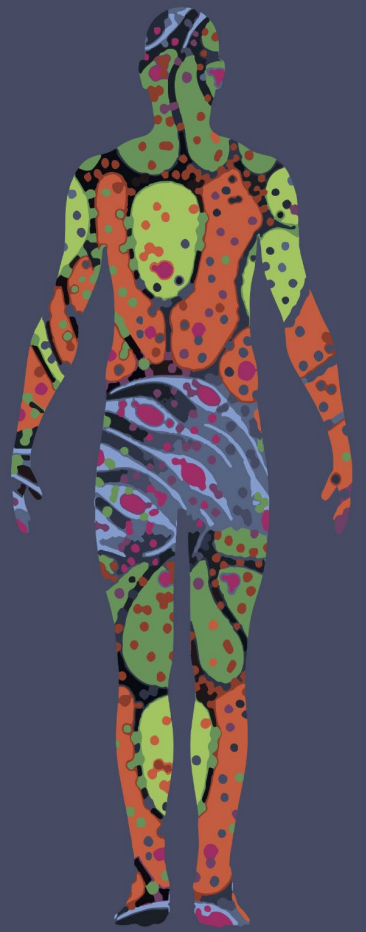


Human Reference Atlas: ASCT+B Tables, 3D Reference Library & CCF User Interfaces

Katy Börner | @katycns
Victor H. Yngve Distinguished Professor of
Intelligent Systems Engineering & Information Science
Luddy School of Informatics, Computing, and Engineering
Indiana University, Bloomington, IN

CFDE April Cross-Pollination Event
Virtual Event

April 6, 2021

HuBMAP

https://commonfund.nih.gov/HuBMAP

Vision

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

Goals

1. Accelerate the development of the next generationof tools and techniques for constructing high resolution spatial tissue maps
2. Generate foundational 3D tissue maps
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

HuBMAP Funded Groups

Rapid Technology Implementation

16 **RTI Members**
4 funded groups

Transformative Technolgy Development

23 **TTD Members**
4 funded groups

Tissue Mapping Centers

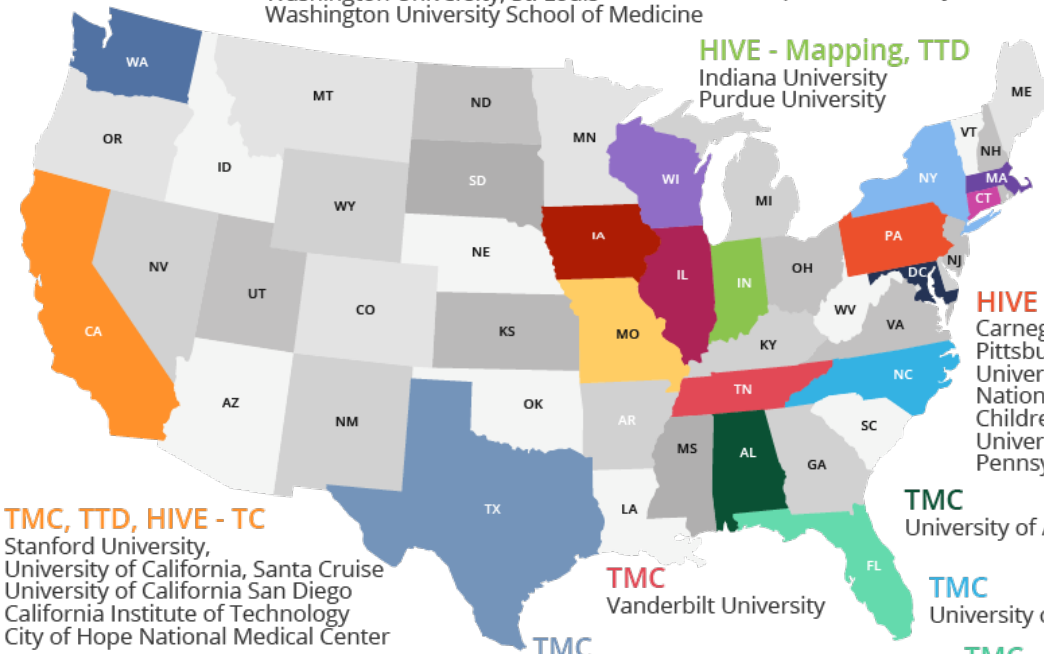
76 **TMC Members**
5 funded groups

HuBMAP Integration Visualization Engagement

87 **HIVE Members**
5 funded groups

202 **Members in**
18 funded groups

HuBMAP Contributing Sites



TMC
University of Washington
Pacific Northwest National Lab

RTI, TTD
Northwestern University

TMC
University of Iowa

TMC
Washington University, St. Louis
Washington University School of Medicine

TTD
Marquette University

HIVE - Mapping, RTI
New York Genome Center
GE Global Research
University of Rochester

HIVE - Mapping, TTD
Indiana University
Purdue University

HIVE - Tools, TTD, RTI, TMC
Harvard University, Medical School
Broad Institute
Dana Farber Institute
Columbia University
Children's Hospital of Boston

TMC, TTD
University of Connecticut
Yale University

HIVE - IEC, HIVE - Tools, RTI, TMC
Carnegie Mellon University
Pittsburgh Supercomputing Center
University of Pittsburgh
National Disease Research Interchange
Children's Hospital of Philadelphia
University of Pennsylvania
Pennsylvania State University

TMC, TTD, HIVE - TC
Stanford University,
University of California, Santa Cruise
University of California San Diego
California Institute of Technology
City of Hope National Medical Center

TMC
Vanderbilt University

TMC
Texas Advanced Computing Center

TMC
University of Alabama, Birmingham

TMC
University of North Carolina, Chapel Hill

TMC
University of Florida

NIH
Common Fund

TMC
University of Zurich

TMC
Delft University of Techology

HIVE- Tools, TMC
European Bioinformatics Institute
Wellcome Sanger Institute

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

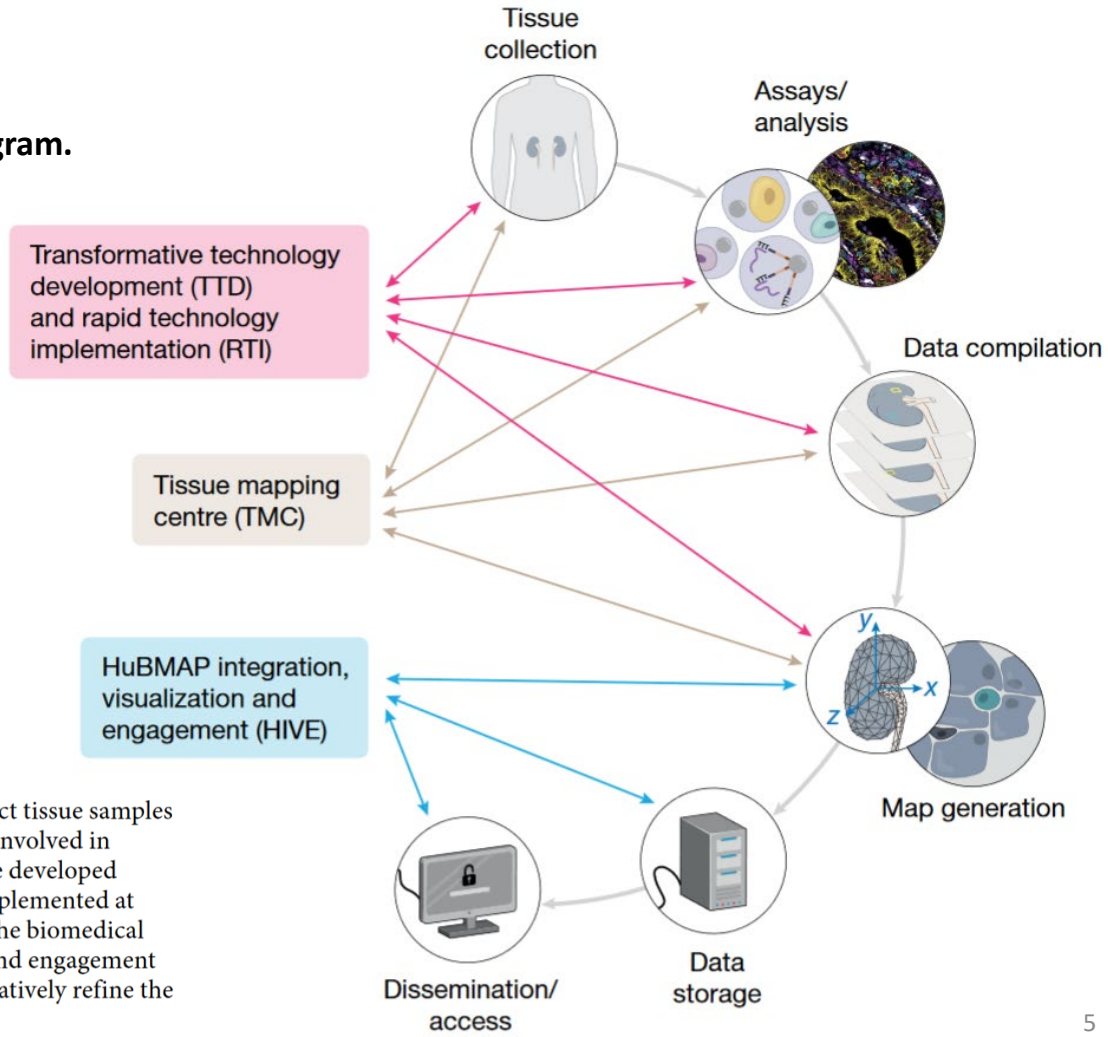


Fig. 1 | The HubMAP consortium. The TMCs will collect tissue samples and generate spatially resolved, single-cell data. Groups involved in TTD and RTI initiatives will develop emerging and more developed technologies, respectively; in later years, these will be implemented at scale. Data from all groups will be rendered useable for the biomedical community by the HuBMAP integration, visualization and engagement (HIVE) teams. The groups will collaborate closely to iteratively refine the atlas as it is gradually realized.

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

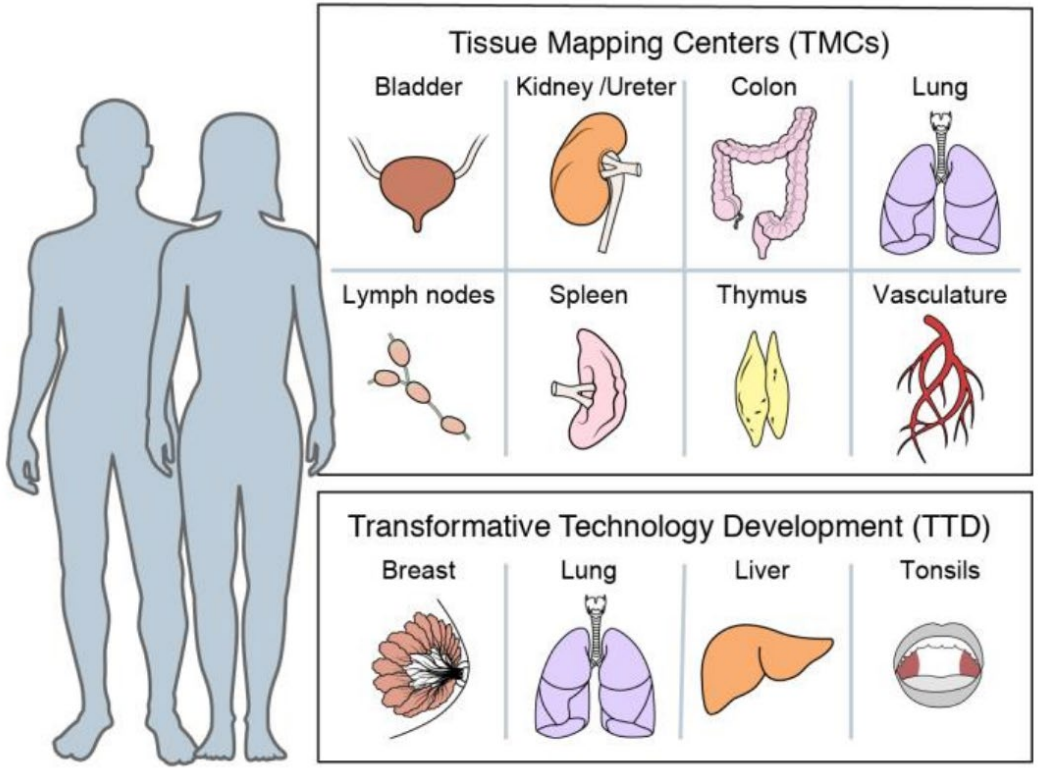


Fig. 2 | Key tissues and organs initially analysed by the consortium. Using innovative, production-grade ('shovel ready') technologies, HuBMAP TMCs will generate data for single-cell, three-dimensional maps of various human tissues. In parallel, TTD projects (and later RTI projects) will refine assays and analysis tools on a largely distinct set of human tissues. Samples from individuals of both sexes and different ages will be studied. The range of tissues will be expanded throughout the program.

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

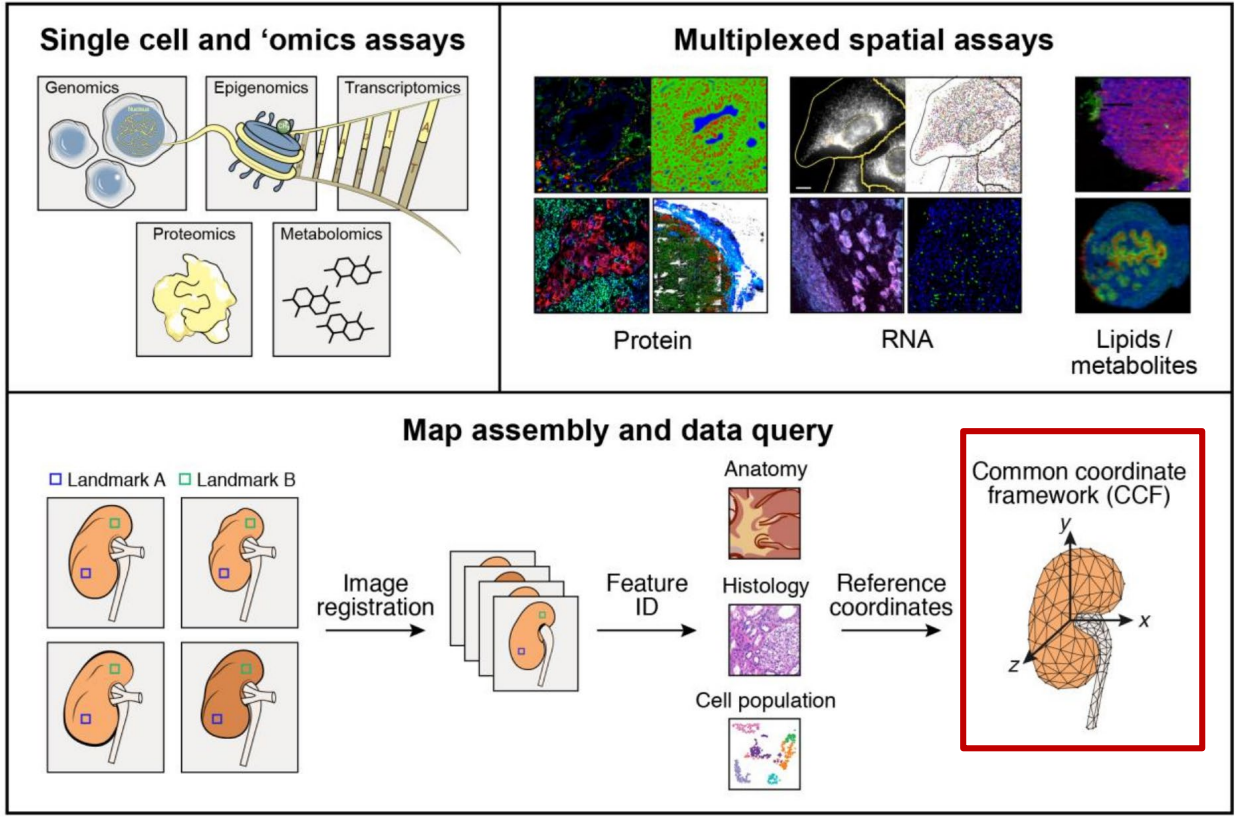


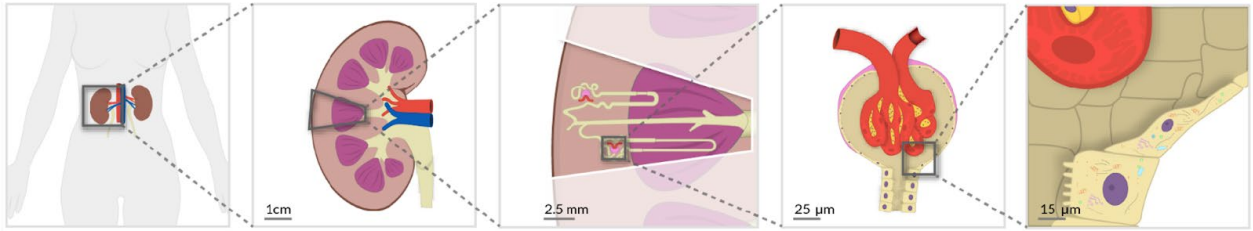
Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic,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

CCF ASCT+B Tables

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

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**

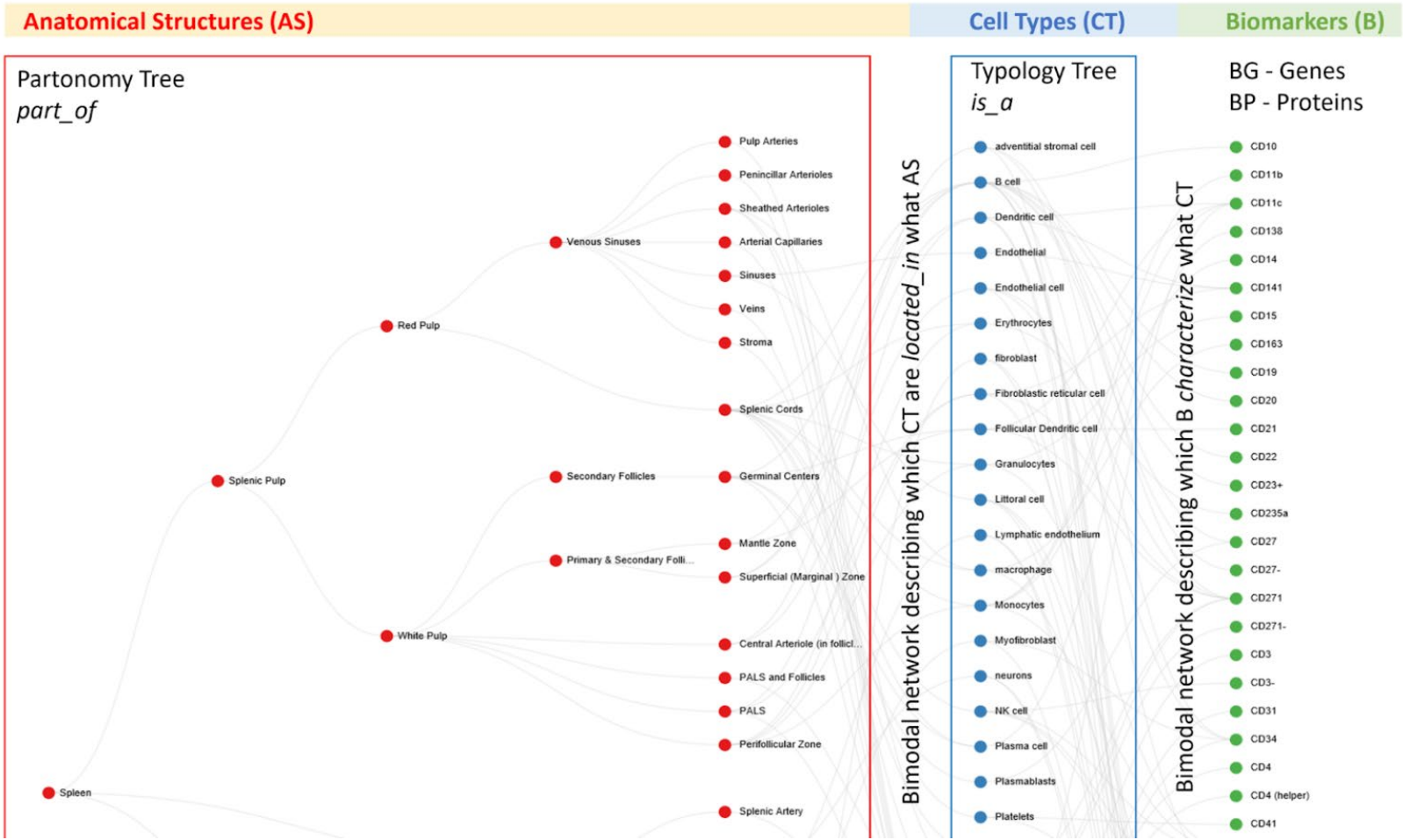
Partial ASCT+B Table from

- 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

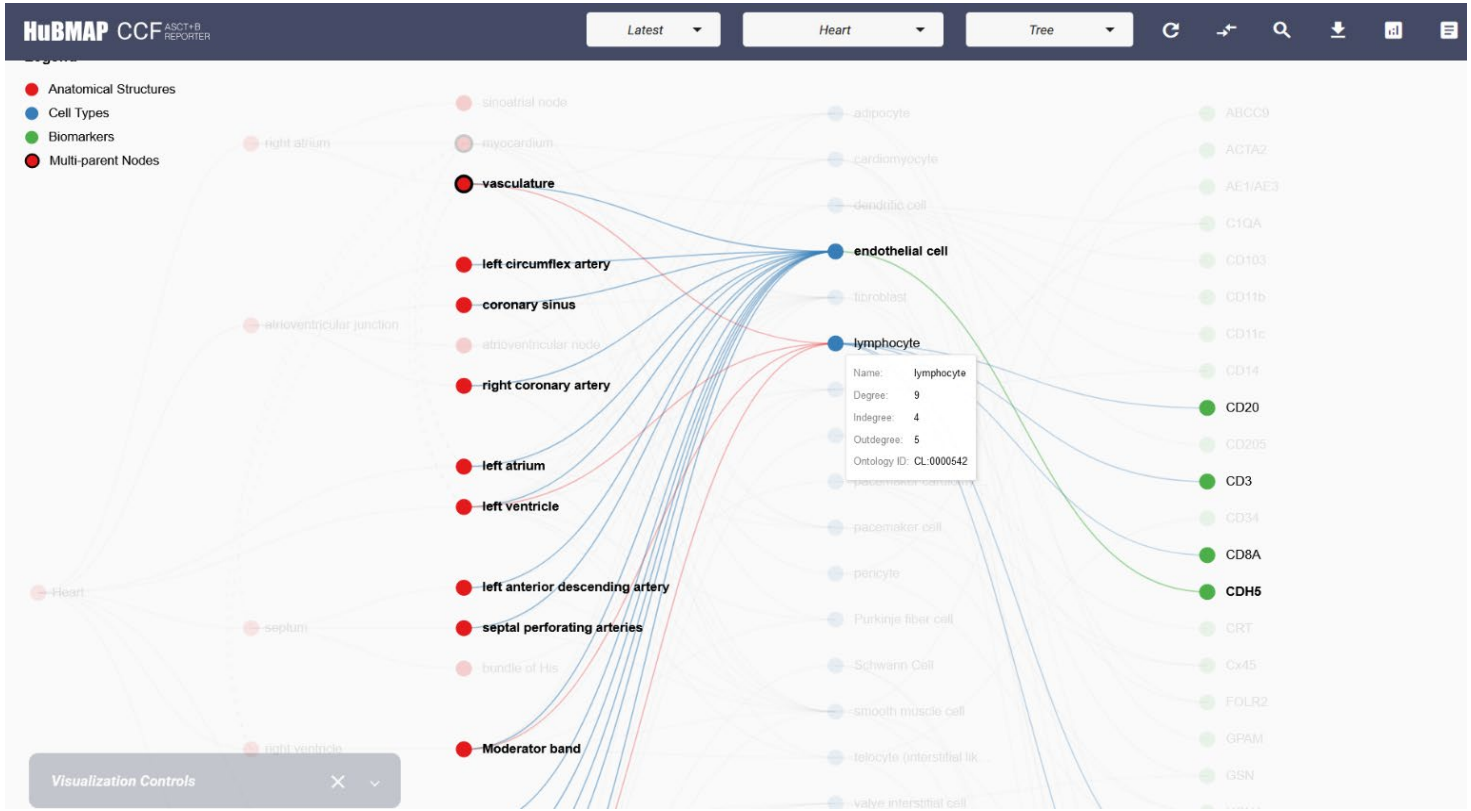
Table 3: Cell types and associated markers from KPMP Pilot 1 transcriptomic studies. Asterisk denotes genes detected by more than one technology. *Italics*, genes detected by a single technology.

Structure/Region	Sub structure/Sub region	Cell Type	Abbreviation	Subset of Marker Genes	Pertinent negatives/comments
Renal Corpuscle	Bowman's Capsule	Parietal epithelial cell	PEC	*CRB2*, CLDN1**	
	Glomerulus	Podocyte	POD	*NPHS2*, PODXL*, NPHS1**	
		Capillary Endothelial Cell	GC-EC	*EHD3*, EMCN*, HECW2*, FLT1*, AQP1**	
		Mesangial Cell	MC	*POSTN*, PIEZO2*, ROBO1*, ITGA8**	
Tubules	Proximal Tubule	Proximal Tubule Epithelial Cell (general)	PT	*CUBN*, LRP2*, SLC13A1*, ALDOB*, GATM**	
		Proximal Convoluted Tubule Epithelial Cell Segment 1	PT-S1	*SLC5A2*, SLC5A12**	There is overlap among the segments
		Proximal Tubule Epithelial Cell Segment 2	PT-S2	*SLC22A6**	
		Proximal Tubule Cell Epithelial Segment 3	PT-S3	*PDZK1IP1*, MT1G**	
	Loop of Henle, Thin Limb	Descending Thin Limb Cell (general)	DTL	*CRYAB*, VCAM1*, AQP1*, SPP1**	*CLDN10* low
		Ascending Thin Limb Cell (general)	ATL	*CRYAB*, TACSTD2*, CLDN3**	*AQP1* low to none
	Loop of Henle, Thick Limb	Thick Ascending Limb Cell (general)	TAL	*SLC12A1*, UMOD**	*SLC12A3* low to none
		Cortex-TAL cell	C-TAL	*SLC12A1*, UMOD**	
		Medulla-TAL cell	M-TAL	*SLC12A1*, UMOD**	
		TAL-Macula Densa cell	TAL-MD	*NOS1*, SLC12A1**	
	Distal Convolution	Distal Convoluted Tubule Cell (general)	DCT	*SLC12A3*, TRPM6**	
		DCT type 1 cell	DCT-1	*SLC12A3*, TRPM6*	*SLC8A1, HSD11B2* (low to none)
		DCT type 2 cell	DCT-2	*SLC12A3*, SLC8A1*, HSD11B2*	Has CNT and DCT signature
	Connecting Tubule	Connecting Tubule Cell (general)	CNT	*SLC8A1*, CALB1, TRPV5*	*SLC12A3* low to none. IC or PC without *SLC8A1* could be in the CNT structure
		CNT-Principal Cell	CNT-PC	*SLC8A1*, AQP2*, SCNN1G**	
		CNT-Intercalated Cell	CNT-IC	*SLC8A1*, CA2, ATP6VOD2**	
		CNT-IC-A cell	CNT-IC-A	*SLC8A1*, SLC4A1*, SLC26A7**	
		CNT-IC-B cell	CNT-IC-B	*SLC8A1*, SLC26A4*, SLC4A9**	
	Collecting Duct	Collecting duct (general) cell	CD	*GATA3**	*GATA3* may be in subpopulation of DCT, CNT and vSMC/P. SLC8A1, CALB1, TRPV5
		CD-PC (general)	CD-PC	*AQP2*, AQP3*, FXYD4*, SCNN1G*, GATA3**	
		C-CD-PC	C-CD-PC		
		M-CD-PC	M-CD-PC		
		Outer medulla-CD-PC	OM-CD-PC		
		Inner Medulla-CD cell	IM-CD	*AQP2*, SLC14A2*	
		Transitional PC-IC cell	tPC-IC	*FXYD4*, SLC4A9*/SLC26A7**	(low to none); Low to No *CALCA* and *KIT* in C-CD-IC-A. It may not be possible to assign IC or PC to CNT or CD structures without regional information of their source.
		CD-IC (general) cell	CD-IC	*CA2, ATP6VOD2**	
		CD-IC-A (general) cell	CD-IC-A	*SLC4A1, SLC26A7*, TMEM213**	
		C-CD-IC-A cell	C-CD-IC-A	*SLC26A7*, SLC4A1**	
		M-CD-IC-A cell	M-CD-IC-A	*SLC26A7*, SLC4A1, KIT*, CALCA*	
		CD-IC-B (general) cell	CD-IC-B	*SLC4A9*, SLC26A4**	
		C-CD-IC-B cell	C-CD-IC-B		
		M-CD-IC-B cell	M-CD-IC-B		
Vessels	Endothelial Cells (non-glomerular)	Endothelial Cell (general)	EC	*EMCN*, PECAM1*, FLT1**	
		EC-Afferent/Efferent Arteriole	EC-AEA	*SERPINE2*, TM4SF1**	likely *PALMD*
		EC-Peritubular capillaries	EC-PTC	*PLVAP**	
		EC-Descending Vasa Recta	EC-DVR	*TM4SF1*, PALMD*	
		EC-Ascending Vasa Recta	EC-AVR	*DNASEIL3**	low to none
		EC-Lymphatics	EC-LYM	*MMRN1*, PROX1*	
Structure/Region	**Sub structure/Sub region**	**Cell Type**	**Abbreviation**	**Subset of Marker Genes**	**Pertinent negatives/comments**
Interstitium	Stroma (non-glomerular)	Vascular Smooth Muscle/Pericyte (general)	vSMC/P	*TAGLN*, ACTA2*, MYH11*, NTRK3, MCAM*	
		vSMC/P-Renin	vSMC/P-REN	*REN*	
		Fibroblast	FIB	*DCN*, ZEB2, C7, LUM*	
	Immune	Macrophages-Resident	MAC-R	*CD163*, IL7R**	
		Macrophage	MAC	*S100A9*	
		Natural Killer Cell	NKC	*NKG7*	
		Dendritic Cell	DC	*APOE*	
		Monocyte	MON	*C1QA, HLA-DRA*	
		T lymphocyte (general)	T	*CD3*	
		T Cytotoxic	T-CYT	*GZMA*	
		B lymphocyte	B	*IGJ*	

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


Anatomical Structures (AS)
Cell Types (CT)
Biomarkers (B)
Partonomy Tree
part_of
Spleen
Splenic Pulp
Red Pulp
Venous Sinuses
Pulp Arteries
Penicillar Arterioles
Sheathed Arterioles
Arterial Capillaries
Sinuses
Veins
Stroma
Splenic Cords
Secondary Follicles
Germinal Centers
Primary & Secondary Folli...
Mantle Zone
Superficial (Marginal) Zone
White Pulp
Central Arteriole (in follicl...
PALS and Follicles
PALS
Perifollicular Zone
Splenic Artery
Bimodal network describing which CT are located_in what AS
Typology Tree
is_a
adventitial stromal cell
B cell
Dendritic cell
Endothelial
Endothelial cell
Erythrocytes
fibroblast
Fibroblastic reticular cell
Follicular Dendritic cell
Granulocytes
Littoral cell
Lymphatic endothelium
macrophage
Monocytes
Myofibroblast
neurons
NK cell
Plasma cell
Plasmablasts
Platelets
BG - Genes
BP - Proteins
Bimodal network describing which B characterize what CT
CD10
CD11b
CD11c
CD138
CD14
CD141
CD15
CD163
CD19
CD20
CD21
CD22
CD23+
CD235a
CD27
CD27-
CD271
CD271-
CD3
CD3-
CD31
CD34
CD4
CD4 (helper)
CD41

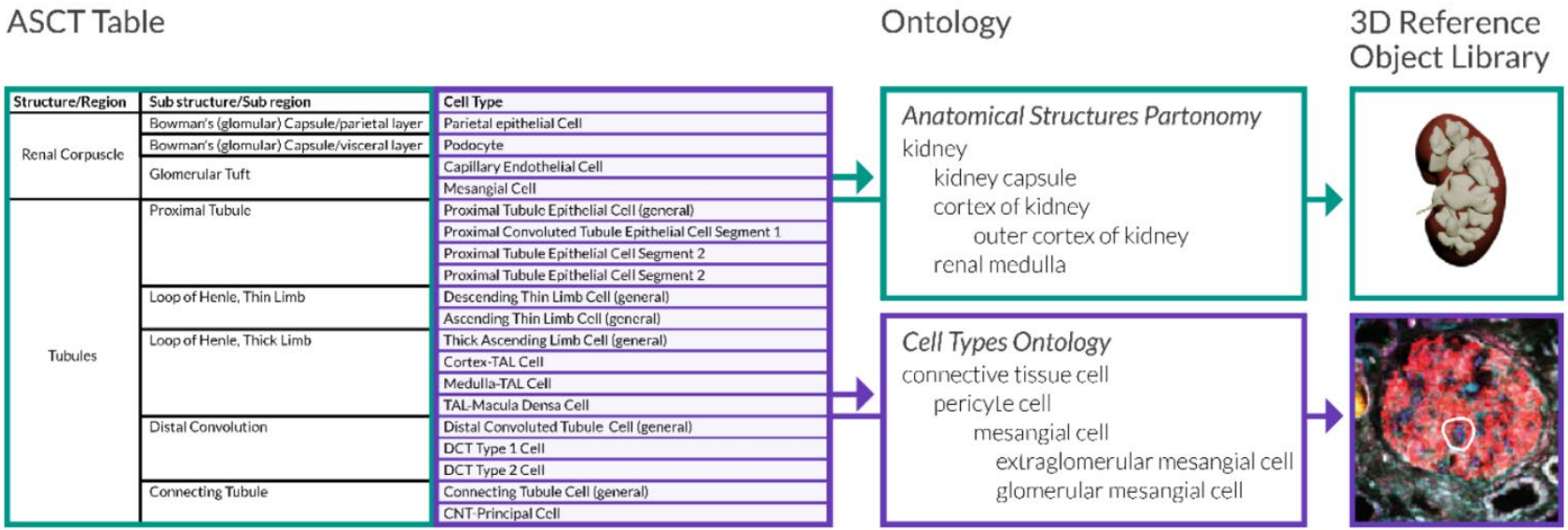
CCF ASCT+B Reporter UI

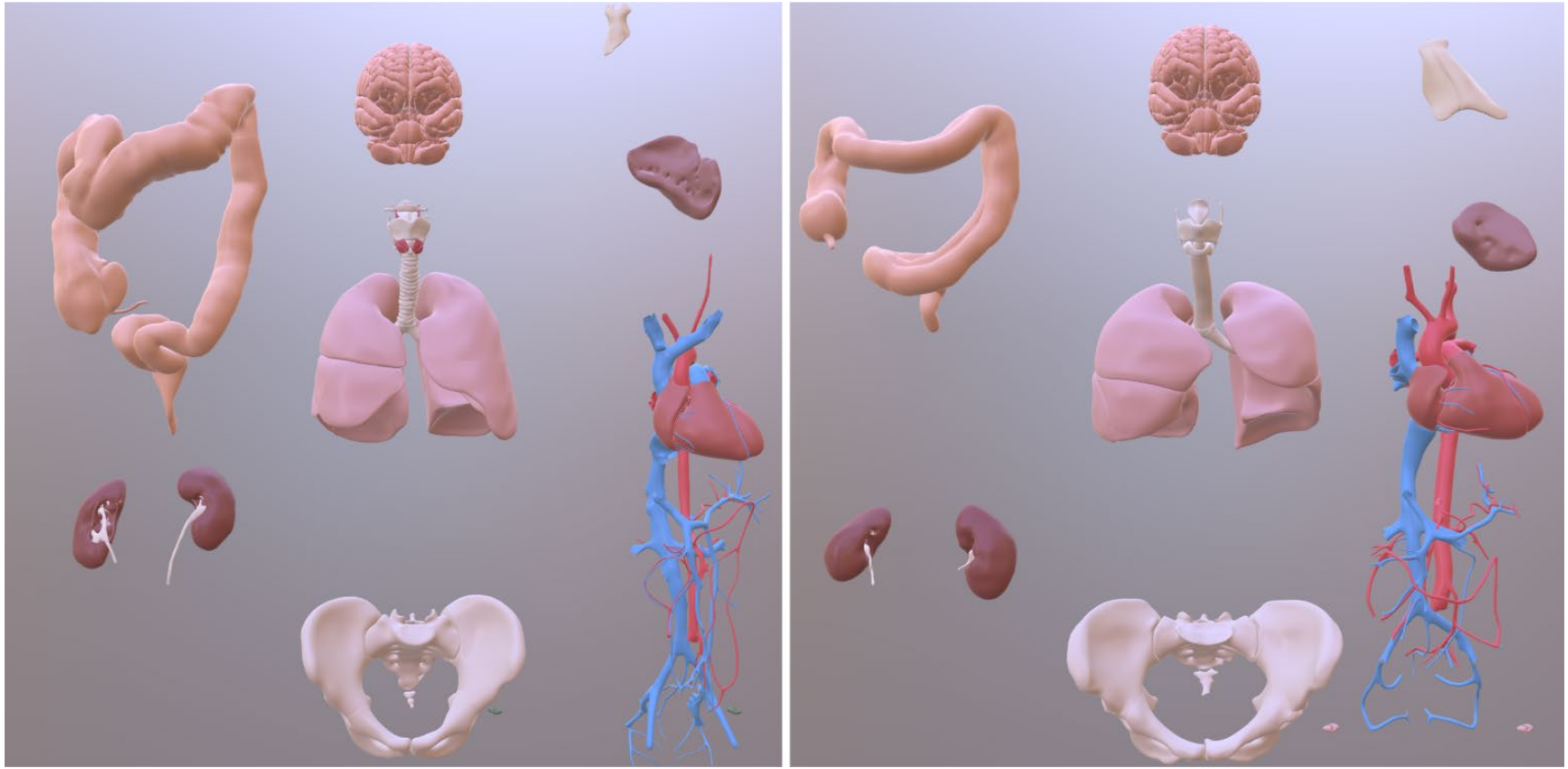


https://hubmapconsortium.github.io/ccf-asct-reporter/

ASCT+B Tables

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).





Overview of CCF 3D Reference Models

ASCT+B Table Working Group

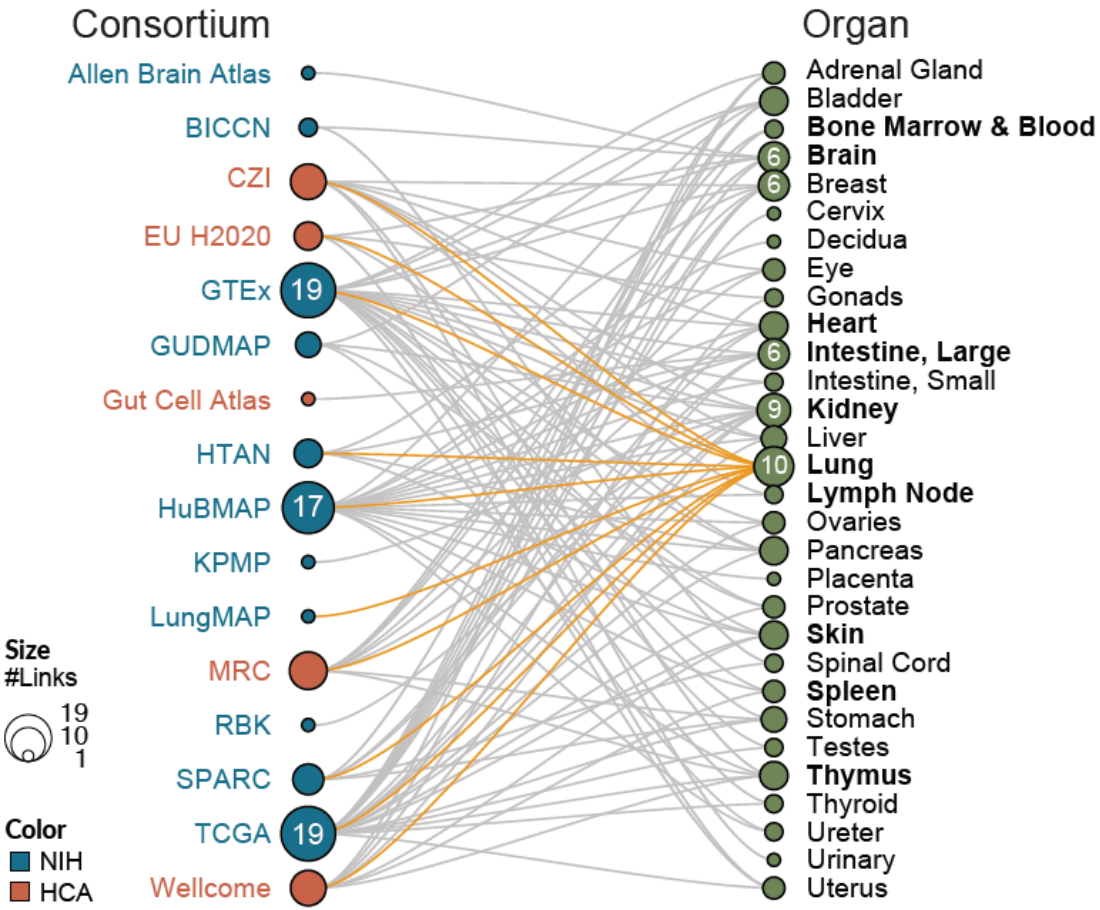
Lead by Katy Börner and Jim Gee; Ellen M Quardokus serves as Knowledge Manager

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

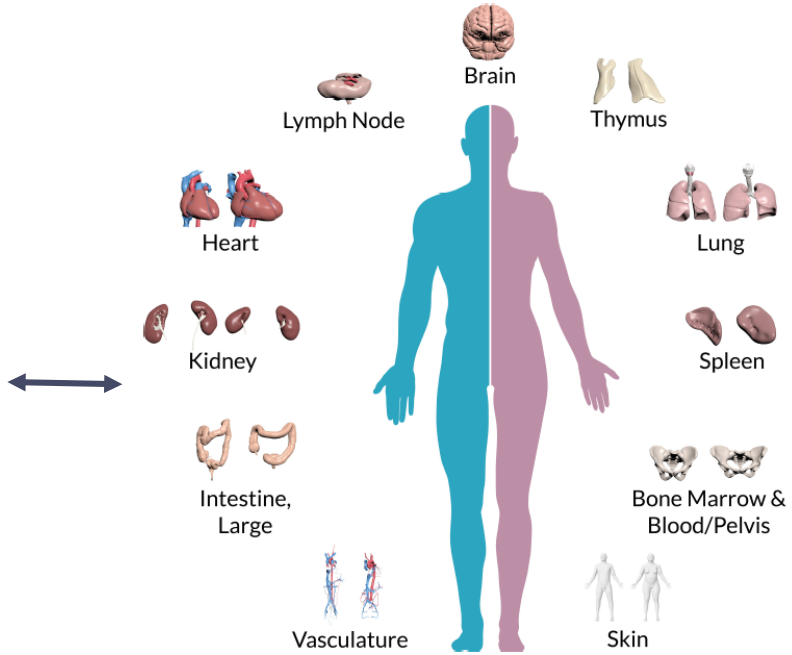
Upcoming meetings in **2021:** April 7, May 5, 11a-noon ET.
Please register to receive invites and updates.

	HuBMAP	RBK	KPMP	SPARC	LungMAP	HTAN	HCA	GUDMAP	Gut Cell Atlas	BICCN	Allen Brain	TCGA	Wellcome	MRC	H2020	GTEx	Total
Kidney	1	1	1	0	0	0	1	1	0	0	0	1	1	1	0	1	9
Liver	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	3
Spleen	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	1	4
Heart	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	4
Lung	1	0	0	1	1	1	1	0	0	0	0	1	1	1	1	1	10
L intestine/Colon	1	0	0	1	0	1	1	0	1	0	0	1	0	0	0	1	7
S intestine	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
Bladder	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0	1	5
Ureters	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
Thymus	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2
Lymph nodes	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
mediastinal lymph node	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Eye	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	3
Brain	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	1	6
Brain stem	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Cerebellum	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	1	3
Spinal cord	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	2
Pancreas	0	0	0	0	0	1	1	0	0	0	0	1	0	0	1	1	5
Breast	0	0	0	0	0	1	1	0	0	0	0	1	1	0	0	1	5
Skin	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	3
Pediatric systems	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	2
Ovaries	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	2
Testes	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	2
Cervix	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1
Uterus	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	5
Blood	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	2
Bone	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Placenta	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Decidua	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Embryo	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
esophagus	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	3
hematopoietic system	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	2
immune system bulk	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Stomach	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	1	3
Thyroid	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	2
Prostate	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	3
Adrenal gland	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	3
Totals	**11**	**1**	**1**	**7**	**1**	**6**	**21**	**4**	**1**	**2**	**2**	**20**	**7**	**5**	**4**	**21**	**114**

Table compiled for, during, and after the NIH-HCA Joint Meeting in March 2020, https://hubmapconsortium.org/nihhca2020


Consortium
Allen Brain Atlas
BICCN
CZI
EU H2020
GTEx
19
GUDMAP
Gut Cell Atlas
HTAN
HuBMAP
17
KPMP
LungMAP
MRC
RBK
SPARC
TCGA
19
Wellcome
Organ
Adrenal Gland
Bladder
Bone Marrow & Blood
Brain
6
Breast
6
Cervix
Decidua
Eye
Gonads
Heart
Intestine, Large
6
Intestine, Small
Kidney
9
Liver
Lung
10
Lymph Node
Ovaries
Pancreas
Placenta
Prostate
Skin
Spinal Cord
Spleen
Stomach
Testes
Thymus
Thyroid
Ureter
Urinary
Uterus
Size
#Links
19
10
1
Color
NIH
HCA

Organ	#AS	#CT	#B Total	#BG	#BP	#AS-AS	#AS-CT	#CT-B
Bone Marrow & Blood/Pelvis	3	46	327	201	126	2	70	710
Brain	187	127	254	254	0	187	127	330
Heart	52	25	48	48	0	61	164	78
Intestine, Large	65	69	94	88	6	389	1,361	197
Kidney	68	63	152	152	0	67	59	257
Lung	161	92	176	172	4	1,633	12,094	286
Lymph Node	41	49	266	108	158	62	135	544
Skin	16	42	70	0	70	17	19	105
Spleen	46	66	255	80	145	68	172	414
Thymus	25	41	511	388	123	38	180	657
Vasculature	870	2	1	1	0	869	606	2
Totals:	**1,534**	**622**	**2,154**	**1,492**	**632**	**3,393**	**14,987**	**3,580**



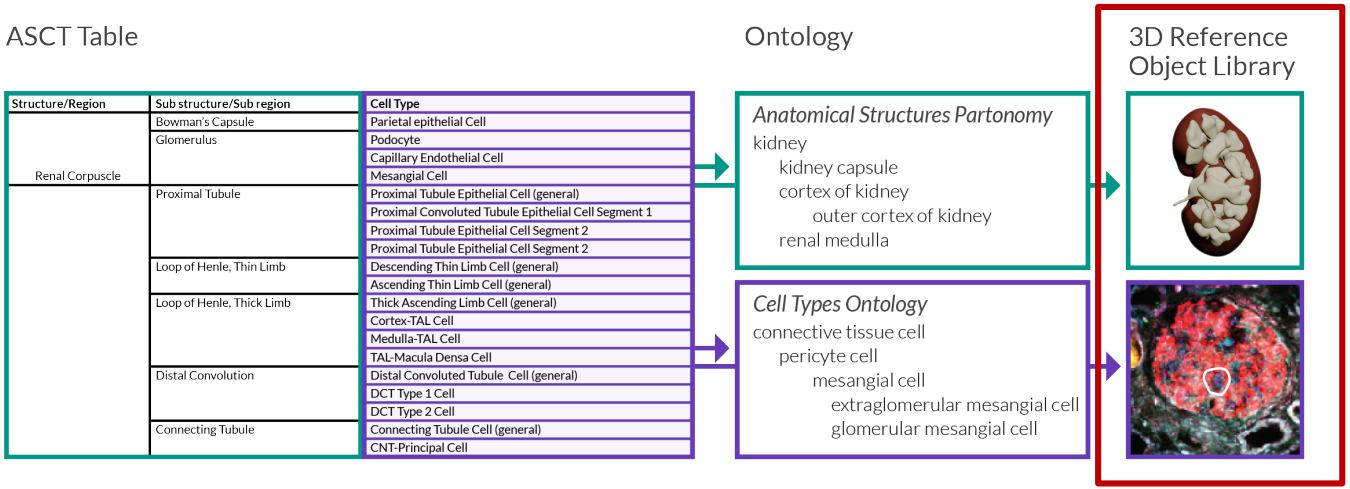
https://hubmapconsortium.github.io/ccf/pages/ccf-anatomical-structures.html

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

CCF Registration User Interface (RUI)

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).

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

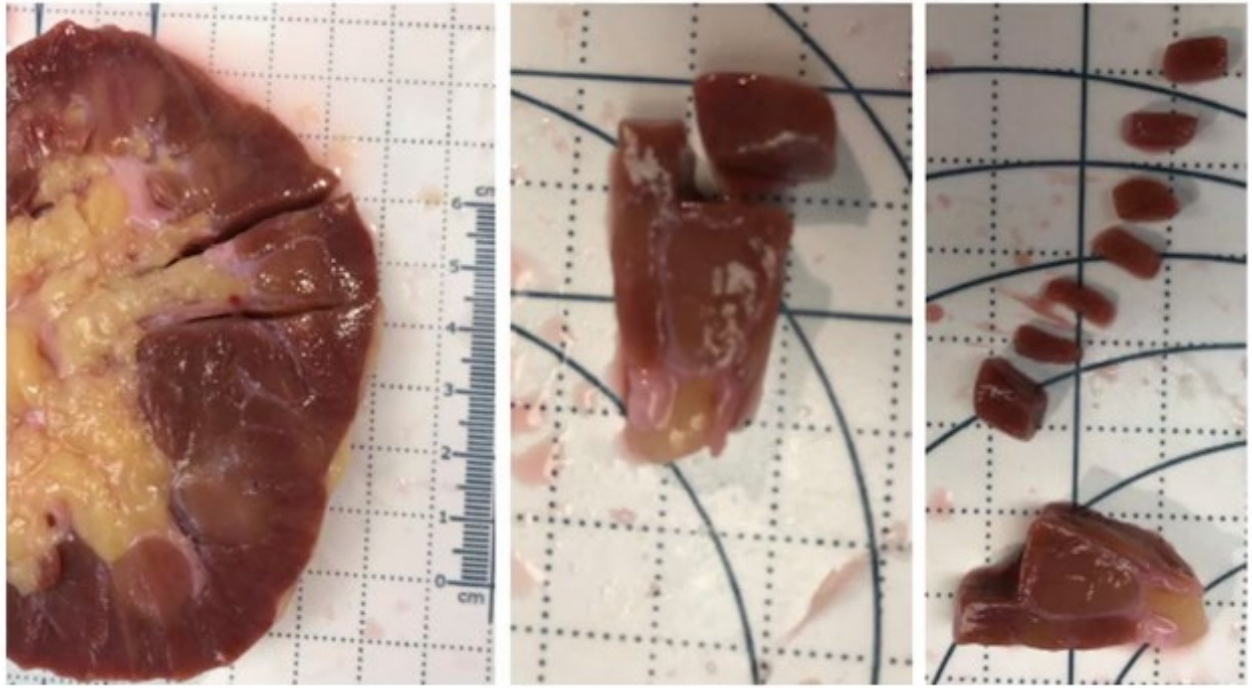
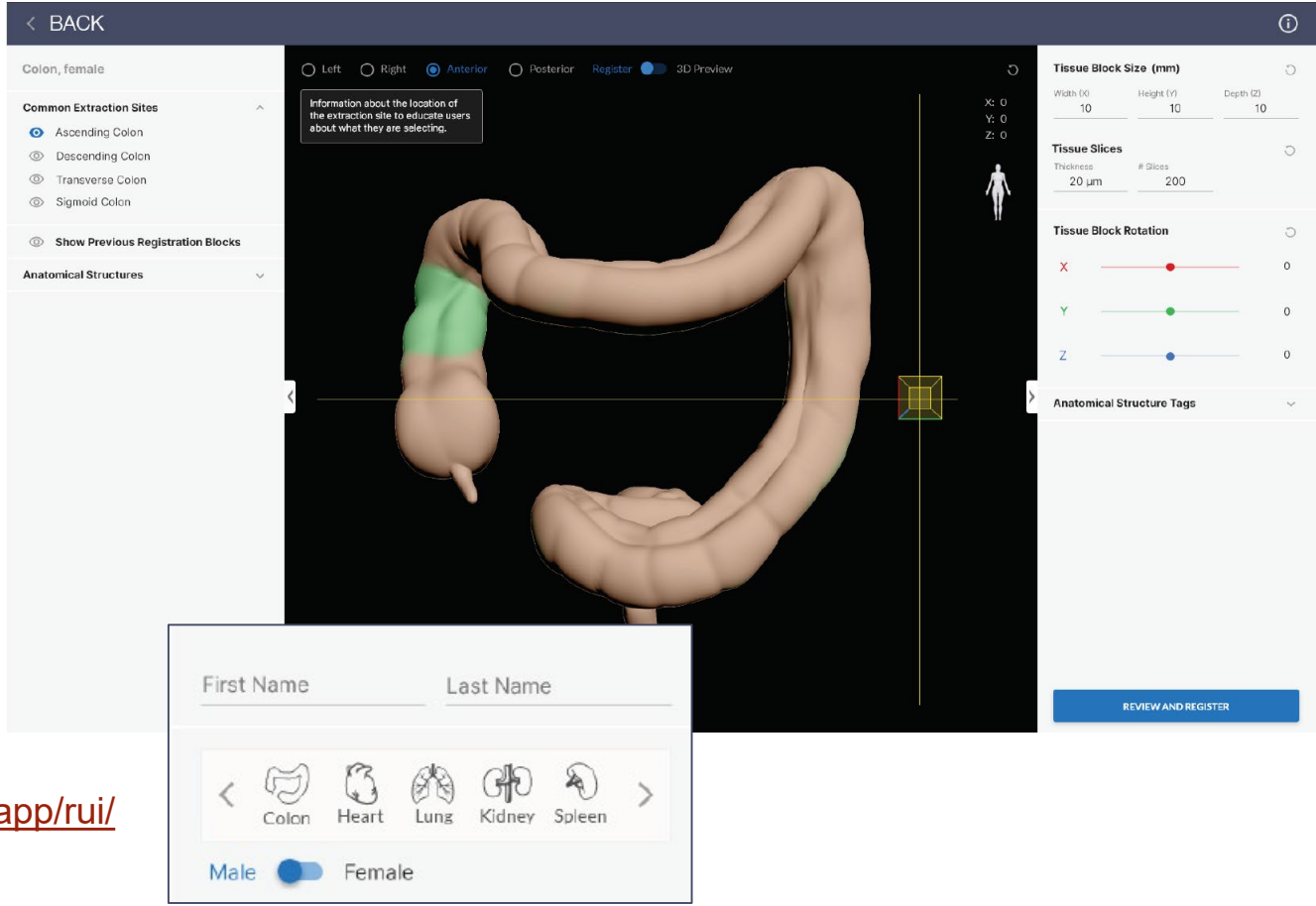


Image provided by Sanjay Jain, TMC-UCSD

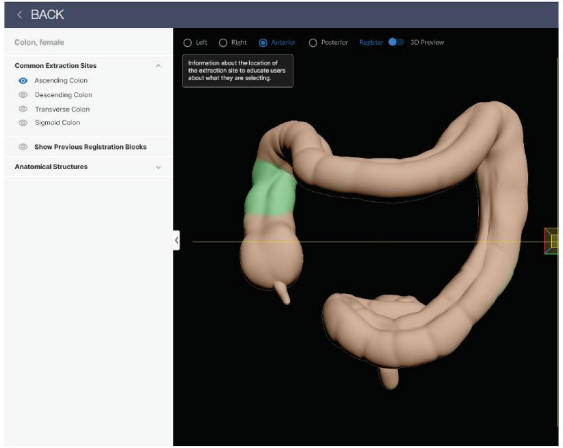
CCF Registration User Interface (RUI) v1.0.0

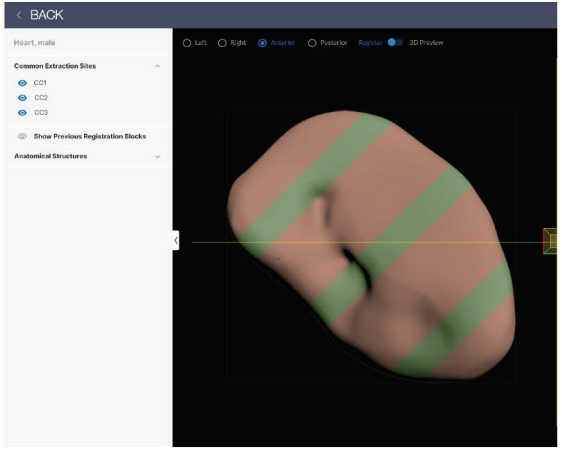
New Features:

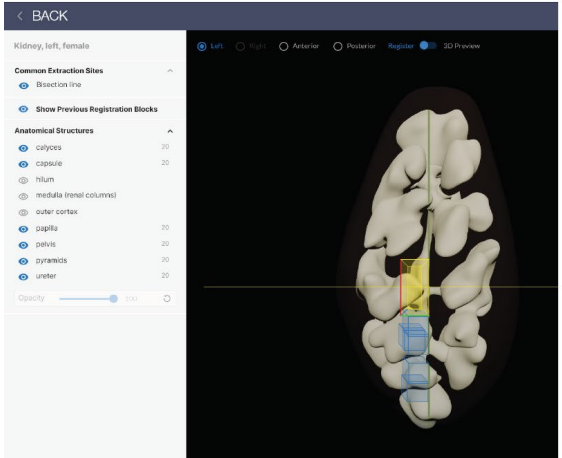
- Organ carousel with 4 reference organs
- Support for tissue extraction sites
- Expanded ontology
- Semantic annotation via collision detection & manual annotation
- Support for non-HuBMAP usage

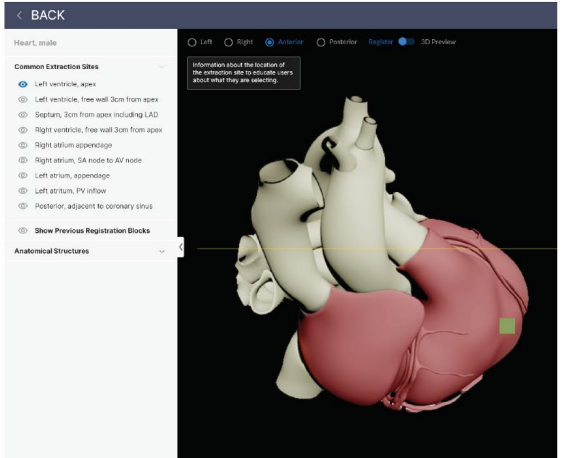


https://hubmap-ccf-ui.netlify.app/rui/









Kidney

- Bisection Line

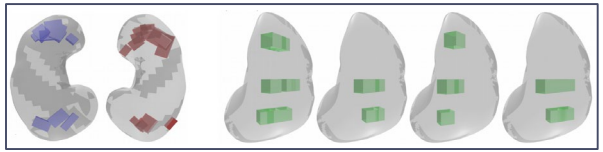
Spleen

- CC1
- CC2
- CC3

Colon

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

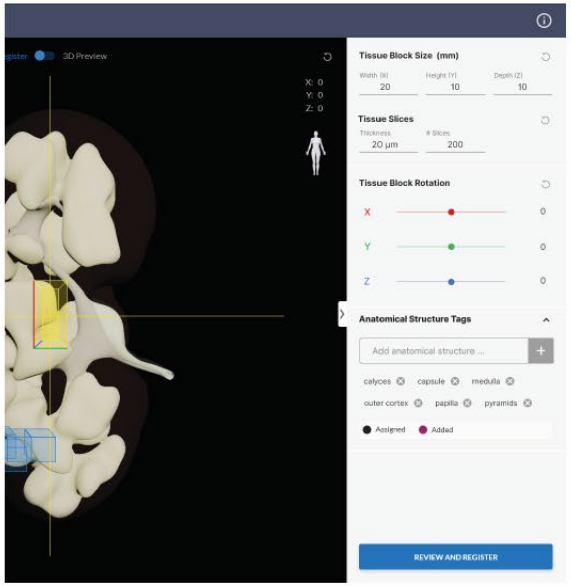
Heart	Extraction Site Mapping
• Left atrium, appendage	7
• Left atrium, PV inflow	8
• Left ventricle, apex	1
• Left ventricle, free wall 3cm from apex	2
• Septum, 3cm from apex including LAD	3
• Posterior, adjacent to coronary sinus	9
• Right atrium appendage	5
• Right atrium, AV (atrioventricular) node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



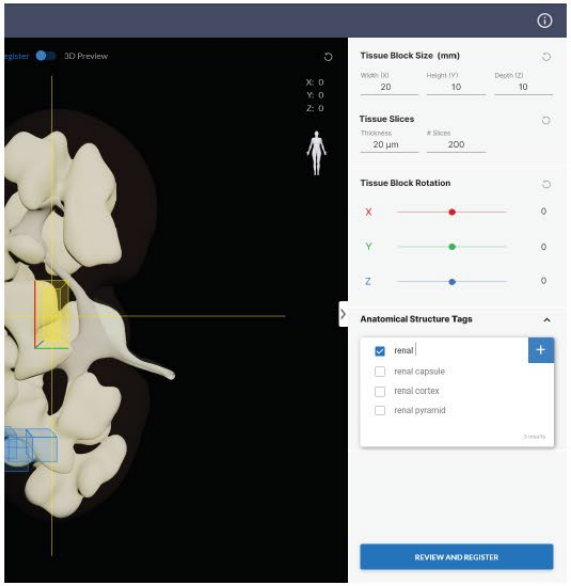
For the first HuBMAP portal release, 48 tissue blocks were registered.

CCF Registration User Interface (RUI) v1.0.0 cont.

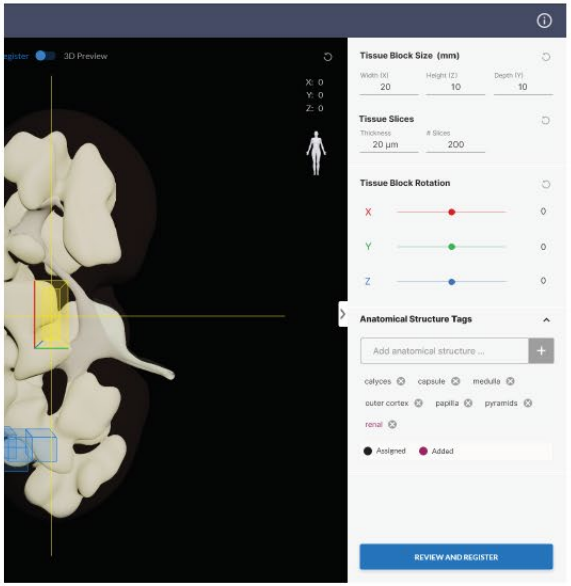
Collision when Tissue Block hits Reference Organ



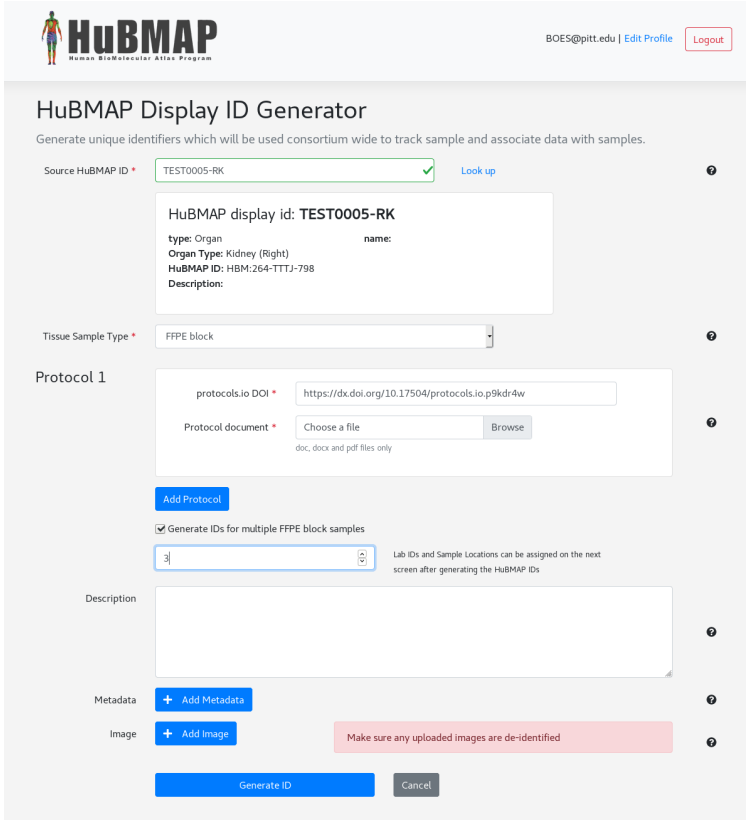
Tag Search behavior

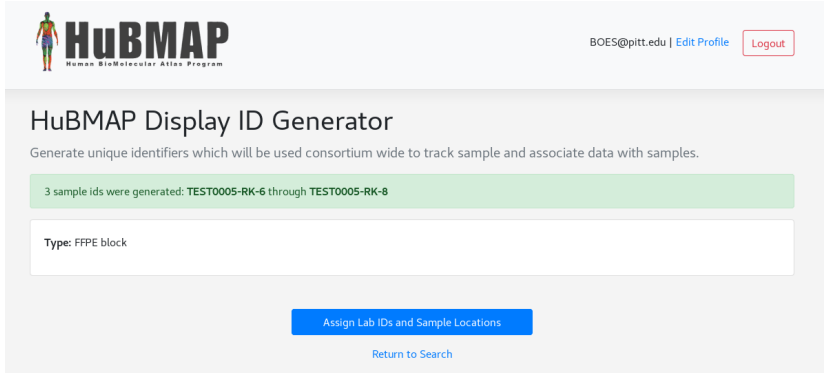


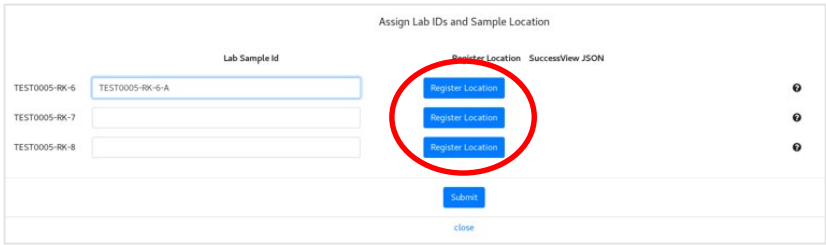
Custom tag added to list



HuBMAP Upload Portal

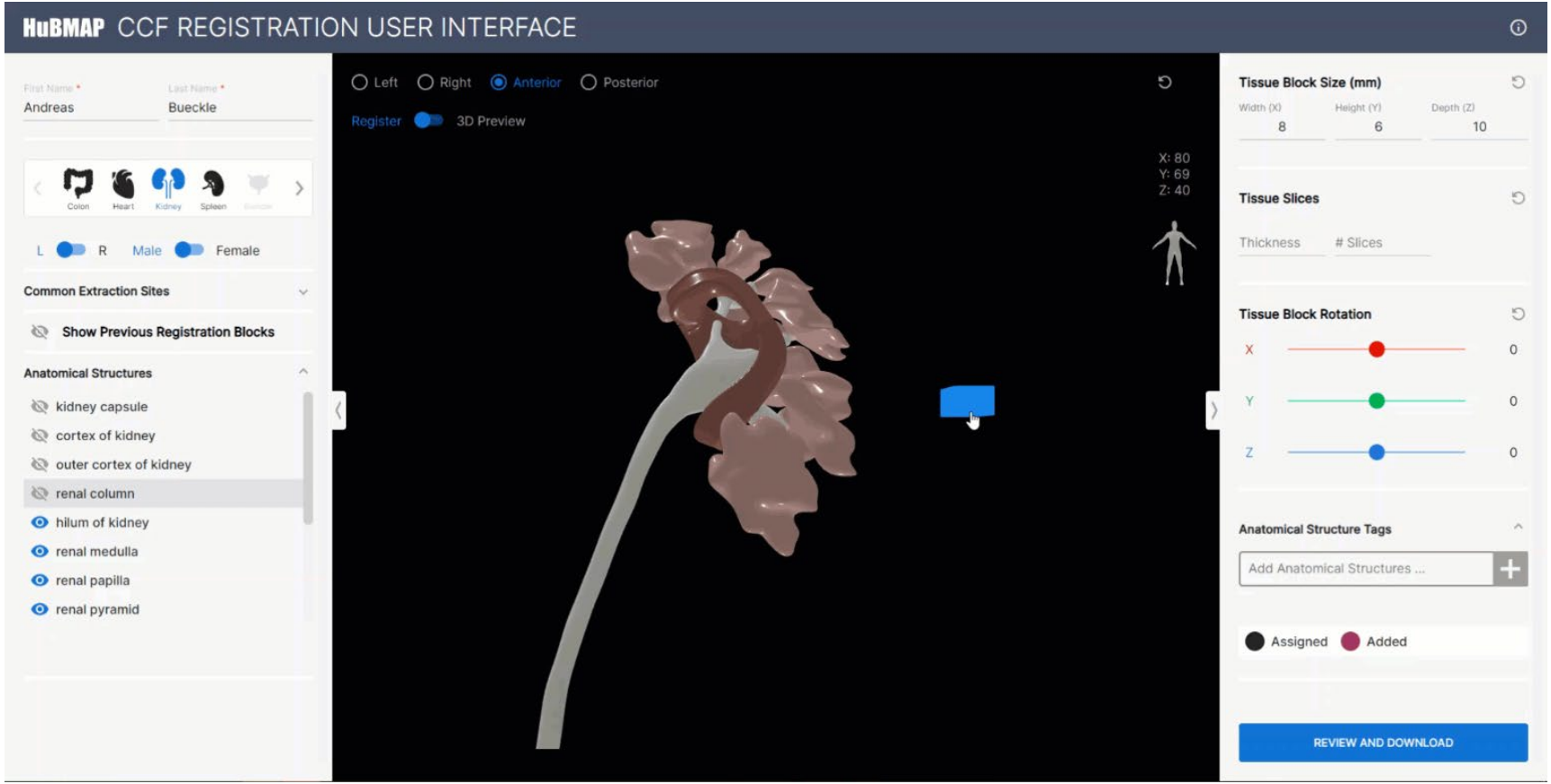




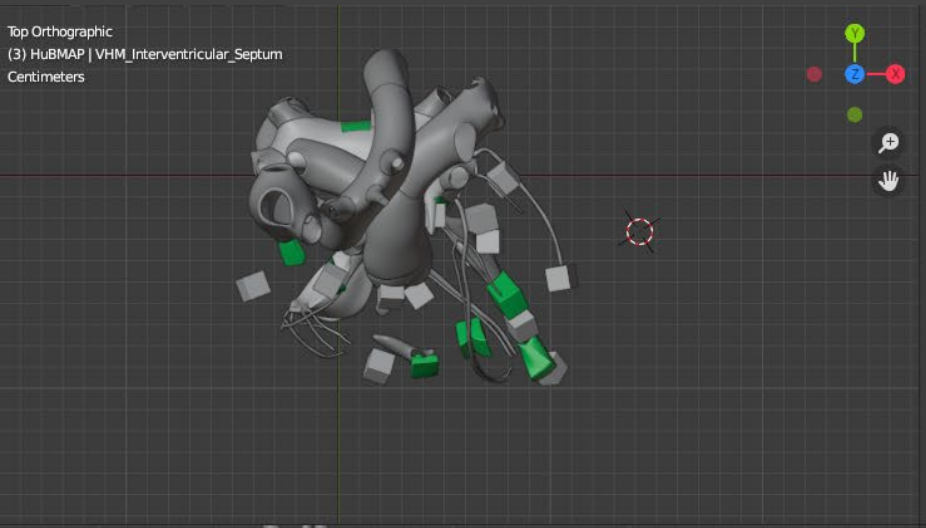


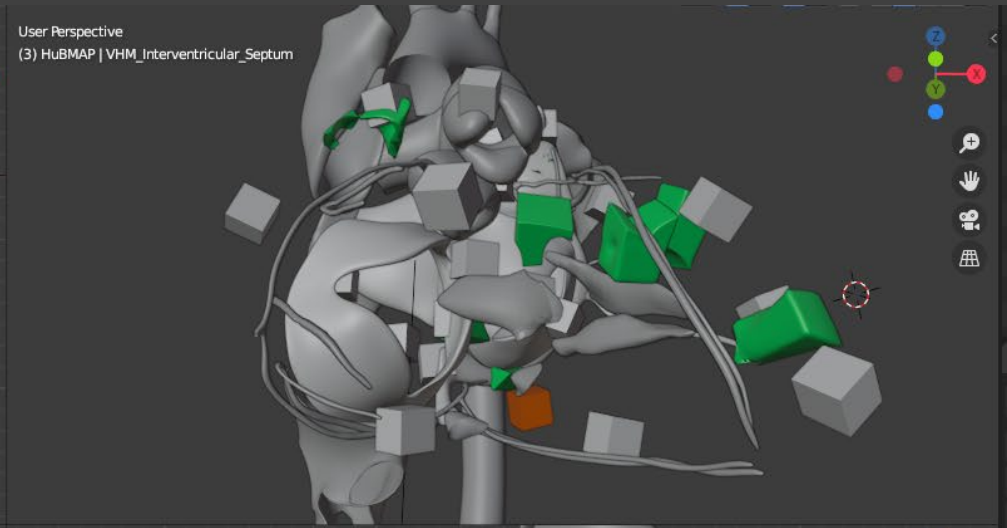
Implemented by the HIVE IEC

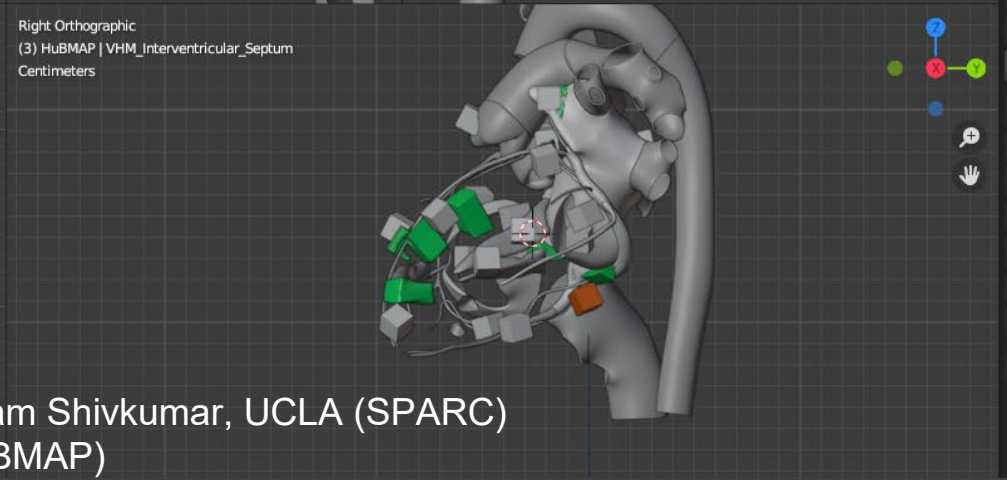
CCF Registration User Interface (RUI)



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

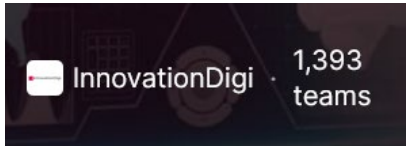






15 extraction sites by Kalyanam Shivkumar, UCLA (SPARC)
10 sites by Shin Lin, UW (HuBMAP)

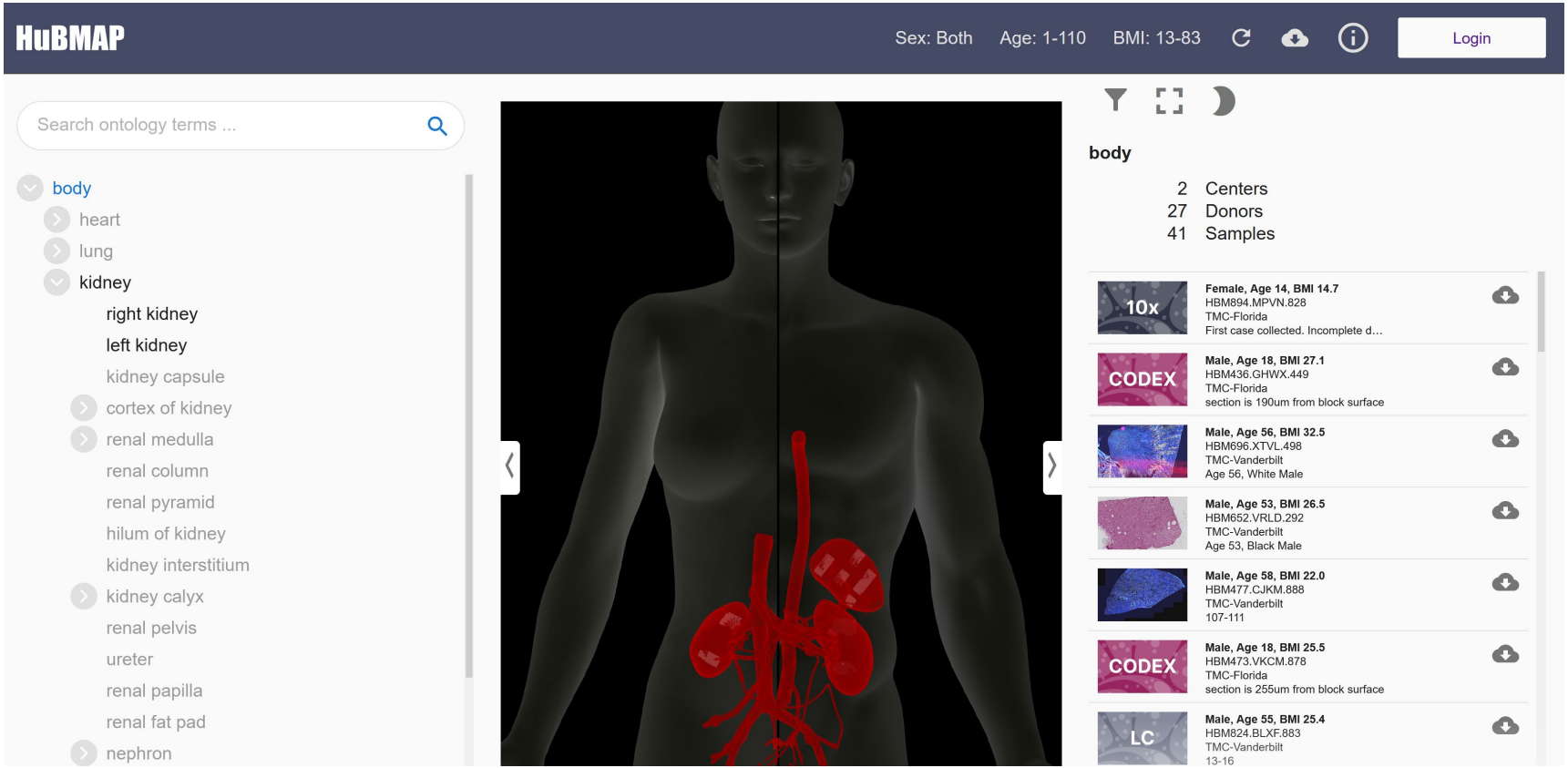
Public private partnership panel with NIH, Google, Broad, Lilly and potentially Roche



https://innovationdigi.com/hubmap-hackathon

CCF Exploration User Interface (EUI)

CCF Exploration User Interface (EUI)



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

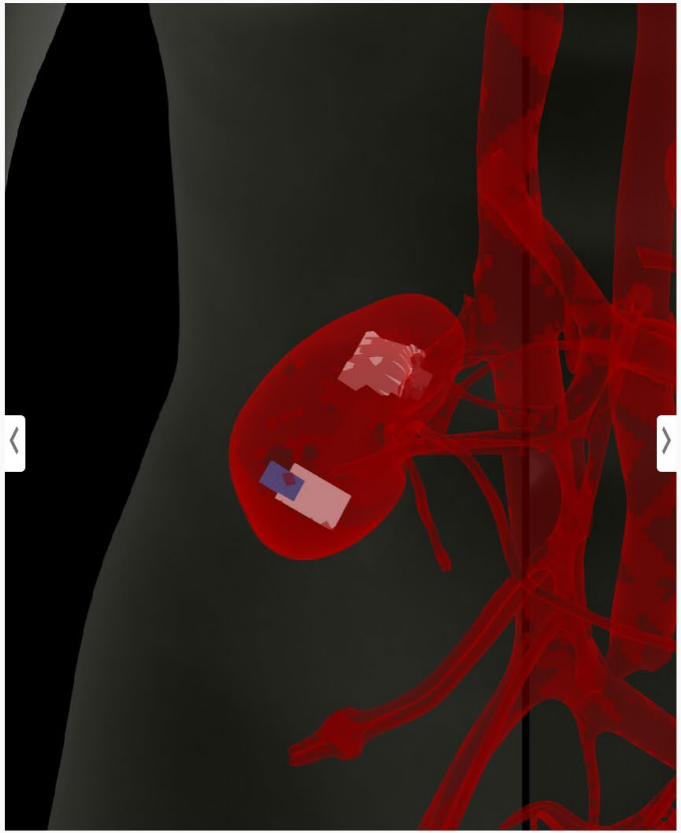
HuBMAP

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

Logout

Search ontology terms ...

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

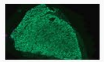


body

1 Centers
9 Donors
40 Samples

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

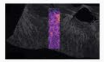
Male, Age 21, BMI 21.8
HBM634.MMGK.572
TMC-Vanderbilt
Age 21 , White Male, Trauma Patient



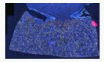
Female, Age 44, BMI 28.0
HBM457.NNQN.252
TMC-Vanderbilt
Age 44, white female.

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

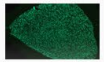
Male, Age 21, BMI 21.8
HBM693.HFFJ.752
TMC-Vanderbilt
Age 21 , White Male, Trauma Patient



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

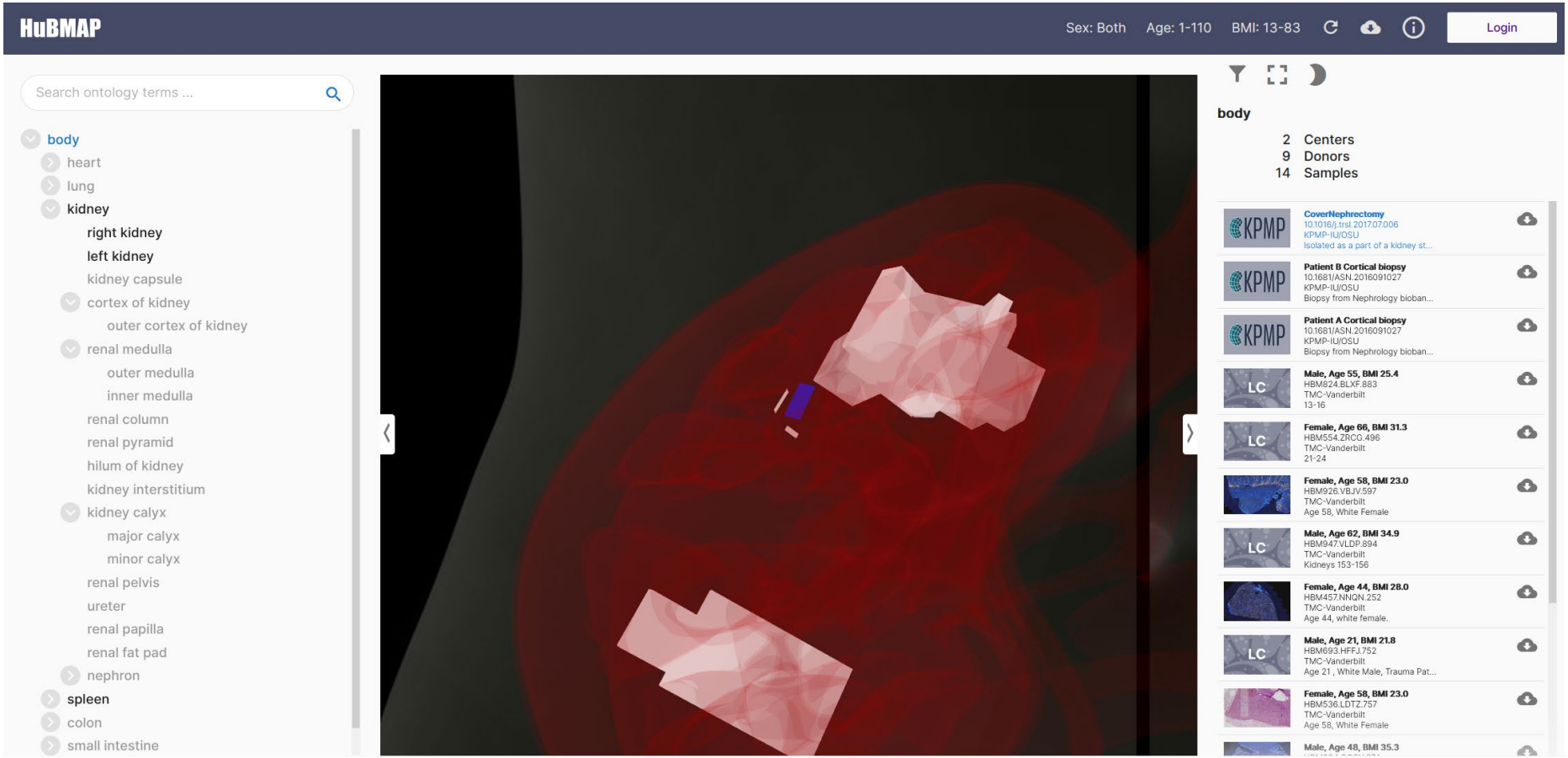


Male, Age 48, BMI 35.3
HBM334.GCCX.874
TMC-Vanderbilt
Age 48, White Male

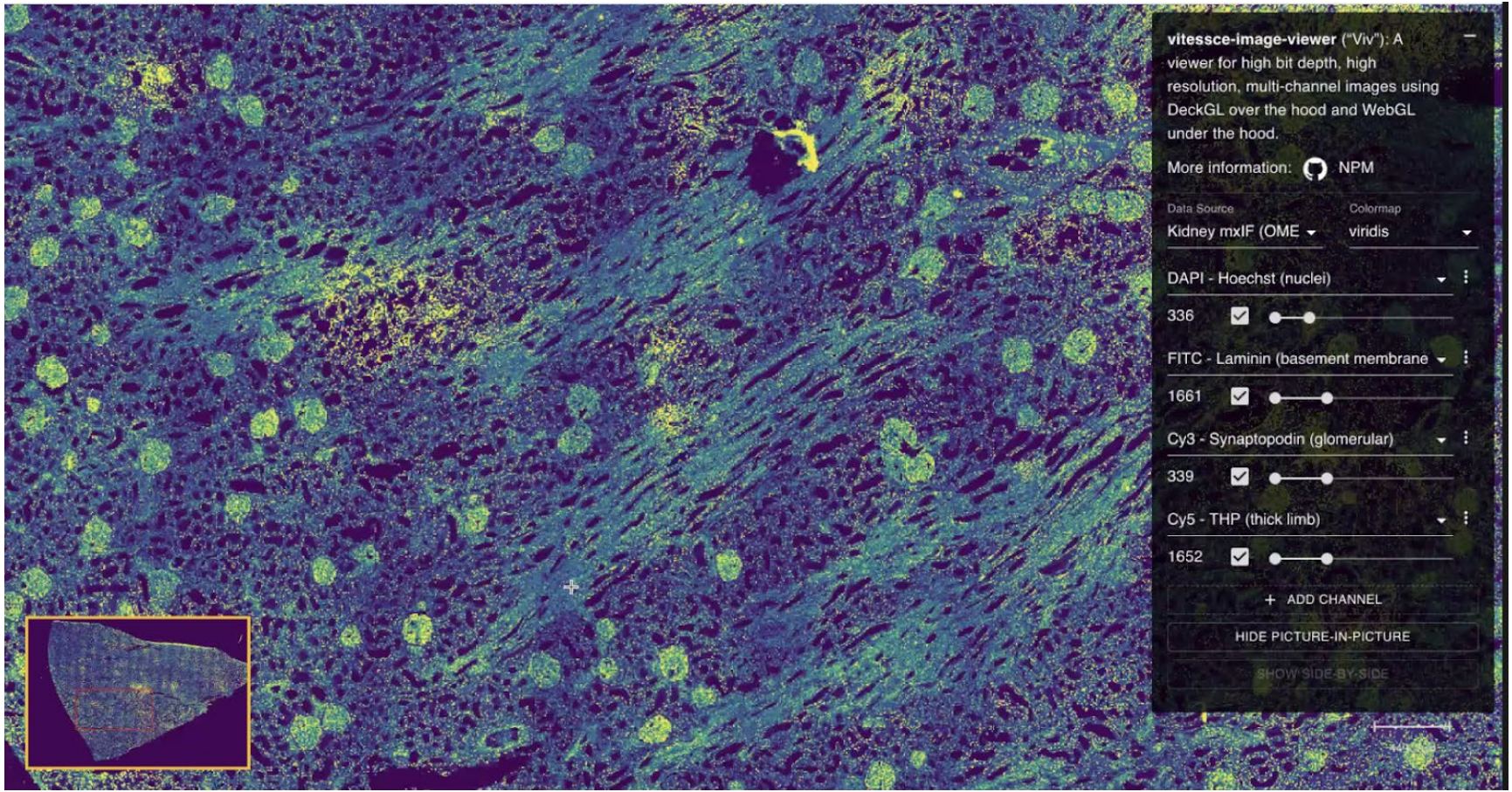


Male, Age 31, BMI 32.6
HBM776.PKJF.786
TMC-Vanderbilt
Age 21, White Male

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



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



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

Human Reference Atlas CCF: Checklist

In support of Common Coordinate Framework (CCF) design (see CCF Portal):

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.

Visible Human MOOC (VHMOOC)

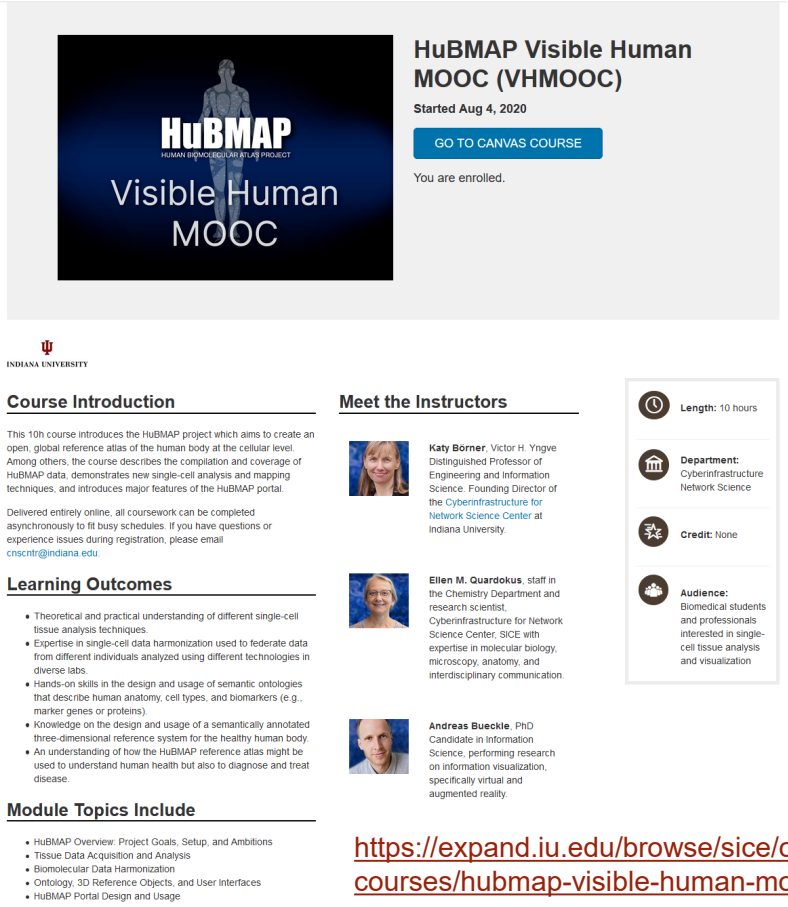
VH Massive Open Online Course (VHMOOC)

Goals

- Communicate tissue data acquisition and analysis,
- Demonstrate single-cell analysis and CCF mapping techniques, and
- Introduce major features of the HuBMAP portal.

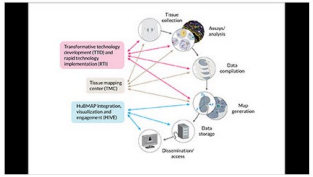
Learning modules come with

- Videos (incl. interviews, tool demos)
- Hands-on exercises
- Self-quizzes



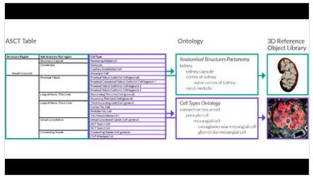
https://expand.iu.edu/browse/sice/cns/courses/hubmap-visible-human-mooc

1st HuBMAP Portal Release (Oct. 2020)



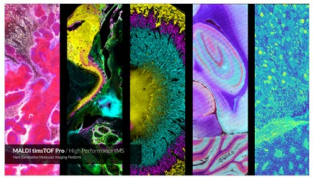
HuBMAP Overview

- Project Goals, Setup, and Ambitions



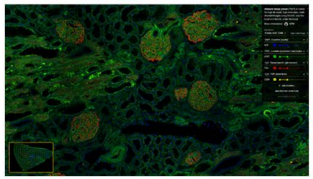
CCF Ontology, 3D Reference Objects, and User Interfaces

- Creating an Atlas of the Human Body



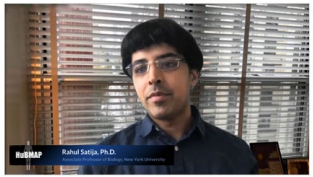
Tissue Data Acquisition and Analysis

- Behind the Scenes at Vanderbilt University



Portal Design and Usage

- Datasets and Software in the 1st HuBMAP Portal Release



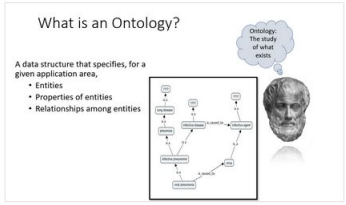
Biomolecular Data Harmonization

- An Introduction to Seurat

Open Consent Your Data

- In Support of Research

2nd HuBMAP Portal Release (Dec. 2020)



Ontologies 101

- A gentle introduction on how to use ontologies to organize the world.

Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) Tables

- What are ASCT+B tables and how they are used.

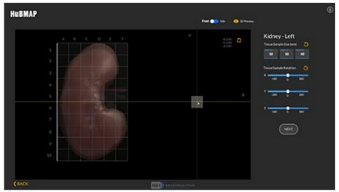
Forthcoming

- CODEX Data and Cell Segmentation by Gary Nolan
- Portal Design and Usage (Summer 2021 Update)

Learning Module Example:

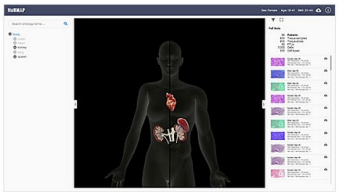
CCF Ontology, 3D Reference Objects, and User Interfaces–Creating an Atlas of the Human Body

Videos



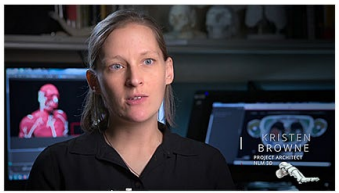
Registration User Interface (RUI)

- RUI Application
- RUI Intro Video



Exploration User Interface (EUI)

- EUI Application
- EUI Intro Video



NLM 3D

- Interview with Kristen Browne

Learning Module Example:

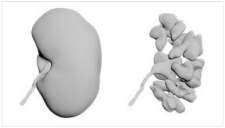
CCF Ontology, 3D Reference Objects, and User Interfaces–Creating an Atlas of the Human Body

Get Involved!

Contribute your expert experience and time.

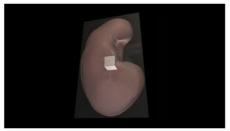
Author or Review ASCT+B Tables

Anatomists, pathologists, biomolecular and other experts are invited to author, edit and/or review Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) tables. Please register to participate.



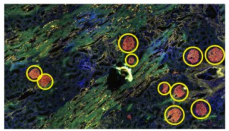
Explore 3D Reference Organs

Download kidney or spleen objects from the HuBMAP Reference Object Library, explore them in a web-based 3D viewer, answer a simple question. Optional: Provide expert comments on the reference organs.



Register Tissue Block via RUI

Use the Registration User Interface (RUI) Prototype to spatially and semantically register three-dimensional tissue blocks within reference organs.



Manually Annotate Human Tissue

Learn how to visually identify functional tissue units in different organs, use human intelligence to annotate them in tissue samples. The resulting data will be used to train machine learning algorithms.

Explore 3D Reference Organs

Started: Aug 30, 2020 at 11:30pm

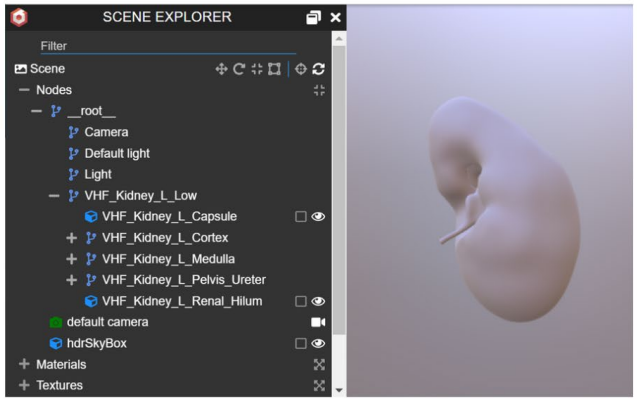
Quiz Instructions

Two 3D reference organs (kidney and spleen) have been made freely available as part of the 1st HuBMAP Portal Release.

The 3D reference objects files are provided in the GLB format, a binary form of the nested Graphics Library Transmission Format (https://www.khronos.org/gltf/). These files can be viewed and explored using free web browser, **Babylon.js** (https://sandbox.babylonjs.com). If you are a programmer, note that these files can also be accessed programmatically via API-neutral runtime asset delivery of 3D scenes and models using the JSON standard.

To explore these 3D models in a web browser:

1. First, visit the Hubmap Github project source objects (https://github.com/hubmapconsortium/hubmap-ontology/tree/master/source_objects/) , and download the GLB file for left female kidney (VHF_Kidney_L_Low.glb, 96KB).
2. Next, visit the **Babylon.js** website and view the 3D kidney by dragging and dropping the GLB file into the browser.
3. In the Scene Explorer on left, click on + symbol to expand Nodes, root, VHF_Kidney_L_Low and other subtrees. Click on eye symbol to turn different parts of the 3D kidney model on/off. Click on square to turn on/off the bounding box (i.e., smallest 3D volume in which all object points lie) for each anatomical structure. To see inner structures, turn outer structures off.



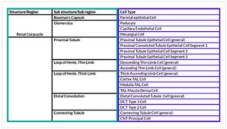
While you explore the kidney, make sure to record the number of renal pyramids for the left female kidney, and report back your finding in the self-check quiz below.

Learning Module Example:

CCF Ontology, 3D Reference Objects, and User Interfaces–Creating an Atlas of the Human Body

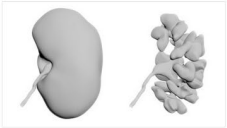
Get Involved!

Contribute your expert experience and time.



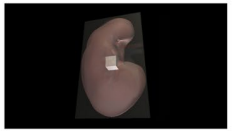
Author or Review ASCT+B Tables

Anatomists, pathologists, biomolecular and other experts are invited to author, edit and/or review Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) tables. Please register to participate.



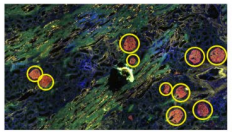
Explore 3D Reference Organs

Download kidney or spleen objects from the HuBMAP Reference Object Library, explore them in a web-based 3D viewer, answer a simple question. Optional: Provide expert comments on the reference organs.



Register Tissue Block via RUI

Use the Registration User Interface (RUI) Prototype to spatially and semantically register three-dimensional tissue blocks within reference organs.



Manually Annotate Human Tissue

Learn how to visually identify functional tissue units in different organs, use human intelligence to annotate them in tissue samples. The resulting data will be used to train machine learning algorithms.

Register Tissue Block via RUI

Due No due date **Points** 5 **Questions** 1 **Time Limit** None

Instructions

The Registration User Interface (RUI) Prototype is a tool developed for HubMAP that supports the registration of three-dimensional (3D) tissue blocks within 3D reference organs. Surgeons and others involved in the tissue procurement process can use the interface to size a virtual tissue block in three dimensions and then to position and rotate the 3D tissue block within a 3D reference organ so its placement mirrors the real-world tissue block extraction site.

The protoype RUI is freely available to use at:
https://hubmapconsortium.github.io/ccf-3d-registration

Registration data can be saved in JSON format to support spatial search and browsing of tissue data in the Exploration User Interface (EUI).

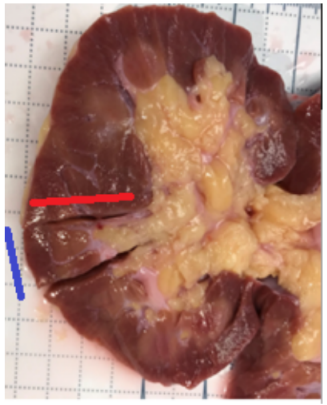


Figure 1. Example kidney tissue block

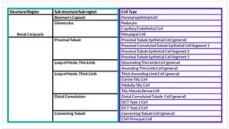
Please register the exemplary kidney tissue block, shown above, using the RUI using these steps (also shown in our tutorial:

Learning Module Example:

CCF Ontology, 3D Reference Objects, and User Interfaces–Creating an Atlas of the Human Body

Get Involved!

Contribute your expert experience and time.



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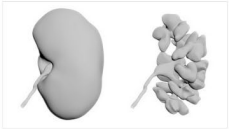

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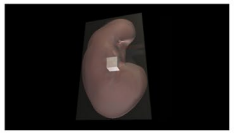

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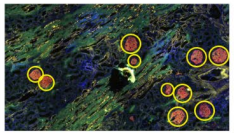


Manually Annotate Human Tissue

Learn how to visually identify functional tissue units in different organs, use human intelligence to annotate them in tissue samples. The resulting data will be used to train machine learning algorithms.

Manually Annotate Human Tissue

–/5 Points

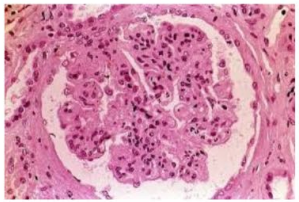
Calculated by:
Most Recent

Unlimited Attempts

Available

Details

Machine learning algorithms can be used to identify and count the number of functional tissue units (FTUs) present in a tissue section. For the kidney, we are interested in identifying and counting the number of glomeruli. Glomeruli have a ball-shaped structure and are composed of capillary blood vessels that filter waste products out of blood to form urine, see Fig. 1.



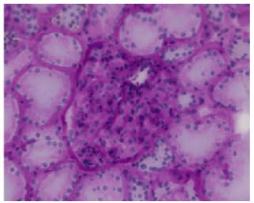
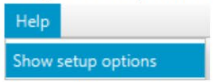


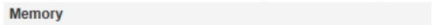
Figure 1. Example of a renal glomeruli

Machine learning algorithms benefit from training data, i.e., human annotations of tissue data that correctly identify glomeruli. For this assignment, please complete the following steps to annotate a kidney tissue sample to help generate machine learning training data and to measure and reduce variability in human annotation data.

1. Install **QuPath** (https://qupath.github.io/)
   - If your installed version is lower than 0.2, please update the QuPath to the latest version by visiting the website or by selecting "***Help – Check for updates (web)***" in the tool menu.
2. To open larger images, update the setting for larger memory in QuPath from
   - Navigate to help and select "Show setup options"



   - Change the maximum memory from the required ***16GB*** to our recommendation of ***32GB***.



NEW Modules Released for XMas 2020

All Sections

Dear all, We are proud to release 2 new modules for XMas 2020: Ontologies 101 A gentle introduction on ho...

Posted on:
Dec 18, 2020 at 9:17am

ASCT+B and RUI Onboarding Videos

All Sections

Hello everyone! As you may know, we have had a big amount of new teams joining HuBMAP recently, so we ...

Posted on:
Nov 19, 2020 at 1:28pm

Azimuth: New App for Reference-Based Single-Cell Analysis Released

All Sections

The Satija Lab, the developers of Seurat (an R toolkit for single cell genomics), has released an exciting new w...

Posted on:
Nov 19, 2020 at 11:31am

HuBMAP "Hacking the Kidney" Kaggle Competition is now live!

All Sections

Dear VHMOOC students, The Kaggle Competition titled HuBMAP: Hacking the Human Kidney is now live! V...

Posted on:
Nov 19, 2020 at 10:47am

Welcome to the course!

U

All Sections

Dear Students, Welcome to the HuBMAP Visible Human MOOC, or VHMOOC! The course opened Tuesday, ...

Posted on:
Sep 1, 2020 at 9am

HuBMAP Visible Human MOOC (VHMOOC)

Started Aug 4, 2020

GO TO CANVAS COURSE

You are enrolled.

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

https://expand.iu.edu/browse/sice/cns/courses/hubmap-visible-human-mooc

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
TMC-Vanderbilt
Vanderbilt University

Sanjay Jain
TMC-UCSD
Washington University, St. Louis

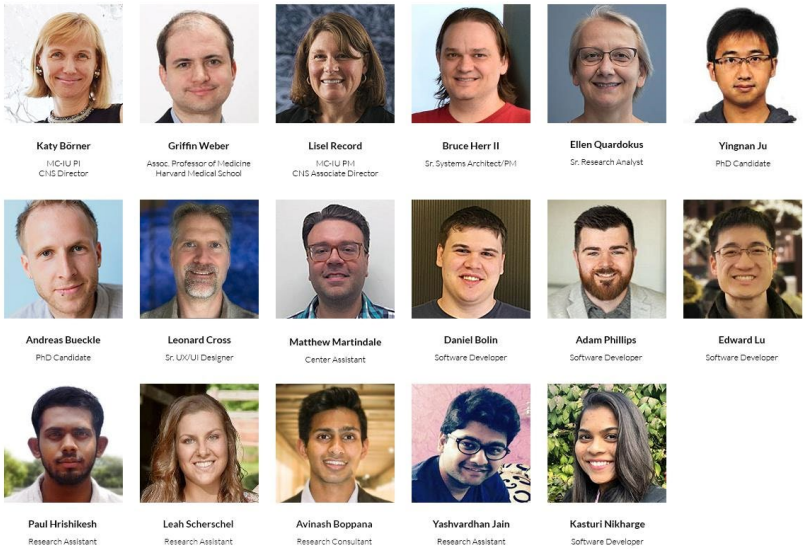
Clive Wasserfall
TMC-UFL
University of Florida

Marda Jorgensen
TMC-UFL
University of Florida

3D Models

Kristen Browne
Medical Imaging and 3D Modeling Specialist
NIAID

MC-IU HIVE Team



Q&A