



Human Reference Atlas Construction and Usage



Katy Börner Intelligent Systems Engineering, Indiana University
Bloomington, IN

With expert input by Bruce W. Herr II, Ellen M. Quardokus, David
Osumi-Sutherland, Rafael Goncalves, Mark Musen

CCB Seminar Series at HMS

May 2, 2022

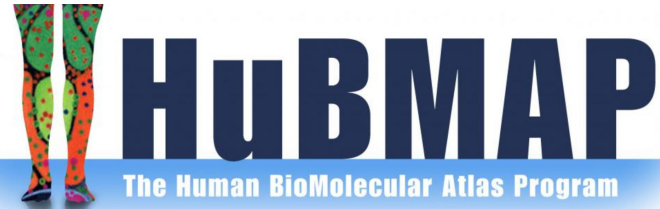
HuBMAP

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

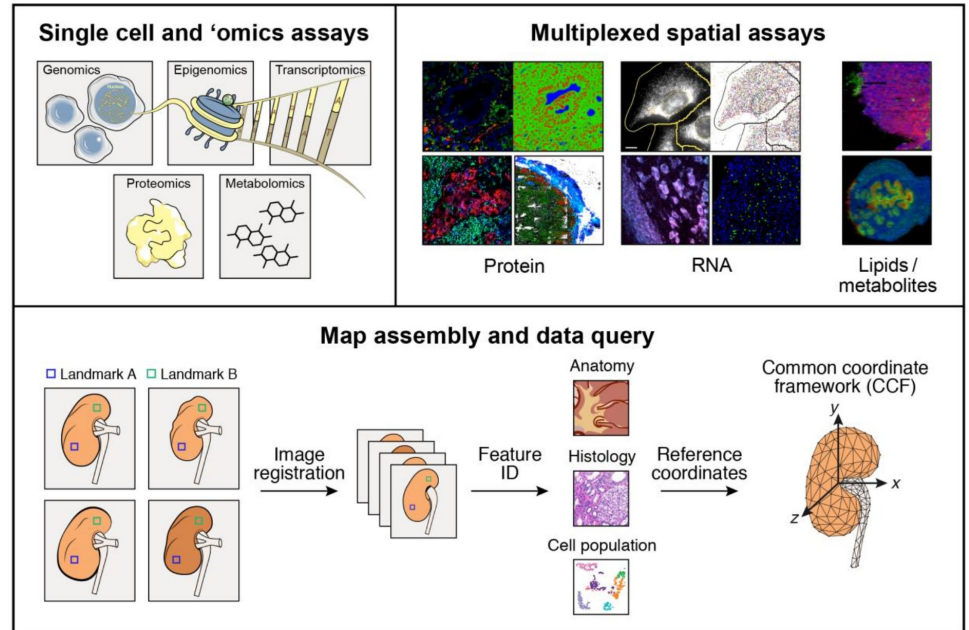
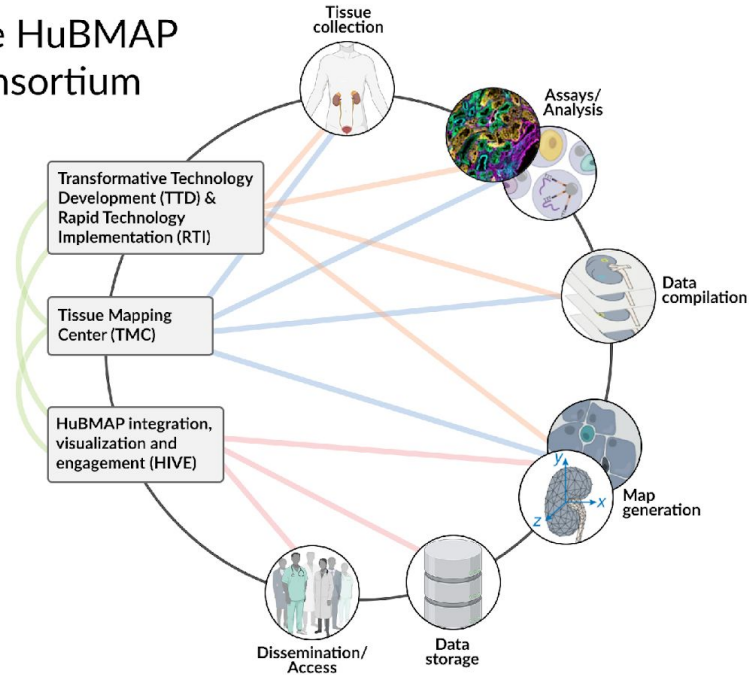


<https://commonfund.nih.gov/HuBMAP>

The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program

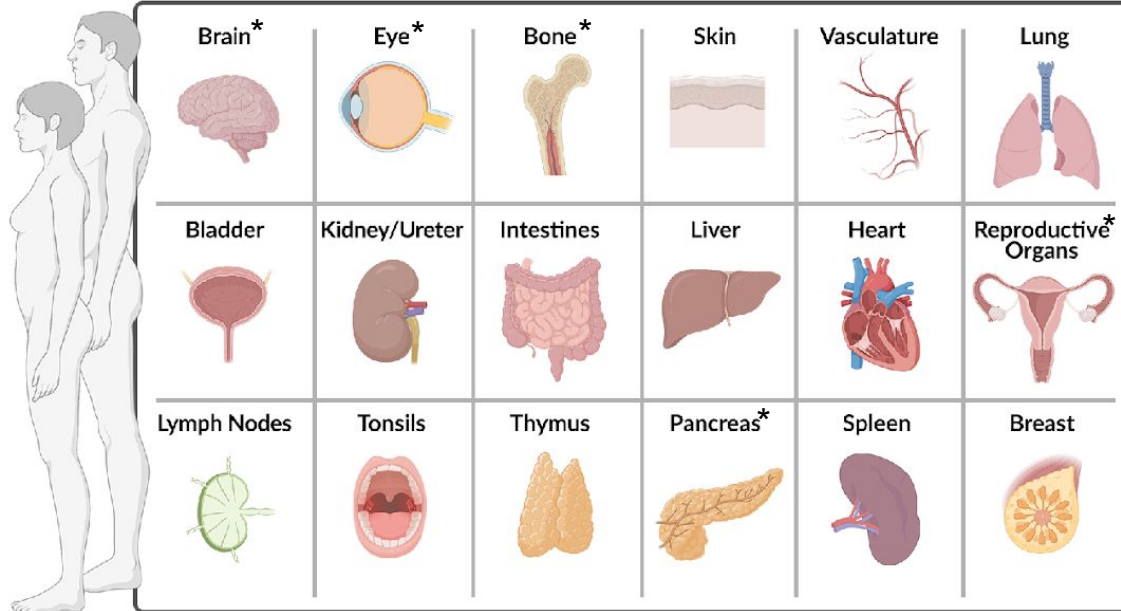
Snyder et al. *Nature*. 574, p. 187-192.

The HuBMAP Consortium



HuBMAP Overview

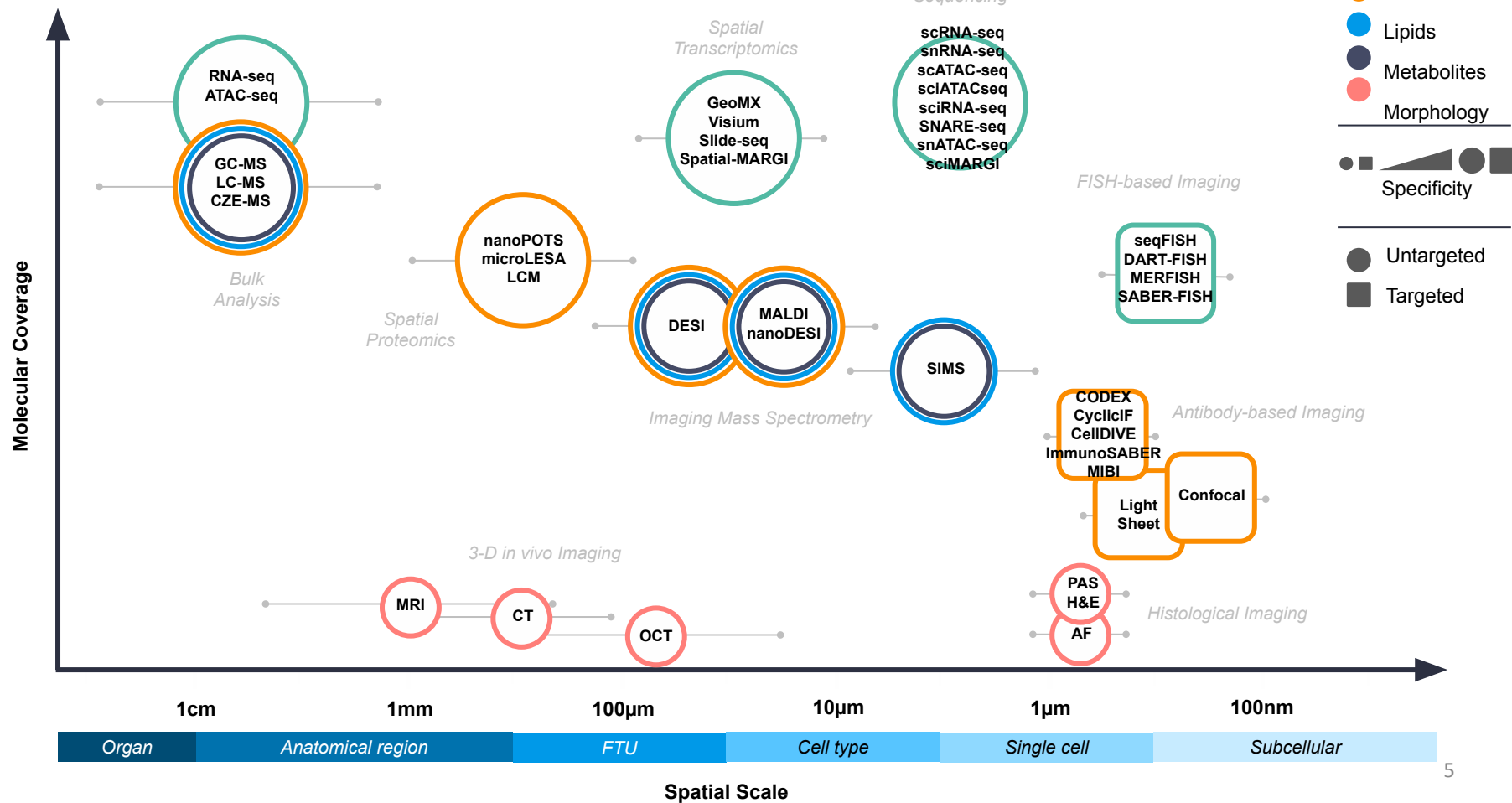
Organ Specific Projects

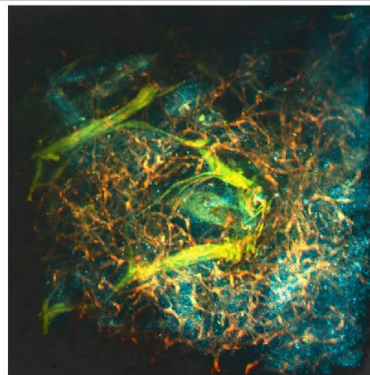
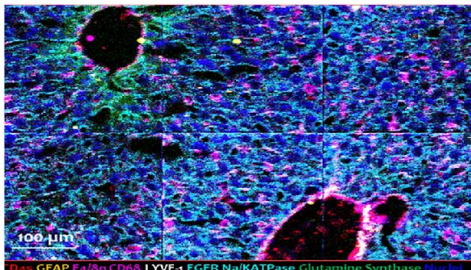
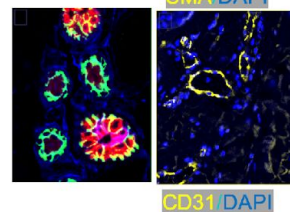
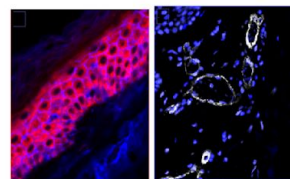
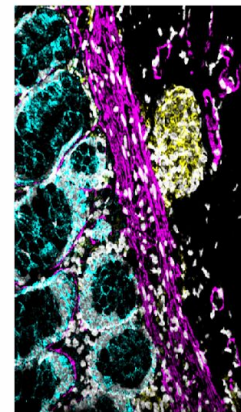
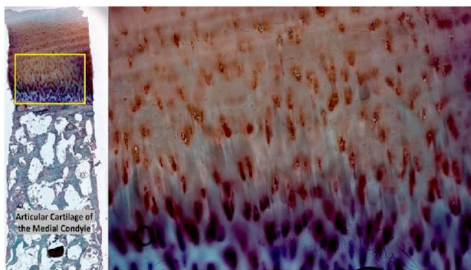
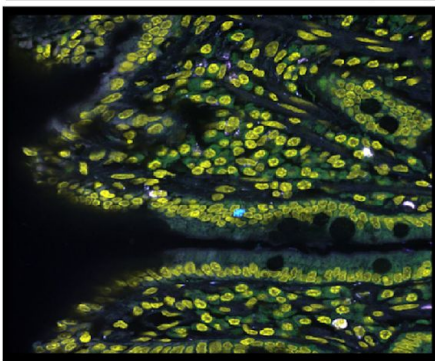
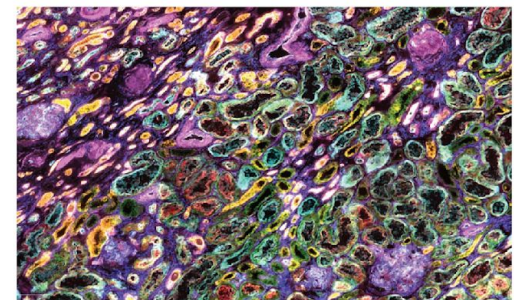
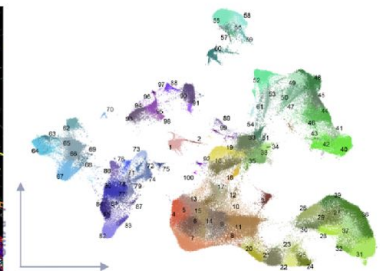
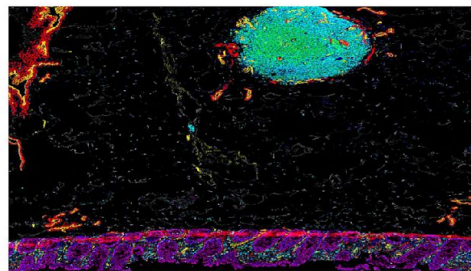
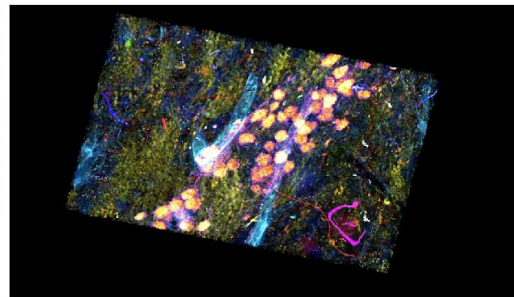
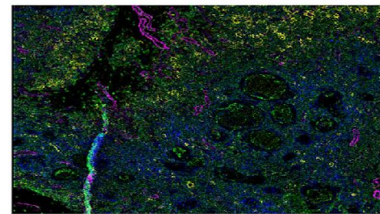
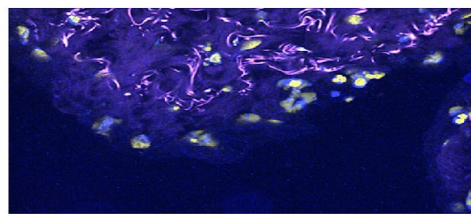
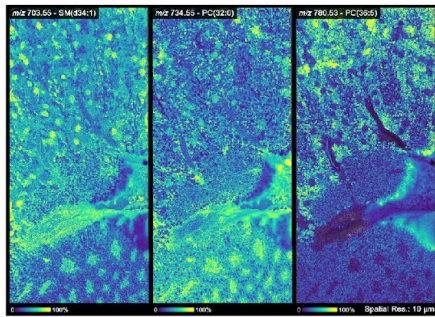


* Newly added organs

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

HuBMAP Technologies





Human BioMolecular Atlas Program

An open, global atlas of the human body at the cellular level

The HuBMAP Data Portal is the central resource for discovery, visualization, and download of single-cell data. Standardized data curation and processing workflow ensure that only high quality is released.

Common Coordinate Framework (CCF) Portal

ASCT+B Reporter

Exploration User Interface (EUI)

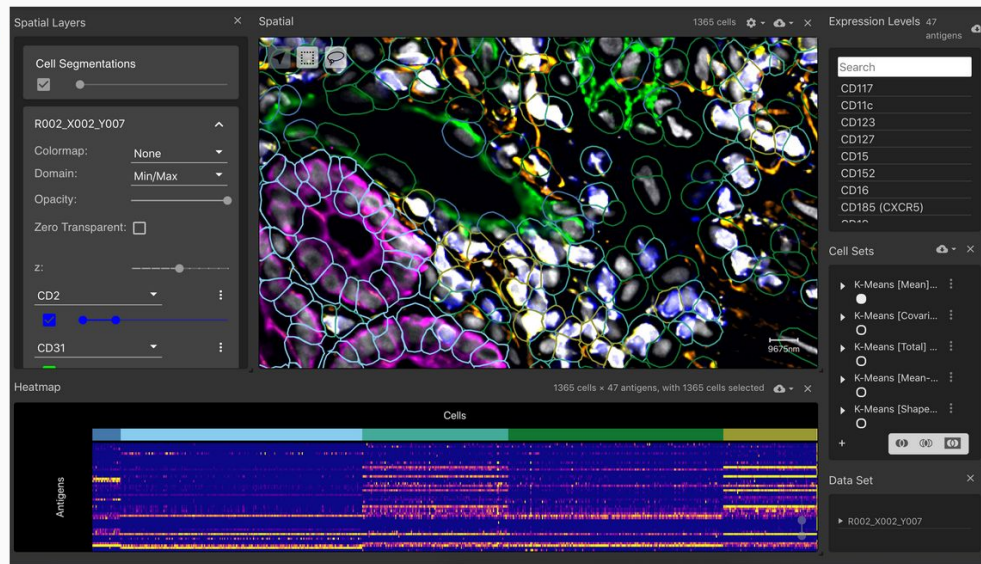
Registration User Interface (RUI)

Azimuth: Reference-based single cell mapping

Explore spatial single-cell data with Vitessce visualizations

View multi-modal assay types with reusable interactive components such as a scatterplot, spatial-imaging plot, genome browser tracks, statistical plots and controller components.

Get Started



In May 2022

86
Donors

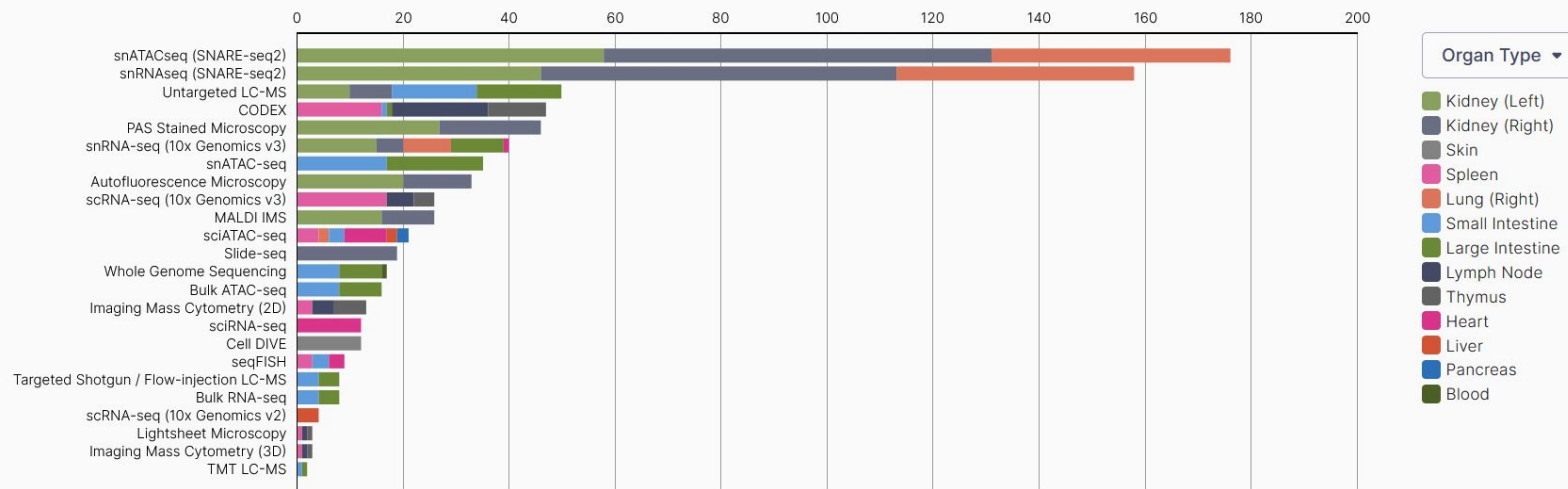
1013
Samples

1031
Datasets

15
Collections

Search Portal

HuBMAP Datasets



<https://portal.hubmapconsortium.org>

13 organs / 24 assay types

HuBMAP Kaggle Competition



Deloitte.

DEERFIELD®

Advancing Healthcare®

Cyber Sponsors



Research Code Competition

HuBMAP - Hacking the Kidney

Identify glomeruli in human kidney tissue images

\$60,000
Prize Money

InnovationDigi · 1,216 teams · 7 days ago

[Overview](#) [Data](#) [Code](#) [Discussion](#) [Leaderboard](#) [Rules](#)

[Join Competition](#)

| Overview | |
|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Description | Our best estimates show there are over 7 billion people on the planet and 300 billion stars in the Milky Way galaxy. By comparison, the adult human body contains 37 trillion cells. To determine the function and relationship among these cells is a monumental undertaking. Many areas of human health would be impacted if we better understand cellular activity. A problem with this much data is a great match for the Kaggle community. |
| Supervised ML Evaluation | |
| Judges Prize | |
| Prizes | Just as the Human Genome Project mapped the entirety of human DNA, the Human BioMolecular Atlas Program (HuBMAP) is a major endeavor. Sponsored by the National Institutes of Health (NIH), HuBMAP is working to catalyze the development of a framework for mapping the human body at a level of glomeruli functional tissue units for the first time in history. Hoping to become one of the world's largest collaborative biological projects, HuBMAP aims to be an open map of the human body at the cellular level. |
| Timeline | |
| Organizers & Sponsors | This competition, "Hacking the Kidney," starts by mapping the human kidney at single cell resolution. |
| Code Requirements | Your challenge is to detect functional tissue units (FTUs) across different tissue preparation pipelines. An FTU is defined as a "three-dimensional block of cells centered around a capillary, such that each cell in this block is within diffusion distance from any other cell in the same block" (de Bono, 2013). The goal of this competition is the implementation of a successful and robust glomeruli FTU detector. |

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

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



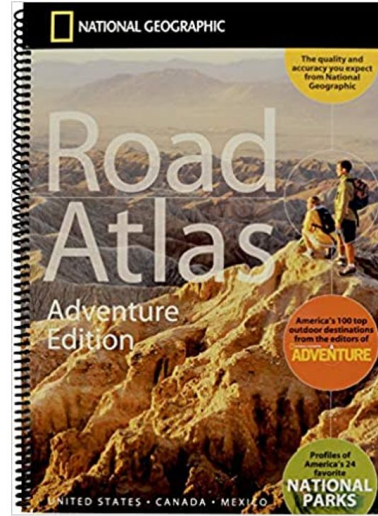
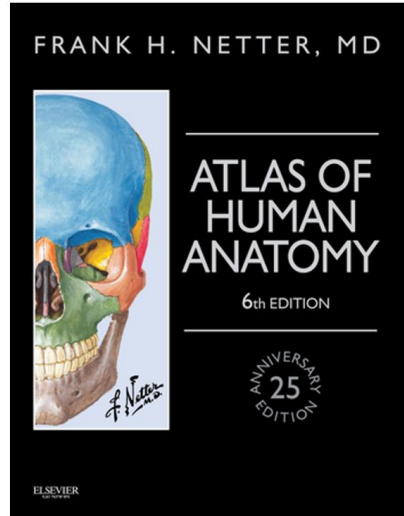
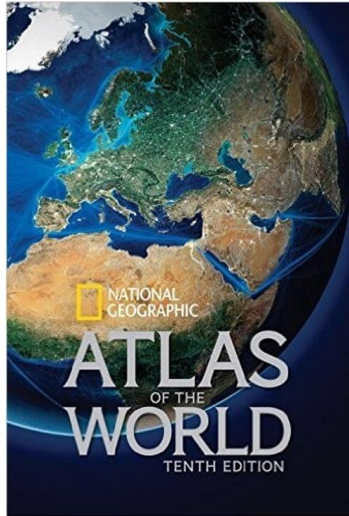
Human Reference Atlas (HRA)



Overall Vision

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

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

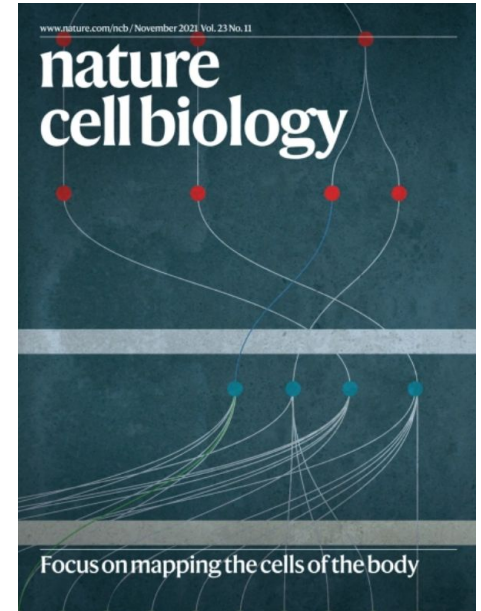


Define Human Reference Atlas

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).

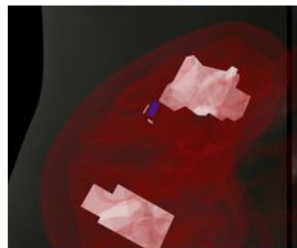
<https://www.nature.com/articles/s41556-021-00788-6>



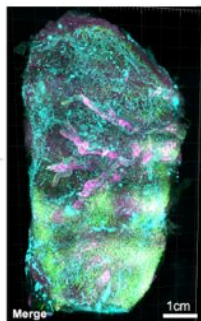
Construct a Human Reference Atlas

Tissue Data

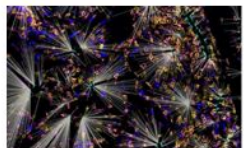
Whole organ data,
e.g., light-sheet data



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)

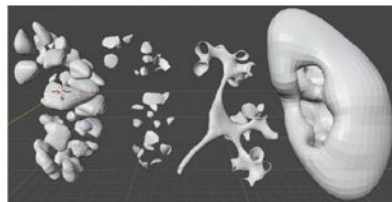
10,000+
Anatomical
Structures

37T Cells

Reference Atlas

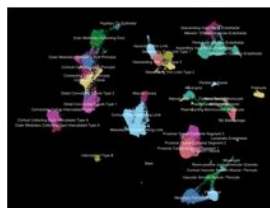


3D coordinate system,
geometric mapping process



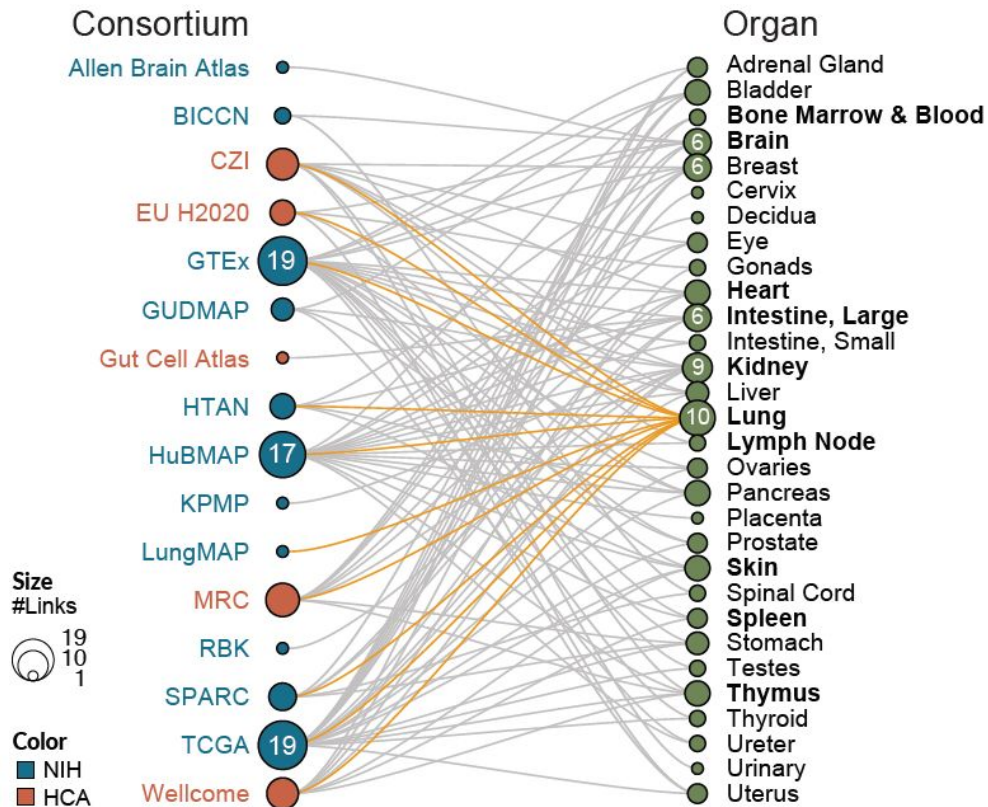
Reference object library with crosswalks to ASCT+B tables,
Synthetic HRA 3D model with cell type populations

2D Reference FTUs



2&3D single cell models
cell graphs

Construct a Human Reference Atlas - Together!

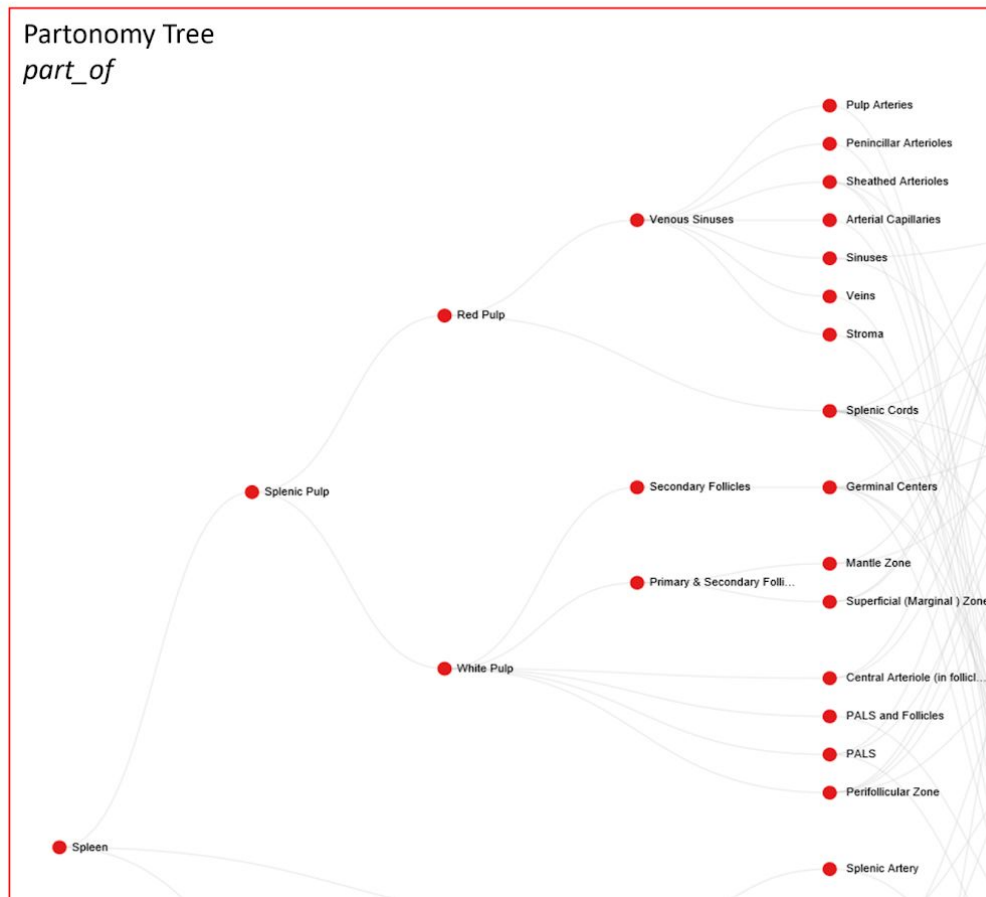


Anatomical Structures (AS)

Cell Types (CT)

Biomarkers (B)

Partonomy Tree
part_of



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

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.

ASCT Table

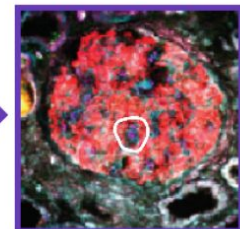
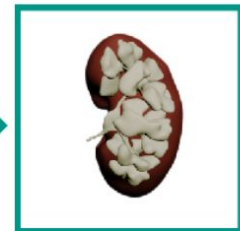
| Structure/Region | Sub structure/Sub region | Cell Type |
|------------------|----------------------------------------------|------------------------------------------------------|
| Renal Corpuscle | Bowman's (glomerular) Capsule/parietal layer | Parietal epithelial Cell |
| | Bowman's (glomerular) 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 |
| | | Proximal Tubule Epithelial Cell Segment 2 |
| | Loop of Henle, Thin Limb | Descending Thin Limb Cell (general) |
| | | Ascending Thin Limb Cell (general) |
| | | Thick Ascending Limb Cell (general) |
| | Loop of Henle, Thick Limb | 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
 pericyte cell
 mesangial cell
 extraglomerular mesangial cell
 glomerular mesangial cell

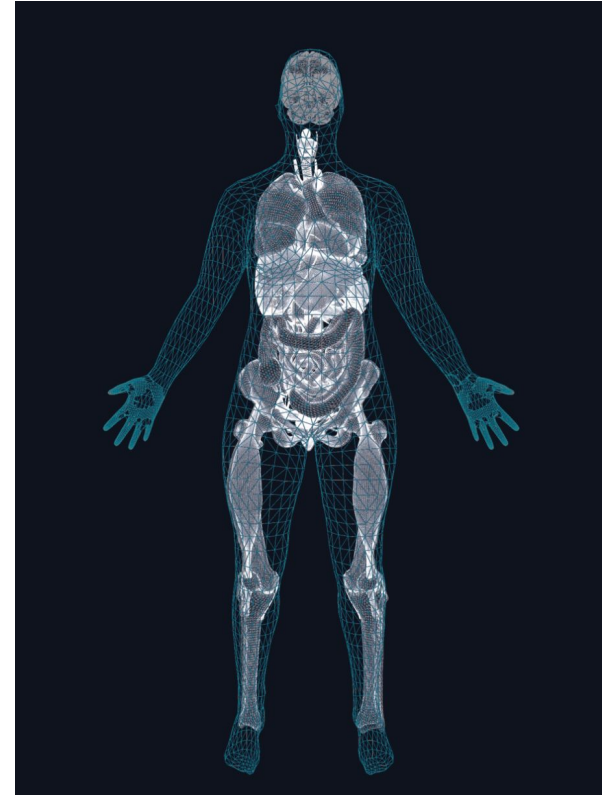
3D Reference Object Library



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 |

Crosswalk



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

<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.

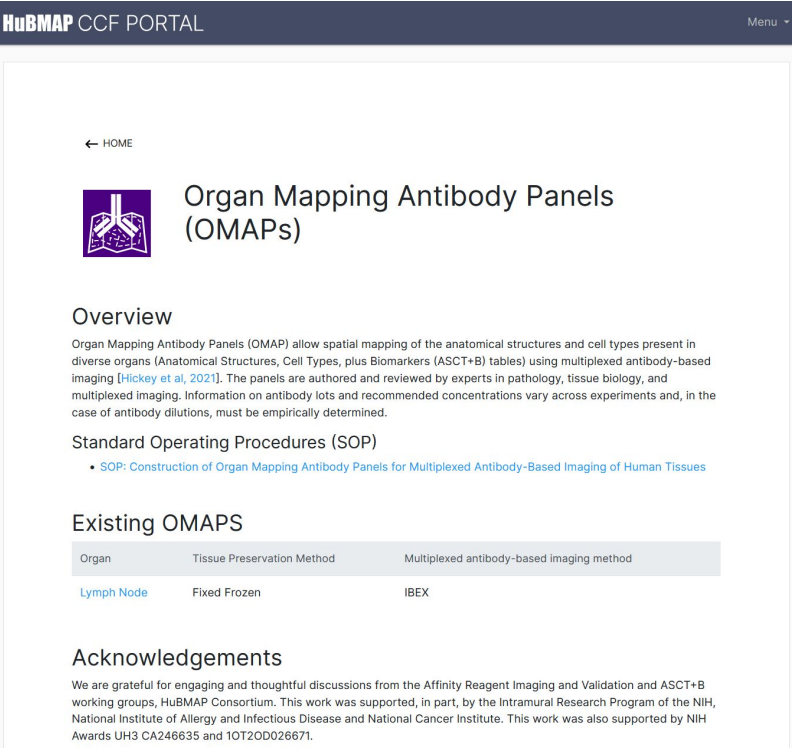
| LABEL | VALUE |
|------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Creator(s): | Gloria Pryhuber; Xin Sun |
| 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. <i>HuBMAP ASCT+B Tables</i> . 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.



HuBMAP CCF PORTAL Menu ▾

[← HOME](#)

Organ Mapping Antibody Panels (OMAPs)

Overview

Organ Mapping Antibody Panels (OMAP) allow spatial mapping of the anatomical structures and cell types present in diverse organs (Anatomical Structures, Cell Types, plus Biomarkers (ASCT+B) tables) using multiplexed antibody-based imaging [Hickey et al, 2021]. The panels are authored and reviewed by experts in pathology, tissue biology, and multiplexed imaging. Information on antibody lots and recommended concentrations vary across experiments and, in the case of antibody dilutions, must be empirically determined.

Standard Operating Procedures (SOP)

- [SOP: Construction of Organ Mapping Antibody Panels for Multiplexed Antibody-Based Imaging of Human Tissues](#)

Existing OMAPs

| Organ | Tissue Preservation Method | Multiplexed antibody-based imaging method |
|----------------------------|----------------------------|-------------------------------------------|
| Lymph Node | Fixed Frozen | IBEX |

Acknowledgements

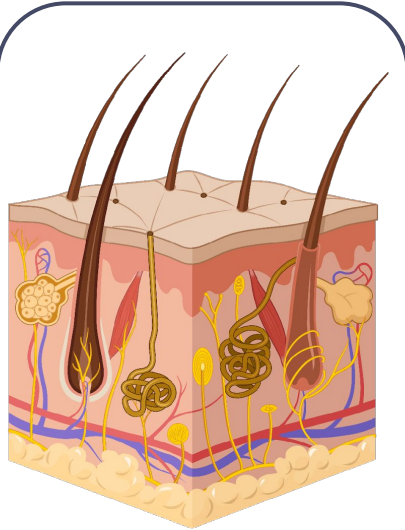
We are grateful for engaging and thoughtful discussions from the Affinity Reagent Imaging and Validation and ASCT+B working groups, HuBMAP Consortium. This work was supported, in part, by the Intramural Research Program of the NIH, National Institute of Allergy and Infectious Disease and National Cancer Institute. This work was also supported by NIH Awards UH3 CA246635 and 10T2OD026671.

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

Interlinking ASCT+B and Affinity Reagent Working Group Efforts

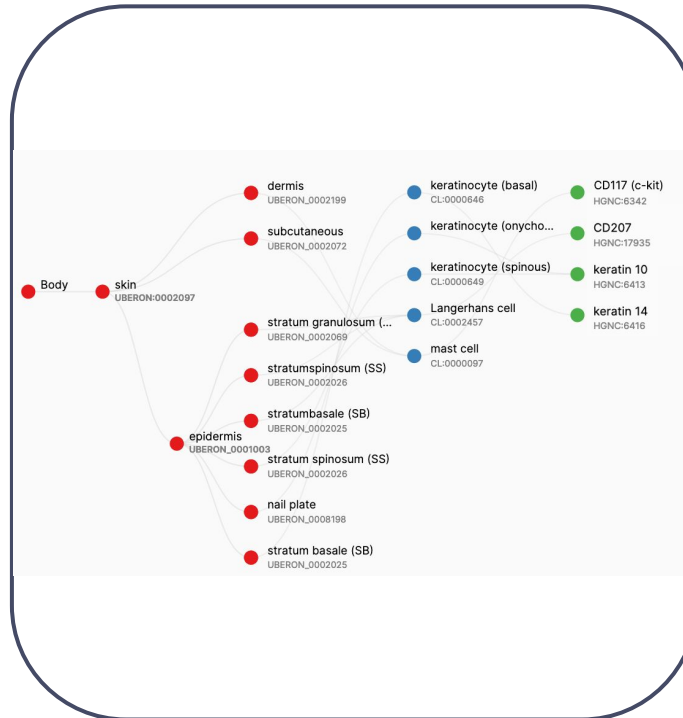
Use Case: Skin-Specific Panel

Skin

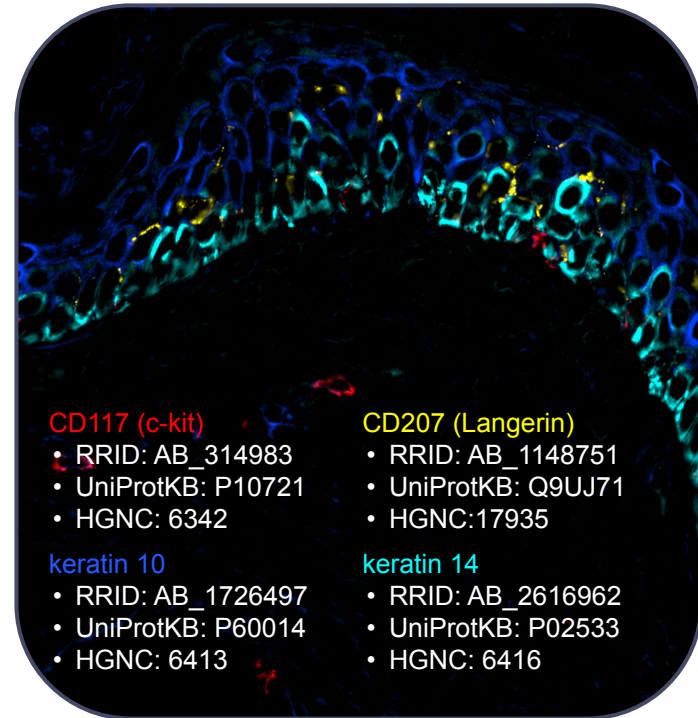


| AS/2 | AS/3 | CT | BP |
|--------------|-------------------------|--------------------------|------------------|
| dermis | | mast cell | CD117 (c-kit) |
| subcutaneous | | mast cell | CD117 (c-kit) |
| epidermis | stratum granulosum (SG) | Langerhans cell | CD207 (Langerin) |
| epidermis | stratum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

Use the Human Reference Atlas for Data Harmonization

HuBMAP Donors Samples Datasets Collections Previews **Atlas & Tools** Documentation My Lists Member Login

Common Coordinate Framework (CCF) Portal
ASCT+B Reporter
Exploration User Interface (EUI)
Registration User Interface (RUI)
Azimuth: Reference-based single cell mapping

Human BioMolecular Atlas Program

An open, global atlas of the human body at the cellular level

The HuBMAP Data Portal is the central resource for discovery, visualization, and download of standardized data. Standardized data curation and processing workflow ensure that only high quality is released.

Navigate healthy human cells with the Common Coordinate Framework

Interact with the human body data with the Anatomical Structures, Cell Types and Biomarkers (ASCT+B) Tables and CCF Ontology. Also explore two user interfaces: the Registration User Interface (RUI) for tissue data registration and Exploration User Interface (EUI) for semantic and spatial data.

Get Started

HuBMAP Search ontology terms ...

- body
 - heart
 - lung
 - kidney
 - right kidney
 - left kidney
 - kidney capsule
 - hilum of kidney
 - renal medulla
 - renal column
 - renal pyramid
 - hilum of kidney
 - kidney interstitium
 - kidney calyx
 - renal pelvis
 - ureter
 - renal papilla
 - renal fat pad
 - epiphon
 - spleen
 - spleen capsule
 - trabeculae of spleen
 - spleen pulp
 - marginal zone of spleen
 - spleen perfollicular zone
 - hilum of spleen
 - colon
 - ascending colon
 - descending colon
 - transverse colon
 - sigmoid colon

body

- 4 Centers
- 28 Donors
- 48 Samples

| Sample ID | Donor | Age | Sex | Cell Type | Marker |
|------------|------------|-----|-----|-----------|--------|
| Patient 1 | 1000000001 | 10 | M | CD45 | CD45 |
| Patient 2 | 1000000002 | 10 | F | CD45 | CD45 |
| Patient 3 | 1000000003 | 10 | M | CD45 | CD45 |
| Patient 4 | 1000000004 | 10 | F | CD45 | CD45 |
| Patient 5 | 1000000005 | 10 | M | CD45 | CD45 |
| Patient 6 | 1000000006 | 10 | F | CD45 | CD45 |
| Patient 7 | 1000000007 | 10 | M | CD45 | CD45 |
| Patient 8 | 1000000008 | 10 | F | CD45 | CD45 |
| Patient 9 | 1000000009 | 10 | M | CD45 | CD45 |
| Patient 10 | 1000000010 | 10 | F | CD45 | CD45 |

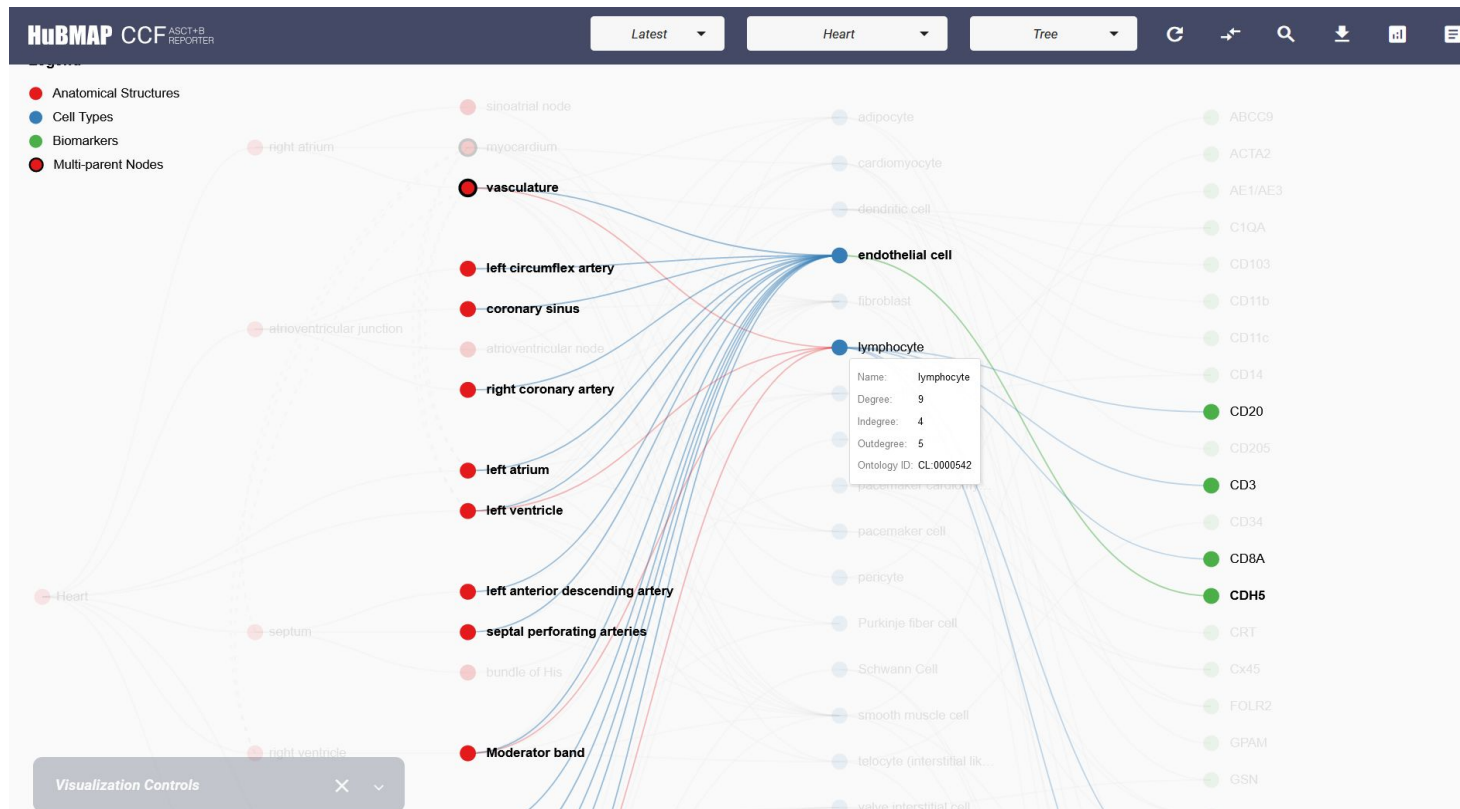
38 Donors

365 Samples

391 Datasets

13 Collections

CCF ASCT+B Reporter UI



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

CCF Registration User Interface (RUI)

The screenshot displays the HuBMAP CCF Registration User Interface (RUI). The interface is divided into several sections:

- Header:** HuBMAP CCF REGISTRATION USER INTERFACE
- User Information:** First Name: Andreas, Last Name: Bueckle
- Orientation:** Radio buttons for Left, Right, **Anterior** (selected), and Posterior.
- Registration Options:** Register (checked), 3D Preview (unchecked)
- Organ Selection:** Colon, Heart, **Kidney** (selected), Spleen, Bladder
- Gender:** L (checked), R (unchecked), Male (checked), Female (unchecked)
- Common Extraction Sites:** Show Previous Registration Blocks
- Anatomical Structures:** kidney capsule, cortex of kidney, outer cortex of kidney, **renal column** (selected), hilum of kidney, renal medulla, renal papilla, renal pyramid
- 3D Model:** A 3D rendering of a kidney with a blue rectangular block placed on its surface. A mouse cursor is visible over the block. Coordinates are shown as X: 80, Y: 69, Z: 40.
- Tissue Block Size (mm):** Width (X): 8, Height (Y): 6, Depth (Z): 10
- Tissue Slices:** Thickness, # Slices
- Tissue Block Rotation:** X, Y, Z rotation sliders, all set to 0.
- Anatomical Structure Tags:** Add Anatomical Structures ... (+)
- Legend:** Assigned (black circle), Added (pink circle)
- Buttons:** REVIEW AND DOWNLOAD

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

CCF Exploration User Interface (EUI)

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

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
 - renal pelvis
 - ureter
 - renal papilla
 - renal fat pad
 - nephron

body

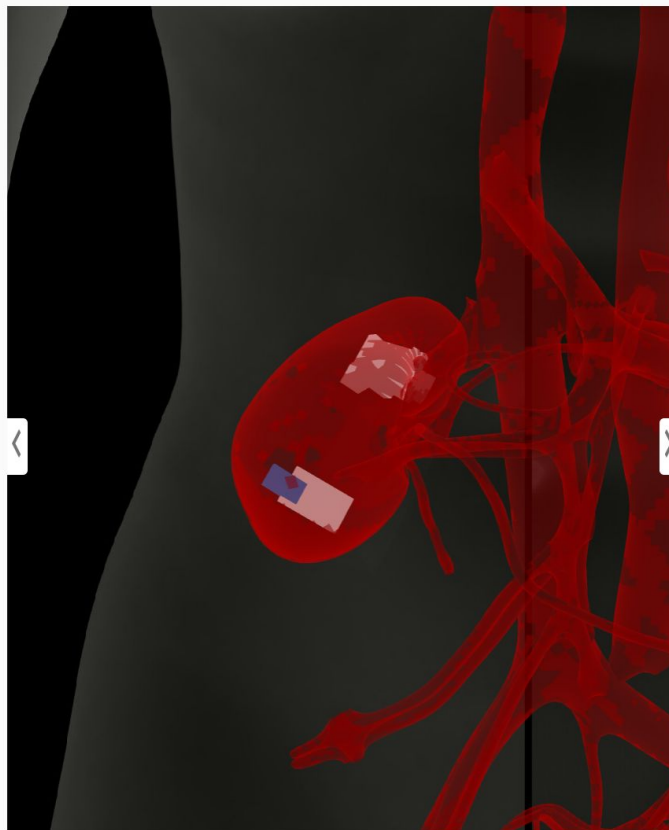
- 2 Centers
- 27 Donors
- 41 Samples

| | | |
|--|------------------------------------------------------------------------------------------------------------|--|
| | Female, Age 14, BMI 14.7 HBM894.MPVN.828 TMC-Florida First case collected. Incomplete d... | |
| | Male, Age 18, BMI 27.1 HBM436.GHWX.449 TMC-Florida section is 190um from block surface | |
| | Male, Age 56, BMI 32.5 HRM696.XTYL.498 TMC-Vanderbilt Age 56, White Male | |
| | Male, Age 53, BMI 26.5 HRM652.VRL.D.292 TMC-Vanderbilt Age 53, Black Male | |
| | Male, Age 58, BMI 22.0 HBM477.CJKM.899 TMC-Vanderbilt 107-111 | |
| | Male, Age 18, BMI 25.5 HBM473.VKCM.878 TMC-Florida section is 255um from block surface | |
| | Male, Age 55, BMI 25.4 HBM824.BLXF.883 TMC-Vanderbilt 13-16 | |

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



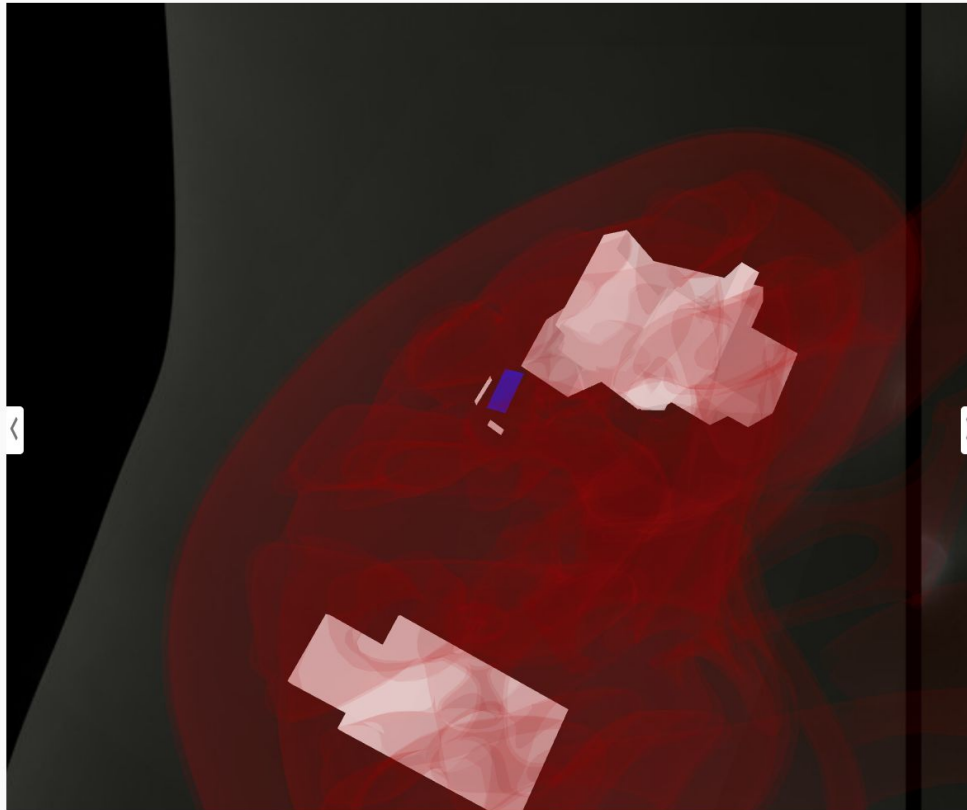
body

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 |  |

Search ontology terms ... 🔍

- body
 - heart
 - lung
 - kidney
 - right kidney
 - left kidney
 - kidney capsule
 - cortex of kidney
 - outer cortex of kidney
 - renal medulla
 - outer medulla
 - inner 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
 - small intestine



body

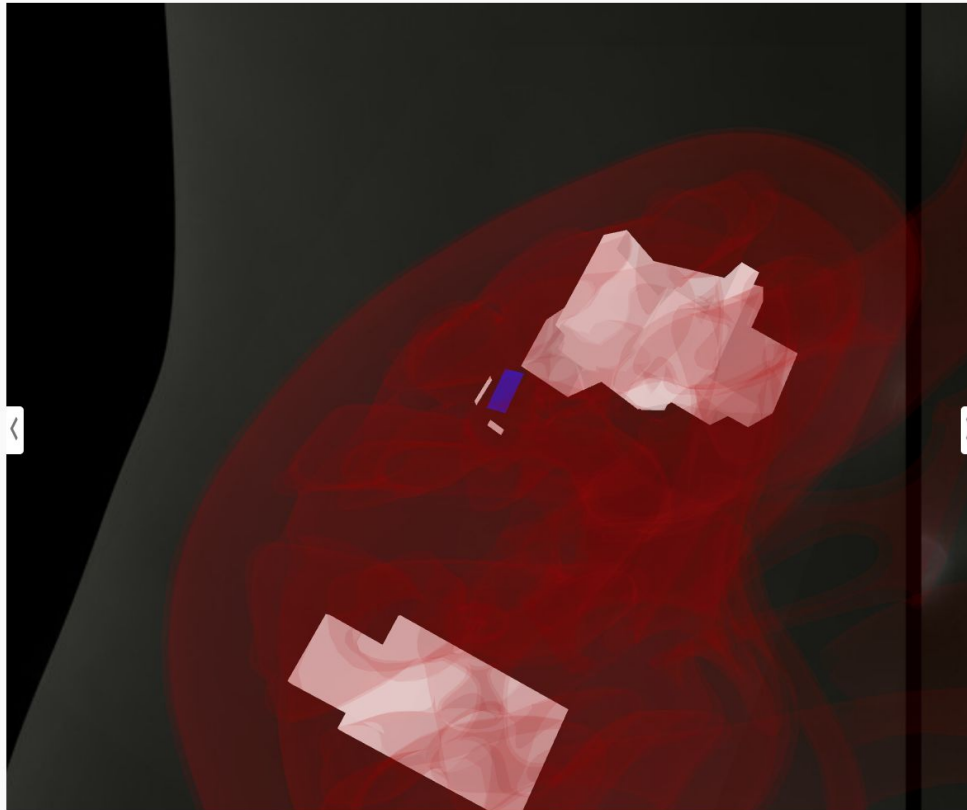
2 Centers
9 Donors
14 Samples

| | | |
|--|--------------------------------------------------------------------------------------------------------------|---|
| | CoverNephrectomy 10.1016/j.trsl.2017.07.006 KPMP-IJCSU Isolated as a part of a kidney st... | + |
| | Patient B Cortical biopsy 10.1681/ASN.2016091027 KPMP-IJCSU Biopsy from Nephrology bioban... | + |
| | Patient A Cortical biopsy 10.1681/ASN.2016091027 KPMP-IJCSU Biopsy from Nephrology bioban... | + |
| | Male, Age 55, BMI 25.4 HBM824.BLXF.883 TMC-Vanderbilt 13-16 | + |
| | Female, Age 66, BMI 31.3 HBM554.ZRCG.496 TMC-Vanderbilt 21-24 | + |
| | Female, Age 58, BMI 23.0 HBM926.VBJV.597 TMC-Vanderbilt Age 58, White Female | + |
| | Male, Age 62, BMI 34.9 HBM947.VLDP.894 TMC-Vanderbilt Kidneys 153-156 | + |
| | Female, Age 44, BMI 28.0 HBM457.NNQN.252 TMC-Vanderbilt Age 44, white female. | + |
| | Male, Age 21, BMI 21.8 HBM693.HFFJ.752 TMC-Vanderbilt Age 21, White Male, Trauma Pat... | + |
| | Female, Age 58, BMI 23.0 HBM536.LDTZ.757 TMC-Vanderbilt Age 58, White Female | + |
| | Male, Age 48, BMI 35.3 | + |

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

Search ontology terms ... 🔍

- body
 - heart
 - lung
 - kidney
 - right kidney
 - left kidney
 - kidney capsule
 - cortex of kidney
 - outer cortex of kidney
 - renal medulla
 - outer medulla
 - inner 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
 - small intestine

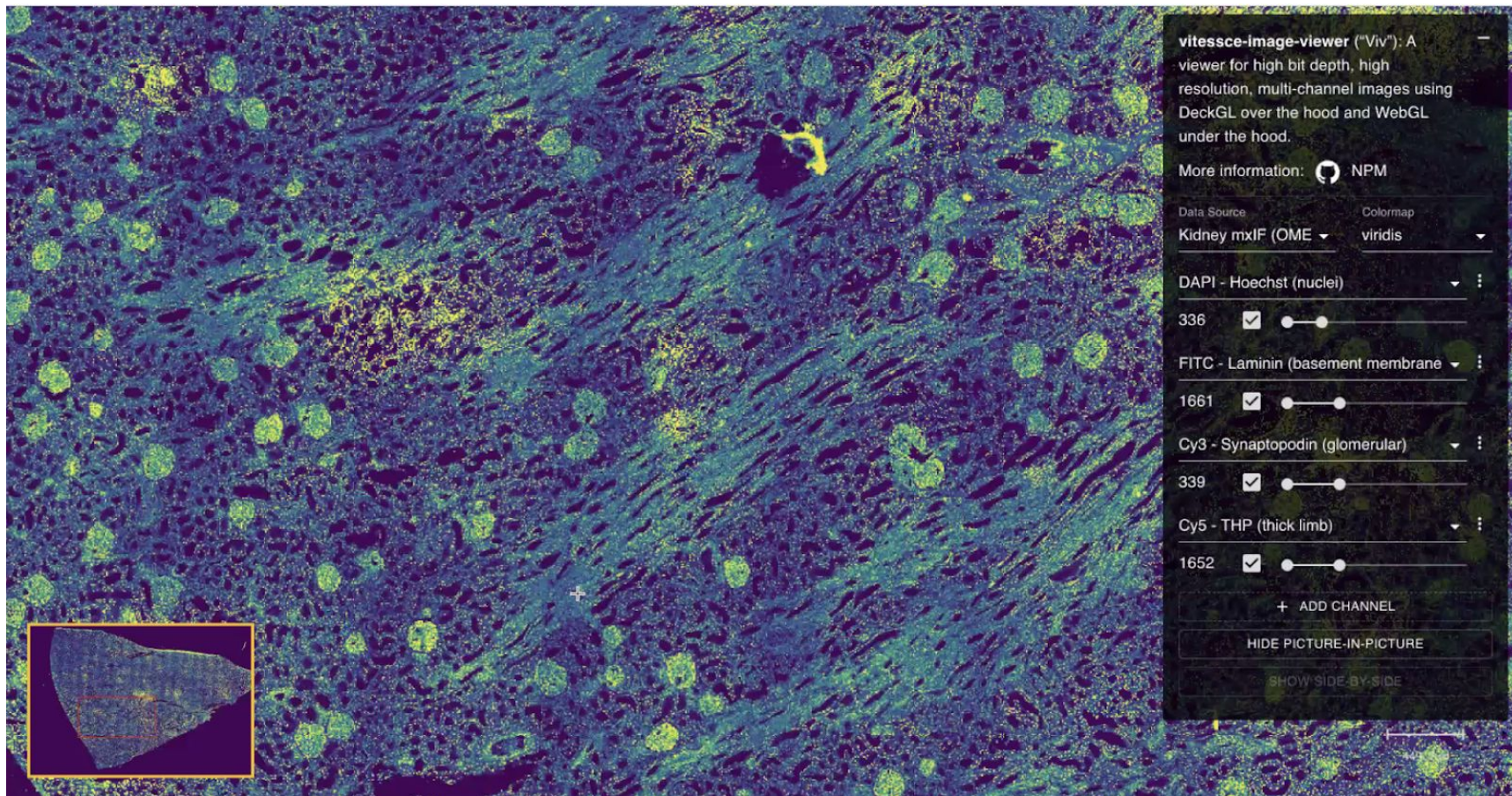


body

2 Centers
9 Donors
14 Samples

| | | |
|--|--------------------------------------------------------------------------------------------------------------|---|
| | CoverNephrectomy 10.1016/j.trsl.2017.07.006 KPMP-IJCSU Isolated as a part of a kidney st... | + |
| | Patient B Cortical biopsy 10.1681/ASN.2016091027 KPMP-IJCSU Biopsy from Nephrology bioban... | + |
| | Patient A Cortical biopsy 10.1681/ASN.2016091027 KPMP-IJCSU Biopsy from Nephrology bioban... | + |
| | Male, Age 55, BMI 25.4 HBM824.BLXF.883 TMC-Vanderbilt 13-16 | + |
| | Female, Age 66, BMI 31.3 HBM554.ZRCG.496 TMC-Vanderbilt 21-24 | + |
| | Female, Age 58, BMI 23.0 HBM926.VBJV.597 TMC-Vanderbilt Age 58, White Female | + |
| | Male, Age 62, BMI 34.9 HBM947.VLDP.894 TMC-Vanderbilt Kidneys 153-156 | + |
| | Female, Age 44, BMI 28.0 HBM457.NNQN.252 TMC-Vanderbilt Age 44, white female. | + |
| | Male, Age 21, BMI 21.8 HBM693.HFFJ.752 TMC-Vanderbilt Age 21, White Male, Trauma Pat... | + |
| | Female, Age 58, BMI 23.0 HBM536.LDTZ.757 TMC-Vanderbilt Age 58, White Female | + |
| | Male, Age 48, BMI 35.3 | + |

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



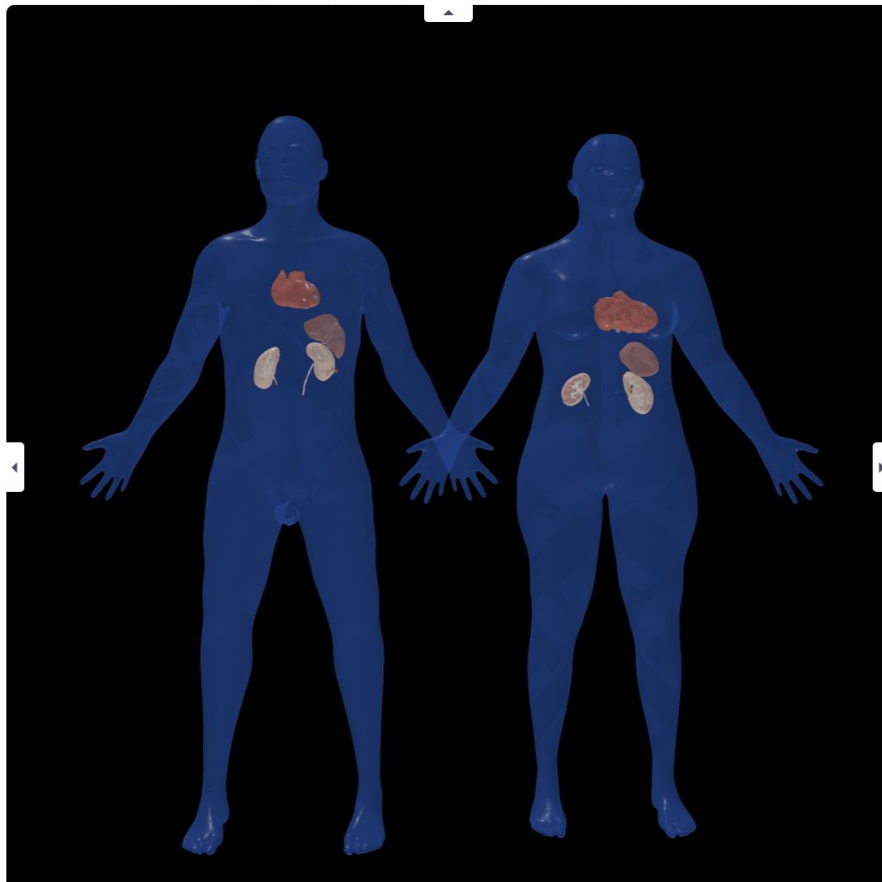
<http://gehlenborglab.org/research/projects/vitessce/>

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



Search ontology terms ...

| body | 196 |
|------------------------------------|-----|
| skin | 0 |
| large intestine | 11 |
| heart | 30 |
| right ventricle | 17 |
| right atrium | 6 |
| inferior vena cava sinoatrial node | 0 |
| superior vena cava coronary sinus | 0 |
| anterior cardiac veins 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 x 10 x 12 millimeter, 12 millimeter, ffpe_blo...

Male, Age 58, BMI 22.0
Entered 12/23/2019, Elizabeth Neumann, TM... ^

Registered 6/9/2020, Elizabeth Neumann, TM...
18 x 10 x 2 millimeter, 0.3 millimeter, fresh_fr...

0 7

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Registered 1/29/2020, Jamie Allen, TMC-V...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres...

Male, Age 58, BMI 22.0
Entered 12/23/2019, Elizabeth Neumann, TM... v

Sex: Both Age: 1-11

Search ontology terms ...

- body
- skin
- large intestine
- heart
 - right ventricle
 - right atrium
 - inferior vena cava
 - sinoatrial node
 - superior vena cava
 - coronary sinus
 - anterior cardiac myocardium
 - sinoatrial nodal area
 - left ventricle
 - atrioventricular junction
 - cardial valve
 - left atrium
 - septum
 - epicardium
- kidney
- spleen
- brain
- lung
- lymph node
- pelvis
- thymus
- vasculature

- 0
- 7
- 29
- 0
- 28
- 66

Configure Spatial Search

Selected Sex/Organ EDIT

Sex: Male Organ: Heart

Probing Sphere Size

min
100mm
 max

RESET PROBING SPHERE RESET CAMERA VIEW

Homing Mode OFF ON

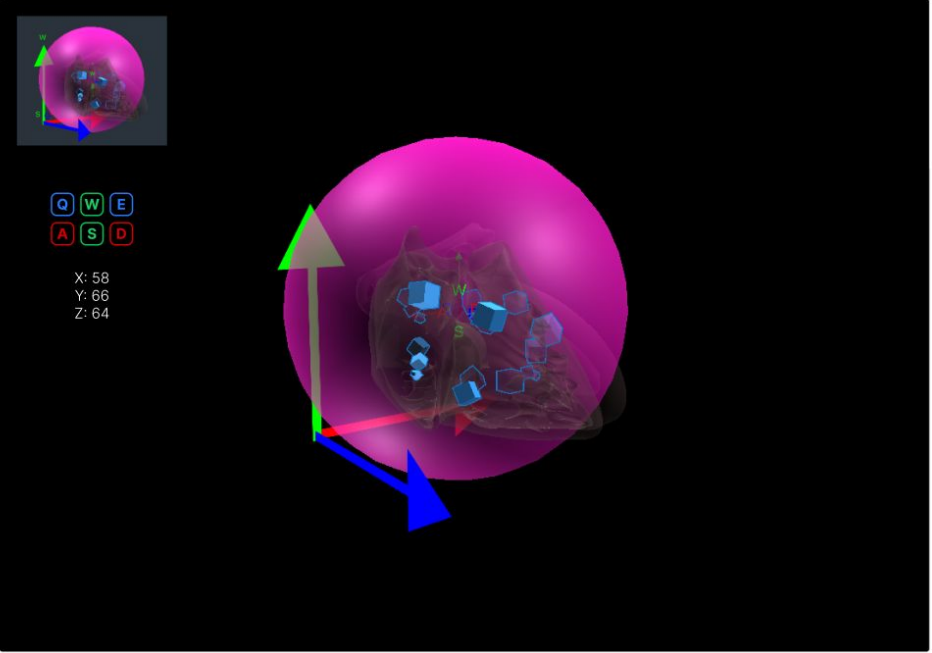
Probing Sphere Collisions

| | |
|------------------------------------------------|----|
| Tissue Block Collisions | 20 |
| Unique Anatomical Structure Collisions | 6 |
| Unique Cell Type Predictions via ASCT+B Tables | 9 |

| Cell Type Collisions | Anatomical Structure Collisions |
|----------------------|---------------------------------|
| R2D2 | 16 |
| CD8 | 16 |
| Epithelial | 13 |
| C3PO | 15 |
| ABCD25 | 16 |
| BB8 | 4 |
| W3W | 9 |
| WWW | 1 |
| RSD4 | 1 |

| | |
|-----------------|---|
| Right Ventricle | 2 |
| Septum | 5 |
| Aortic Valve | 1 |
| Right Atrium | 4 |
| Left Ventricle | 4 |
| Left Atrium | 1 |

APPLY SPATIAL SEARCH



X: 58
Y: 66
Z: 64



Data Providers

locks
ections
atasets

BMI 27.1
2020, Marda Jorgensen, TMC-F-...
7/2020, Marda Jorgensen, TMC-...
millimeter, 12 millimeter, fpe_blo-...
ODEX

BMI 22.0
/2019, Elizabeth Neumann, TM-...
9/2020, Elizabeth Neumann, TM-...
millimeter, 0.3 millimeter, fresh_fr-...
LC AF PAS
ed 1/29/2020, Jamie Allen, TMC-V-...
0.3 millimeter, 0.3 millimeter, fres-...
ed 1/29/2020, Jamie Allen, TMC-V-...
0.3 millimeter, 0.3 millimeter, fres-...
ed 1/29/2020, Jamie Allen, TMC-V-...
0.3 millimeter, 0.3 millimeter, fres-...
ed 1/29/2020, Jamie Allen, TMC-V-...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres-...
Registered 1/29/2020, Jamie Allen, TMC-V-...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres-...
Registered 1/29/2020, Jamie Allen, TMC-V-...
18 x 10 x 0.3 millimeter, 0.3 millimeter, fres-...
Registered 1/29/2020, Jamie Allen, TMC-V-...
18 x 10 x 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

HuBMAP Donors Samples Datasets Other ▾ Atlas & Tools ▾ Resources ▾ My Lists Member Login

Sections
Summary
Visualization
Provenance
Metadata
Files
Attribution

Dataset
HBM545.NTKZ.536
snRNA-seq (SNARE-seq2) [Salmon] | Kidney (Left) Published | Public Access | Save Version 1 ▾

Creation Date: 2022-02-07 Modification Date: 2022-02-13

Visualization

Scatterplot (UMAP) 7897 cells × Expression by Cell Set Cell Sets

Select a gene.

- Leiden
- Predicted ASCT Cell ...
 - B cell (4)
 - Connecting Tu...
 - Cortical Collec...
 - Cortical Thick...
 - Descending T...
 - Descending T...
 - Descending V...

Expression Levels 34857 genes

Search

- ENSG000000000003.15
- ENSG000000000005.6
- ENSG000000000419.13

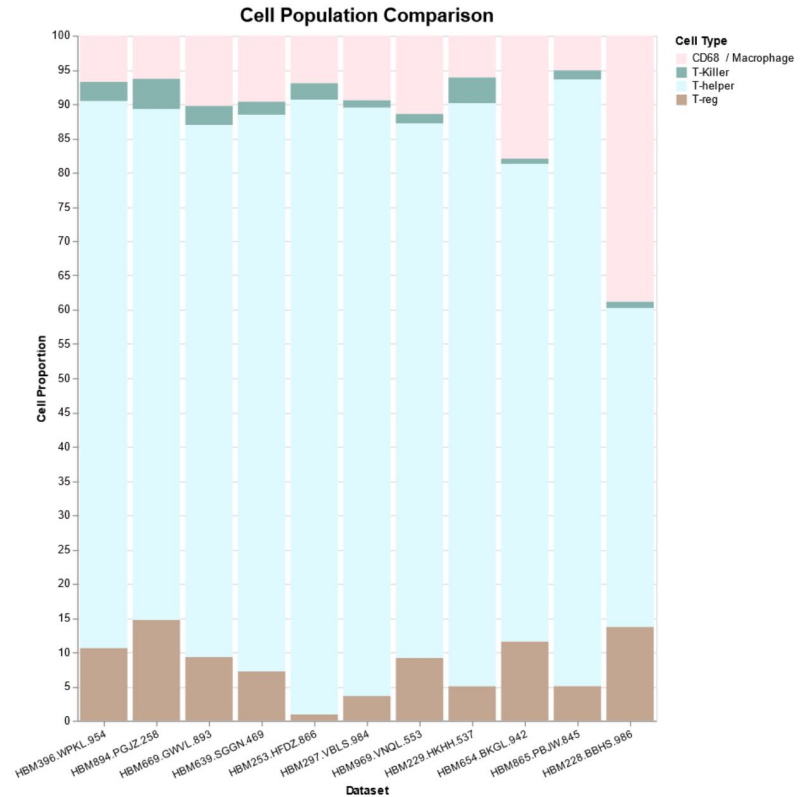
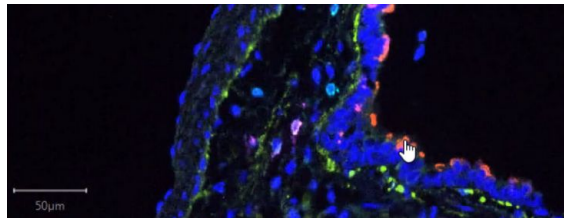
Heatmap 7897 cells × 79 genes, with 3972 cells selected

Cells Analysis Details

Use the Human Reference Atlas

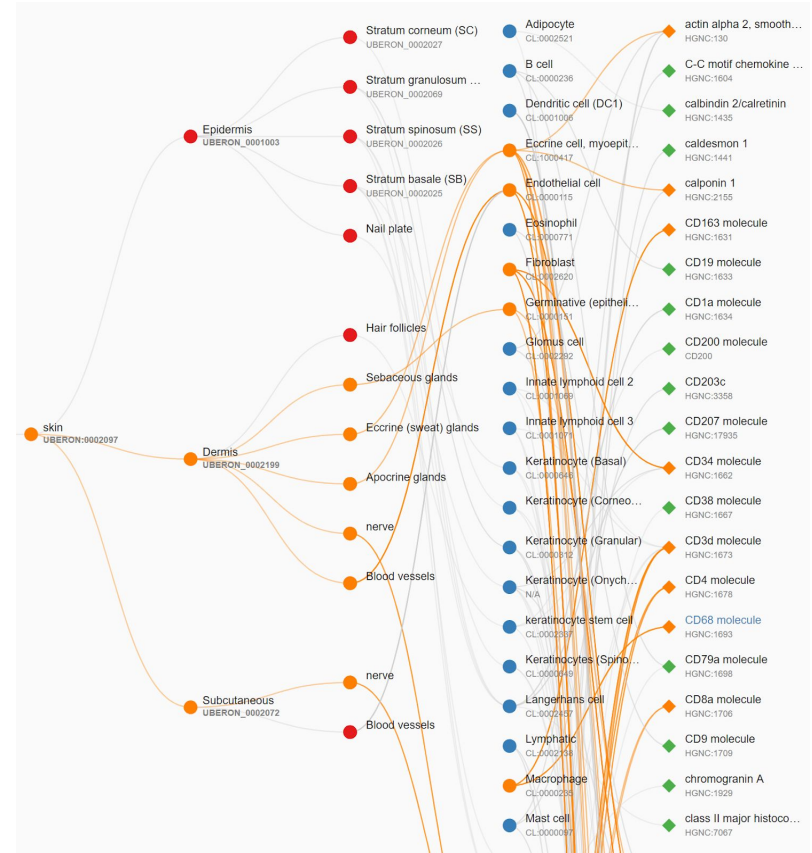
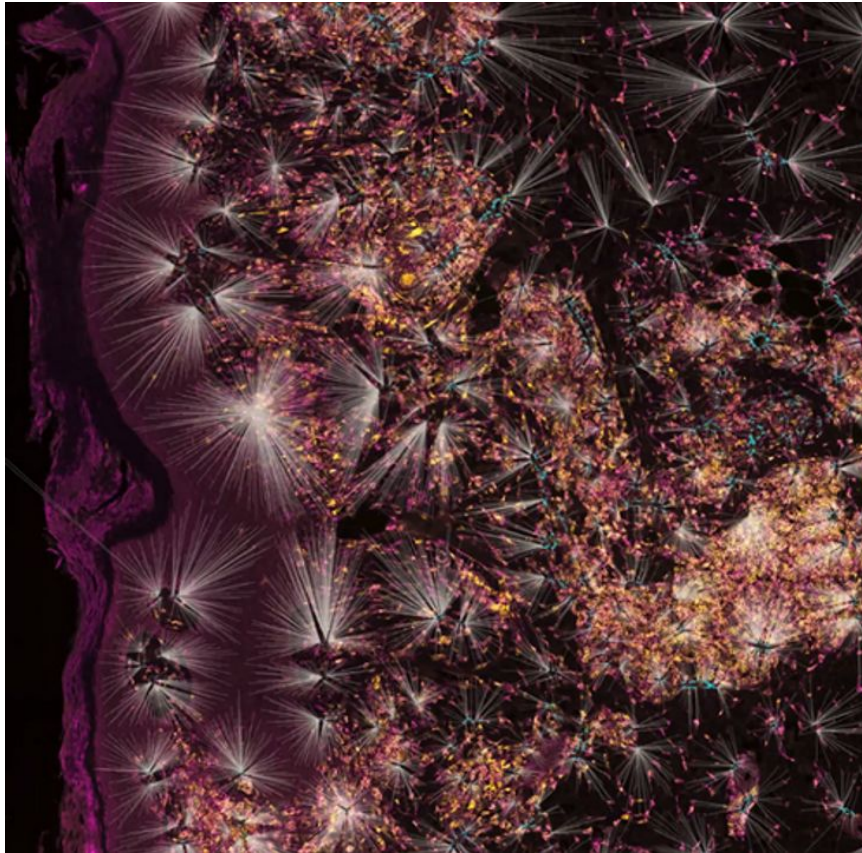


Via ASCT+B
Tables to CT



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

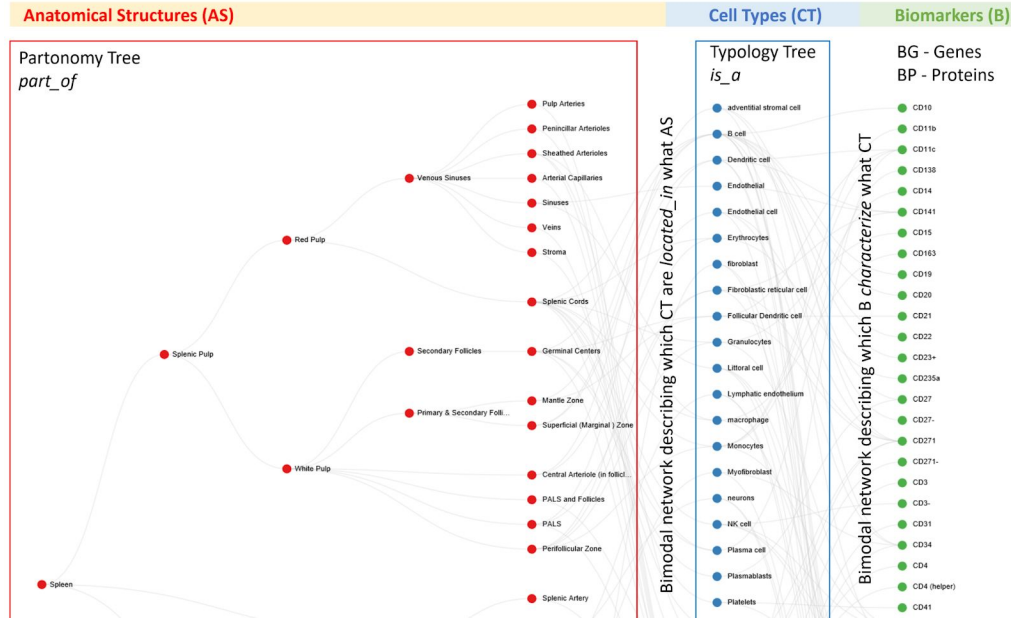
Possible/Planned Queries via CCF HRA Ontology

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



**Azimuth
Maps**
**Validated
Antibodies
(OMAPs)**

2D/3D Maps
& Ontology
Crosswalks



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 of 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

