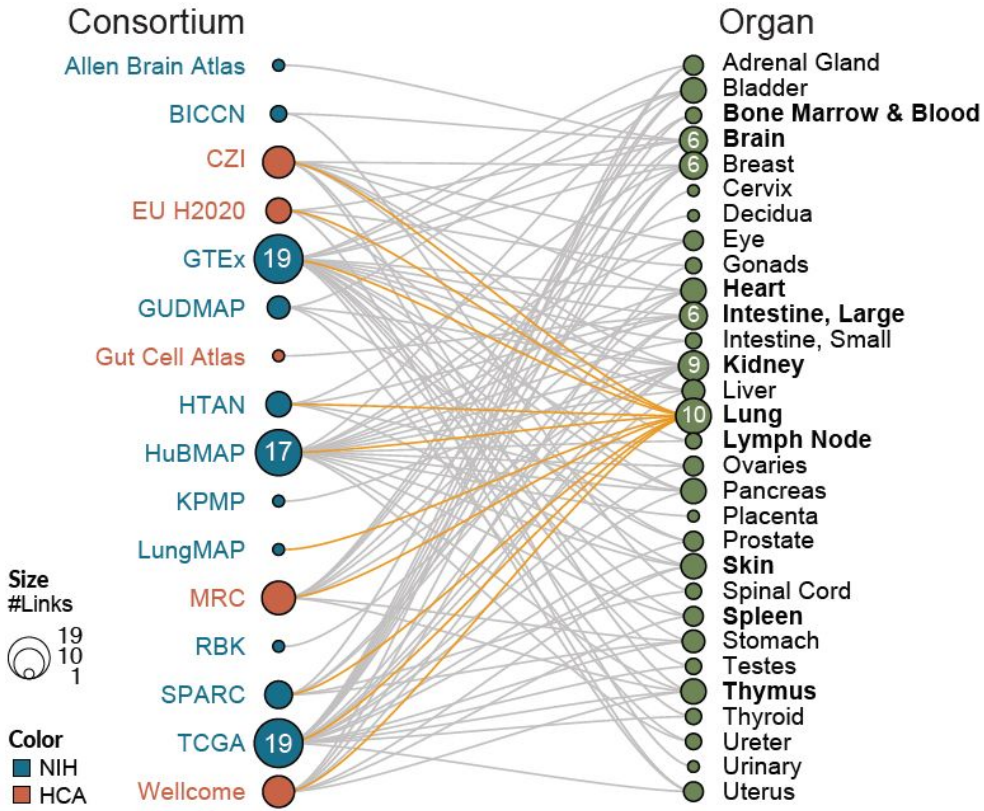
2D Reference FTUs

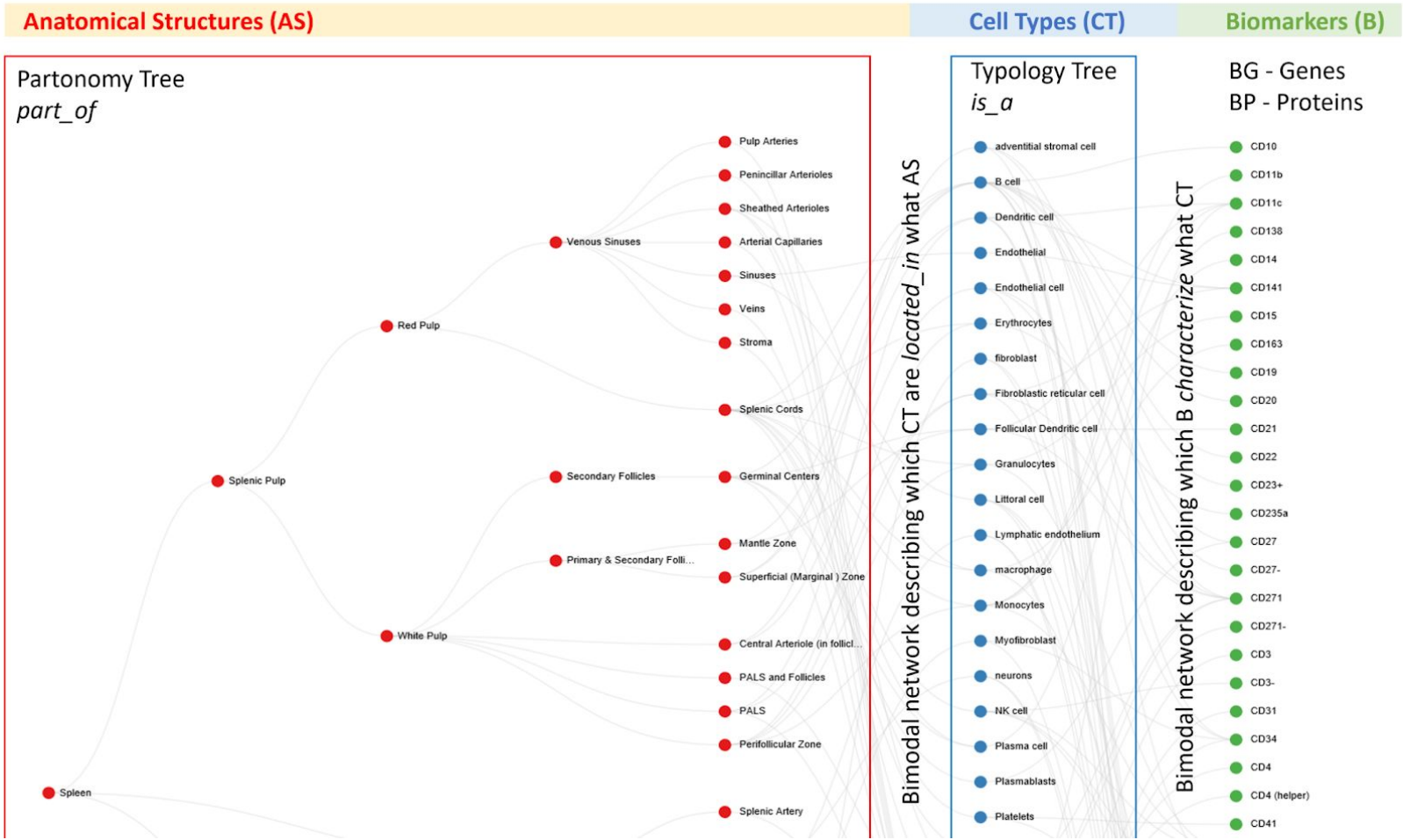
Reference object library with crosswalks to ASCT+B tables,
Synthetic HRA 3D model with cell type populations



2&3D single cell models
cell graphs

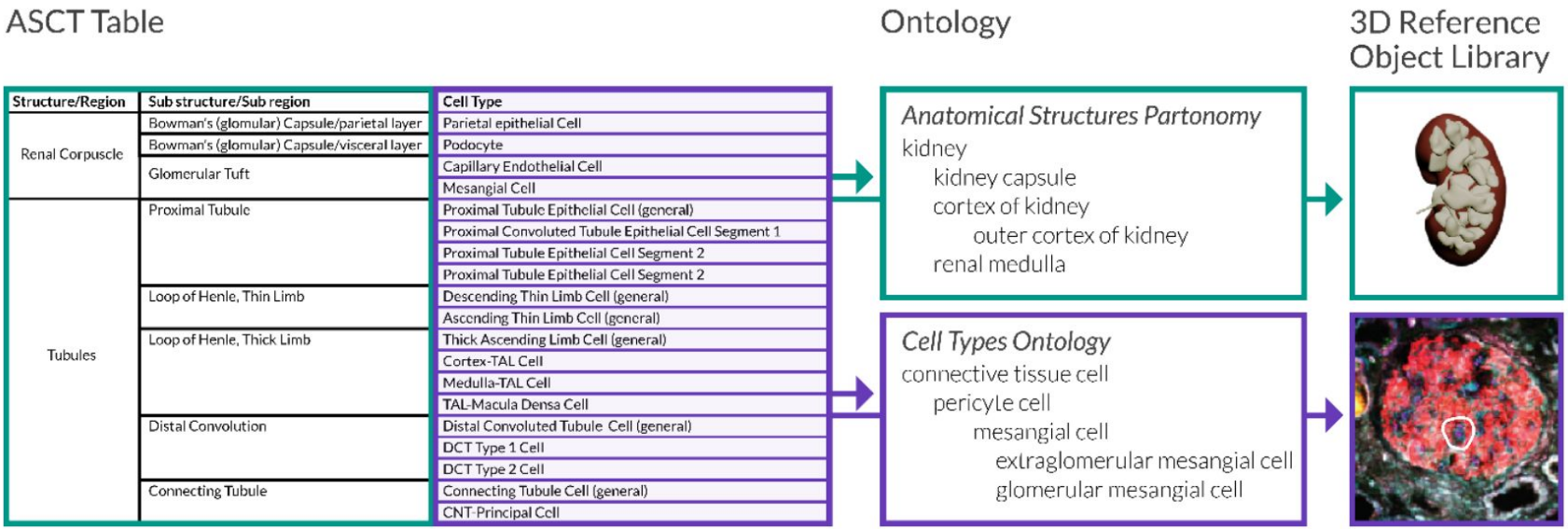
Construct a Human Reference Atlas - Together!




Anatomical Structures (AS)
Cell Types (CT)
Biomarkers (B)
Partonomy Tree
part_of
Spleen
Splenic Pulp
Red Pulp
Venous Sinuses
Pulp Arteries
Penicillar Arterioles
Sheathed Arterioles
Arterial Capillaries
Sinuses
Veins
Stroma
Splenic Cords
Secondary Follicles
Germinal Centers
Primary & Secondary Folli...
Mantle Zone
Superficial (Marginal) Zone
White Pulp
Central Arteriole (in follicl...
PALS and Follicles
PALS
Perifollicular Zone
Splenic Artery
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
BG - Genes
BP - Proteins
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

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.



Choose **version** of ASCT+B datasets: 2nd Release, December '21

Organ	#AS	#CT	#B Total	#BG	#BP	#AS-AS	#AS-CT	#CT-B
Blood	1	30	159	112	47	1	30	506
Blood Vasculature	841	2	1	1	0	869	606	2
Bone Marrow	1	47	262	198	64	1	47	838
Brain	183	127	257	257	0	183	127	346
Eye	26	53	136	61	75	27	58	404
Fallopian Tube	55	22	25	13	12	72	65	32
Heart	50	23	45	45	0	60	183	74
Kidney	61	62	150	150	0	62	60	257
Knee	32	19	14	0	14	32	8	17
Large Intestine	54	57	167	84	83	287	1,156	352
Liver	17	30	62	16	46	17	31	75
Lung	146	83	180	174	6	909	1065	267
Lymph Node	34	45	223	106	117	43	86	499
Lymph Vasculature	4	1	1	1	0	4	2	1
Ovary	71	7	13	7	6	109	12	5
Pancreas	32	32	44	42	2	162	229	101
Peripheral Nervous System	782	1	2	1	1	803	609	2
Prostate	4	12	31	31	0	4	12	36
Skin	15	36	70	0	70	17	19	101
Small Intestine	38	48	13	13	0	69	185	13
Spleen	37	61	194	85	109	50	129	424
Thymus	17	52	394	318	76	28	39	620
Ureter	7	14	30	30	0	7	14	61
Urinary Bladder	16	15	30	30	0	16	16	63
Uterus	58	19	45	39	6	73	28	65
Totals:	**2,582**	**898**	**2,548**	**1,814**	**734**	**3,905**	**4,816**	**5,161**

https://hubmapconsortium.github.io/ccf/pages/ccf-anatomical-structures.html

Crosswalk

https://hubmapconsortium.github.io/ccf/pages/ccf-3d-reference-library.html (NLM VHP organs)
https://community.brain-map.org/t/allen-human-reference-atlas-3d-2020-new/ (brain)
https://www3.cs.stonybrook.edu/~ari/ (male colon)

Anatomical Structures, Cell Types, plus Biomarkers (ASCT+B) table for Lung v1.0

Description

Anatomical Structures, Cell Types, plus Biomarkers (ASCT+B) tables aim to capture the nested *part_of* structure of anatomical human body parts, the typology of cells, and biomarkers used to identify cell types. The tables are authored and reviewed by an international team of experts.

LABEL	VALUE
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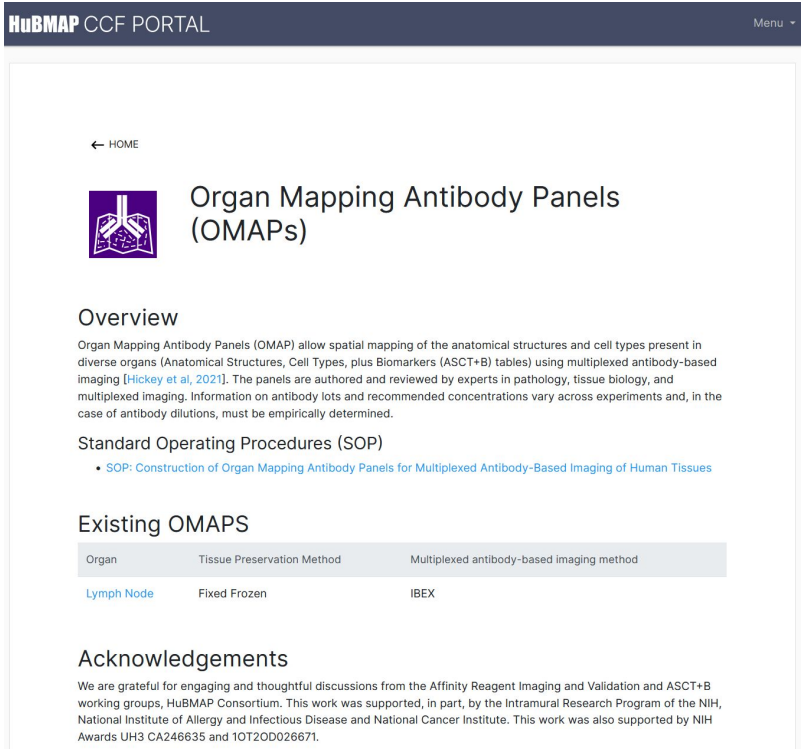
Creator ORCID:	0000-0002-9185-3994; 0000-0001-8387-4966
Project Lead:	Katy Börner
Project Lead ORCID:	0000-0002-3321-6137
Creation Date:	2021-03-12
License:	Creative Commons Attribution 4.0 International (CC BY 4.0)
Publisher:	HuBMAP
Funder:	National Institutes of Health
Award Number:	OT2OD026671
HuBMAP ID:	HBM868.DWJZ.874
Data Table:	Lung v1.0
DOI:	https://doi.org/10.48539/hbm868.dwjz.874
How to Cite This Data Table:	Gloria Pryhuber; Xin Sun. HuBMAP ASCT+B Tables. Lung v1.0 https://doi.org/10.48539/hbm868.dwjz.874
How to Cite ASCT+B Tables Overall:	Quardokus, Ellen, Hrishikesh Paul, Bruce W. Herr II, Lisel Record, Katy Börner. 2021. *HuBMAP ASCT+B Tables*. https://hubmapconsortium.github.io/ccf/pages/ccf-anatomical-structures.html. Accessed on March 12, 2021.

Construct a Human Reference Atlas

In close collaboration with Affinity Reagents Working Group led by Andrea J. Radtke, Ellen Quardokus, Jeannie Camarillo, Neil Kelleher, and Ronald N. Germain we will publish six more OMAPs by June 15, 2022:

1. Skin Liz McDonough (GE; colleague Fiona Ginty) (technology: Cell Dive)
2. Intestines John Hickey (Nolan/Snyder labs)(technology: CODEX)
3. Lung Gloria Pryhuber (HuBMAP/LungMAP) (technology: Cell Dive)
4. Kidney Elizabeth Neumann (TMC-VU) (technology: CODEX)
5. Pancreas Anna Martinez Casals (SciLifeLab Sweden; colleague Emma Lundberg) (technology: CODEX)
6. Liver Presha Rajbhandari From Stockwell lab (technology: SIM)
7. Lymph node (Andrea Radtke) (revised) (technology: IBEX); Christopher Werlein (stellar reviewer!)

All OMAPs are linked to respective ASCT+B tables.
Aim to submit *Nature Methods* Correspondence in May 2022.

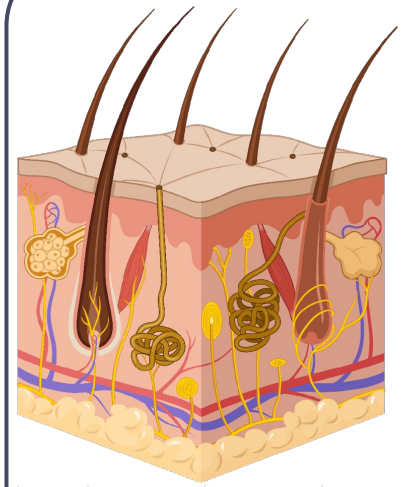


https://hubmapconsortium.github.io/ccf/pages/omap.html

Interlinking ASCT+B and Affinity Reagent Working Group Efforts

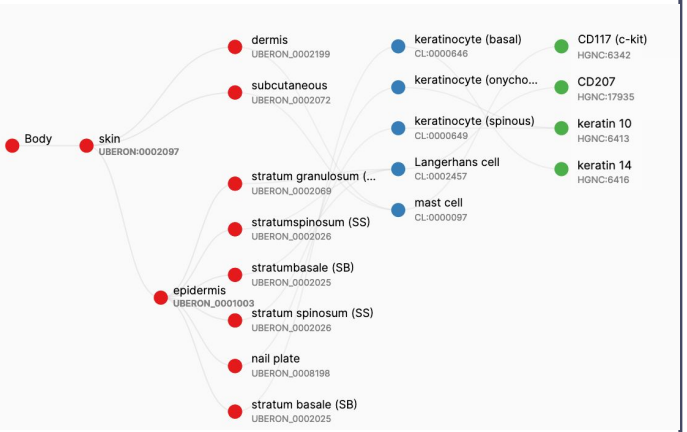
Use Case: Skin-Specific Panel

Skin

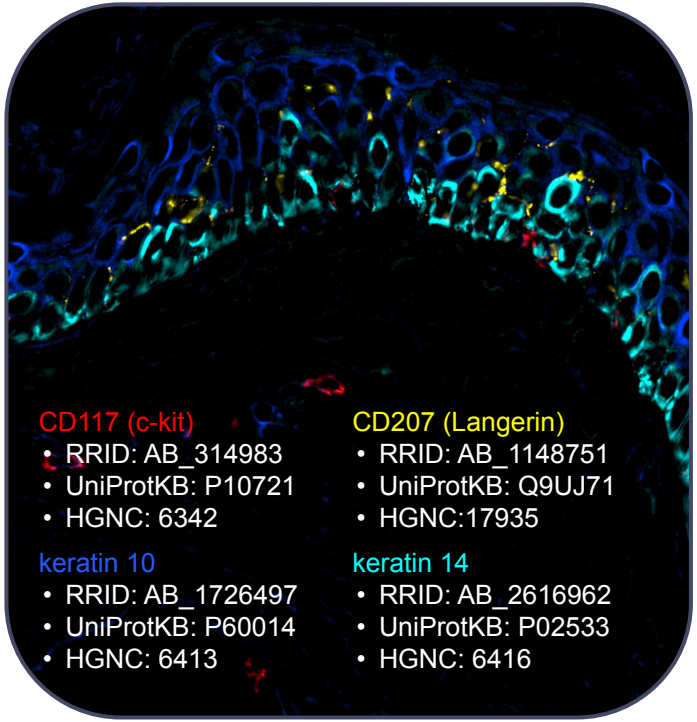


AS/2	AS/3	CT	BP
dermis		mast cell	CD117 (c-kit)
subcutaneous		mast cell	CD117 (c-kit)
epidermis	stratum granulosum (SG)	Langerhans cell	CD207 (Langerin)
epidermis	stratumspinosum (SS)	Langerhans cell	CD207 (Langerin)
epidermis	stratumbasale (SB)	Langerhans cell	CD207 (Langerin)
epidermis	stratum spinosum (SS)	keratinocyte (spinous)	keratin 10
epidermis	nail plate	keratinocyte (onychocyte)	keratin 10
epidermis	stratum basale (SB)	keratinocyte (basal)	keratin 14

ASCT + B



4 Affinity Reagent / pBiomarker Pairs

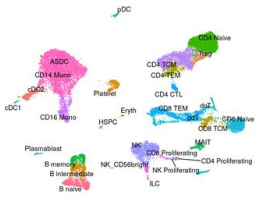


Thanks go to Andrea R., Ellen Q., Rich L, Neil K. (MC-IU & RTI-Northwestern)

Construct a Human Reference Atlas

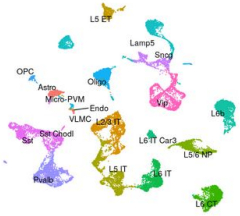
https://azimuth.hubmapconsortium.org

Human - PBMC



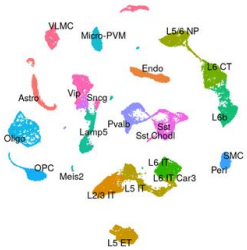
Learn more | Go to App

Human - Motor Cortex



Learn more | Go to App

Mouse - Motor Cortex



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Human - Pancreas

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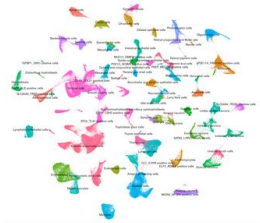
Human - Fetal Development



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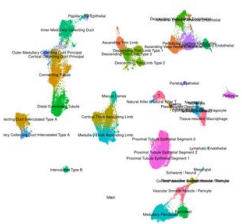
Human - Kidney



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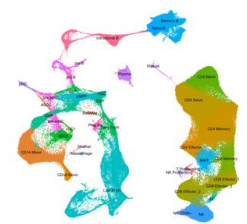
Human - Bone Marrow



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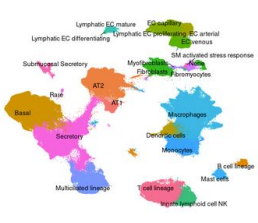
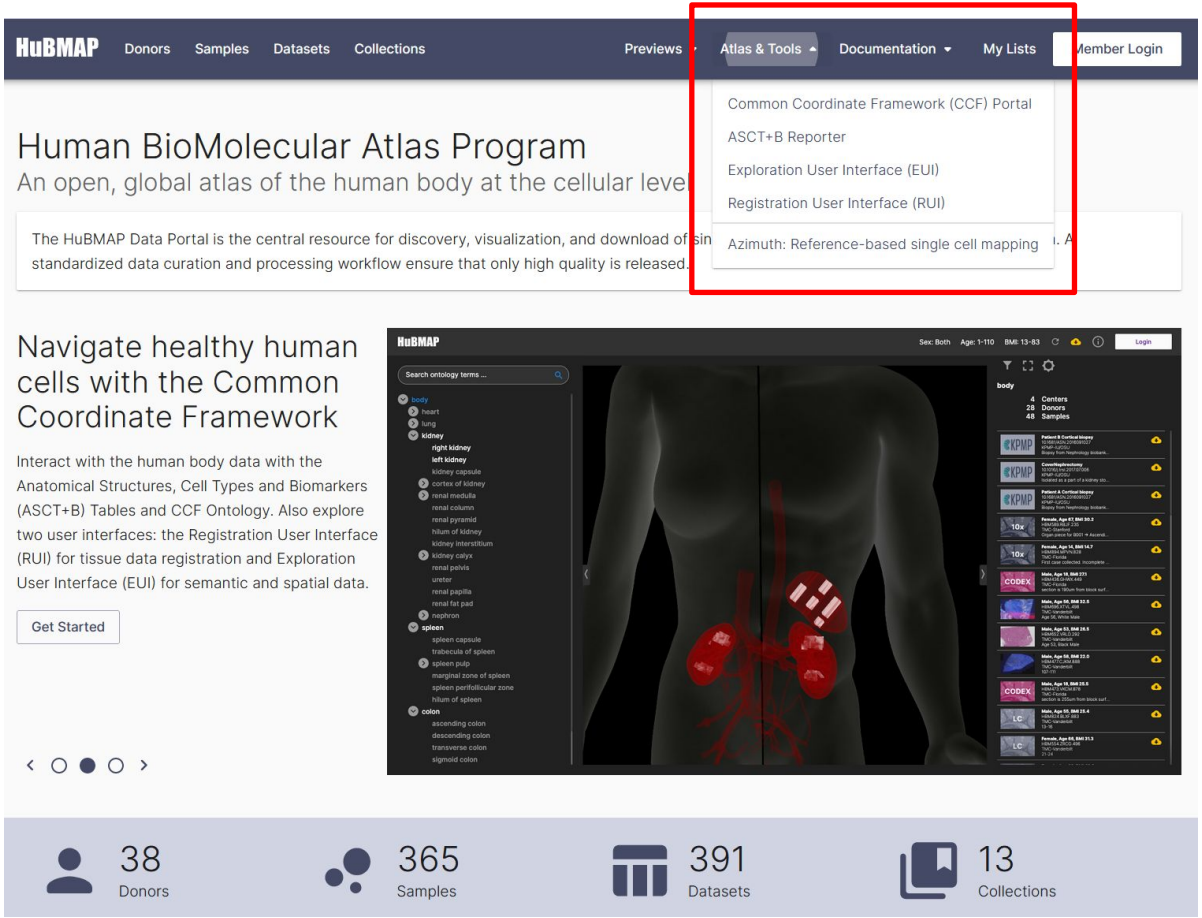
Human - Lung v2 (HLCA)

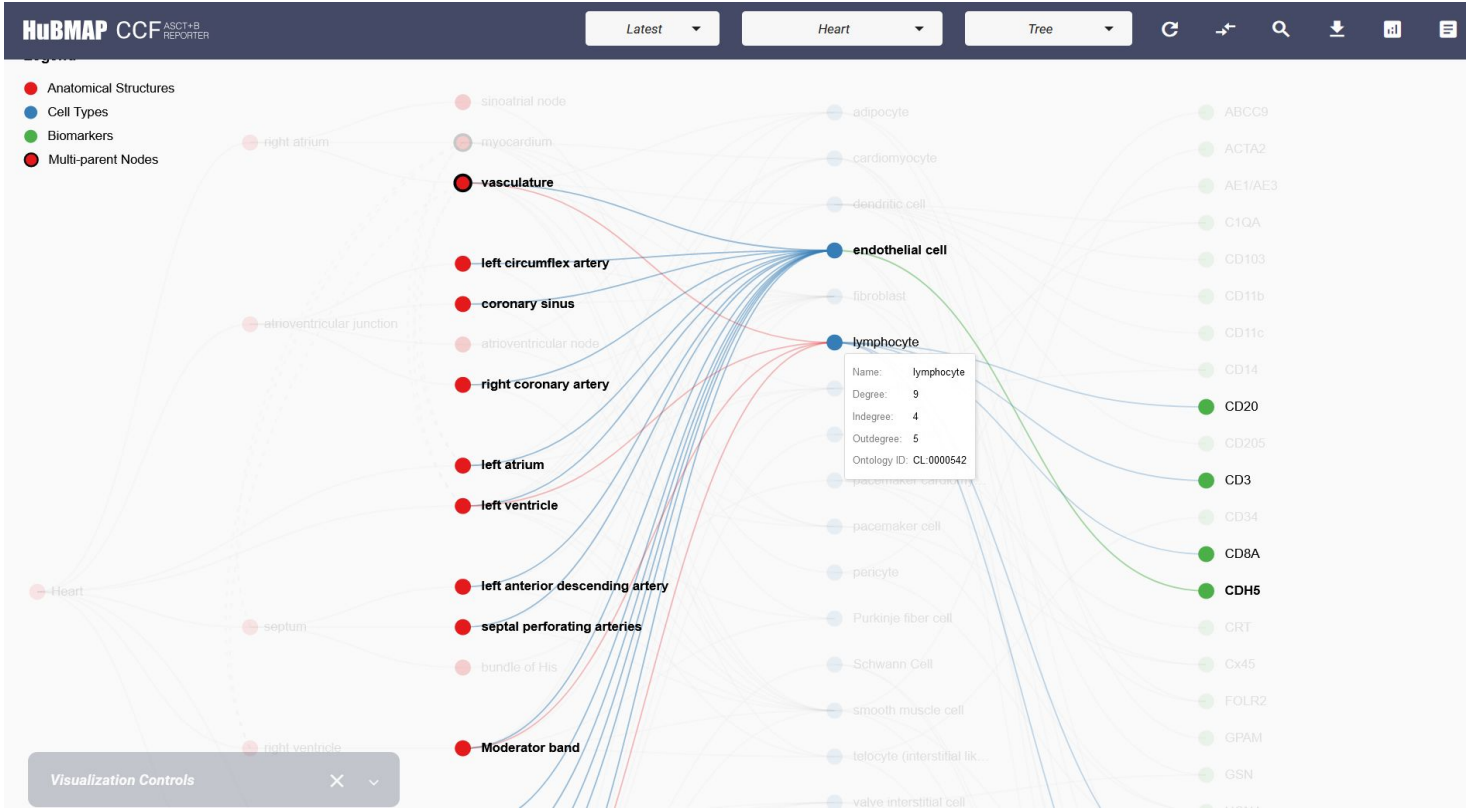


Learn more | Go to App

Use the Human Reference Atlas for Data Harmonization



CCF ASCT+B Reporter UI

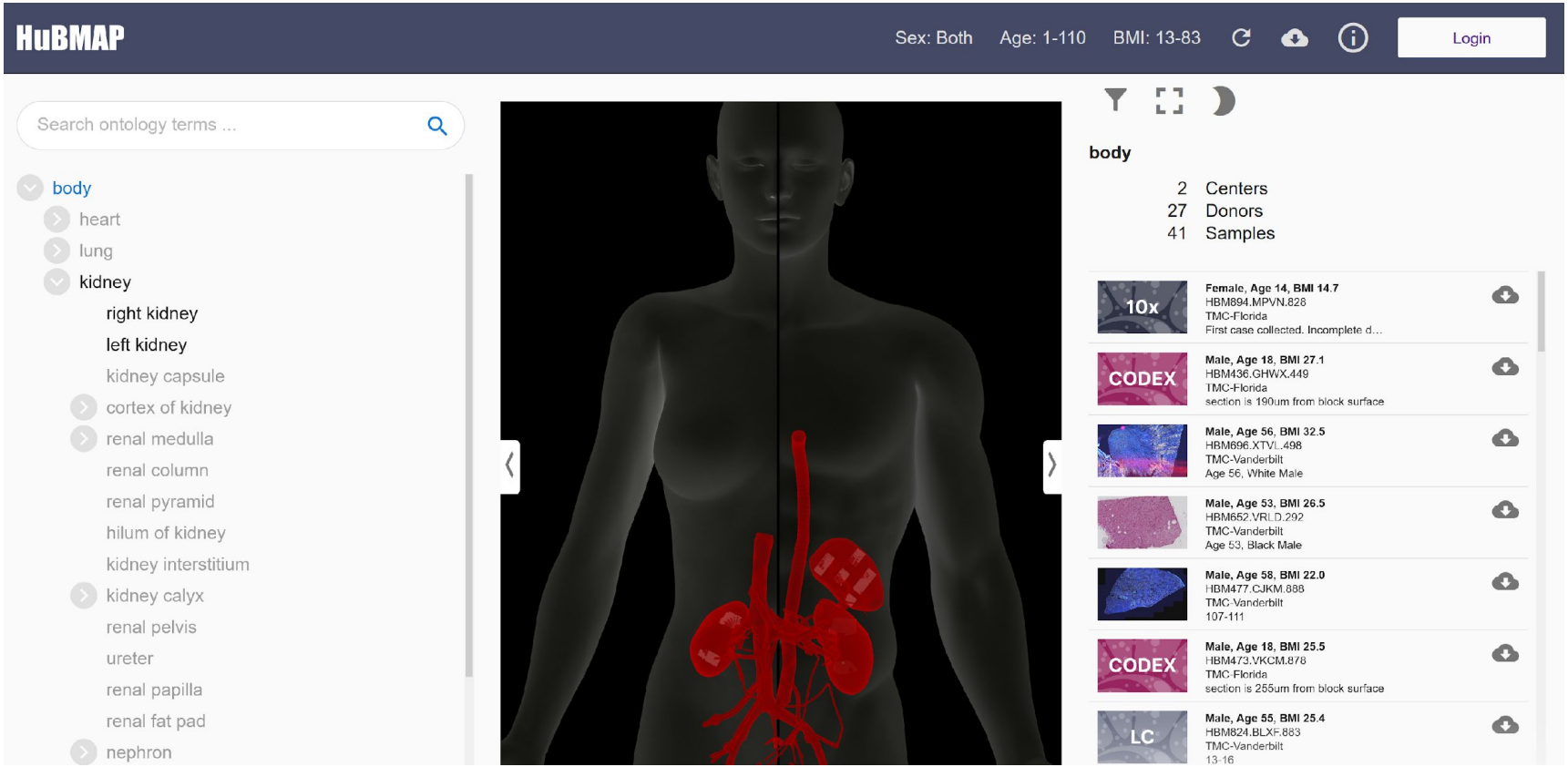


https://hubmapconsortium.github.io/ccf-asct-reporter/

CCF Registration User Interface (RUI)

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

CCF Exploration User Interface (EUI)



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

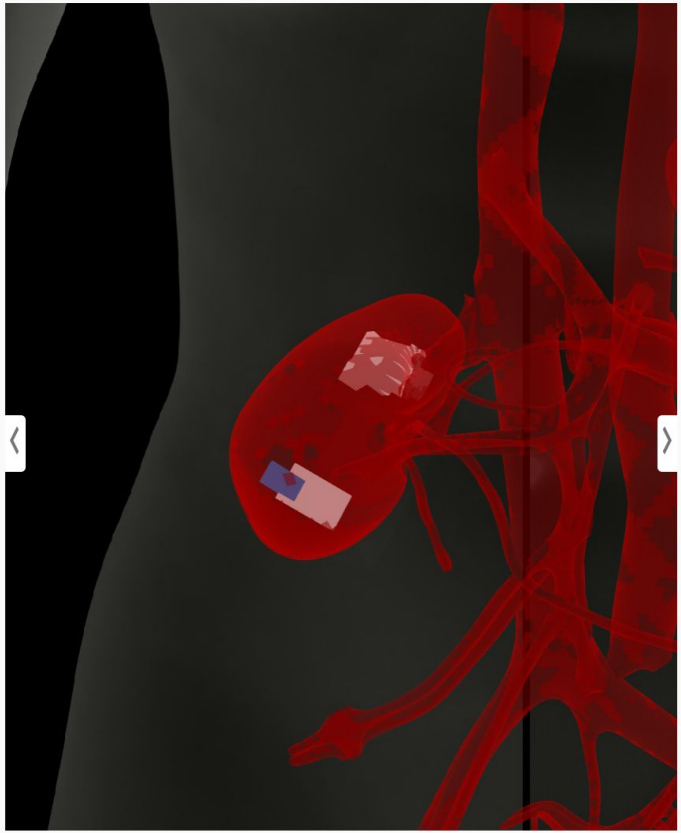
HuBMAP

Sex: Both Age: 1-110 BMI: 13-83

Logout

Search ontology terms ...

- body
  - heart
  - lung
  - kidney
    - right kidney
    - left kidney
    - kidney capsule
    - cortex of kidney
    - renal medulla
    - renal column
    - renal pyramid
    - hilum of kidney
    - kidney interstitium
    - kidney calyx
      - major calyx
      - minor calyx
    - renal pelvis
    - ureter
    - renal papilla
    - renal fat pad
  - nephron
  - spleen
  - colon

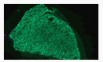


body

1 Centers
9 Donors
40 Samples

Male, Age 55, BMI 25.4
HBM695.RTLJ.484
TMC-Vanderbilt
13-16

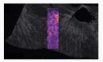
Male, Age 21, BMI 21.8
HBM634.MMGK.572
TMC-Vanderbilt
Age 21 , White Male, Trauma Patient



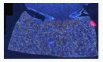
Female, Age 44, BMI 28.0
HBM457.NNQN.252
TMC-Vanderbilt
Age 44, white female.

Female, Age 44, BMI 28.0
HBM465.VKHL.532
TMC-Vanderbilt
Age 44, white female.

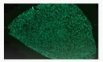
Male, Age 21, BMI 21.8
HBM693.HFFJ.752
TMC-Vanderbilt
Age 21 , White Male, Trauma Patient



Female, Age 58, BMI 23.0
HBM536.LDTZ.757
TMC-Vanderbilt
Age 58, White Female

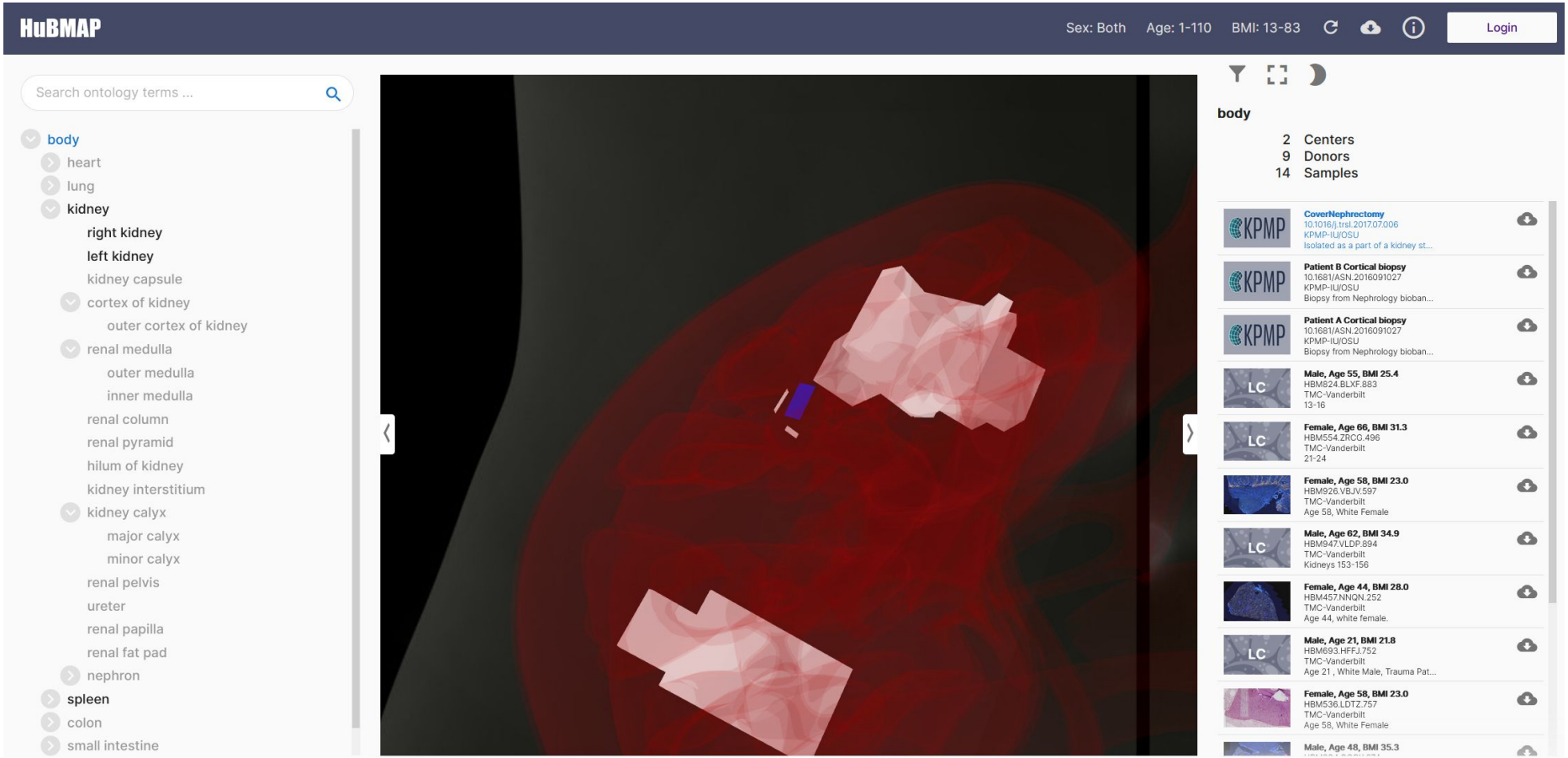


Male, Age 48, BMI 35.3
HBM334.GCCX.874
TMC-Vanderbilt
Age 48, White Male

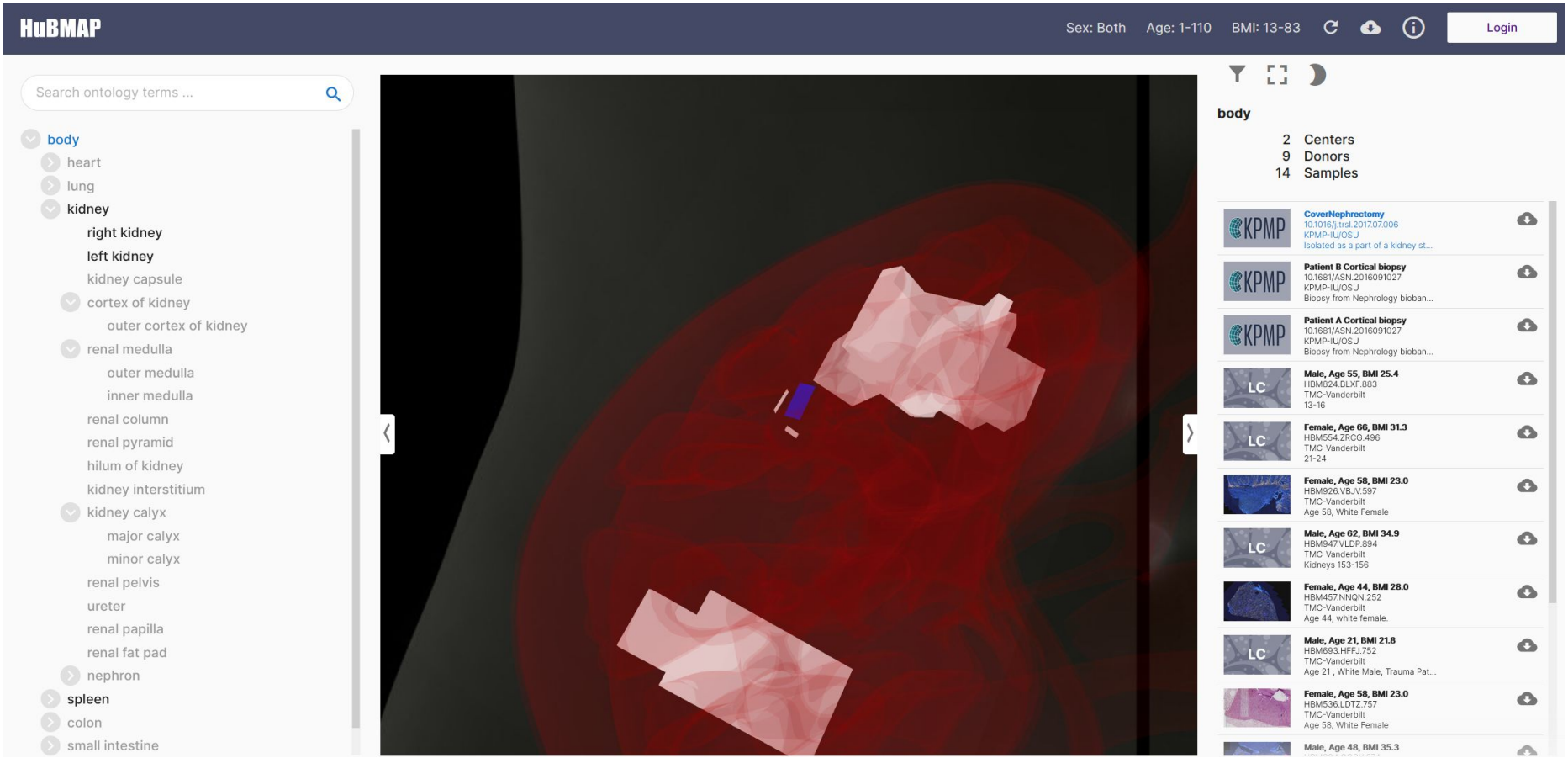


Male, Age 31, BMI 32.6
HBM776.PKJF.786
TMC-Vanderbilt
Age 21, White Male

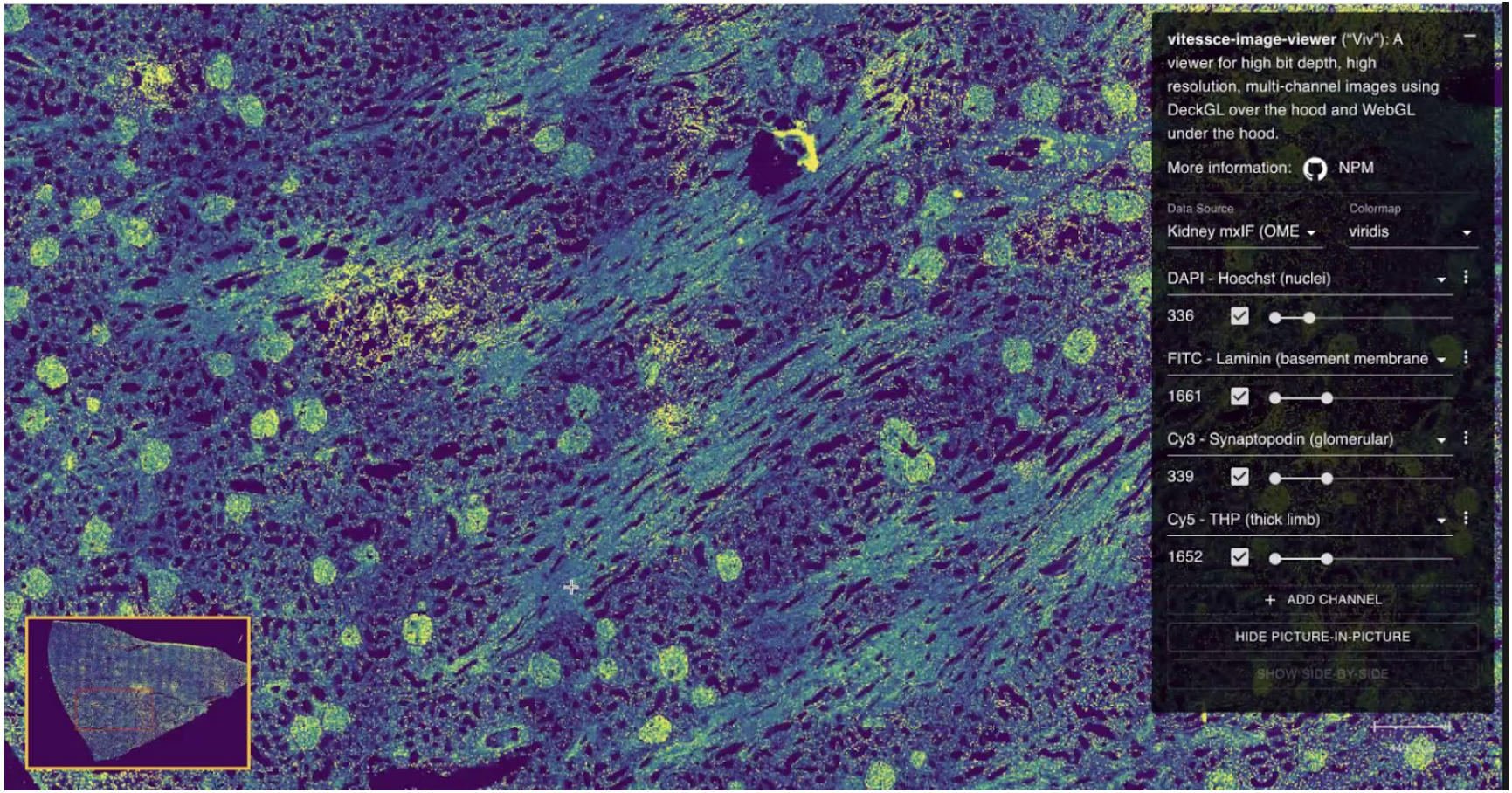
Female, Age 66, BMI 31.3
HBM284.TRCV.726



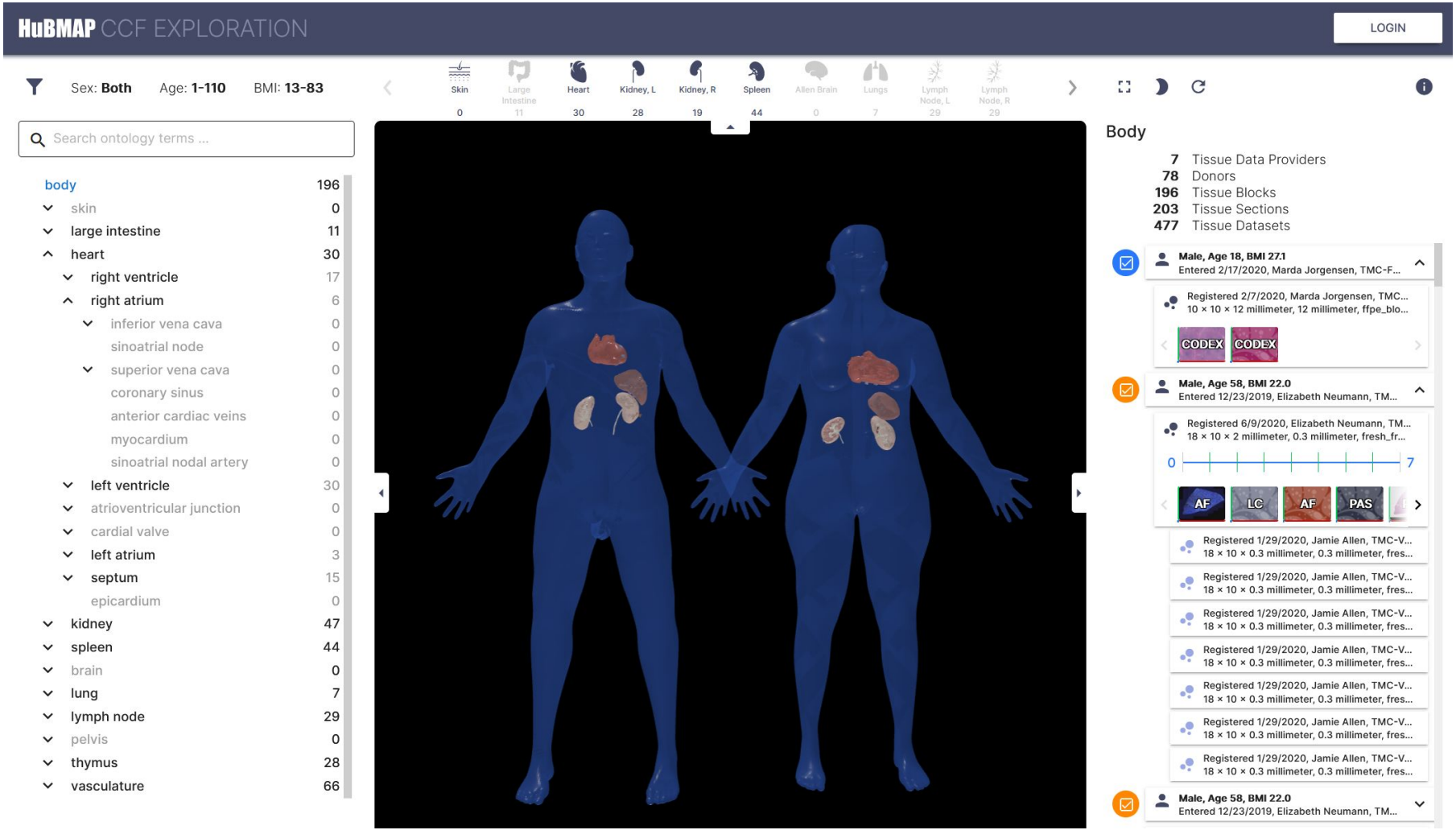
Register your data via https://hubmap-ccf-ui.netlify.app/rui/ so it can be spatially/semantically explored in EUI.

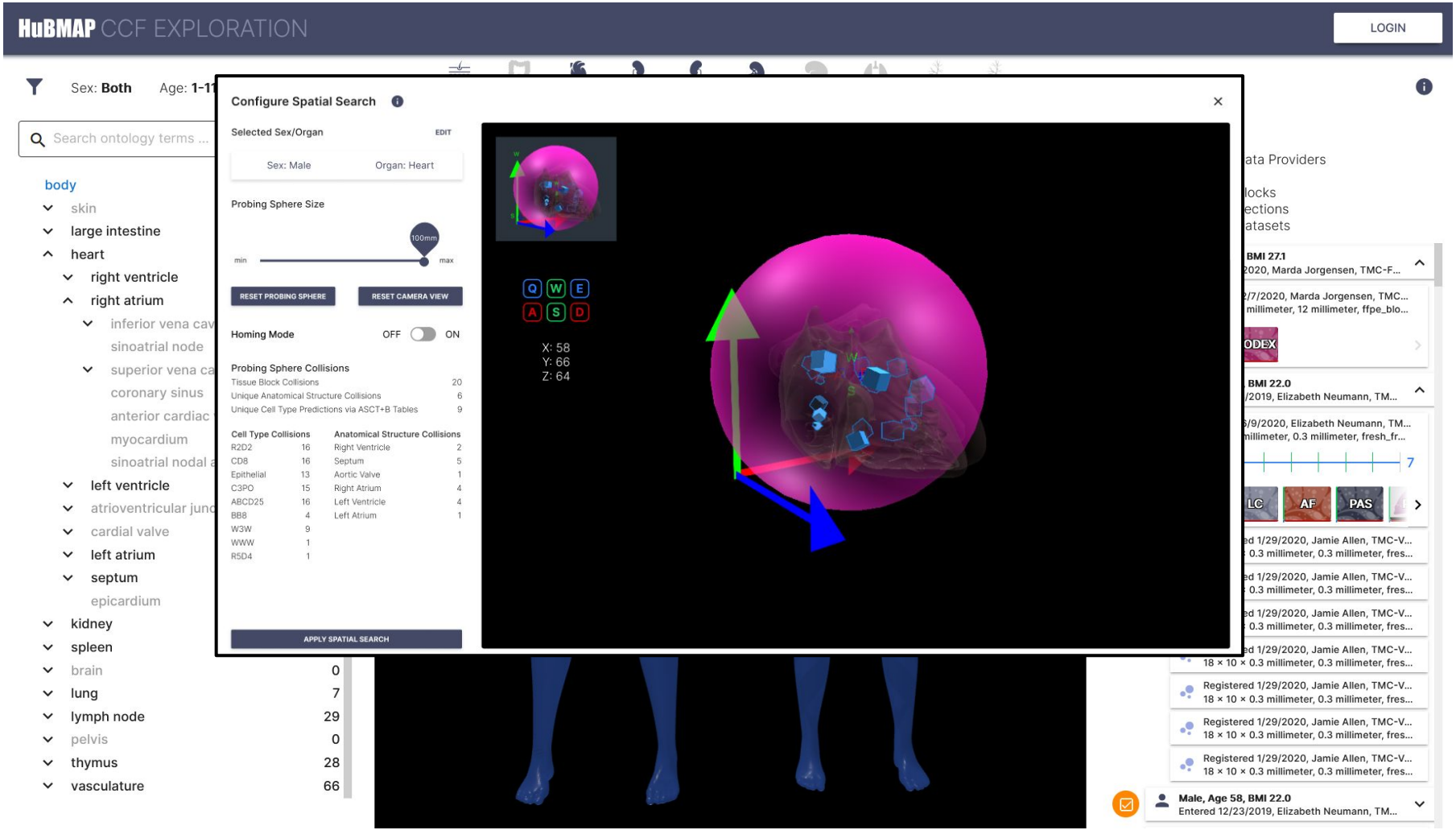


Register your data via https://hubmap-ccf-ui.netlify.app/rui/ so it can be spatially/semantically explored in EUI.



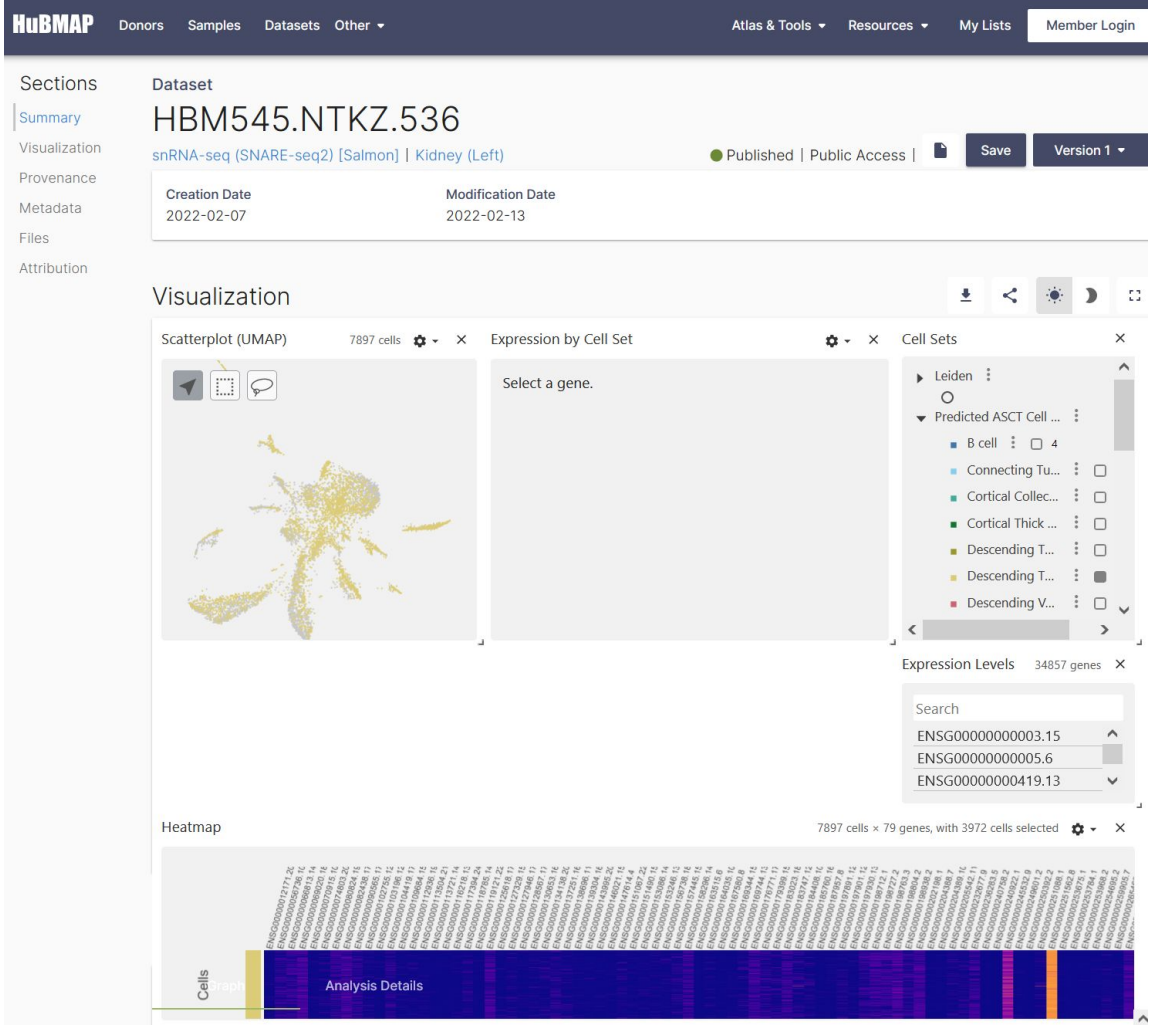
http://gehlenborglab.org/research/projects/vitessce/


HuBMAP CCF EXPLORATION
LOGIN
Sex: Both
Age: 1-110
BMI: 13-83
Skin 0
Large Intestine 11
Heart 30
Kidney, L 28
Kidney, R 19
Spleen 44
Allen Brain 0
Lungs 7
Lymph Node, L 29
Lymph Node, R 29
Search ontology terms ...
body 196
skin 0
large intestine 11
heart 30
right ventricle 17
right atrium 6
inferior vena cava 0
sinoatrial node 0
superior vena cava 0
coronary sinus 0
anterior cardiac veins 0
myocardium 0
sinoatrial nodal artery 0
left ventricle 30
atrioventricular junction 0
cardial valve 0
left atrium 3
septum 15
epicardium 0
kidney 47
spleen 44
brain 0
lung 7
lymph node 29
pelvis 0
thymus 28
vasculature 66
Body
7 Tissue Data Providers
78 Donors
196 Tissue Blocks
203 Tissue Sections
477 Tissue Datasets
Male, Age 18, BMI 27.1
Entered 2/17/2020, Marda Jorgensen, TMC-F...
Registered 2/7/2020, Marda Jorgensen, TMC...
10 × 10 × 12 millimeter, 12 millimeter, ffpe_blo...
CODEX
CODEX
Male, Age 58, BMI 22.0
Entered 12/23/2019, Elizabeth Neumann, TM...
Registered 6/9/2020, Elizabeth Neumann, TM...
18 × 10 × 2 millimeter, 0.3 millimeter, fresh_fr...
0
7
AF
LC
AF
PAS
Registered 1/29/2020, Jamie Allen, TMC-V...
18 × 10 × 0.3 millimeter, 0.3 millimeter, fres...
Male, Age 58, BMI 22.0
Entered 12/23/2019, Elizabeth Neumann, TM...


HuBMAP CCF EXPLORATION
LOGIN
Sex: Both
Age: 1-11
Search ontology terms ...
body
skin
large intestine
heart
right ventricle
right atrium
inferior vena cav
sinoatrial node
superior vena ca
coronary sinus
anterior cardiac
myocardium
sinoatrial nodal a
left ventricle
atrioventricular junc
cardial valve
left atrium
septum
epicardium
kidney
spleen
brain 0
lung 7
lymph node 29
pelvis 0
thymus 28
vasculature 66
Configure Spatial Search
Selected Sex/Organ
EDIT
Sex: Male
Organ: Heart
Probing Sphere Size
100mm
min
max
RESET PROBING SPHERE
RESET CAMERA VIEW
Homing Mode
OFF
ON
Probing Sphere Collisions
Tissue Block Collisions 20
Unique Anatomical Structure Collisions 6
Unique Cell Type Predictions via ASCT+B Tables 9
Cell Type Collisions
R2D2 16
CD8 16
Epithelial 13
C3PO 15
ABCD25 16
BB8 4
W3W 9
WWW 1
R5D4 1
Anatomical Structure Collisions
Right Ventricle 2
Septum 5
Aortic Valve 1
Right Atrium 4
Left Ventricle 4
Left Atrium 1
APPLY SPATIAL SEARCH
Q W E
A S D
X: 58
Y: 66
Z: 64
ata Providers
locks
ections
atasets
BMI 27.1
2020, Marda Jorgensen, TMC-F...
2/7/2020, Marda Jorgensen, TMC...
millimeter, 12 millimeter, ffpe_blo...
ODEX
BMI 22.0
/2019, Elizabeth Neumann, TM...
6/9/2020, Elizabeth Neumann, TM...
millimeter, 0.3 millimeter, fresh_fr...
7
LC
AF
PAS
ed 1/29/2020, Jamie Allen, TMC-V...
0.3 millimeter, 0.3 millimeter, fres...
Registered 1/29/2020, Jamie Allen, TMC-V...
18 × 10 × 0.3 millimeter, 0.3 millimeter, fres...
Male, Age 58, BMI 22.0
Entered 12/23/2019, Elizabeth Neumann, TM...

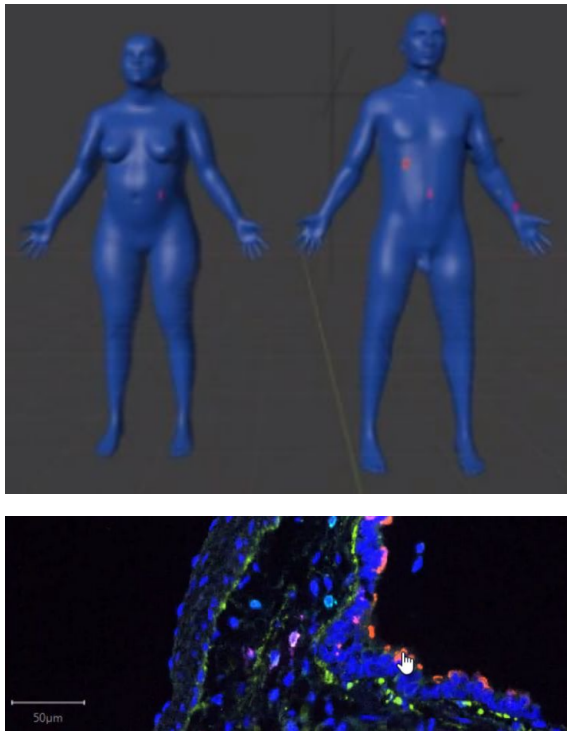
Use the Human Reference Atlas for Data Harmonization

snRNA-seq assays now have ASCT+B CT annotations

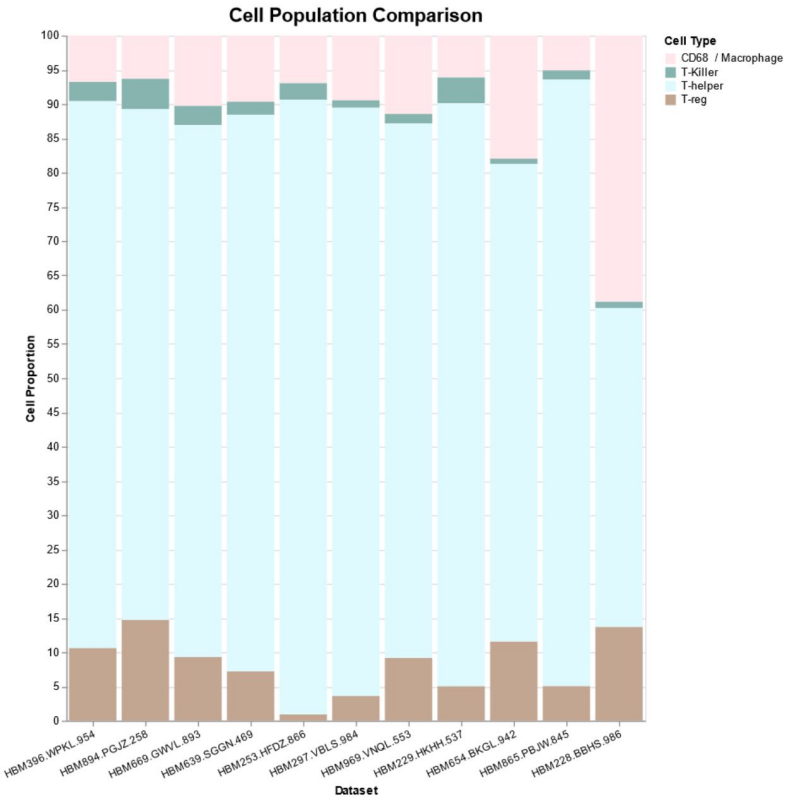


https://portal.hubmapconsortium.org/browse/dataset/d1e9f509063984326570cf603c5654f2

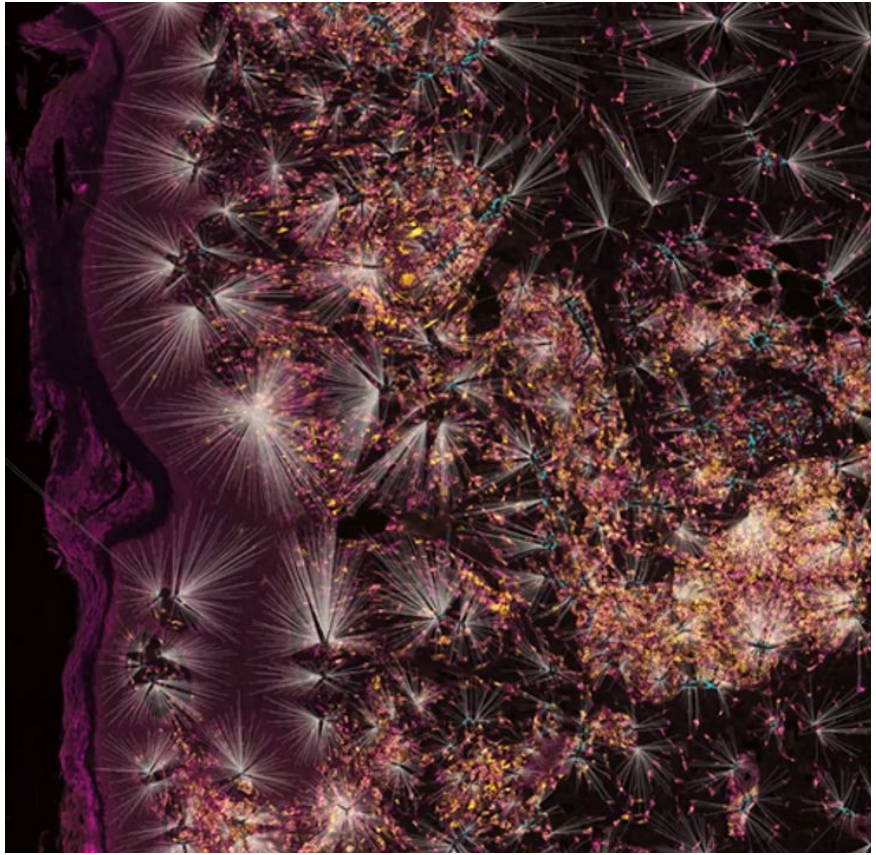
Use the Human Reference Atlas

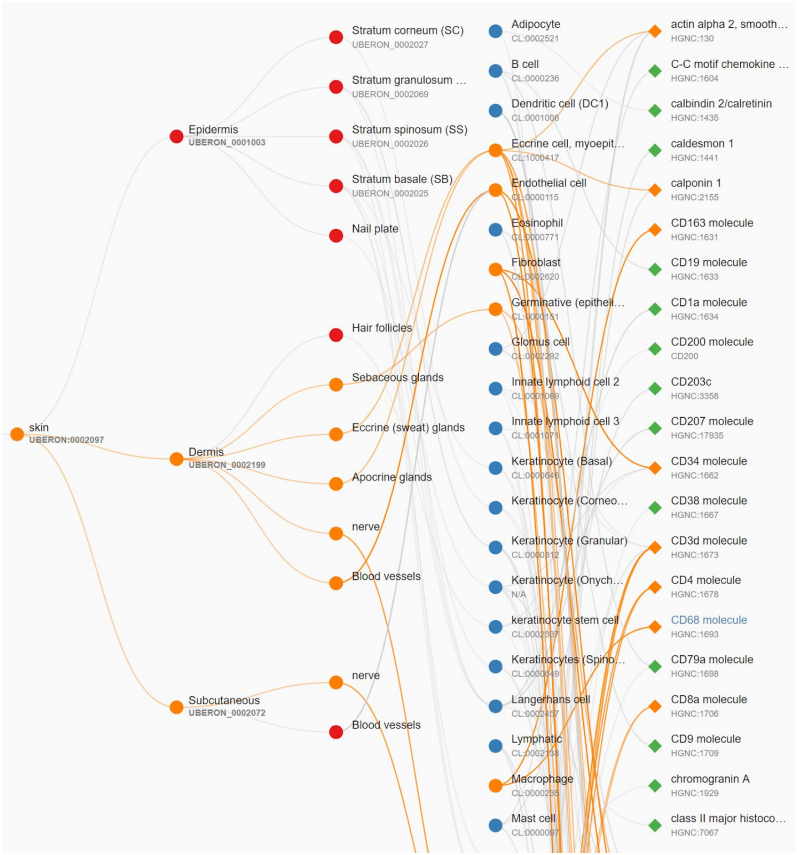


Via ASCT+B
Tables to CT



Human Digital Twin: Automated Cell Type Distance Computation and 3D Atlas Construction in Multiplexed Skin Biopsies. Soumya Ghose, Yingnan Ju, Chrystal Chadwick, Elizabeth McDonough, Anup Sood, Yousef Al-Kofahi, Katy Börner, Fiona Ginty. Submitted. https://www.biorxiv.org/content/10.1101/2022.03.30.486438v1





Human Digital Twin: Automated Cell Type Distance Computation and 3D Atlas Construction in Multiplexed Skin Biopsies. Soumya Ghose, Yingnan Ju, Chrystal Chadwick, Elizabeth McDonough, Anup Sood, Yousef Al-Kofahi, Katy Börner, Fiona Ginty. Submitted. https://www.biorxiv.org/content/10.1101/2022.03.30.486438v1

Access the Human Reference Atlas / CCF.OWL 1.7

Indiana U, Stanford U, and EBI are collaborating closely on using Linked Open Data/Semantic Web Standards in support of ontology development and reasoning. Linked open data compatible with the Semantic Web is used as the ground truth. The CCF.OWL is published on Bioportal, https://bioportal.bioontology.org/ontologies/CCF/

All CCF UIs (e.g., RUI, EUI, ASCT+B Reporter) and APIs (e.g., to update Jonathan's Knowledge Graph) are using the CCF.OWL 1.7 data (2.0 coming in April). Queries can be expressed in SPARQL and exposed as standard HTTP APIs to support a whole ecosystem of collaborative and compatible APIs, libraries, UIs.

ASCT+B API Links:

- API Endpoint (includes interactive documentation): https://asctb-api.herokuapp.com
- API Documentation: https://hubmapconsortium.github.io/ccf-asct-reporter/docs/api
- OpenAPI specification: https://asctb-api.herokuapp.com/asctb-api-spec.yaml

CCF-API Links:

- API Endpoint (includes interactive documentation): https://ccf-api.hubmapconsortium.org
- API Documentation and OpenAPI specification: https://ccf-api.hubmapconsortium.org
- API Database backend is n3.js: https://github.com/rdfjs/N3.js
- Code to instantiate/use CCF Database: https://github.com/hubmapconsortium/ccf-ui/tree/main/projects/ccf-database
- Published Python, TypeScript, JavaScript, and Angular libraries forthcoming

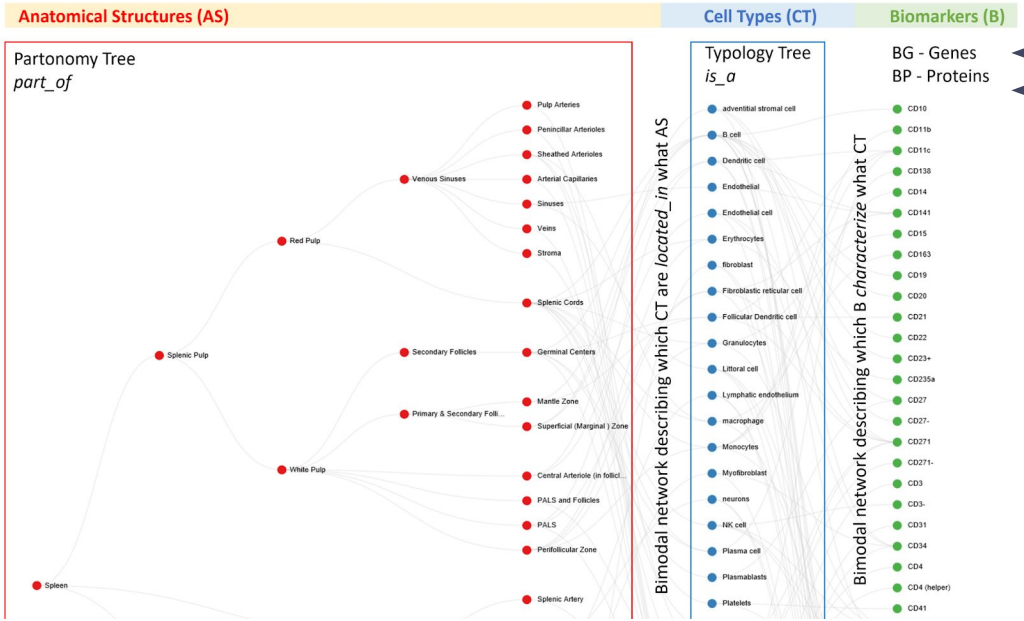
Possible/Planned Queries via CCF HRA Ontology

1. Query for a subset of AS, CT, B* in the HRA or associated experimental datasets; filtered by demographics. [EAS for AS+CT, S for B]
2. Find cell types are present in a certain AS (body to organ to FTU). [S]
3. What Bs characterize a certain CT in a specific AS. [S]
4. What kind of biomarker is a given marker (e.g., gene, protein). [S]
5. What extraction sites exist for the heart? [S] How many tissue blocks exist for what extraction site? [EAS]
6. Given a 3D spatial location, retrieve all tissue blocks in this location. [EA* (by end of June)]
7. Given the location of an image/tissue registered in the CCF RUI, get the cell types present and any associated biomarkers. [EAS – roughly via collisions, S to get biomarkers]
8. Given one or more anatomical structure IDs, retrieve cell type population information (#cells per cell type) for each. [EAS*]
9. Given cell type population information for a tissue block, compute the likely spatial location of the block based on similarity in CT population with RUI-registered tissue blocks. [EAS*]
10. Given cell type population information for a tissue block, retrieve all other tissue blocks that have similar cell type populations and show the spatial location of RIU-registered tissue blocks in the EUI. [EAS*]
11. What cells are co-expressed (access different Bs) or co-located (in 2D or 3D)? [EAS*]
12. Given a 3D spatial location OR cell type population, retrieve all experimental data (DOIs) and publication citation evidence (DOIs if available). [EAS*]

E = Exploration User Interface; A = CCF-API; S = SPARQL; * = planned support;

HRA Validation/ Expansion

New ATLAS publications



2D/3D Maps & Ontology Crosswalks

Azimuth Maps

Validated Antibodies (OMAPs)

New ATLAS datasets

BF – Proteoforms
BL – Lipids
BM – Metabolites

Constructing a Meta-HRA

There is interest to add the atlas data/work reported in major papers to the Human Reference Atlas (HRA). They make wonderful high-resolution inserts!
GE Skin paper is DONE and serves as a good example.

If you

- used the kidney Azimuth reference, your CxG data is already part of the HRA.
- used OMAPs, your CxP data is covered.
- registered all tissue blocks, spatial search in EUI is soon possible.

In general, we need for each paper:

- (HuBMAP) IDs for all healthy adult tissue blocks so we can API-retrieve sex, age, BMI, etc.
- RUI register ALL these tissue blocks so we have spatial size, location, rotation (the RUI now supports 50+ organs at https://hubmapconsortium.github.io/ccf-ui/rui) and
- Compile an ASCT+B table with all AS, CT, Bs used in the study (should be a matter or deleting rows in the relevant master tables, see https://hubmapconsortium.github.io/ccf/pages/ccf-anatomical-structures.html).

Questions for the (Bioconductor) Experts

- How might you use ASCT+B tables to advance research/practice? Please share sample queries, e.g., “retrieve AS/location of my favorite CT/B* across 30 organs.”
- Are you interested to run spatial queries? If yes, which, e.g., “retrieve all CTs/B*s in a 3D volume.”

- What other datasets could be used to extend the ASCT+B tables or provide experimental evidence for existing AS, CT, B?

- How comfortable are you with ontologies and semantic web technologies?
- Would you prefer direct access to technologies like SPARQL, RDF, and JSON-LD or would you prefer APIs to be higher level?

Q&A