



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

Andreas Bueckle, MC-IU (HuBMAP)

Ph.D. Candidate in Information Science
Research Assistant
Luddy School of Informatics, Computing, and Engineering
Indiana University, Bloomington, IN

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.

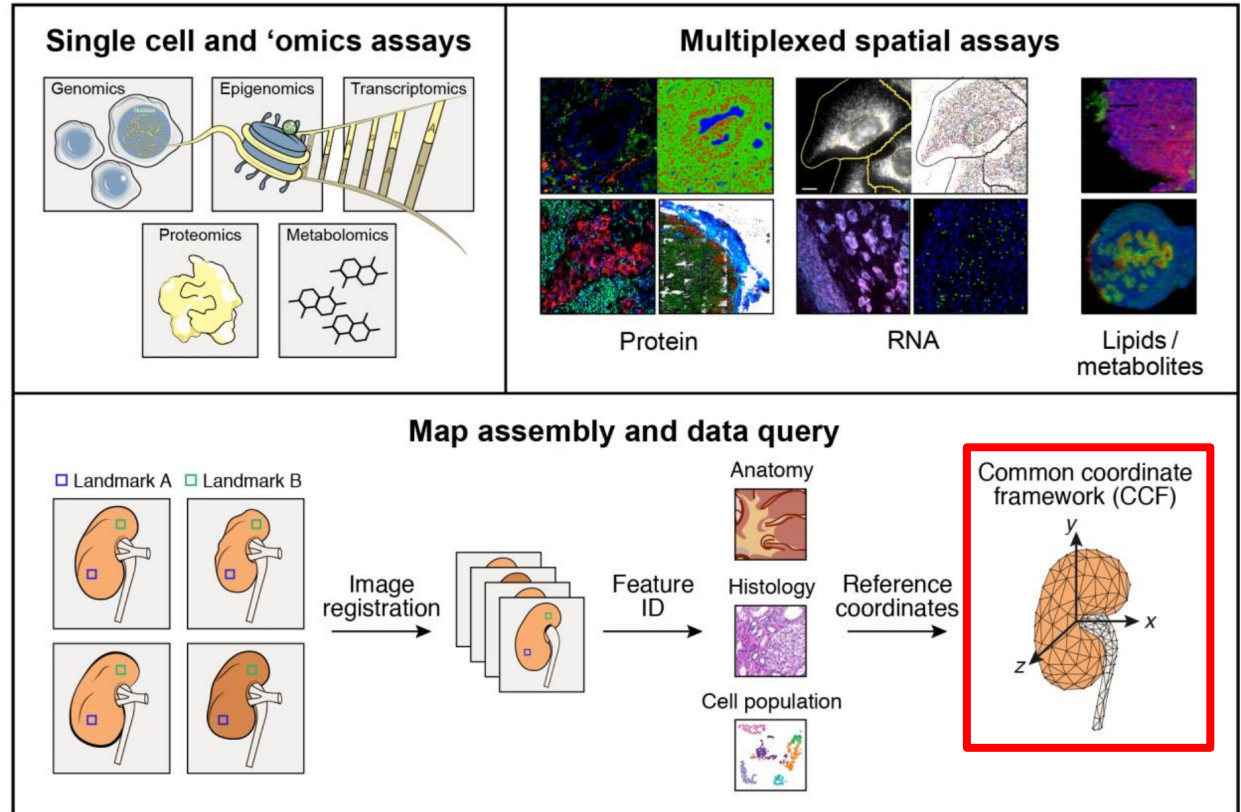


Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic,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

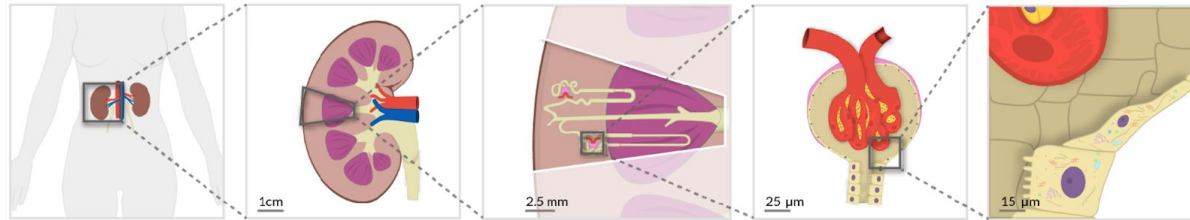
- enable biomedical experts to semantically annotate tissue samples and to precisely describe their locations in the human body (“registration”),
- align multi-modal tissue data extracted from different individuals to a reference coordinate system (“mapping”) and,
- provide tools for searching and browsing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

- Body
- Kidney (Left, Right)
- Aorta
- Renal artery
- Renal vein
- Ureter

Organ

- Renal capsule
- Renal pyramid
- Renal cortex
- Renal medulla
- Renal calyx
- Renal pelvis

Functional Tissue Unit

- Nephron
- Renal corpuscle
- Proximal convoluted tubule
- Loop of Henle
- Distal convoluted tubule
- Connecting tubule
- Collecting duct

FTU Sub-structure(s)

- Bowman's capsule
- Glomerulus
- Efferent arteriole
- Afferent arteriole

Cellular

- 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/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

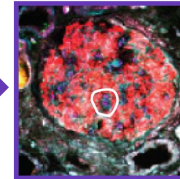
Structure/Region	Sub structure/Sub region	Cell Type	
Renal Corpuscle	Bowman's Capsule	Parietal epithelial Cell	
	Glomerulus	Podocyte Capillary Endothelial Cell Mesangial Cell	
Renal Tubule	Proximal Tubule	Proximal Tubule Epithelial Cell (general) Proximal Convoluted Tubule Epithelial Cell Segment 1 Proximal Tubule Epithelial Cell Segment 2 Proximal Tubule Epithelial Cell Segment 2	
		Loop of Henle, Thin Limb	Descending Thin Limb Cell (general) Ascending Thin Limb Cell (general)
			Loop of Henle, Thick Limb
		Distal Convolution	Cortex-TAL Cell Medulla-TAL Cell TAL-Macula Densa Cell
			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



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

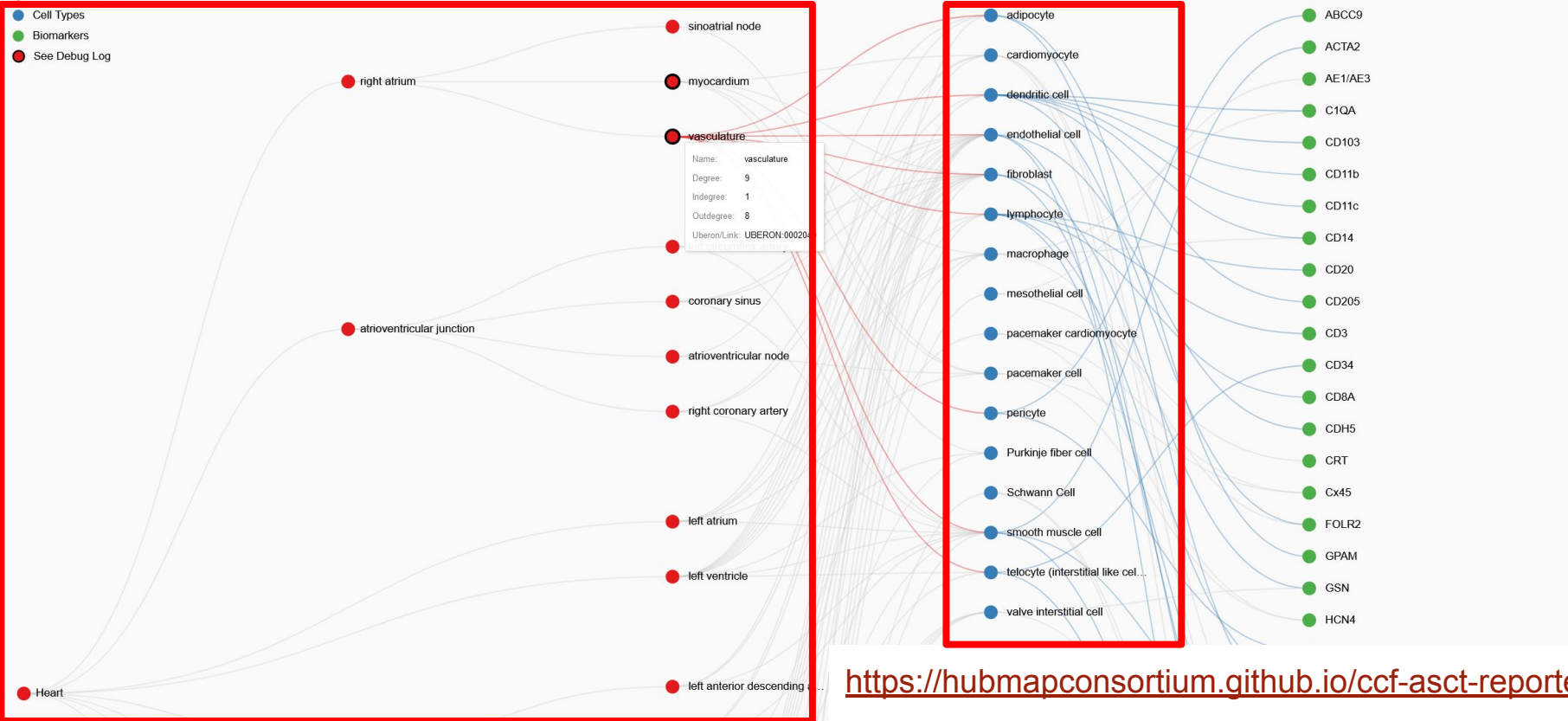
Biomarkers

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>

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

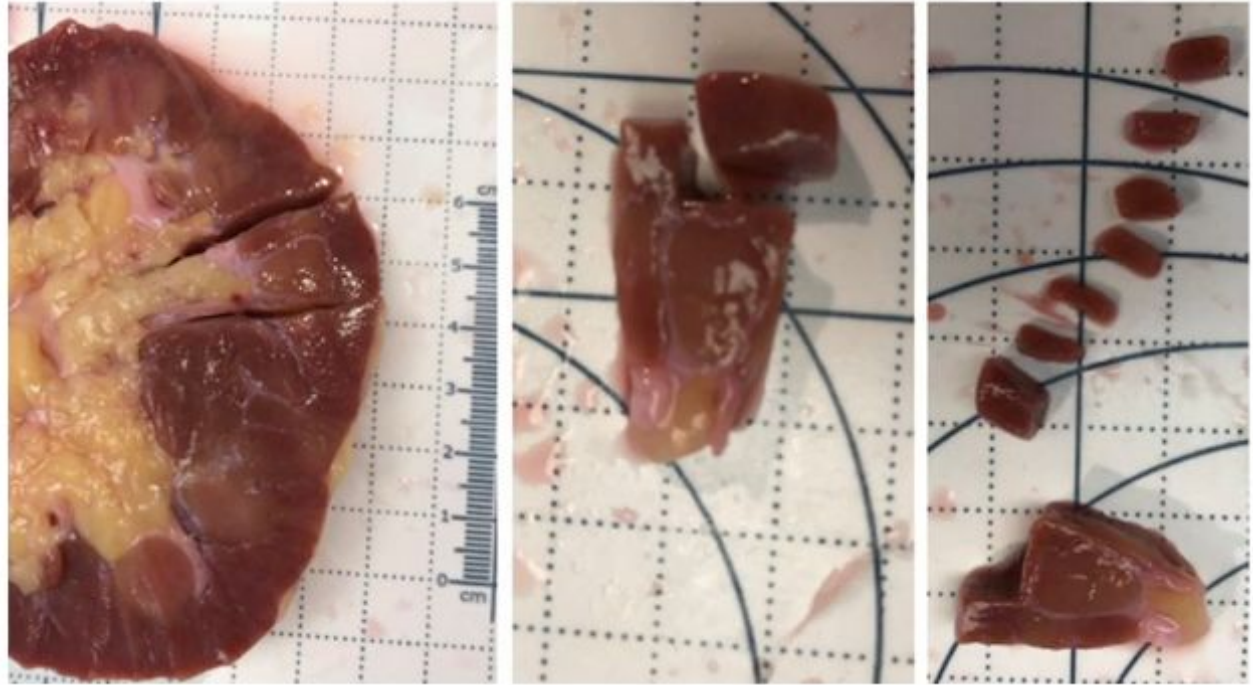
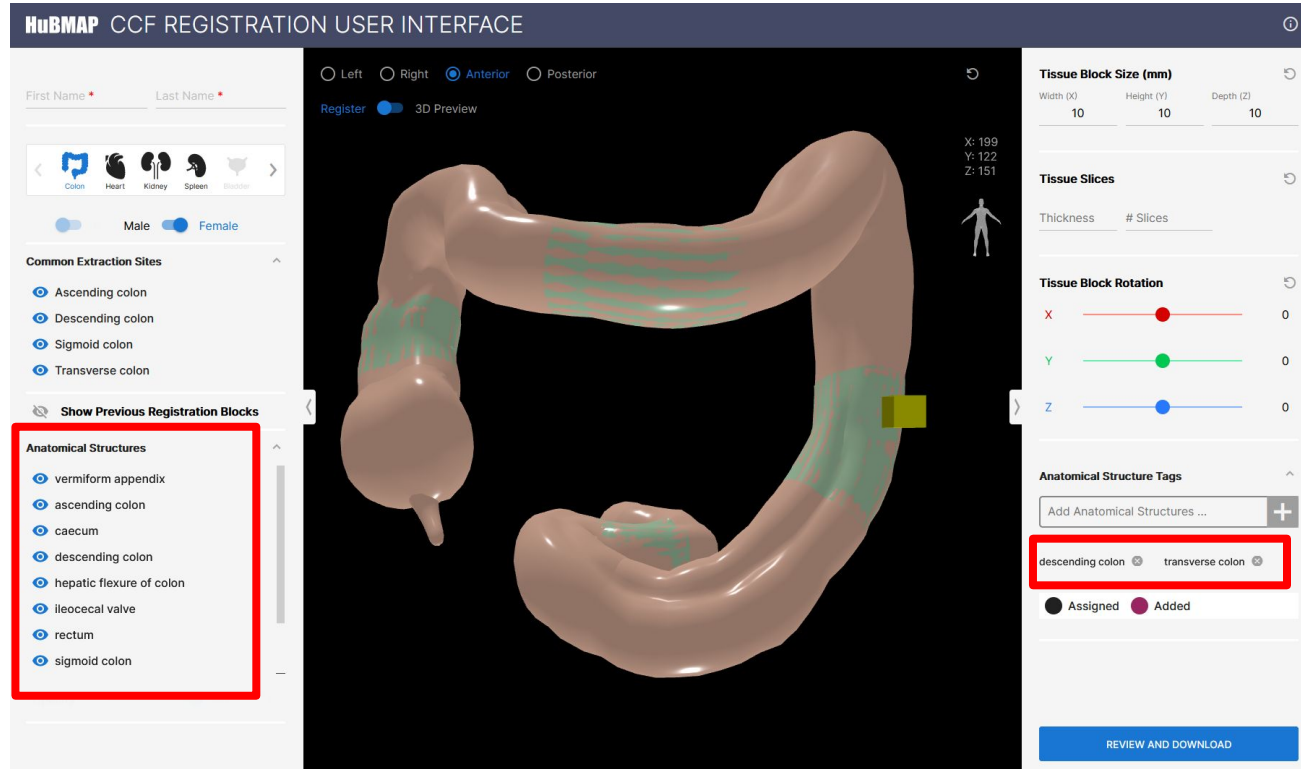


Image provided by Sanjay Jain, TMC-UCSD

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

HuBMAP CCF REGISTRATION USER INTERFACE

First Name: Andreas Last Name: Bueckle

Register 3D Preview

Left Right Anterior Posterior

Colon Heart Kidney Spleen Bladder

L R Male Female

Common Extraction Sites

Show Previous Registration Blocks

Anatomical Structures

- kidney capsule
- cortex of kidney
- outer cortex of kidney
- renal column
- hilum of kidney
- renal medulla
- renal papilla
- renal pyramid

X: 80 Y: 69 Z: 40

Tissue Block Size (mm)

Width (X)	Height (Y)	Depth (Z)
8	6	10

Tissue Slices

Thickness # Slices

Tissue Block Rotation

X 0 Y 0 Z 0

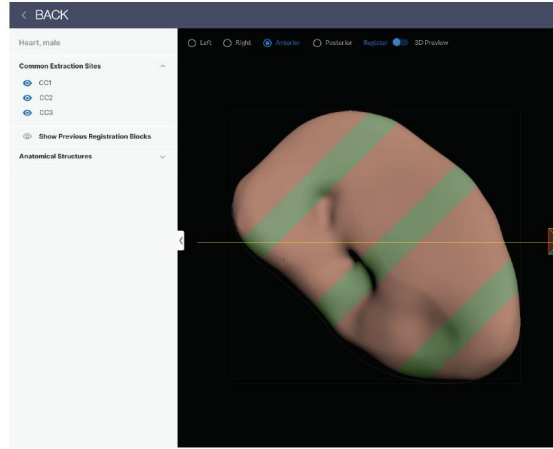
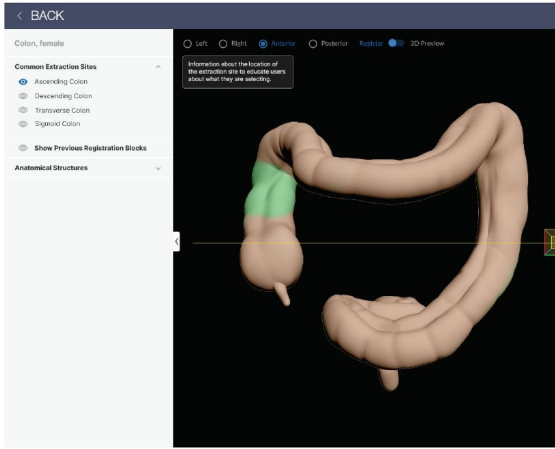
Anatomical Structure Tags

Add Anatomical Structures ...

Assigned Added

REVIEW AND DOWNLOAD

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



Kidney

- Bisection Line

Spleen

- CC1
- CC2
- CC3

Colon

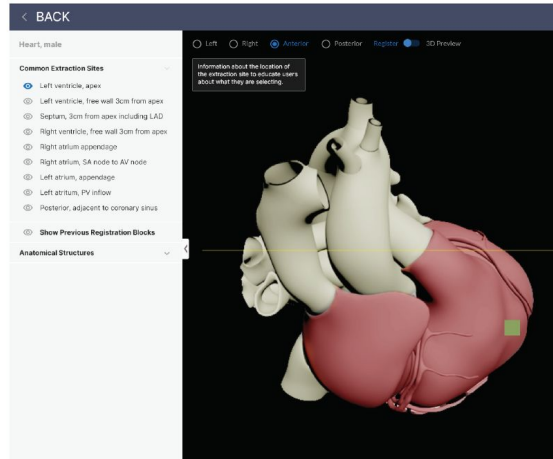
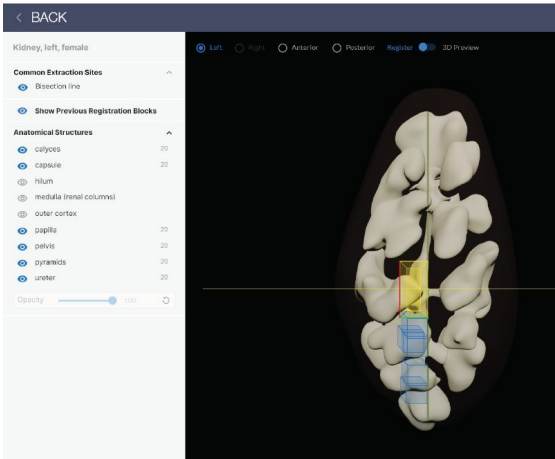
- Ascending Colon
- Descending Colon
- Transverse Colon
- Sigmoid Colon

Heart

- Left atrium, appendage
- Left atrium, PV inflow
- Left ventricle, apex
- Left ventricle, free wall 3cm from apex
- Septum, 3cm from apex including LAD
- Posterior, adjacent to coronary sinus
- Right atrium appendage
- Right atrium, AV (atrioventricular) node
- Right atrium, SA (sinoatrial) node
- Right ventricle, free wall 3cm from apex

Extraction Site Mapping

- 7
- 8
- 1
- 2
- 3
- 9
- 5
- 6a
- 6b
- 4



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

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
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

CODEX Male, Age 18, BMI 25.5
HBM473.VKCM.876
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>

CCF Exploration User Interface (EUI)

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

Search ontology terms ...

- body
 - heart
 - lung
 - kidney
 - spleen
 - colon
 - small intestine
 - rectum

body

- 2 Centers
- 27 Donors
- 41 Samples

	Female, Age 58, BMI 23.0 HBM926.VBJV.597 TMC-Vanderbilt Age 58, White Female	
	Male, Age 46, BMI 22.3 HBM946.ZWHV.257 TMC-Vanderbilt 48-51	
	Female, Age 76, BMI 37.5 HBM543.NGQC.475 TMC-Vanderbilt Age 76, white female.	
	Male, Age 55, BMI 30.0 HBM258.DDTW.423 TMC-Vanderbilt 52-55	
	Female, Age 38, BMI 42.3 HBM396.JRWZ.394 TMC-Vanderbilt 17-20	
	Male, Age 62, BMI 34.9 HBM947.VLDP.894 TMC-Vanderbilt Kidneys 153-156	
	Female, Age 44, BMI 48.2 HBM629.PPWR.872 TMC-Vanderbilt 25-28	
	Male, Age 18, BMI 27.1 HBM748.ZDKH.494 TMC-Florida Section is 400um from face edge ...	

<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 cnsctr@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. Yingve 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



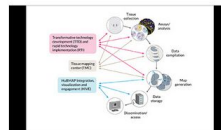
Department:
Cyberinfrastructure
Network Science



Credit: None

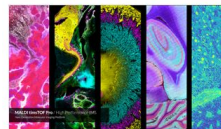


Audience:
Biomedical students and professionals interested in single-cell tissue analysis and visualization



HuBMAP Overview

- Project Goals, Setup, and Ambitions



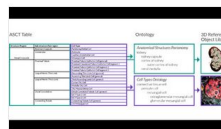
Tissue Data Acquisition and Analysis

- Behind the Scenes at Vanderbilt University



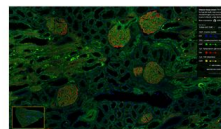
Biomolecular Data Harmonization

- 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

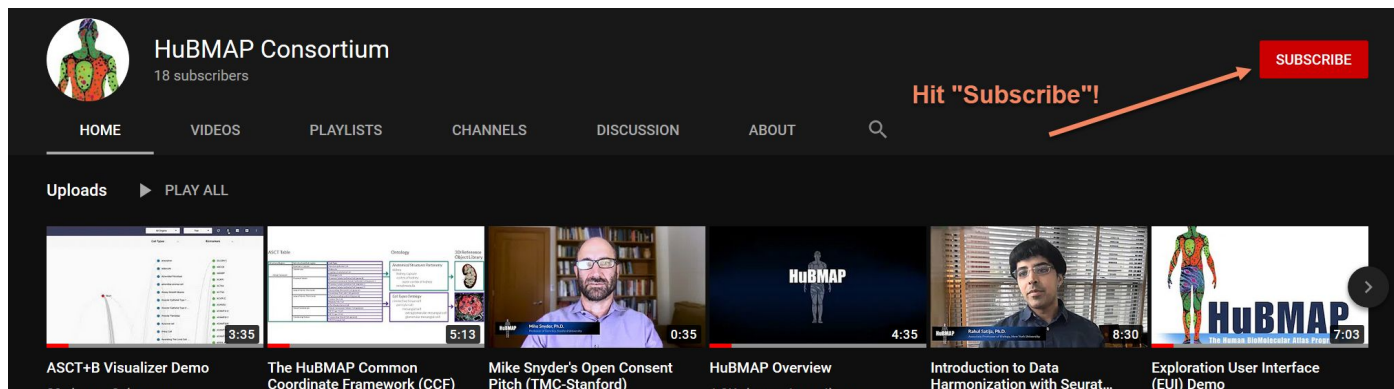
Videos

- 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:



The image shows a screenshot of the HuBMAP Consortium YouTube channel page. The channel name is "HuBMAP Consortium" with 18 subscribers. The navigation menu includes HOME, VIDEOS, PLAYLISTS, CHANNELS, DISCUSSION, and ABOUT. A red "SUBSCRIBE" button is visible in the top right corner, with an orange arrow pointing to it and the text "Hit 'Subscribe!'". Below the navigation menu, the "Uploads" section is displayed, showing a row of video thumbnails with their titles and durations:

- ASCT+B Visualizer Demo (3:35)
- The HuBMAP Common Coordinate Framework (CCF) (5:13)
- Mike Snyder's Open Consent Pitch (TMC-Stanford) (0:35)
- HuBMAP Overview (4:35)
- Introduction to Data Harmonization with Seurat... (8:30)
- Exploration User Interface (EU) Demo (7:03)

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



Jeffrey Spraggins
TMC-Vanderbilt
Vanderbilt University



Sanjay Jain
TMC-UCSD
Washington University,
St. Louis



Clive Wasserfall
TMC-UFL
University of Florida



Marda Jorgensen
TMC-UFL
University of Florida



Kristen Browne
Medical Imaging and
3D Modeling Specialist
NIAID

3D Models

MC-IU HIVE Team



Katy Börner
MC-IU PI
CNS Director



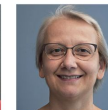
Griffin Weber
Assoc. Professor of Medicine
Harvard Medical School



Lisel Record
MC-IU PI
CNS Associate Director



Bruce Herr II
Sr. Systems Architect/PM



Ellen Quardokus
Sr. Research Analyst



Yingnan Ju
PhD Candidate



Andreas Bueckle
PhD Candidate



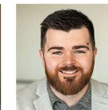
Leonard Cross
Sr. UX/UI Designer



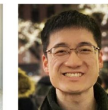
Matthew Martindale
Center Assistant



Daniel Bolin
Software Developer



Adam Phillips
Software Developer



Edward Lu
Software Developer



Paul Hrishikesh
Research Assistant



Leah Scherschel
Research Assistant



Avinash Boppa
Research Consultant



Q&A

