

Common Coordinates and User Interfaces for Registering Human Tissue Data at Multiple Scales

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Intelligent Systems for Molecular Biology, Virtual Conference July 14,2020



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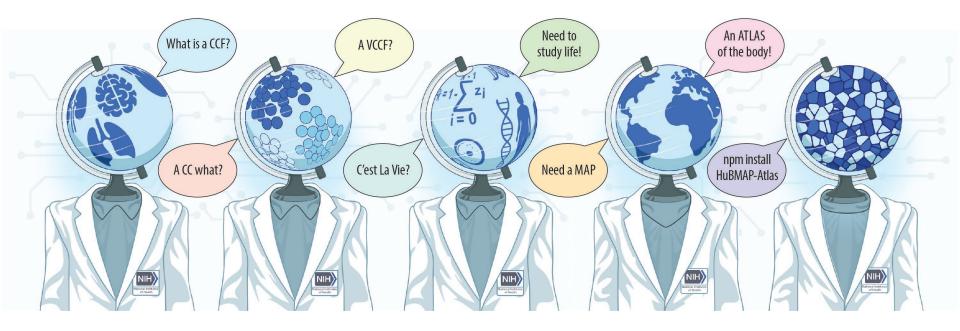
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28TH CONFERENCE ON Intelligent Systems for Molecular Biology JULY 13-16, 2020



What is a CCF?

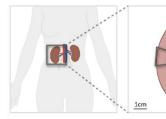
The Common Coordinate System (CCF) consists of ontologies and reference object libraries, computer software, e.g., user interfaces, and training materials that

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

CCF Requirements

The CCF must capture major anatomical structures, cell types, and biomarkers (ASCT+B) 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 calvx
 - Renal pelvis

Functional Tissue Unit

- Nephron
- Renal corpuscle

2.5 mm

- Proximal convoluted tubule
- Loop of Henle
- Distal convoluted tubule
- Connecting tubule
- Collecting duct

FTU Sub-structure(s) Cellular

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

- 25 µm 15 un
 - - Parietal epithelial cell
 - Capillary
 - endothelial cell
 - Mesangial cell
 - Podocvte

ASCT Tables

Anatomical Structures and Cell Types (ASCT) tables aim to capture the partonomy of anatomical structures, cell types, and major biomarkers (genomic, epigenomic, transcriptomic, proteomic, lipidomic, and metabolomic).

| Structure/Re | Substructure/Sub | Cell Type | Subset of Marker Genes |
|--------------|------------------|----------------------------|--------------------------|
| gion | region | | |
| Renal | Bowman's Capsule | Parietal epithelial cell | CRB2*, CLDN1* |
| Corpuscle | 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; 828665. 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/R egion | Sub structure/Sub region | Cell Type | Abbreviation | Subset of Marker Genes | Pertinent negatives/com ments |
|----------------------|------------------------------|---|--------------|---|-------------------------------------|
| | Bowman's Capsule | Parietal epithelial cell | PEC | CRB2*, CLDN1* | |
| Renal | Glomerulus | Podocyte | POD | NPHS2*, PODXL*, NPHS1* | |
| Corpuscle | | Capillary Endothelial Cell | GC-EC | EHD3*, EMCN*, HECW2*, FLT1*, AQP1* | |
| | | Mesangial Cell | MC | POSTN*, PIEZO2*, ROBO1*, ITGA8* | |
| | Proximal Tubule | Proximal Tubule Epithelial Cell (general) | PT | CUBN*, LRP2*, SLC13A1*, ALDOB*, GATM* | |
| | | Proximal Convoluted Tubule Epithelial Cell Segment 1 | PT-S1 | SLC5A2*, SLC5A12* | These is seed as |
| | | Proximal Tubule Epithelial Cell Segment 2 | PT-S2 | SLC22A6* | There is overlap among the |
| | | Proximal Tubule Cell Epithelial Segment 3 | PT-S3 | PDZK1IP1*, MT1G* | - segments |
| | Loop of Henle, Thin Limb | lenle, Thin Descending Thin Limb Cell (general) | | 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* | |
| Tubules | | 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 | |
| | | CNT-Principal Cell | CNT-PC | SLC8A1*, AQP2*, SCNN1G* | SLC12A3 low to none. IC or PC |
| | | CNT-Intercalated Cell | CNT-IC | SLC8A1*, CA2, ATP6VOD2* | without SLC8A1 |
| | | CNT-IC-A cell | CNT-IC-A | SLC8A1*, SLC4A1*, SLC26A7* | - could be in the CNT structure |
| | | CNT-IC-B cell | CNT-IC-B | SLC8A1*, SLC26A4*, SLC4A9* | |
| | Collecting Duct | Collecting duct (general) cell | CD | GATA3* | GATA3 may be |
| | | CD-PC (general) | CD-PC | | in subpopulation |
| | | C-CD-PC | C-CD-PC | AQP2*, AQP3*, FXYD4*, | of DCT, CNT |
| | | M-CD-PC | M-CD-PC | SCNN1G*, GATA3* | and vSMC/P. |
| | | Outer medulla-CD-PC | OM-CD-PC | | SLC8A1, |
| | | Inner Medulla-CD cell | IM-CD | AQP2*, SLC14A2 | CALB1, TRPV5 |

| | | Transitional PC-IC cell | tRC,IC | FXYD4*, SLC4A9*/SLC26A7* | (low to none); Low to No |
|----------------------|--|--------------------------------|--------------|----------------------------------|-------------------------------------|
| | | CD-IC (general) cell | CD-IC | CA2, ATP6VOD2* | CALCA and KIT |
| | | CD-IC-A (general) cell | CD-IC-A | SLC4A1, SLC26A7*, TMEM213* | in C-CD-IC-A. I may not be |
| | | C-CD-IC-A cell | C-CD-IC-A | SLC26A7*, SLC4A1* | possible to |
| | | M-CD-IC-A cell | M-CD-IC-A | SLC26A7*, SLC4A1, KIT*, CALCA | assign IC or PC to_CNT or CD |
| | | CD-IC-B (general) cell | CD-IC-B | | structures |
| | | C-CD-IC-B cell | C-CD-IC-B | SLC4A9*, SLC26A4* | without regional |
| | | M-CD-IC-B cell | M-CD-IC-B | | information of their source. |
| | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* | |
| | | EC-Afferent/Efferent Arteriole | EC-AEA | SERPINE2*, TM4SF1* | likely PALMD |
| | | EC-Peritubular capillaries | EC-PTC | PLVAP* | |
| Vessels | Endothelial Cells (non- glomerular) | 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/R egion | Sub structure/Sub region | Cell Type | Abbreviation | Subset of Marker Genes | Pertinent negatives/com ments |
| Interstitium | Stroma (non- | Vascular Smooth | VSMC/P | TAGLN*, ACTA2*, | |
| | glomerular) | Muscle/Pericyte (general) | | 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 | 1 |
| | | Natural Killer Cell | NKC | NKG7 | |
| | | Dendritic Cell | DC | APOE | |
| | | Monocyte | MON | C1QA, HLA-DRA | |
| | | T lymphocyte (general) | T | CD3 | |
| | | T Cytotoxic | T-CYT | GZMA | 1 |
| | | B lymphocyte | В | 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; 828665. doi:10.1101/828665

ASCT Table Meetings

Meetings take place monthly to

- Review and approve tables.
- Formalize and unify table design language.
- Discuss table usage.

We are working on

- Converting tables into machine readable formats.
- Compare tables against Uberon, CL, and other ontologies.
- Compare tables against cell types identified in harmonized HuBMAP data and data generated by other efforts.

Experts are welcome to <u>register</u>.

ASCT Table Design

The CCF Session at the NIH-HCA meeting—co-organized with Peter Hunter (SPARC) and James Gee (BICCN)—brought together experts across consortia.

In follow up meetings, 10 ASCT tables have been created via collaborations across consortia. Ontology experts, including Chris Mungall and Mark Musen, provided expert comments.

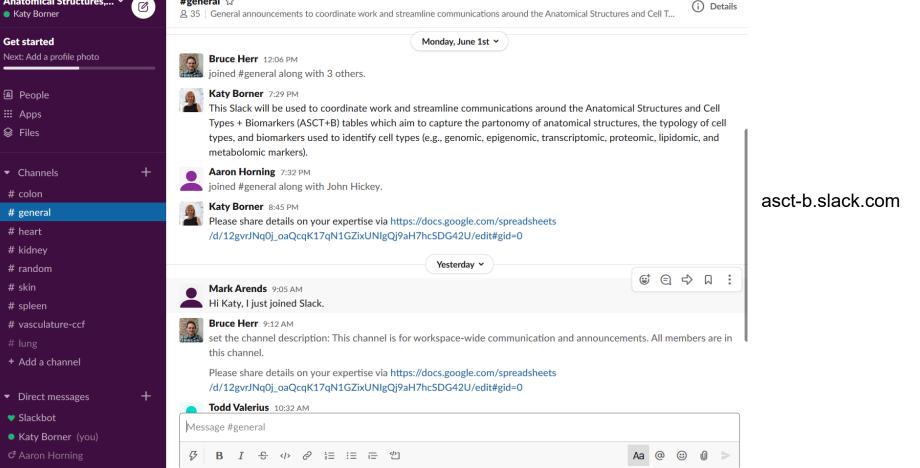


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#general ☆

Details

Anatomical Structures,... > Katy Borner



| | HuBMAP | RBK | КРМР | 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 |

Example: Converting tables into machine readable formats- Kidney vasculature

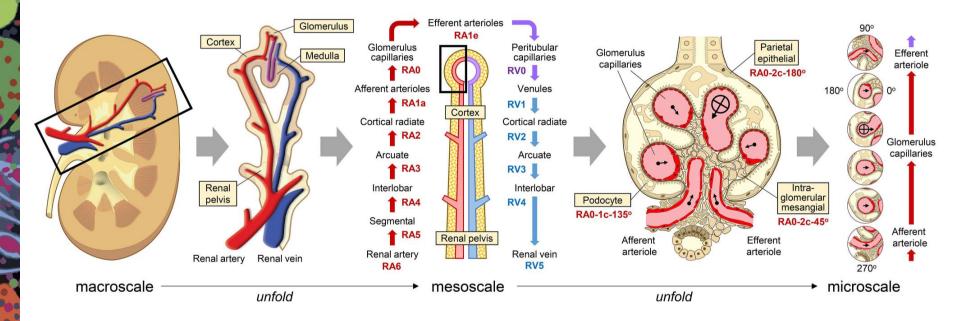
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| /asculature | renal atery [L/R] | | | | Endothelial | Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
|------------------|-----------------------------|-------------------------------------|--------------------------|--|--------------|----------------------------|--------|-----------------------------------|
| | | segmental arteries [sup | erior, inferior, anterio | or, posterior] | | | | |
| | | interlobar aterties | | | | | | |
| | | arcuate aterties | | | | | | |
| | | cortical radiate ateries | | | | | | |
| | | {cortex} | afferent arterioles | | EC-Afferent | /Efferent Arteriole | EC-AEA | SERPINE2*, TM4SF1* |
| | | . · | {nephron} | glomerulus capillaries {glomerulus} | Capillary En | dothelial Cell | GC-EC | EHD3*, EMCN*, HECW2*, FLT1*, AQP1 |
| | | | efferent arterioles | | EC-Afferent | /Efferent Arteriole | EC-AEA | SERPINE2*, TM4SF1* |
| | | | {nephron} | peritubular capillaries | EC-Peritubu | ılar capillaries | EC-PTC | PLVAP* |
| | | | | descending vasa recta | EC-Descend | ling Vasa Recta | EC-DVR | TM4SF1*, PALMD |
| | | | | ascending vasa recta | EC-Ascendi | ng Vasa Recta | EC-AVR | DNASEIL3* |
| | renal vein [L/R) | cortical radiate veins {cortex} | venules | · · · · · · · · · · · · · · · · · · · | Endothelial | Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| | | arcuate veins interlobar veins | | | - | | | |
| | | | | | | | | |
| asculature renal | l artery [L/R] | | | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| asculature renal | l artery [L/R] segmental ar | teries [superior, inferior, anterio | r, posterior] | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| | | | | | | 5 I.U. I. I.O. I.C. I. | 50 | |

| Vasculature | renal artery [L/R] | segmental arteries [superior, inferior, anteri | or, posterior] | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
|-------------|--------------------|--|-------------------------------|-------------------------------------|--------------------------------|--------|------------------------------------|
| Vasculature | renal artery [L/R] | interlobar arterties | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal artery [L/R] | arcuate arteries | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | afferent arterioles {nephron} | | EC-Afferent/Efferent Arteriole | EC-AEA | SERPINE2*, TM4SF1* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | afferent arterioles {nephron} | glomerulus capillaries {glomerulus} | Capillary Endothelial Cell | GC-EC | EHD3*, EMCN*, HECW2*, FLT1*, AQP1* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | efferent arterioles {nephron} | | EC-Afferent/Efferent Arteriole | EC-AEA | SERPINE2*, TM4SF1* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | efferent arterioles {nephron} | peritubular capillaries | EC-Peritubular capillaries | EC-PTC | PLVAP* |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | efferent arterioles {nephron} | descending vasa recta | EC-Descending Vasa Recta | EC-DVR | TM4SF1*, PALMD |
| Vasculature | renal artery [L/R] | cortical radiate arteries {cortex} | efferent arterioles {nephron} | ascending vasa recta | EC-Ascending Vasa Recta | EC-AVR | DNASEIL3* |
| Vasculature | renal vein [L/R) | cortical radiate veins {cortex} | venules {nephron} | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal vein [L/R) | cortical radiate veins {cortex} | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal vein [L/R) | arcuate veins | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| Vasculature | renal vein [L/R) | interlobar veins | | | Endothelial Cell (general) | EC | EMCN*, PECAM1*, FLT1* |
| | | | | | | | |

Capturing vasculature details is critically important for a vasculature based CCF



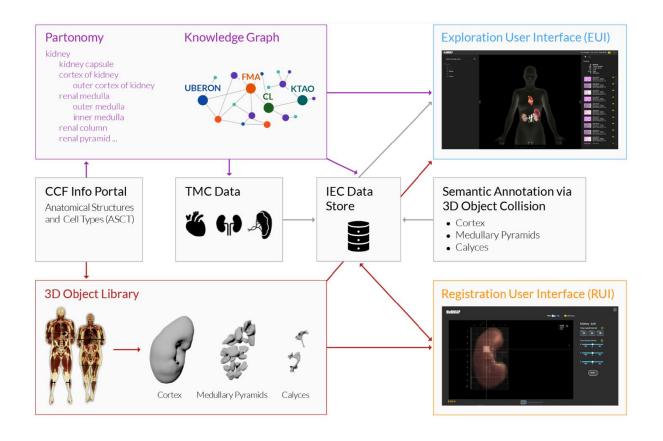
Weber, Griffin M, Yingnan Ju, and Katy Börner. 2020. <u>"Considerations for Using the Vasculature as a Coordinate System to Map All the Cells in the Human Body"</u>. *Frontiers in Cardiovascular Medicine* 7 (29): doi: 10.3389/fcvm.2020.00029.

ASCT Table Usage

ASCT tables guide **CCF Ontology** and **3D Reference Object Library** design that semantically name and spatially place tissue data from different individuals into one CCF (i.e., <u>mapping</u>).

| ASCT Table | 2 | | | Ontology | Reference ect Library |
|------------------|--|---|----------|--|------------------------------|
| Structure/Region | Sub structure/Sub region Bowman's Capsule Glomerulus | Cell Type Parietal epithelial Cell Podocyte Capillary Endothelial Cell Mesanzial Cell | | Anatomical Structures Partonomy kidney kidney capsule | |
| | 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 | | cortex of kidney outer cortex of kidney renal medulla | |
| | 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 Medulla-TAL Cell TAL-Macula Densa Cell | → | Cell Types Ontology connective tissue cell pericyte cell | |
| | Distal Convolution | Distal Convoluted Tubule Cell (general) DCT Type 1 Cell DCT Type 2 Cell | | mesangial cell extraglomerular mesangial cell | 0 |
| | Connecting Tubule | Connecting Tubule Cell (general) CNT-Principal Cell | | glomerular mesangial cell | |

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



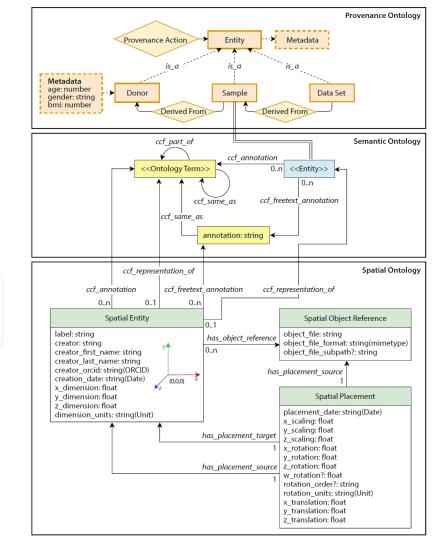
Data gathered in the ASCT tables is used in Ontology Design (topleft) and 3D Object Library (bottom-left).

Two interfaces on right: **Registration User Interface (RUI)** supports semantic and spatial annotation of tissue data.

Exploration User Interface (EUI) supports semantic and spatial exploration of tissue data. Construction and Usage of a Human Body Common Coordinate Framework Containing Provenance, Semantic, and Spatial Ontologies

Documentation of three CCF ontologies 2.5 mm 25 um 15 um HUBMAP Body Organ Tissue Block FTU Cell Atlas reference Used for Used for RUI 7-Stack of Human or ML Human or ML system navigation registration tissue sections segmented segmented

Börner K, Quardokus EM, Herr, II BW, Cross LE, Record EG, Ju Y, Bueckle A, Sluka JP, Silverstein J, Browne K, Jain S, Wasserfall CH, Jorgensen ML, Spraggins JM, Patterson NH, Weber GM. 2020. Conceptualization, Construction, and Usage of a Human Body Common Coordinate Framework. In preparation.





3D Object Library

The CCF 3D Reference Object Library provides anatomically correct reference organs. The organs are developed by a specialist in 3D medical illustration and approved by organ experts.

Initially, reference objects were created using data from the Visible Human male and female datasets provided by the National Library of Medicine.

For the 1st HuBMAP Portal Release, kidney and spleen reference organs are freely available in GLB format.

https://hubmapconsortium.github.io/ccf/pages/ccf-3d-reference-library.html

HUBMAP CCF Portal ← HOME CCF 3D Reference Object Library **. Reference Organs** COLON HEART KIDNEY SPI FEN MALE: Kidney, L MALE: Kidney, R 0 0 # Anatomical Structures 38 # Anatomical Structures 39 9/3 Calyces (minor/major) Calvces (minor/major Capsule 1 Capsule Hilum 1 Hilum Medulla (renal columns) Medulla (renal columns) Outer Cortex Outer Cortex Papilla 9 Papilla 10 Pelvis Pelvis Pyramids 9 **Pyramids** 10 Ureter Ureter Artery Artery Voins Voine FEMALE: Kidney, L FEMALE: Kidney, R 0 ~ 44 # Anatomical Structures # Anatomical Structures Calvces (minor/major) 10/4 Calvces (minor/major) 10/3Capsule Capsule Hilum Hilum Medulla (renal columns) Medulla (renal columns) Outer Cortex Outer Cortes Papilla 11 Papilla 10 Pelvis 1 Pelvis 11 Pyramids 10 Pyramide

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1

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Ureter

Veins

Ureter

Artery

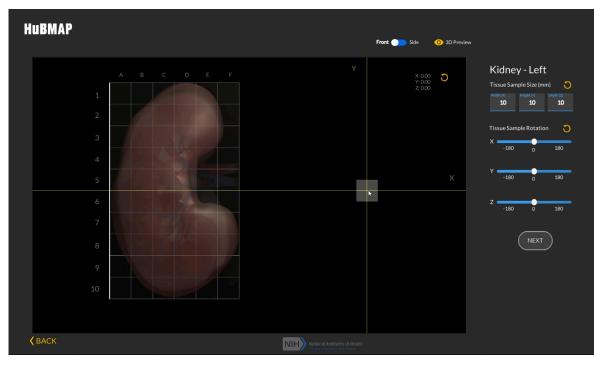
Veins

CCF Registration

Registration User Interface (RUI) is used to document the tissue extraction site by registering tissue blocks within a3D reference organ.

24 kidney and 24 spleen tissue blocks have been registered.





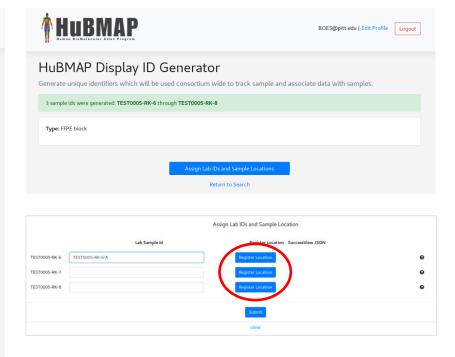
https://hubmapconsortium.github.io/ccf-3d-registration

1st Portal Release: Upload Portal

| Å | HUBMAP |
|------|----------------------------------|
| - 11 | Human BioMolecular Atlas Program |

| DES@pitt.edu Edit Profile | Logout |
|-----------------------------|--------|
|-----------------------------|--------|

| |)isplay ID Generator tiflers which will be used consortium wide to track sample and associate data with samples. |
|----------------------|---|
| Source HuBMAP ID * | TEST0005-RK 🗸 Look up |
| | HuBMAP display id: TEST0005-RK type: Organ Type: Kidney (Right) HuBMAP ID: HBM:264-TTTJ-798 Description: |
| Tissue Sample Type * | FFPE block |
| Protocol 1 | protocols lo DOI * https://dx.doi.org/10.17504/protocols.io.p9kdr4w Protocol document * Choose a file Browse doc. docs and pdf files only |
| Description | Add Protocol Image: Construction of the state of the stat |
| Description | |
| Metadata | + Add Metadata |
| Image | + Add Image Make sure any uploaded images are de-identified |
| | Generate ID Cancel |

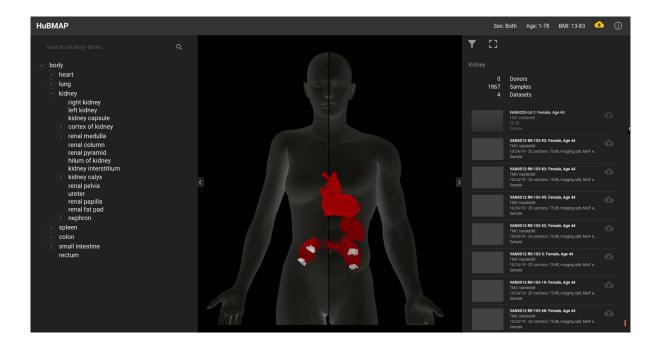


Thanks go to the IEC for providing screenshots

CCF Exploration

Exploration User Interface (EUI) supports exploring 2D/3D tissue samples across multiple scales using spatial, semantic, clinical, and provenance data.

Version 1.0.0 will features the HuBMAP Tissue Viewer



Version 1.0.0 Previous version is at https://hubmapconsortium.github.io/ccf-ui/

1st Portal Release

| UBMAP Donors Sam | ples | Datasets Collection | s | Showcases | - CCF | Documentati | on Logout |
|--|------|---------------------|------------------------------|--|---------------|-------------|------------------------|
| Datasets | | | | | | | |
| Q Search | | 327 results found | | | | | Newest 👻 |
| Data Type | | ID | Group | Data Types | Organ | Status | Last Modified |
| Unexpected code Untargeted LC-MS CODEX | | HBM268.DLTB.229 | University of Florida TMC | derived data from CODEX through Cytokit | Lymph Node | Processing | 2020-07-12 03:52:18 |
| Autofluorescence Microscopy | | HBM277.GMVW.283 | University of Florida TMC | derived data from CODEX through Cytokit | Spleen | Error | 2020-07-12 03:50:50 |
| □ seqFish View all | | HBM643.RRCT.235 | University of Florida TMC | derived data from CODEX through Cytokit | Thymus | Error | 2020-07-12 03:45:56 |
| Organ | | HBM487.RCRF.347 | University of Florida TMC | derived data from CODEX through Cytokit | Spleen | Processing | 2020-07-12 02:23:00 |
| Kidney (Eert) Kidney (Right) | | HBM795.MLVP.544 | University of Florida TMC | derived data from CODEX through Cytokit | Lymph Node | QA | 2020-07-12 02:21:34 |
| Spleen Large Intestine | | HBM267.BZKT.867 | University of Florida TMC | CODEX | Spleen | QA | 2020-07-12 01:10:55 |
| View all | | HBM623.TSMG.452 | University of Florida TMC | CODEX | Lymph Node | QA | 2020-07-11 22:48:08 |
| Specimen Type Cryosections/curls from | | HBM339.XXWC.842 | University of Florida TMC | CODEX | Thymus | QA | 2020-07-11 22:43:08 |
| fresh frozen OCT Fresh Frozen Tissue Section | | HBM426.LLTT.655 | University of Florida TMC | CODEX | Lymph Node | QA | 2020-07-11 22:36:17 |
| Flash frozen, liquid nitrogen | 48 | HBM342.JTKN.834 | University of Florida TMC | CODEX | Lymph Node | QA | 2020-07-11 22:26:55 |
| FFPE slide Single cell cryopreserved | | HBM337.FSXL.564 | University of Florida TMC | CODEX | Spleen | QA | 2020-07-11 22:24:10 |
| View all | | HBM869.VZJM.366 | University of Florida TMC | CODEX | Lymph Node | QA | 2020-07-11 22:10:49 |
| New | | HBM987.XGTH.368 | University of Florida TMC | CODEX | Spleen | QA | 2020-07-11 22:09:23 |
| CA Error Processing | | HBM647.MFQB.496 | University of Florida TMC | CODEX | Spleen | QA | 2020-07-11 22:07:25 |

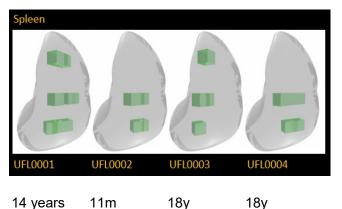
Early draft of HuBMAP interface.

Official first release is on Aug 4,2020.

Exemplary Use Case

Compare cell types in ASCT tables with cell types identified in HuBMAP data. Spleen example: Data from five tissue blocks from 4 spleens were harmonized.

Male

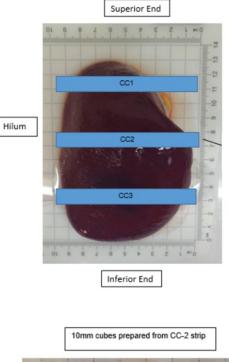


Male

Female

Male

UFL0001-SP-2-8, cube 1 UFL0001-SP-3-4, cube 3 UFL0002-SP-2-2, cube 3 UFL0003-SP-2-2, cube 1 UFL0004-SP-2-1, cube 4





Data provided by TMC-UFL

Exemplary Use Case

Seurat harmonization results: Cell counts and prediction scores

| UFL0001-SP-3-4, cube 3 | | UFL0003-SP-2-2, cube 1 | | UFL0002-SP-2-2, cube 3 | | UFL0001-SP-2-8, cube 1 | | UFL0004-SP-2-1, cube 4 | | |
|---------------------------------------|----------------------|---------------------------------------|----------------------|---------------------------------------|----------------------|---------------------------------------|----------------------|---------------------------------------|------|--|
| IBM336.FWTN.636 | 6010 HBM396.RPRR.624 | | 9382 HBM472.NTNN.543 | | 8738 HBM556.QMSM.776 | | 5273 HBM984.GRBB.858 | | 6328 | |
| alpha-beta T cell | 372 | alpha-beta T cell | 773 | alpha-beta T cell | 1497 | alpha-beta T cell | 515 | alpha-beta T cell | 878 | |
| B cell | 1349 | B cell | 4463 | B cell | 6550 | B cell | 1407 | B cell | 2803 | |
| CD141-positive myeloid dendritic cell | 55 | CD141-positive myeloid dendritic cell | 89 | CD141-positive myeloid dendritic cell | 19 | CD141-positive myeloid dendritic cell | 44 | CD141-positive myeloid dendritic cell | 1 | |
| CD14-positive monocyte | 1851 | CD14-positive monocyte | 2242 | CD14-positive monocyte | 238 | CD14-positive monocyte | 872 | CD14-positive monocyte | 802 | |
| CD1c-positive myeloid dendritic cell | 185 | CD1c-positive myeloid dendritic cell | 18 | | | CD1c-positive myeloid dendritic cell | 162 | CD1c-positive myeloid dendritic cell | 19 | |
| erythroblast | 177 | erythroblast | 42 | erythroblast | 17 | erythroblast | 89 | | | |
| gamma-delta T cell | 151 | gamma-delta T cell | 57 | gamma-delta T cell | 30 | gamma-delta T cell | 176 | gamma-delta T cell | 1241 | |
| hematopoietic stem cell | 73 | hematopoietic stem cell | 84 | hematopoietic stem cell | 56 | hematopoietic stem cell | 79 | hematopoietic stem cell | 30 | |
| low-quality | 93 | low-quality | 71 | low-quality | 94 | low-quality | 129 | low-quality | 13: | |
| natural killer cell | 594 | natural killer cell | 1307 | natural killer cell | 84 | natural killer cell | 460 | natural killer cell | 26 | |
| plasma cell | 460 | plasma cell | 171 | plasma cell | 101 | plasma cell | 360 | plasma cell | 75 | |
| plasmablast | 22 | plasmablast | 7 | plasmablast | 28 | plasmablast | 1 | plasmablast | 36 | |
| splenic endothelial cell | 424 | splenic endothelial cell | 47 | splenic endothelial cell | 6 | splenic endothelial cell | 588 | splenic endothelial cell | 1 | |
| splenic fibroblast | 15 | splenic fibroblast | 5 | splenic fibroblast | 6 | splenic fibroblast | 20 | splenic fibroblast | 1 | |
| splenic macrophage | 189 | splenic macrophage | 6 | splenic macrophage | 12 | splenic macrophage | 371 | splenic macrophage | 26 | |

| 3M336.FWTN.636 1 HBM396.RPRR.624 | | HBM472.NTNN.543 | | HBM556.QMSM.776 | | HBM984.GRBB.858 | | | |
|---------------------------------------|---|---------------------------------------|-------------|---------------------------------------|-------------|---------------------------------------|-------------|---------------------------------------|-------------|
| alpha-beta T cell | 1 | alpha-beta T cell | 0.81531392 | alpha-beta T cell | 0.935717083 | alpha-beta T cell | 0.852839869 | alpha-beta T cell | 0.819379533 |
| B cell | 1 | B cell | 0.966724409 | B cell | 0.978509075 | B cell | 0.958394632 | B cell | 0.963947327 |
| CD141-positive myeloid dendritic cell | 1 | CD141-positive myeloid dendritic cell | 0.714928889 | CD141-positive myeloid dendritic cell | 0.870885148 | CD141-positive myeloid dendritic cell | 0.890455775 | CD141-positive myeloid dendritic cell | 0.615445273 |
| CD14-positive monocyte | 1 | CD14-positive monocyte | 0.940118127 | CD14-positive monocyte | 0.937989865 | CD14-positive monocyte | 0.938657155 | CD14-positive monocyte | 0.963592885 |
| CD1c-positive myeloid dendritic cell | 1 | CD1c-positive myeloid dendritic cell | 0.563719677 | | | CD1c-positive myeloid dendritic cell | 0.803740621 | CD1c-positive myeloid dendritic cell | 0.783471674 |
| erythroblast | 1 | erythroblast | 0.532657229 | erythroblast | 0.694290983 | erythroblast | 0.978894926 | | |
| gamma-delta T cell | 1 | gamma-delta T cell | 0.539497766 | gamma-delta T cell | 0.502216796 | gamma-delta T cell | 0.740586674 | gamma-delta T cell | 0.904053159 |
| hematopoietic stem cell | 1 | hematopoietic stem cell | 0.726385726 | hematopoietic stem cell | 0.764763311 | hematopoietic stem cell | 0.75724491 | hematopoietic stem cell | 0.648865012 |
| low-quality | 1 | low-quality | 0.680657174 | low-quality | 0.68445931 | low-quality | 0.649134708 | low-quality | 0.728998052 |
| natural killer cell | 1 | natural killer cell | 0.770988817 | natural killer cell | 0.623959124 | natural killer cell | 0.833128238 | natural killer cell | 0.718629642 |
| plasma cell | 1 | plasma cell | 0.945743141 | plasma cell | 0.947816498 | plasma cell | 0.954210246 | plasma cell | 0.82474102 |
| plasmablast | 1 | plasmablast | 0.445989963 | plasmablast | 0.593308367 | plasmablast | 0.535441087 | plasmablast | 0.558989332 |
| splenic endothelial cell | 1 | splenic endothelial cell | 0.921750546 | splenic endothelial cell | 0.649250648 | splenic endothelial cell | 0.949515886 | splenic endothelial cell | 0.555504115 |
| splenic fibroblast | 1 | splenic fibroblast | 0.883399167 | splenic fibroblast | 0.886345281 | splenic fibroblast | 0.878256094 | splenic fibroblast | 0.820886903 |
| splenic macrophage | 1 | splenic macrophage | 0.646221909 | splenic macrophage | 0.827945537 | splenic macrophage | 0.853436501 | splenic macrophage | 0.880481635 |

Data provided by MC-NYGC

HUBN Visible Human MOOC

HuBMAP Visible Human MOOC

Starts Aug 4, 2020

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



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

Ш INDIANA UNIVERSITY

Course Introduction

** Enrollment is currently closed and begins July 20, 2020, **

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.

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



Ellen M. Quardokus, staff in the Chemistry Department and research scientist, Cyberinfrastructure for Network Science Center, SICE with

microscopy, anatomy, and

Andreas Bueckle, PhD

Candidate in Information

specifically virtual and augmented reality.

Science, performing research

on information visualization,

expertise in molecular biology, interdisciplinary communication.



Î

Length: 10 hours

Department:

Credit: None

Cyberinfrastructure

Network Science

HuBMAP-Postdoc Position

The Department of Intelligent Systems Engineering at Indiana University, Bloomington, is seeking a Postdoctoral Fellow within the NIH funded Human BioMolecular Atlas Program (HuBMAP). The postdoctoral fellow will help identify and catalog knowledge about the structure of the vascular pathways in the human body (arteries, veins, capillaries, and lymph vessels). This will be conducted primarily through a literature search to find (1) descriptions of the named vascular pathways and microvascular architecture in different organs of the body; (2) descriptions of the variability of the vascular system across different individuals; (3) imaging studies that show the physical 3D structure of vascular pathways; and (4) studies that identify biomolecular signatures unique to different parts of the vascular system, such as how gene expression varies in endothelial cells across the body. The postdoctoral fellow should have a background in human anatomy or related fields such as systems biology, cell biology, radiology, or pathology.

To apply, please contact Katy Borner, <u>katy@indiana.edu</u>

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





TMC-UCSD

St. Louis







3D Models

Jeffrey Spraggins TMC-Vanderbilt Vanderbilt University

Saniav Jain Clive Wasserfall TMC-UFL Washington University, University of Florida

Marda Jorgensen TMC-UFL University of Florida

Kristen Browne Medical Imaging and 3D Modeling Specialist NIAID













Katy Börner MC-IU PI CNS Director

Griffin Weber Assoc. Professor of Medicine Harvard Medical School

Lisel Record MC-IU PM CNS Associate Director

Bruce Herr II Sr. Systems Architect/PM Ellen Quardokus Sr. Research Analyst

Yingnan Ju PhD Candidate











Leonard Cross Andreas Bueckle PhD Candidate Sr. UX/UI Designer

Matthew Martindale Center Assistant

Adam Phillins Software Developer



Daniel Bolin

Software Developer









