The HuBMAP Common Coordinate Framework (CCF) Registration User Interface (RUI)

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Gut Cell Atlas Annual Convening

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

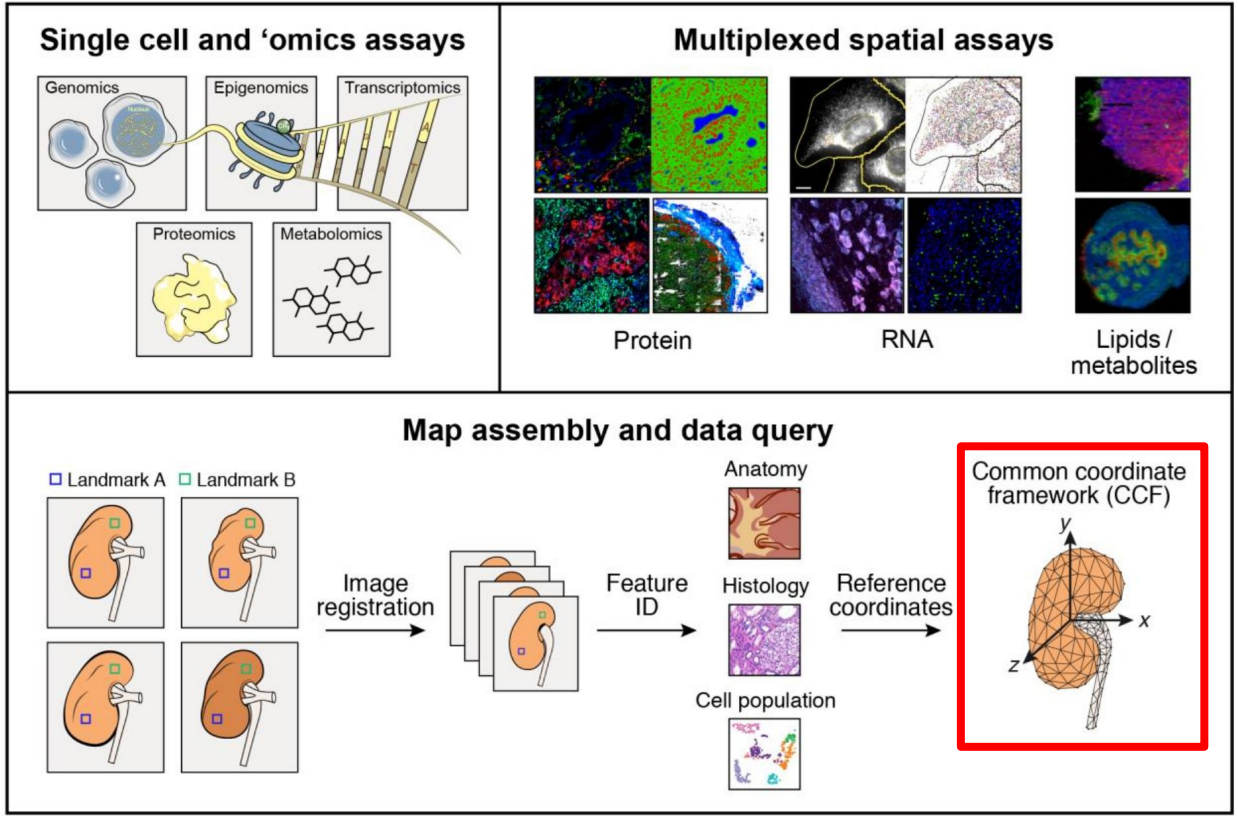


Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic, 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

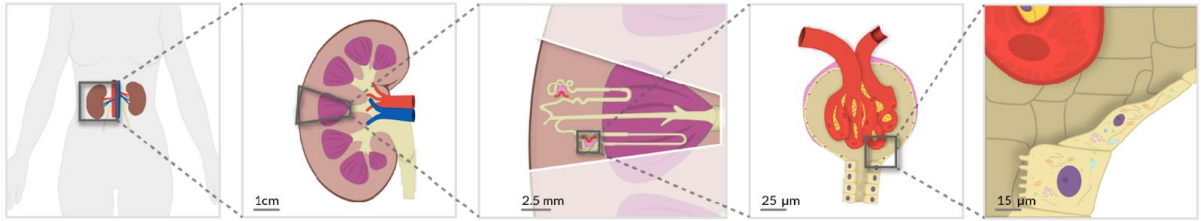
- enable biomedical experts to semantically annotate tissue samples and to precisely describe their locations in the human body ("registration"),
- align multi-modal tissue data extracted from different individuals to a reference coordinate system ("mapping") and,
- provide tools for searching and browsing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

See CCF Portal and SciTech Webinar from Oct 12, 2020.

CCF Requirements

The CCF must capture major **anatomical structures, cell types, and biomarkers** and their interrelations across **multiple levels of resolution**.

It should be **semantically explicit** (using existing ontologies, e.g., Uberon, CL) and **spatially explicit** (e.g., using 3D reference organs for registration and exploration).



Body	Organ	Functional Tissue Unit	FTU Sub-structure(s)	Cellular
• Body • Kidney (Left, Right) • Aorta • Renal artery • Renal vein • Ureter	• Renal capsule • Renal pyramid • Renal cortex • Renal medulla • Renal calyx • Renal pelvis	• Nephron • Renal corpuscle • Proximal convoluted tubule • Loop of Henle • Distal convoluted tubule • Connecting tubule • Collecting duct	• Bowman's capsule • Glomerulus • Efferent arteriole • Afferent arteriole	• Parietal epithelial cell • Capillary endothelial cell • Mesangial cell • Podocyte

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).

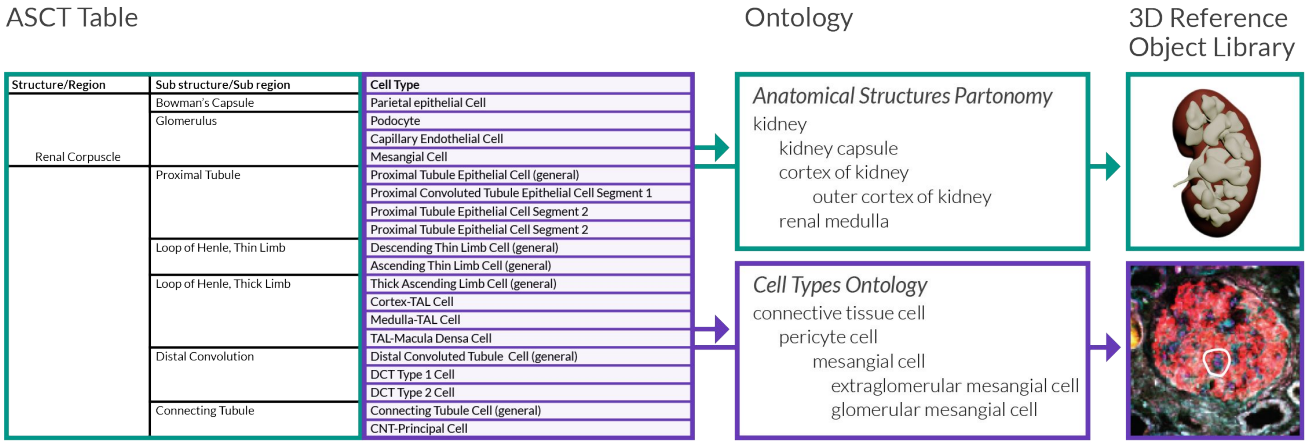
Structure/Region	Substructure/Subregion	Cell Type	Subset of Marker Genes
Renal Corpuscle	Bowman's Capsule	Parietal epithelial cell	*CRB2*, CLDN1**
	Glomerulus	Podocyte	*NPHS2*, PODXL*, NPHS1**
		Capillary Endothelial Cell	*EHD3*, EMCN*, HECW2*, FLT1*, AQP1**
		Mesangial Cell	*POSTN*, PIEZO2*, ROBO1*,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

Partial ASCT Table from

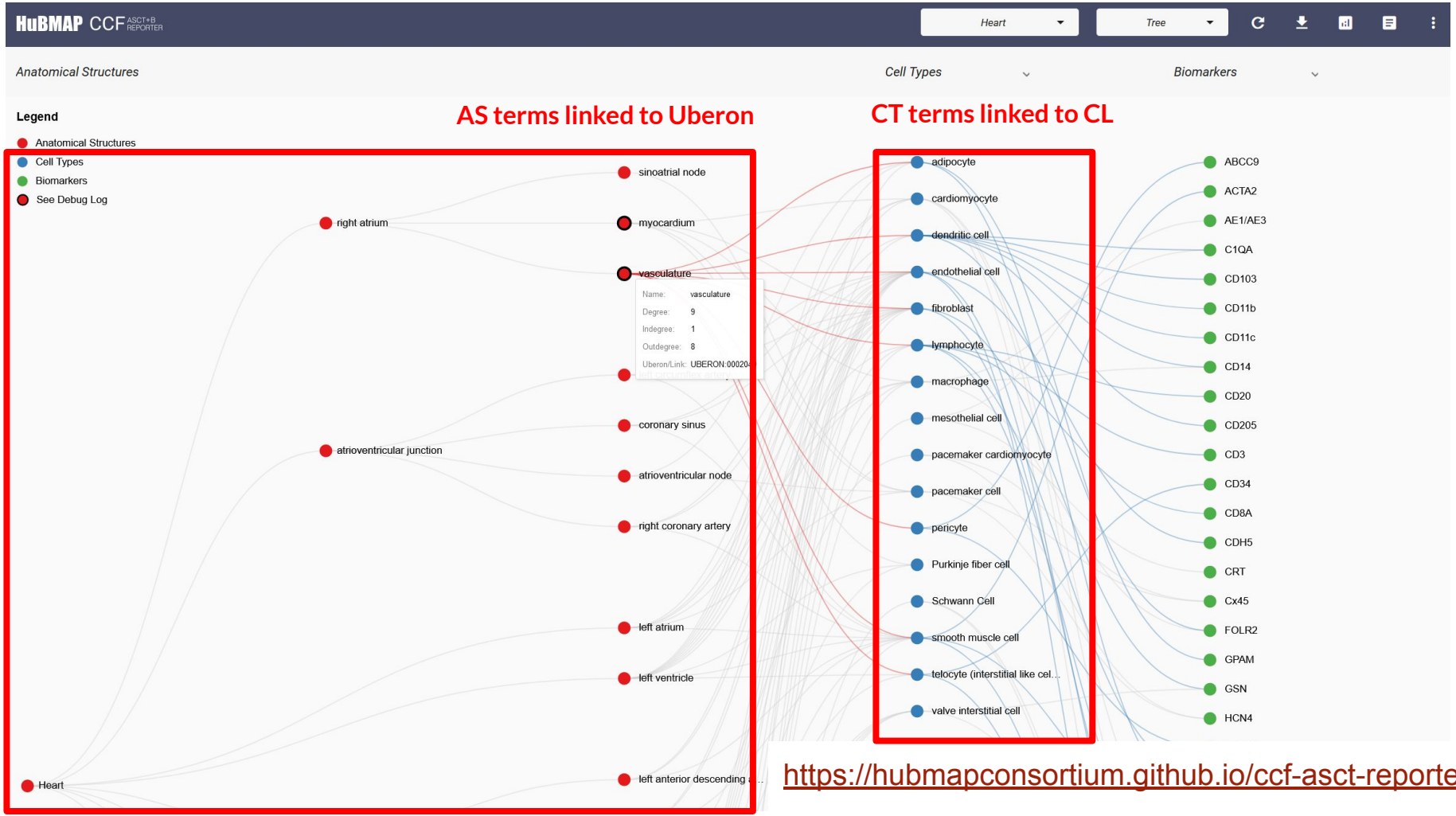
- El-Achkar et al. A Multimodal and Integrated Approach to Interrogate Human Kidney Biopsies with Rigor and Reproducibility: The Kidney Precision Medicine Project. bioRxiv. 2019, Updated Aug 2020. doi:10.1101/828665

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).



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



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

Document the tissue extraction site by registering tissue blocks within a 3D reference organ.

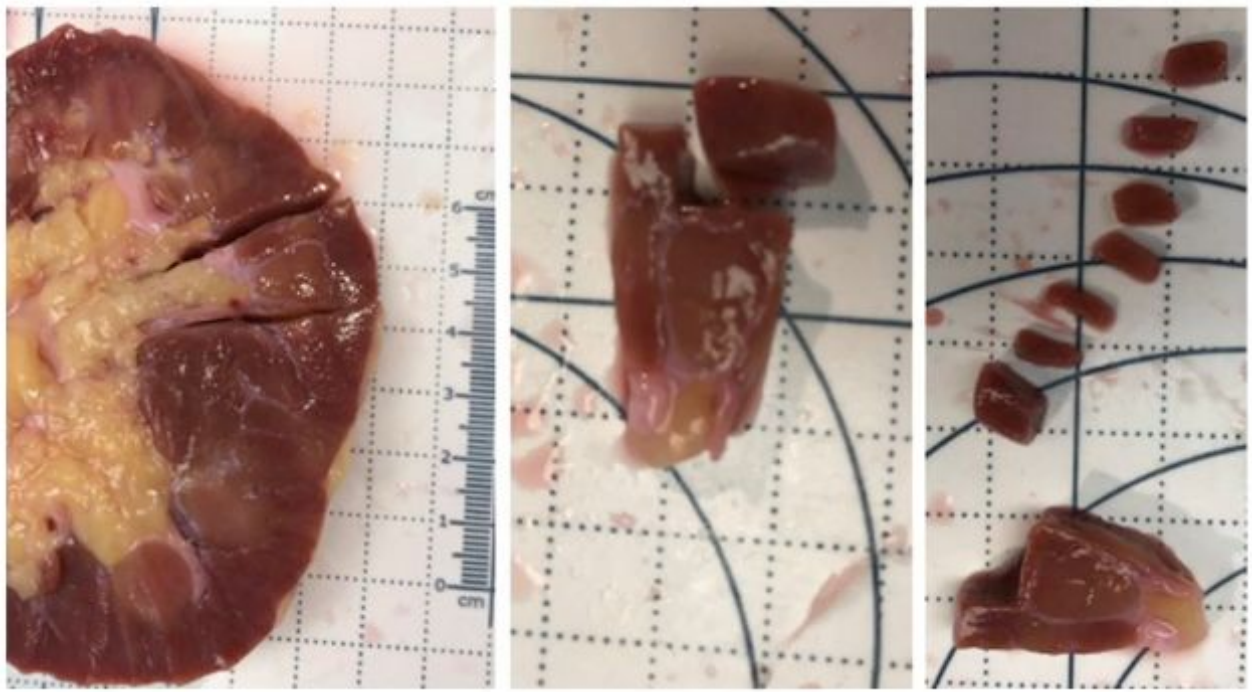


Image provided by Sanjay Jain, TMC-UCSD

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

AS terms from ASCT+B

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

CCF Registration User Interface (RUI) v1.0.0

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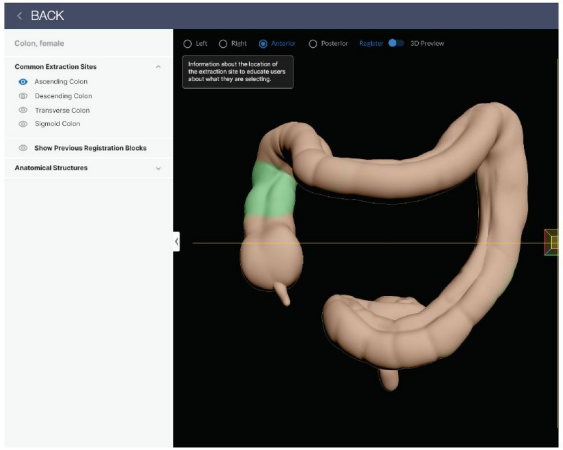
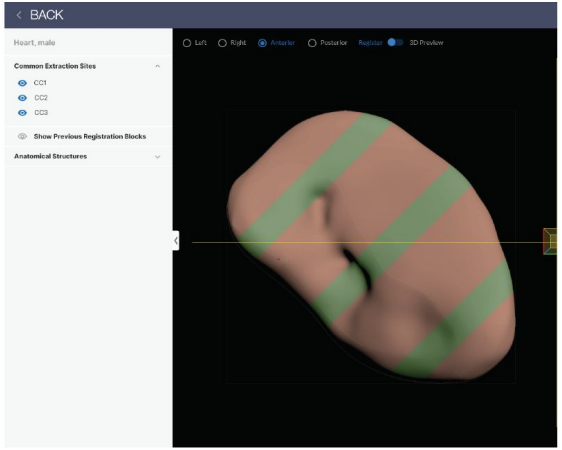
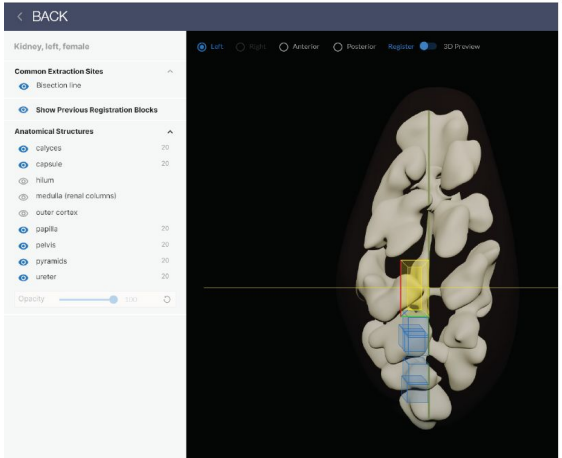
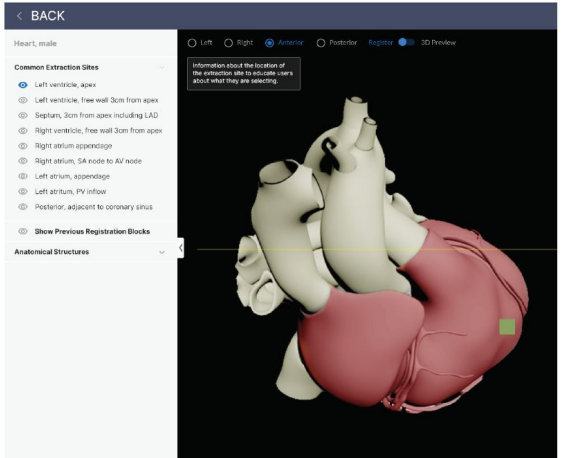








Kidney

- Bisection Line

Spleen

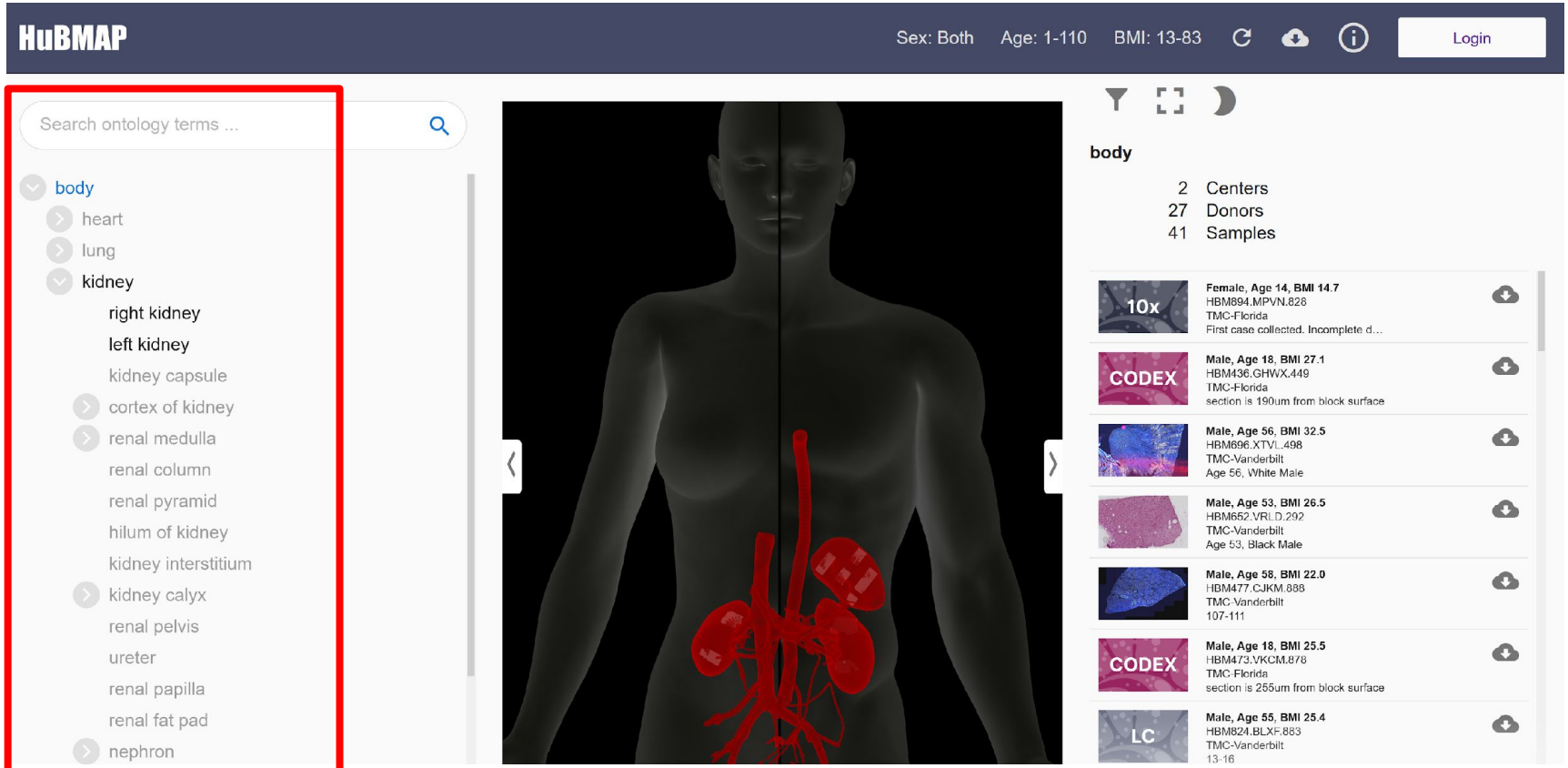
- CC1
- CC2
- CC3

Colon

- Ascending Colon
- Descending Colon
- Transverse Colon
- Sigmoid Colon

Heart	Extraction Site Mapping
• Left atrium, appendage	7
• Left atrium, PV inflow	8
• Left ventricle, apex	1
• Left ventricle, free wall 3cm from apex	2
• Septum, 3cm from apex including LAD	3
• Posterior, adjacent to coronary sinus	9
• Right atrium appendage	5
• Right atrium, AV (atrioventricular) node	6a
• Right atrium, SA (sinoatrial) node	6b
• Right ventricle, free wall 3cm from apex	4

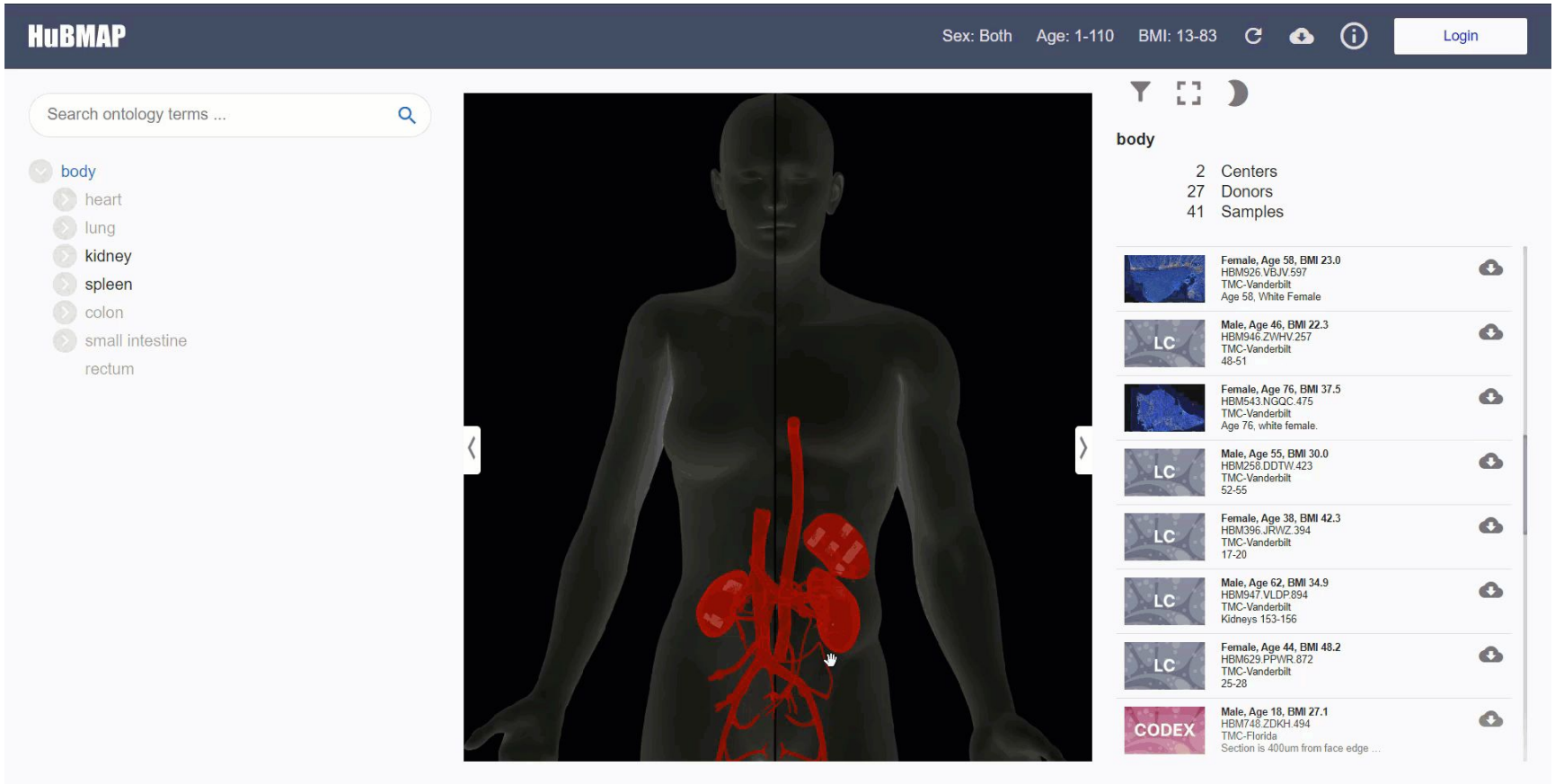
CCF Exploration User Interface (EUI)



AS terms from ASCT+B

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

CCF Exploration User Interface (EUI)



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

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.

Please register to receive invites and updates.
The next meeting is on Dec 3, 1:30p EST.

HuBMAP Visible Human MOOC (VHMOOC)

Started Aug 4, 2020

To enroll, first **log in**. If you don't have an account, **create an IU Guest account**.

Register via:
https://tinyurl.com/vhmooc

INDIANA UNIVERSITY

Course Introduction

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

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

Learning Outcomes

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

Module Topics Include

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

Meet the Instructors

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

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

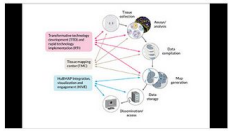
Andreas Bueckle, PhD Candidate in Information Science, performing research on information visualization, specifically virtual and augmented reality.

Length: 10 hours

Department: Cyberinfrastructure Network Science

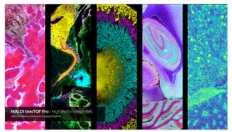
Credit: None

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



HuBMAP Overview

- Project Goals, Setup, and Ambitions

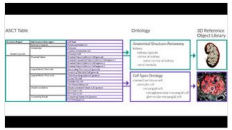


Tissue Data Acquisition and Analysis

- Behind the Scenes at Vanderbilt University

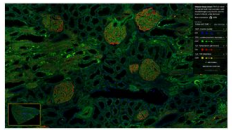
Biomolecular Data Harmonization

- An Introduction to Seurat



CCF Ontology, 3D Reference Objects, and User Interfaces

- Creating an Atlas of the Human Body



Portal Design and Usage

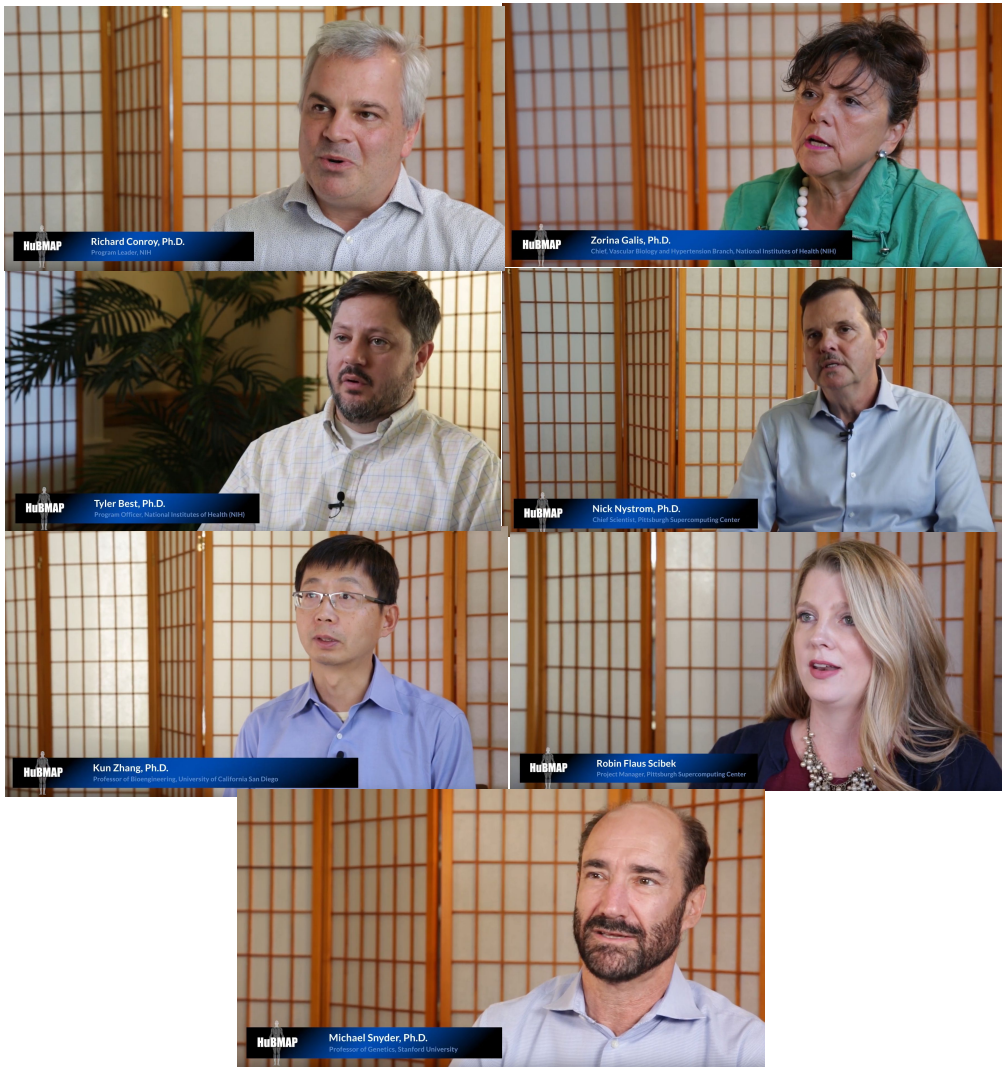
- Datasets and Software in the 1st HuBMAP Portal Release

Open Consent Your Data

- In Support of Research

Videos

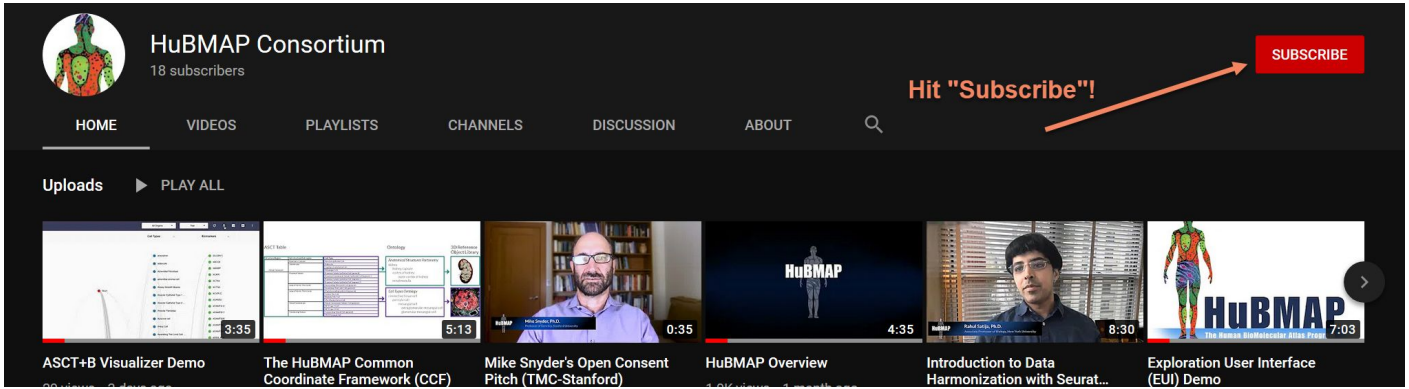
- Six initial videos during 2019/2020
- More video to come 2020/2021
- Pictured here are f2f interviews at Annual Meeting at Stanford in Sept 2019



Relevant links

- Sign up on IU Expand:

- Subscribe on YouTube:



Acknowledgements

HuBMAP Consortium (https://hubmapconsortium.org)

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

NIH National Institutes of Health

Opportunity Pool Awardee
KIDNEY PRECISION MEDICINE PROJECT
kpmp.org

NSF

TMCs

Jeffrey Spraggins
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Vanderbilt University

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3D Models

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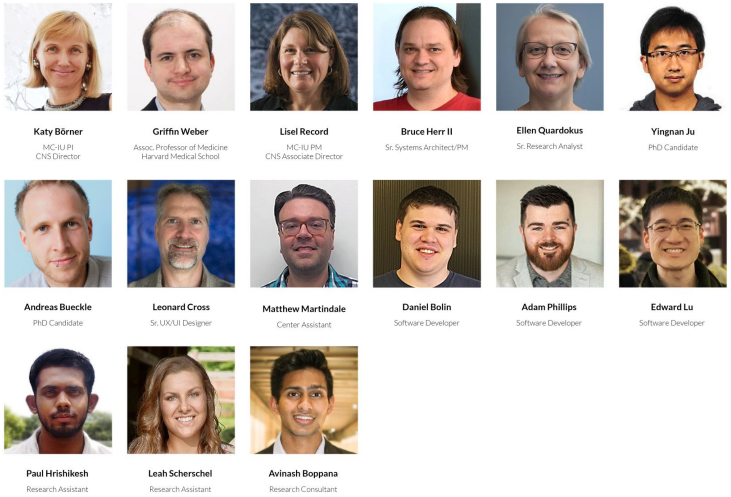
NIAID

MC-IU HIVE Team



Q&A