



Anatomical Structures, Cell Types and Biomarkers (ASCT+B) Tables: Design & Usage

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HTAN All-hands Meeting, Cross-Consortium Presentation

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

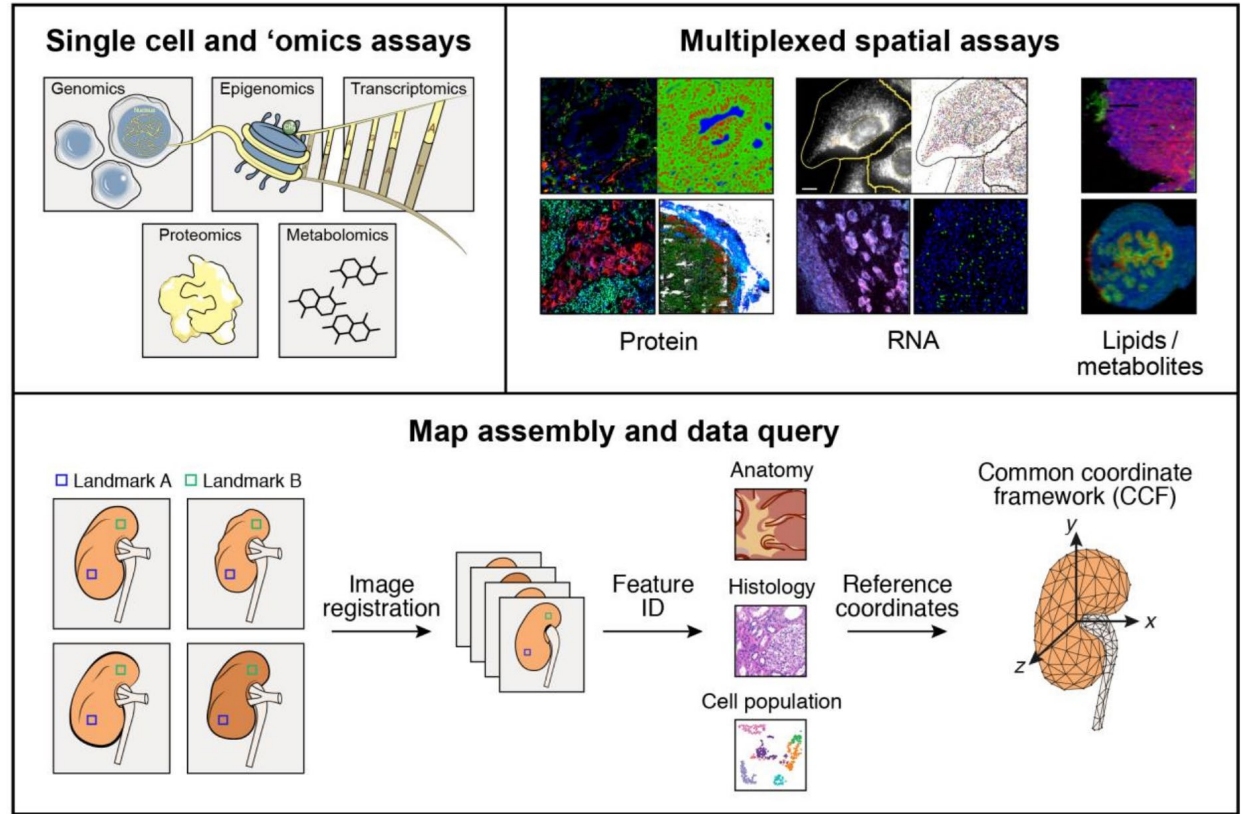


Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic, and/or metabolomic. To achieve these ends, centres will apply a combination of imaging, 'omics and mass spectrometry

techniques to specimens collected in a reproducible manner from specific sites in the body. These data will be then be integrated to arrive at a high-resolution, high-content three-dimensional map for any given tissue. To ensure inter-individual differences will not be confounded with collection heterogeneity, a robust CCF will be developed.

What is a CCF?

The Common Coordinate System (CCF) consists of ontologies and reference object libraries, computer software (e.g., user interfaces), and training materials that

- enable biomedical experts to semantically annotate tissue samples and to precisely describe their locations in the human body (“registration”),
- align multi-modal tissue data extracted from different individuals to a reference coordinate system (“mapping”) and,
- provide tools for searching and browsing HuBMAP data at multiple levels, from the whole body down to single cells (“exploration”).

See [CCF Portal](#) and [SciTech Webinar from Oct 12, 2020](#).

ASCT+B Tables

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

Structure/Region	Substructure/Sub region	Cell Type	Subset of Marker Genes
Renal Corpuscle	Bowman's Capsule	Parietal epithelial cell	<i>CRB2*</i> , <i>CLDN1*</i>
	Glomerulus	Podocyte	<i>NPHS2*</i> , <i>PODXL*</i> , <i>NPHS1*</i>
		Capillary Endothelial Cell	<i>EHD3*</i> , <i>EMCN*</i> , <i>HECW2*</i> , <i>FLT1*</i> , <i>AQP1*</i>
		Mesangial Cell	<i>POSTN*</i> , <i>PIEZO2*</i> , <i>ROBO1*</i> , <i>ITGA8*</i>

Partial ASCT Table from

- El-Achkar et al. A Multimodal and Integrated Approach to Interrogate Human Kidney Biopsies with Rigor and Reproducibility: The Kidney Precision Medicine Project. bioRxiv. 2019, Updated Aug 2020. doi:10.1101/828665

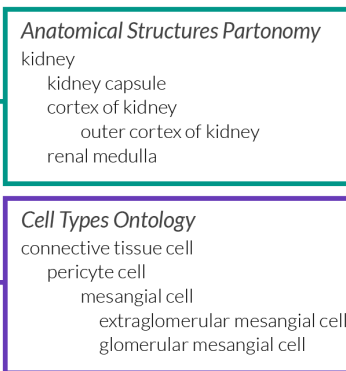
ASCT+B Table Usage

ASCT+B tables guide **CCF Ontology** and **3D Reference Object Library** design that semantically name and spatially place tissue data from different donors into one CCF (i.e., mapping).

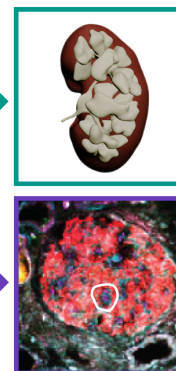
ASCT Table

Structure/Region	Sub structure/Sub region	Cell Type
Renal Corpuscle	Bowman's Capsule	Parietal epithelial Cell
	Glomerulus	Podocyte
		Capillary Endothelial Cell
Renal Tubule	Proximal Tubule	Mesangial Cell
		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
	Distal Convolution	Medulla-TAL Cell
		TAL-Macula Densa Cell
		Distal Convoluted Tubule Cell (general)
Connecting Tubule	DCT Type 1 Cell	
	DCT Type 2 Cell	
	Connecting Tubule Cell (general)	
		CNT-Principal Cell

Ontology



3D Reference Object Library



Tissue blocks are registered into the CCF using the Registration User Interface (RUI), and they can be explored via the Exploration User Interface (EUI).

Anatomical Structures

Cell Types

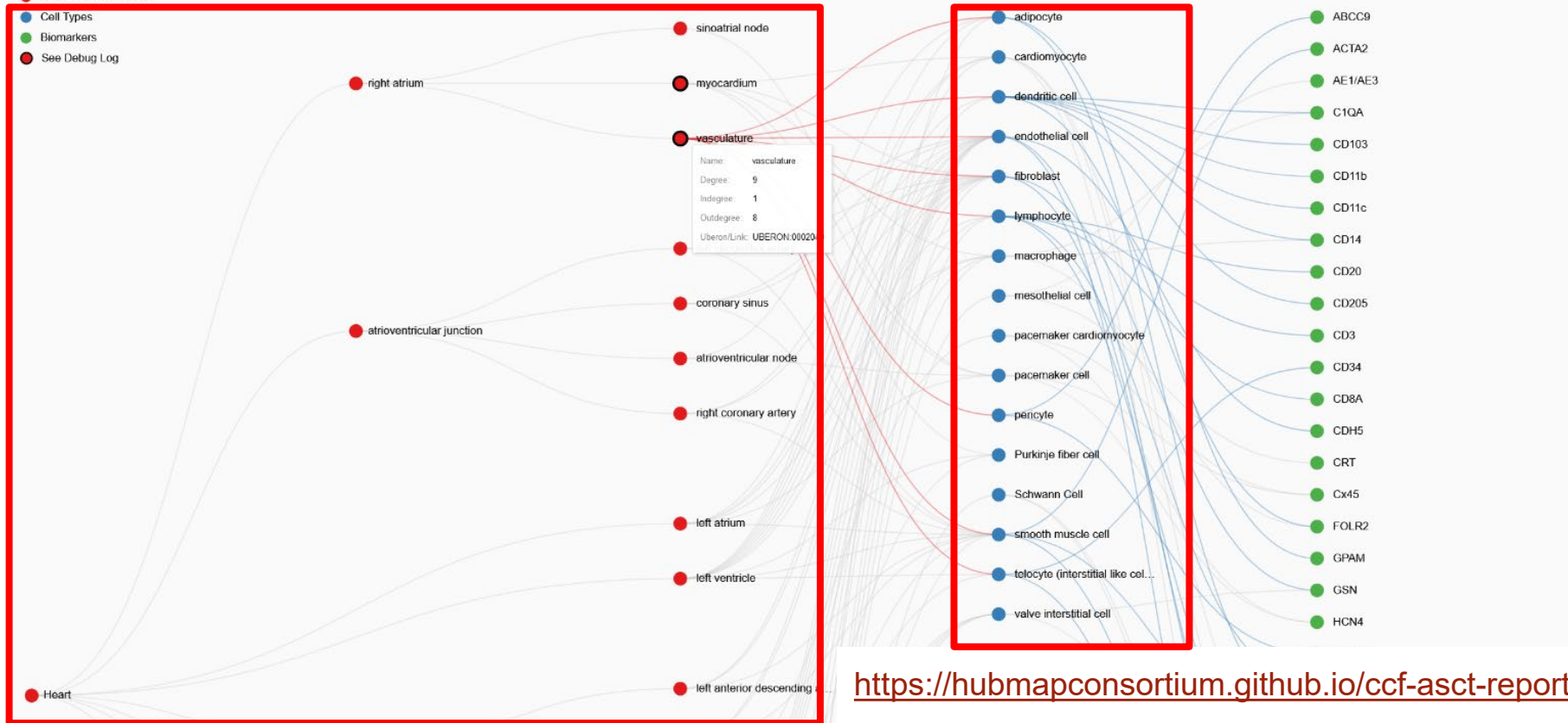
Biomarkers

Legend

- Anatomical Structures
- Cell Types
- Biomarkers
- See Debug Log

AS terms linked to Uberon

CT terms linked to CL



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

CCF Registration User Interface (RUI) v1.0.0

New Features:

- Organ carousel with 4 reference organs
- Support for tissue extraction sites
- Expanded ontology
- Semantic annotation via collision detection & manual annotation
- Support for non-HuBMAP usage

HuBMAP CCF REGISTRATION USER INTERFACE

First Name * Last Name *

Register 3D Preview

Left Right **Anterior** Posterior

X: 199 Y: 122 Z: 151

Width (X) Height (Y) Depth (Z)
10 10 10

Tissue Slices
Thickness # Slices

Tissue Block Rotation
X 0
Y 0
Z 0

Anatomical Structure Tags
Add Anatomical Structures ... +
descending colon **transverse colon**
Assigned Added

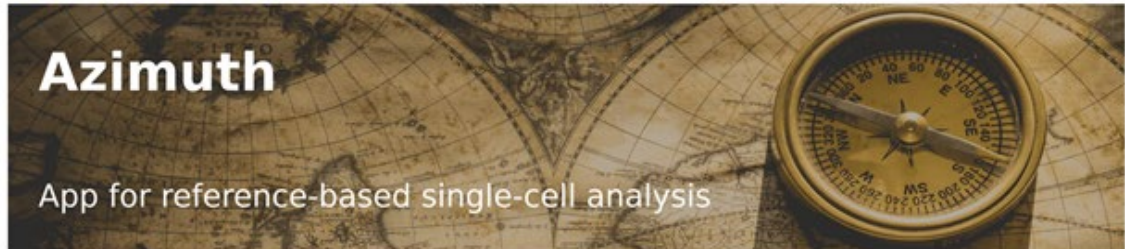
REVIEW AND DOWNLOAD

Anatomical Structures

- vermiform appendix
- ascending colon
- caecum
- descending colon
- hepatic flexure of colon
- ileocecal valve
- rectum
- sigmoid colon

AS terms from ASCT+B

<https://hubmap-ccf-ui.netlify.app/rui/>



Azimuth

App for reference-based single-cell analysis

QC Filters

min nCount_RNA: 400, max nCount_RNA: 25000
 min nFeature_RNA: 27, max nFeature_RNA: 3200
 min percent_mt: 0, max percent_mt: 50

33148 cells remain after current filters. [Map cells to reference](#)

Violin Plots: nCount_RNA, nFeature_RNA, percent_mt

	0%	25%	50%	75%	100%
nCount per cell	400.00	1483.00	1891.00	2438.00	33000.00
Genes detected per cell	57.00	604.00	732.00	875.00	3293.00
Mitochondrial percentage per cell	0.00	1.75	2.25	2.94	10.27

Reference t-SNE Plot: Shows cell clusters colored by Cell Type (CT) terms from ASCT+B. A legend on the right lists terms such as ASCT, B, B1, B2, B3, B4, B5, B6, B7, B8, B9, B10, B11, B12, B13, B14, B15, B16, B17, B18, B19, B20, B21, B22, B23, B24, B25, B26, B27, B28, B29, B30, B31, B32, B33, B34, B35, B36, B37, B38, B39, B40, B41, B42, B43, B44, B45, B46, B47, B48, B49, B50, B51, B52, B53, B54, B55, B56, B57, B58, B59, B60, B61, B62, B63, B64, B65, B66, B67, B68, B69, B70, B71, B72, B73, B74, B75, B76, B77, B78, B79, B80, B81, B82, B83, B84, B85, B86, B87, B88, B89, B90, B91, B92, B93, B94, B95, B96, B97, B98, B99, B100.

Query t-SNE Plot: Shows the same cell clusters as the reference plot, but colored by the query cell type.

Summary: 33148 cells uploaded, 33148 cells after filtering, Success: Mapping complete.

CCF Exploration User Interface (EUI)

The screenshot displays the HuBMAP CCF Exploration User Interface (EUI). At the top, the HuBMAP logo is on the left, and user information (Sex: Both, Age: 1-110, BMI: 13-83) and navigation icons (refresh, download, help) are on the right. A 'Login' button is also present.

On the left side, there is a search bar labeled 'Search ontology terms ...' with a magnifying glass icon. Below it is a list of ontology terms under the 'body' category, which is highlighted with a red box. The terms include: heart, lung, kidney (with sub-terms: 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, and nephron.

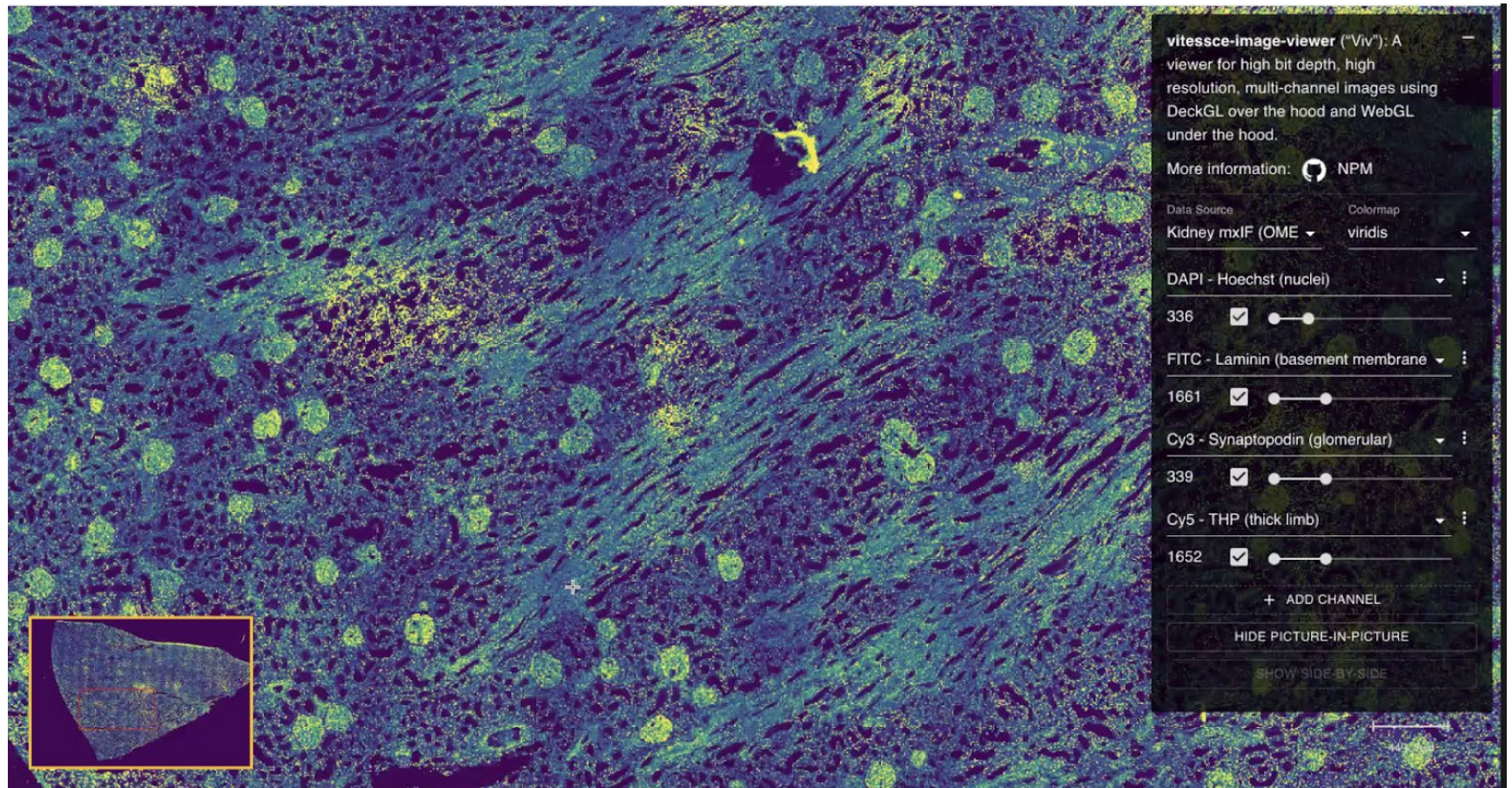
The central part of the interface features a 3D human model with the kidneys highlighted in red. Navigation arrows are visible on the left and right sides of the model.

On the right side, there is a 'body' section with summary statistics: 2 Centers, 27 Donors, and 41 Samples. Below this is a list of sample cards, each with a thumbnail image, a title, and a download icon. The sample cards are:

- 10x: Female, Age 14, BMI 14.7; HBM894.MPVN.828; TMC-Florida; First case collected. Incomplete d...
- CODEX: Male, Age 18, BMI 27.1; HBM436.GHWX.449; TMC-Florida; section is 190um from block surface
- Male, Age 56, BMI 32.5; HBM696.XTVL.498; TMC-Vanderbilt; Age 56, White Male
- Male, Age 53, BMI 26.5; HBM652.VRLD.292; TMC-Vanderbilt; Age 53, Black Male
- Male, Age 58, BMI 22.0; HBM477.CJKM.888; TMC-Vanderbilt; 107-111
- CODEX: Male, Age 18, BMI 25.5; HBM473.VKCM.878; TMC-Florida; section is 255um from block surface
- LC: Male, Age 55, BMI 25.4; HBM824.BLXF.883; TMC-Vanderbilt; 13-16

AS terms from ASCT+B

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



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

Human Reference CCF Atlas: Checklist

Common Coordinate Framework (CCF) Design:

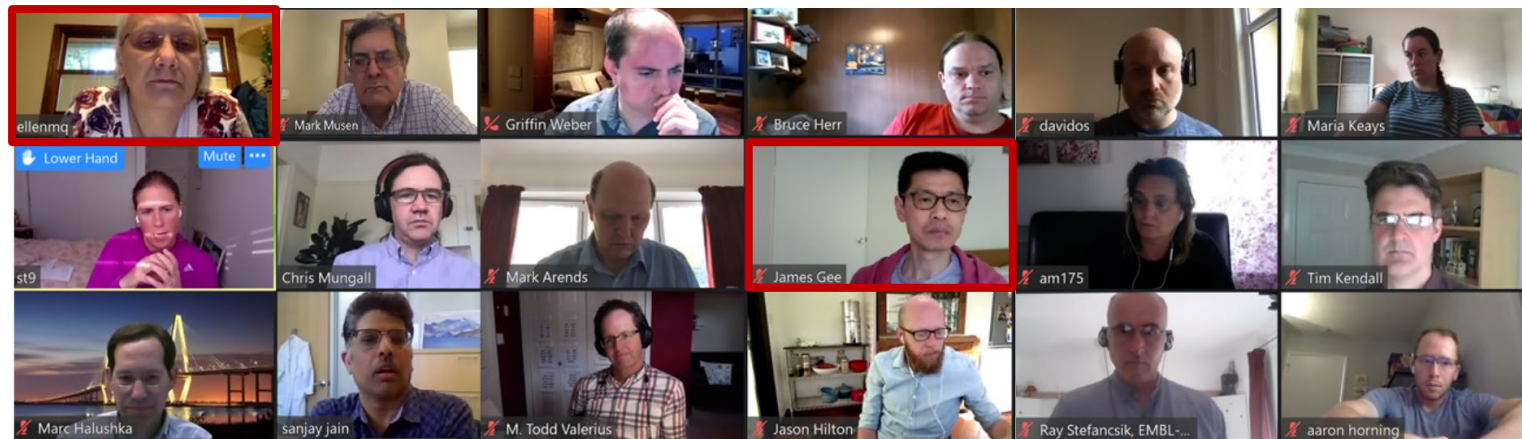
1. Make sure the Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) that you use/submit are listed in the [ASCT+B tables](#). The tables are authored and reviewed by an international team of anatomists, pathologists, physicians, and other experts, see this [SOP](#).
2. Spatially register all tissue samples using the CCF Registration User Interface (RUI) in the Ingest Portal. End of October 2020, kidney, spleen, heart, colon registration are supported. For other organs, see [SOP](#).
3. After submitting data, review data in the [CCF Exploration User Interface](#) and make sure spatial, semantic, and other metadata are correct.
4. For functional tissue unit (FTU) segmentation, submit a list of FTUs for your organ(s) and make sure FTU names and all relevant cell types (CT) are captured in the ASCT+B table. Use assays/biomarkers (B) that make it possible to identify FTUs—initially manually, later automatically. Submit tissue with 1000 FTUs manually identified FTUs.
5. In support of the [Vasculature-based CCF](#), provide cell segmentation data for blood vessels and different cell types.

For questions, email infoccf@indiana.edu.

ASCT+B Table Working Group

Meetings take place monthly to review and approve tables, formalize and unify table design language, discuss and expand table usage, see [WG Charter](#).

Next meetings: Dec 3, 1:30p EST. In 2021: Jan 6, Feb 3, March 3, 11a-noon ET.
Please [register](#) to receive invites and updates.





HuBMAP
Human BioMolecular Atlas Program

Hacking the Kidney Hackathon



PARTICIPATION OPENS
NOV 5TH, 10:00 AM EST

TOTAL PRIZE MONEY **\$60,000** TO BE AWARDED TO
THE WINNING TEAMS!

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<https://innovationdigi.com/hubmap-hackathon>

HuBMAP: Hacking the Kidney

Identify glomeruli in human kidney tissue images



InnovationDigi

\$60,000

Prize Money

[Overview](#) [Data](#) [Notebooks](#) [Leaderboard](#) [Rules](#) [Team](#) [Host](#)

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i This competition is not yet live; only competition hosts can currently view it.

Overview

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Description

Supervised ML
Evaluation

Judges Prize

Prizes

Timeline

Organizers &
Sponsors

+ Add Page

Our best estimates show there are over 7 billion people on the planet and 300 billion stars in the Milky Way. 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.

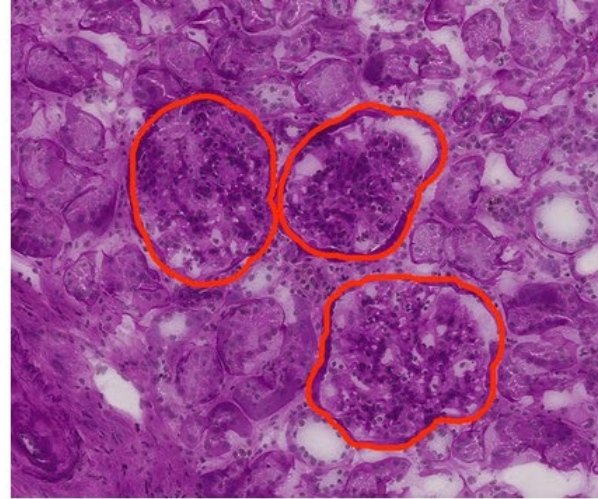
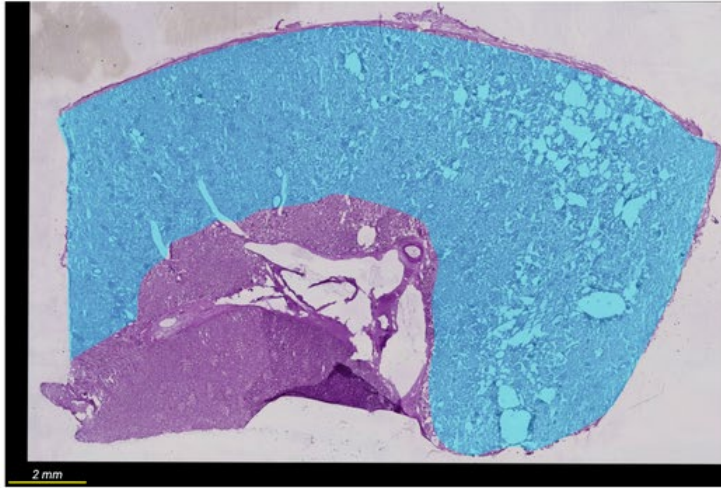
Just as the Human Genome Project mapped the entirety of human DNA, the [Human BioMolecular Atlas Program](#) (HuBMAP) is a major endeavor. Sponsored by the National Institutes of Health (NIH), HuBMAP is working to catalyze the development of a framework for mapping the human body at a level of glomeruli 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.

This competition, "Hacking the Kidney," starts by mapping the human kidney at single cell resolution.

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.

You will also have the opportunity to present your findings to a panel of judges for additional consideration. Successful submissions will construct the tools, resources, and cell atlases needed to determine how the relationships between cells can affect the health of an individual.

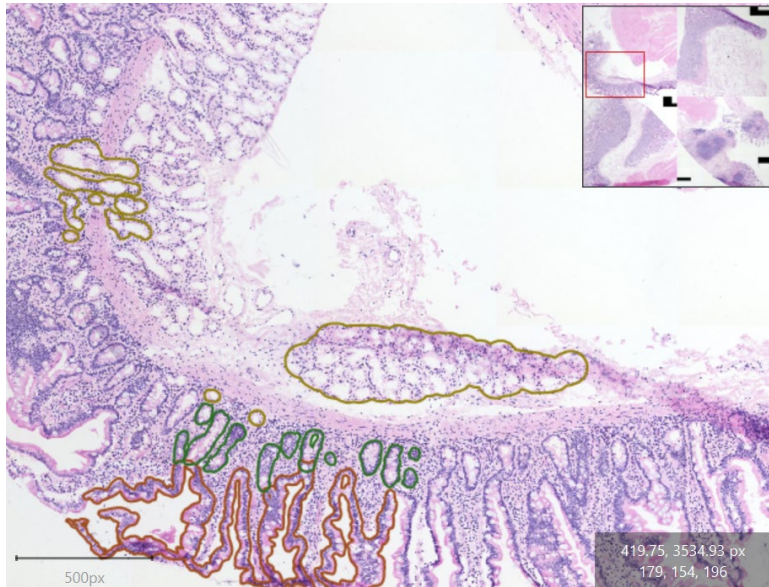
Advancements in HuBMAP will accelerate the world's understanding of the relationships between cell and tissue organization and function and human health. These datasets and insights can be used by researchers in cell and tissue anatomy, pharmaceutical companies to develop therapies, or even parents to show their children the magnitude of the human body.



PAS stained tissue sections provided by TMC-VU.
Cortex segmentations (left) and glomeruli segmentations (right)

Small Intestine

Provided by Jeanne Shen, TMC-Stanford



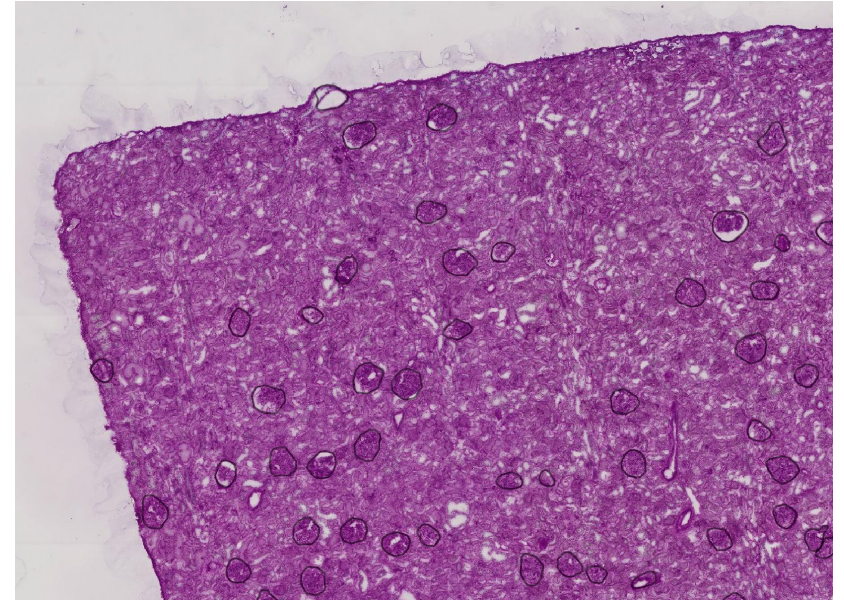
Red brown: Small intestinal villus epithelium

Green: Small intestinal crypt

Brown: Small intestinal Brunner's gland

Kidney

Provided by Heath Patterson, TMC-VU



Black: Glomeruli

Used in HuBMAP Kaggle Competition

Acknowledgements

HuBMAP Consortium (<https://hubmapconsortium.org>)



Thanks go to all the **patients** that agreed to volunteer healthy tissue and open use of their data.



TMCs



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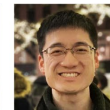
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Q&A

