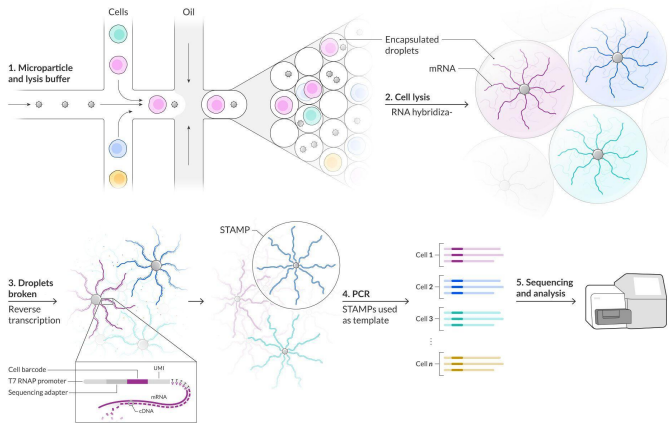
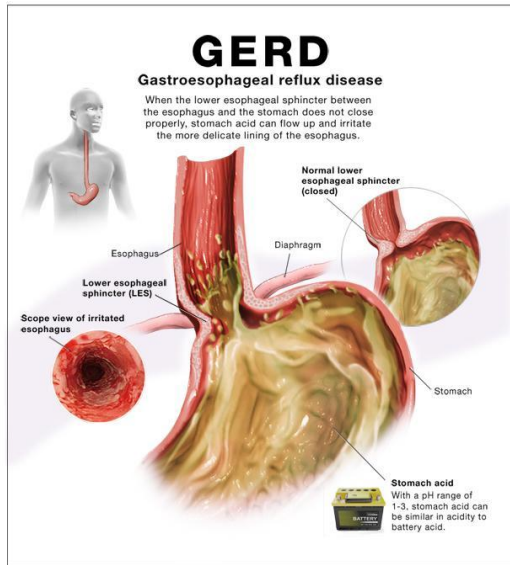
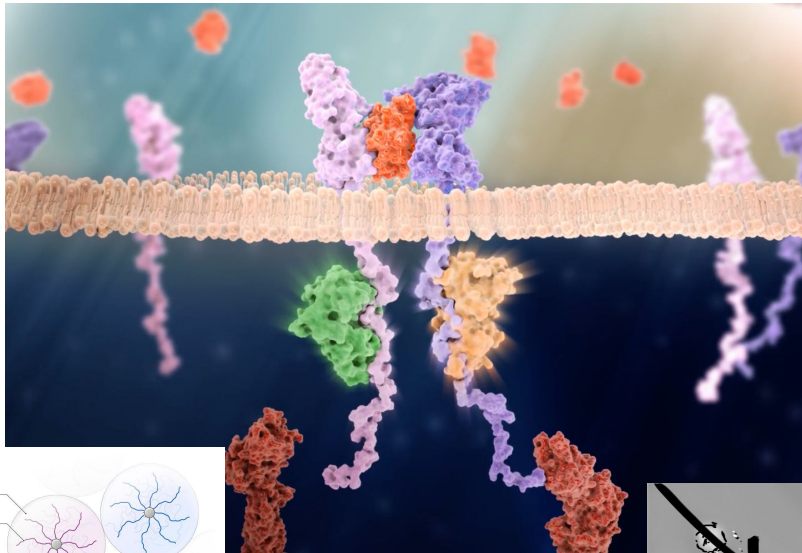
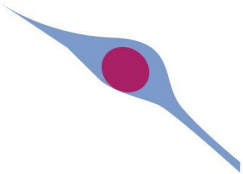


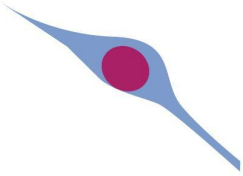
Mapping the Human Body at Single-Cell Resolution: Developing the Human Reference Atlas

Rachel Bajema, Indiana University- Bloomington
Heidi Schlelein, Indiana University- Bloomington



Who are medical illustrators?





What is HuBMAP (The Human BioMolecular Atlas Program)?

- Creating a computable, open-source map of the human body at single-cell resolution
- 18 funded components with over 350 researchers in more than 50 research institutions across the U.S. and Europe
- Initiatives:



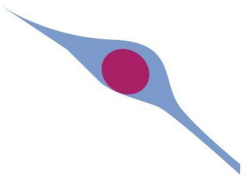
1. ***HuBMAP Integration, Visualization and Engagement:*** Building an atlas tissue maps; tools for visualizing, searching and modeling data; Infrastructure, Engagement and Communications

Indiana University Bloomington > Luddy School of Informatics, Computing, and Engineering > Cyberinfrastructure for Network Science Center (CNS)



Funded by
the NIH
Common
Fund

2. **Rapid Technology Implementation:** Enhancing, large-scale validation, integration of emerging new technologies
3. **Tissue Mapping Centers:** Collect and analyze a range of normal tissues
4. **Transformative Technology Development:** Analyze tissue, validation of new methods for mapping the body at high resolution



Tissue Mapping Centers (TMC)

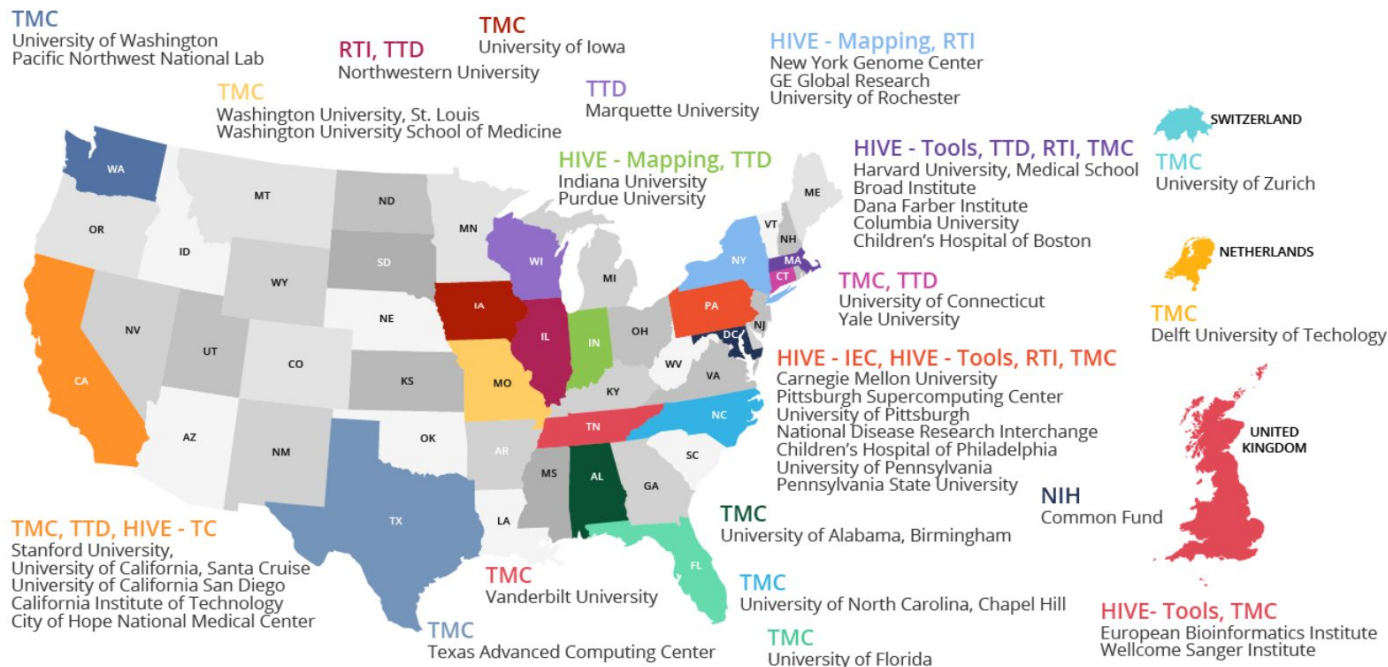
Where data comes from

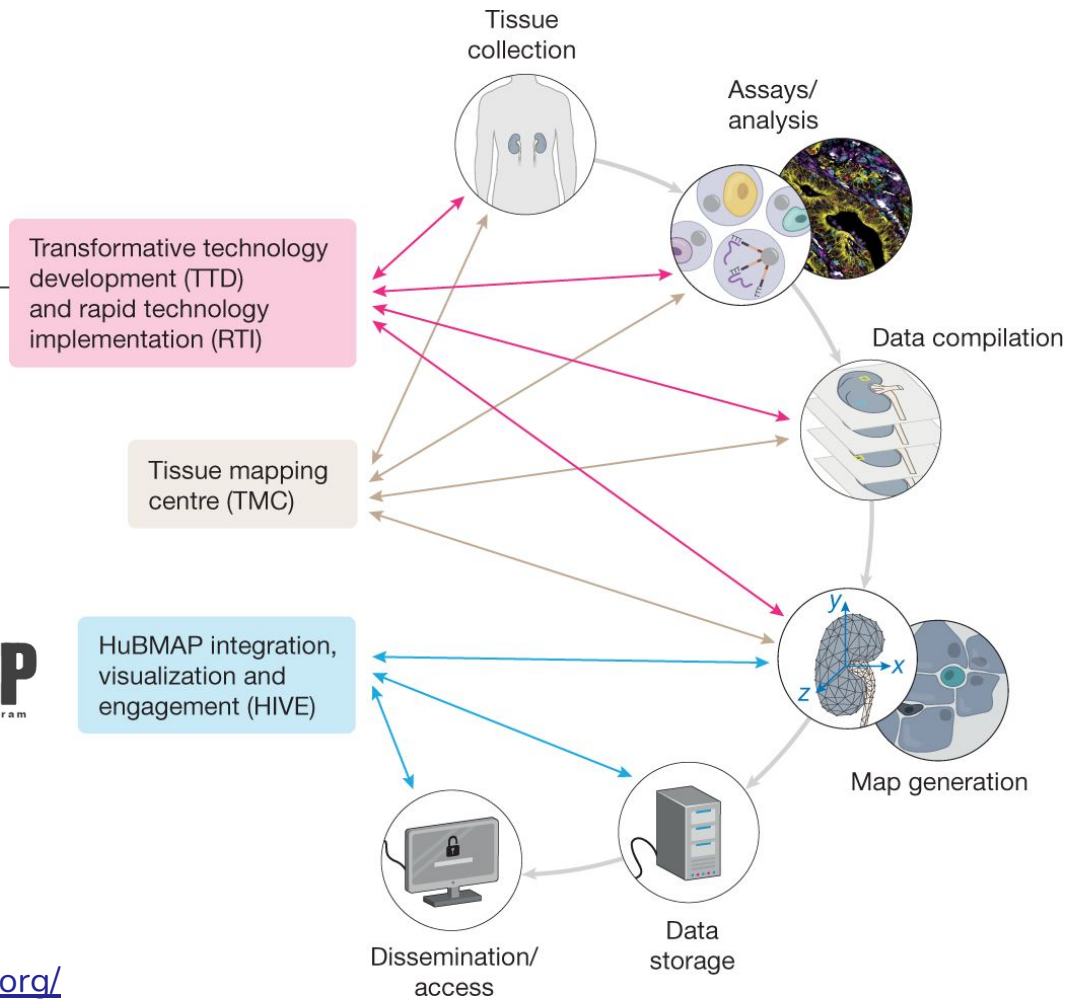
Over 20 different organs from more than 80 donors comprise the samples and datasets (>1000 of each) across 3 main modalities:

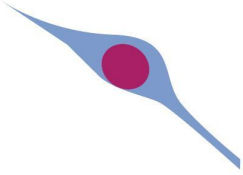
- mass spectrometry
- microscopy
- sequencing

New Assay types are published as they become available.

HuBMAP Contributing Sites

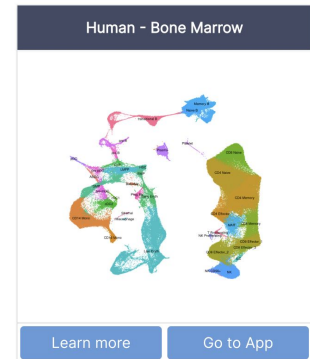
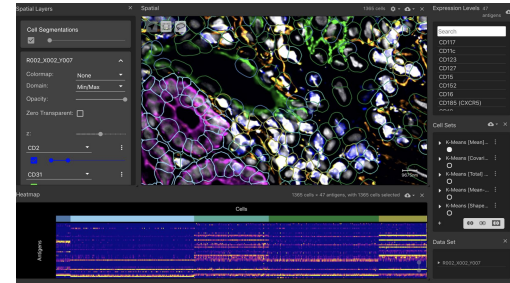
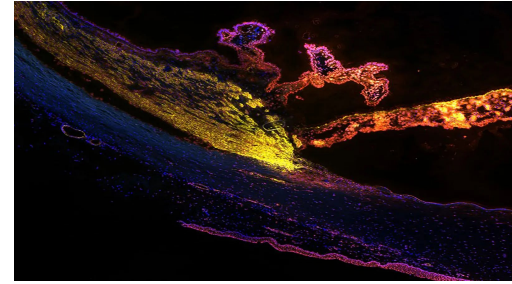






Why another Human Atlas? Why Single-Cell?

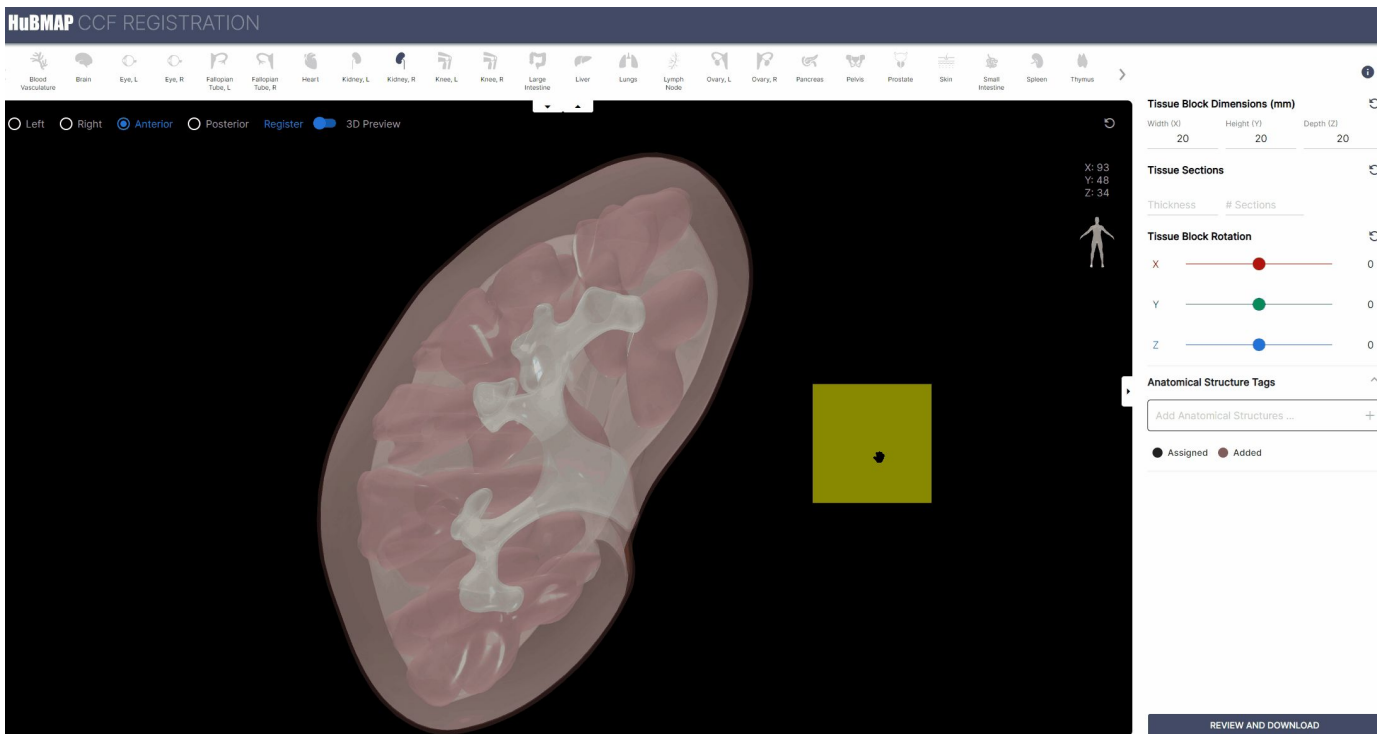
- Our goal is multiscale, multidimensional mapping of the human body from the whole body level to the individual cell
- Now possible to classify cells by their expression profiles (level at which RNA or protein is expressed from each gene)
- Large scale data sets can be interpreted by machine learning and visualization tools to find how cells are related to and interact with each other
- Enables the creation of cellular reference maps of the position, function and characteristics of every cell type in the human body





Registration User Interface (RUI)

A new way to preserve spatial relationships between different tissue samples from around the world into searchable one 3D space



HuBMAP CCF REGISTRATION

Navigation icons: Blood Vasculture, Brain, Eye, L, Eye, R, Fallopian Tube, L, Fallopian Tube, R, Heart, Kidney, L, Kidney, R, Knee, L, Knee, R, Large Intestine, Liver, Lung, Lymph Node, Ovary, L, Ovary, R, Pancreas, Pelvis, Prostate, Skin, Small Intestine, Spleen, Thymus

View controls: Left Right Anterior Posterior Register 3D Preview

Coordinates: X: 93, Y: 48, Z: 34

Tissue Block Dimensions (mm)

Width (X)	Height (Y)	Depth (Z)
20	20	20

Tissue Sections

Thickness	# Sections

Tissue Block Rotation

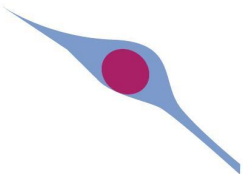
X: 0
Y: 0
Z: 0

Anatomical Structure Tags

Add Anatomical Structures ... +

Assigned Added

REVIEW AND DOWNLOAD



Exploration User Interface (EUI)

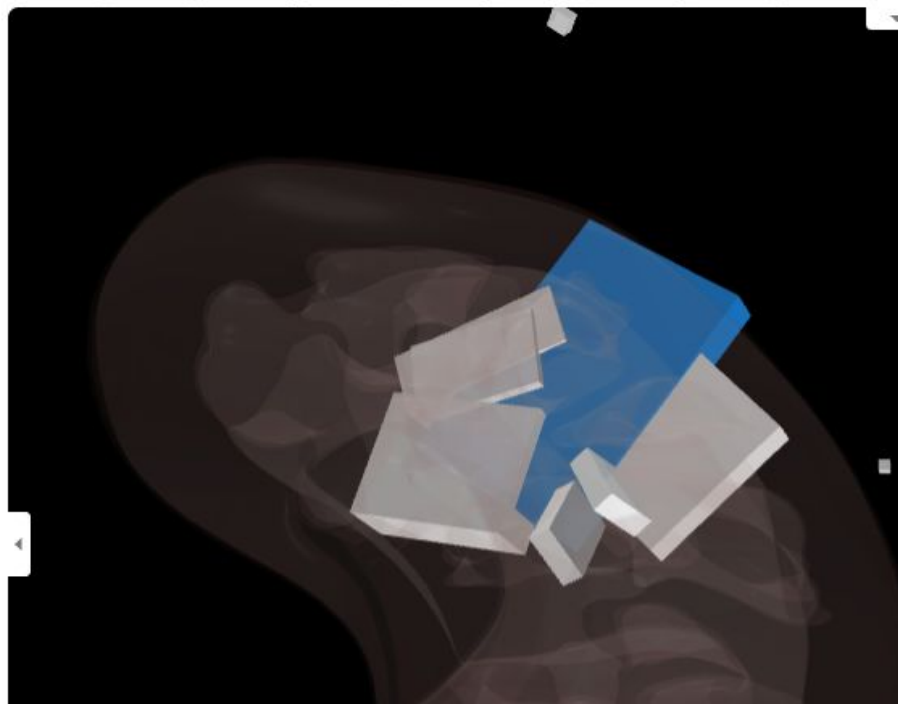
A way to explore the vast amounts of data entered into the RUI

Anyone can access this data

Q Search anatomical structures...

▼ heart	31
^ kidney	72
▼ papilla	16
kidney capsule	33
▼ nephron	0
▼ interstitium	0
^ renal medulla	28
renal pyramid	28
inner medulla of kidney	0
▼ kidney outer medulla outer stripe	0
▼ kidney outer medulla inner stripe	0
▼ vessels	0
▼ renal cortex	32
right kidney	36

Q Search cell types...

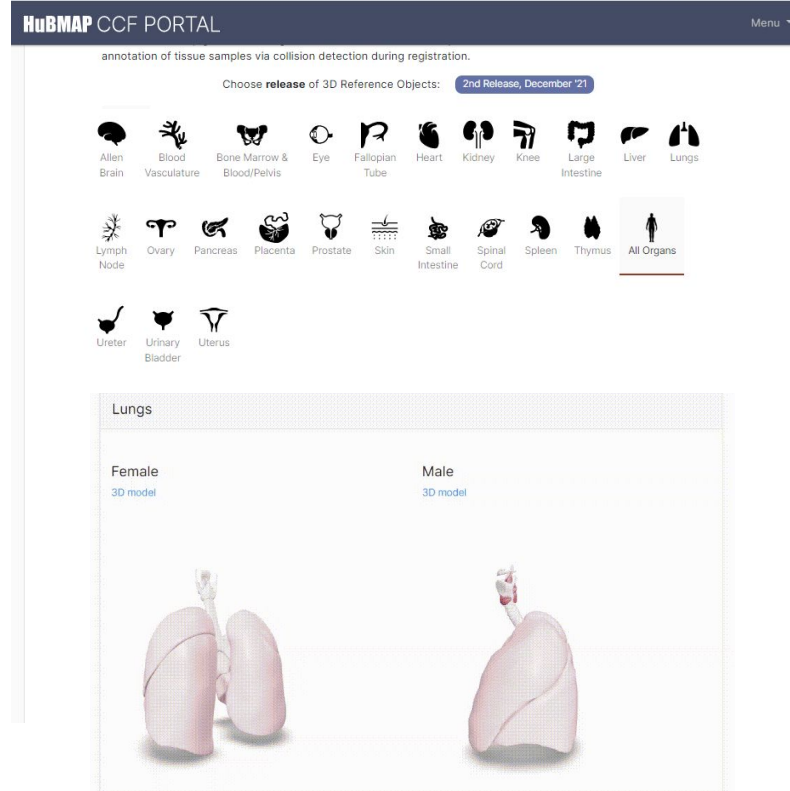




3D Reference Organ Library

Glb and fbx files of all 25 organs centrally located

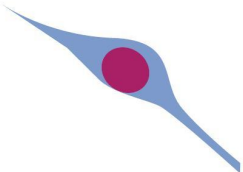
- Free for all to use under Creative Commons license,
- Created for RUI
- Each organ has metadata related to Uberon terms that link to the ASCT+B Table



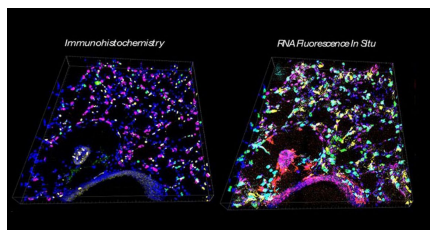
The screenshot displays the HuBMAP CCF Portal interface. At the top, it says "HuBMAP CCF PORTAL" and "Menu". Below that, it indicates "annotation of tissue samples via collision detection during registration." and "Choose release of 3D Reference Objects: 2nd Release, December '21".

The main content area shows a grid of 25 organ icons, each with a label: Allen Brain, Blood Vasculature, Bone Marrow & Blood/Pelvis, Eye, Fallopian Tube, Heart, Kidney, Knee, Large Intestine, Liver, Lungs, Lymph Node, Ovary, Pancreas, Placenta, Prostate, Skin, Small Intestine, Spinal Cord, Spleen, Thymus, Ureter, Urinary Bladder, and Uterus. The "All Organs" icon is highlighted with a red underline.

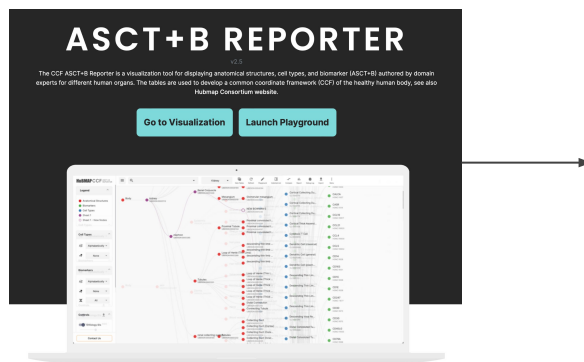
Below the grid, there is a section titled "Lungs" with two sub-sections: "Female 3D model" and "Male 3D model". Each sub-section shows a 3D model of the respective lung.



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



Data from assays/analysis indicates which anatomical structures, cell types and biomarkers are present in a tissue sample



Connected to cell ontology: standard set of research-confirmed cell types

- Forces agreement on terminology and interpretation of data

- Text output (.csv) defines organizational hierarchy (relationships) for each organ

- Organ
- Anatomical structures
- Cell types
- Biomarkers

- Used to define functional tissue units (FTUs) for each organ
- FTUs are related to vascular mapping, a concurrent effort
- FTUs chosen for illustration

Partial ASCT+B table for Large Intestine

AS/4/LABEL	AS/4/ID	AS/4/NOTES	CT/1	CT/1/LABEL	CT/1/ID
colonic epithelium	UBERON:0000397		absorptive	enterocyte of epithelium of large intestine	CL:0002071
colonic epithelium	UBERON:0000397		goblet	large intestine crypt goblet cell	CL:1000321
epithelium of crypt of Lieberkuhn	UBERON:0011184		epithelial stem cell	intestinal crypt stem cell of large intestine	CL:0009016
epithelium of crypt of Lieberkuhn	UBERON:0011184		Paneth	paneth cell of epithelium of large intestine	CL:0009009
epithelium of crypt of Lieberkuhn	UBERON:0011184		neuroendocrine	neuroendocrine cell	CL:0000165
epithelium of crypt of Lieberkuhn	UBERON:0011184		absorptive	enterocyte of epithelium of large intestine	CL:0002071
epithelium of crypt of Lieberkuhn	UBERON:0011184		goblet	large intestine crypt goblet cell	CL:1000321
epithelium of crypt of Lieberkuhn	UBERON:0011184		transient amplifying cell	transit amplifying cell of large intestine	CL:0009011
epithelium of crypt of Lieberkuhn	UBERON:0011184		tuft cell	intestinal tuft cell	CL:0019032
colonic epithelium	UBERON:0000397	Tissue resident lymphocytes; interepithelial lymphocytes	surface intraepithelial CD8+ alpha positive alpha/beta lymphocyte	CD8-alpha-alpha-positive, alpha-beta intraepithelial T cell	CL:0000915
colonic epithelium	UBERON:0000397	Tissue resident lymphocytes; interepithelial lymphocytes	surface intraepithelial CD8+ lymphocyte gamma/delta		CL:0008364
colonic epithelium	UBERON:0000397	Tissue resident lymphocytes; interepithelial lymphocytes	surface intraepithelial CD8+ alpha beta positive alpha/beta lymphocyte	CD8-alpha-beta-positive, alpha-beta intraepithelial T cell	CL:0000796
colonic epithelium	UBERON:0000397	Tissue resident lymphocytes; interepithelial lymphocytes	surface intraepithelial CD4+ lymphocyte	CD4-positive, alpha-beta intraepithelial T cell	CL:0000793
colonic epithelium	UBERON:0000397	Tissue resident lymphocytes; interepithelial lymphocytes	surface intraepithelial CD4-CD8- lymphocyte alpha/beta	CD4-negative, CD8-negative, alpha-beta intraepithelial T cell	CL:0000935
crypt of Lieberkuhn of colon	UBERON:0013485		eosinophil	mature eosinophil	CL:0000041
lamina propria of mucosa of colon	UBERON:0007177		subepithelial membrane		
lamina propria of mucosa of colon	UBERON:0007177		pericryptal fibroblastic sheath		
lamina propria of mucosa of colon	UBERON:0007177		capillary endothelium	capillary endothelial cell	CL:0002144
lamina propria of mucosa of colon	UBERON:0007177		lymphatic endothelium	endothelial cell of lymphatic vessel	CL:0002138
lamina propria of mucosa of colon	UBERON:0007177		pericyte	pericyte cell	CL:0000669
lamina propria of mucosa of colon	UBERON:0007177		myofibroblast	myofibroblast cell	CL:0000186
lamina propria of mucosa of colon	UBERON:0007177		fibroblast	fibroblast	CL:0000057
lamina propria of mucosa of colon	UBERON:0007177		nerve/schwann cell	Schwann cell	CL:0002573
lamina propria of mucosa of colon	UBERON:0007177		ganglion		
lamina propria of mucosa of colon	UBERON:0007177		neuroendocrine cell	neuroendocrine cell	CL:0000165
gut-associated lymphoid tissue	UBERON:0001962		M cell	M cell of gut	CL:0000682
gut-associated lymphoid tissue	UBERON:0001962		B cell	lymphocyte of large intestine lamina propria	CL:0009018
gut-associated lymphoid tissue	UBERON:0001962		CD4+ T cell	lymphocyte of large intestine lamina propria	CL:0009018
gut-associated lymphoid tissue	UBERON:0001962		regulatory CD4+ T cell	lymphocyte of large intestine lamina propria	CL:0009018
gut-associated lymphoid tissue	UBERON:0001962		CD8+ T cell	macrophage	CL:0009018
gut-associated lymphoid tissue	UBERON:0001962		macrophage	macrophage	CL:0000235
gut-associated lymphoid tissue	UBERON:0001962		NK cell	lymphocyte of large intestine lamina propria	CL:0009018
gut-associated lymphoid tissue	UBERON:0001962		ILF lymphatic endothelium	endothelial cell of lymphatic vessel	CL:0002138

Currently more than 25,000 nodes and edges in the ASCT+B knowledge graph

https://docs.google.com/spreadsheets/d/1d_KWKnQq3HT5nzDmfhlvFG4P_qdviu0vyhGZ6QHgNik/edit#gid=2043181688

2D Functional Tissue Unit (FTU) Illustrations

Pancreas islets of Langerhans (0.1 mm)

Pulmonary alveolar parenchyma (0.2 mm)

Renal corpuscle (0.2 mm)

Prostatic glandular acinus (0.2 mm)

Crypt of Lieberkuhn (0.5-0.7 mm)

0.2 mm

Detailed description: This block contains five illustrations of functional tissue units. At the top left is a circular cluster of colorful cells representing the Pancreas islets of Langerhans. Below it is a cluster of pink, sac-like structures representing pulmonary alveolar parenchyma. To the right is a long, narrow, finger-like projection representing a crypt of Lieberkuhn. Below that is a circular structure with a central capillary and surrounding cells representing a renal corpuscle. At the bottom left is a circular glandular structure with a central opening representing a prostatic glandular acinus. A horizontal scale bar labeled '0.2 mm' is positioned at the bottom center of this block.

Liver lobule (1-2.5 mm)

Thymus lobule (0.5-2 mm)

0.5 mm

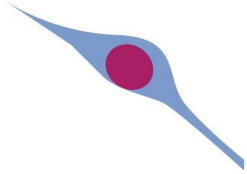
Detailed description: This block contains two illustrations of lobules. The top illustration is a circular liver lobule with a central vein and radiating cords of hepatocytes. Two small inset boxes show histological sections of the liver tissue. The bottom illustration is a triangular thymus lobule with a dense population of small lymphocytes. Two small inset boxes show histological sections of the thymus tissue. A horizontal scale bar labeled '0.5 mm' is positioned at the bottom center of this block.

Nephron tubule (3-5 mm)

1 mm

H

Detailed description: This block contains a large illustration of a nephron tubule, showing a long, branching structure with various segments. Several circular insets show cross-sections of different parts of the tubule. A horizontal scale bar labeled '1 mm' is positioned at the bottom left. At the bottom right is a red circular logo with a white letter 'H' inside.



HuBMAP CCF Portal: where it all lives

Explore and use

Everything is open source- all recreatable,
can be used for any purpose















<https://hubmapconsortium.github.io/ccf/index.html>

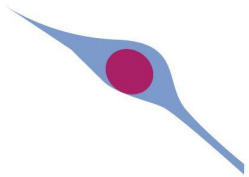


The Human Body Atlas: High-Resolution, Functional Mapping of Voxel, Vector, and Meta Datasets

MC-IU team within the HuBMAP HIVE

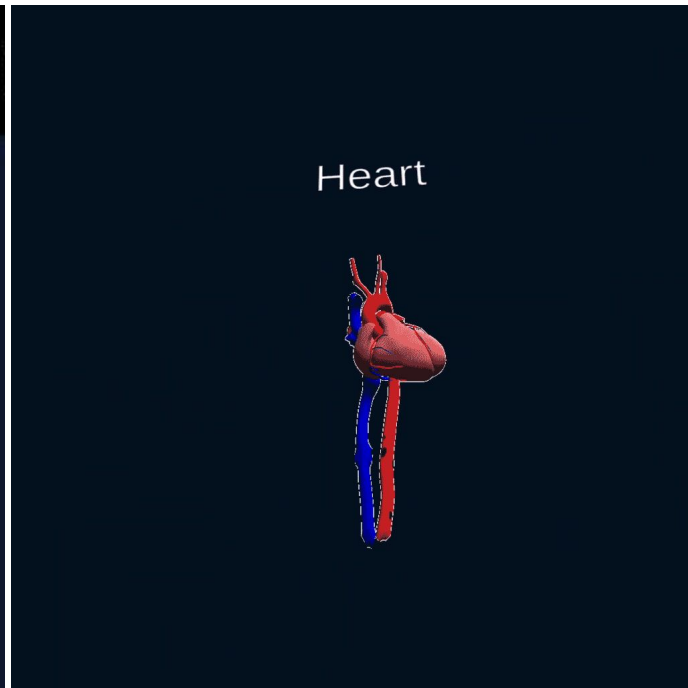
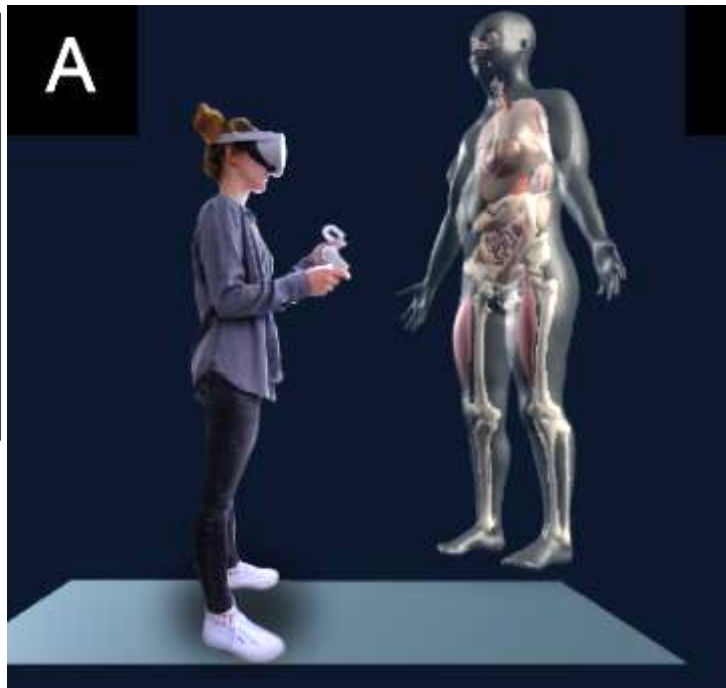
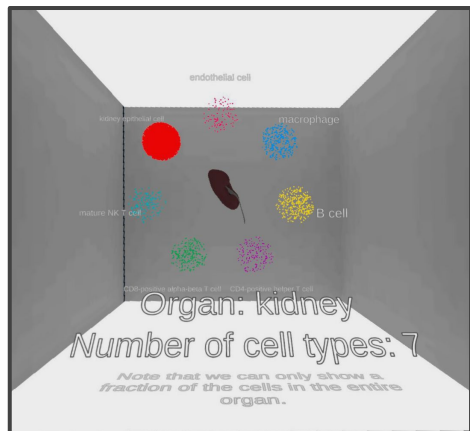
The ultimate goal of the HIVE Mapping effort is to develop a common coordinate framework (CCF) for the healthy human body. This framework will support cataloging different types of individual cells, understanding the functions of and relationships between those cell types, and modeling their individual and collective function. During the initial three years of HuBMAP, the MC-IU team has built many elements of the CCF. We co-organized the construction of ASCT+B Tables and implemented a CCF Ontology. We collaborated with NIAID at NIH on the design of a 3D Reference Object Library. Lastly, we developed three interactive user interfaces. The CCF ASCT+B Reporter supports the authoring and interactive review of ASCT+B Tables. The CCF Registration User Interface (RUI) supports uniform tissue data registration across organs and labs. The CCF Exploration User Interface (EUI) supports exploration of semantically and spatially explicit data—from the whole body to the single cell level. For an introduction to HuBMAP goals, data, and code visit the Visible Human MOOC (VHMOOC).

 CCF Anatomical Structures, Cell Types and Biomarkers (ASCT+B) Tables	 CCF Ontology
 CCF 3D Reference Object Library	 CCF 2D Reference FTU Library
 CCF ASCT+B Reporter	 Organ Mapping Antibody Panels (OMAPs)
 CCF Registration User Interface (RUI)	 ASCT+B Cell Types Data from Azimuth
 CCF Exploration User Interface (EUI)	 Visible Human MOOC (VHMOOC)
 Kaggle Competition and Awards	 HRA Millitome



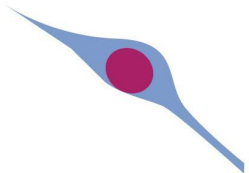
Visual resource

Organ VR Gallery



<https://osf.io/z9gm3/>

For test build: contact Andi Bueckle at abueckle@iu.edu



Visual resource

Vitesse

Principal Investigator:
Nils Gehlenborg

<http://vitesse.io/>



Sections

Summary

Visualization

Provenance

Metadata

Files

Attribution

Dataset

HBM975.NQTF.737

CODEX [Cytokit + SPRM] | Small Intestine

Published | Public Access |

Save

Version 1

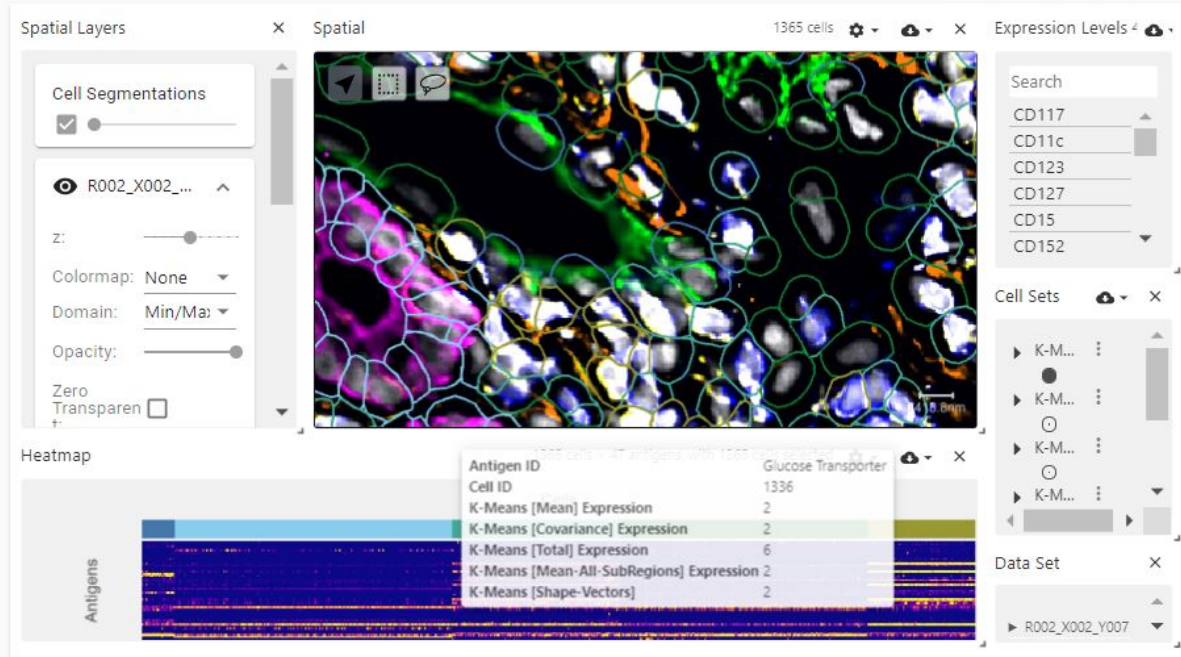
Publication Date

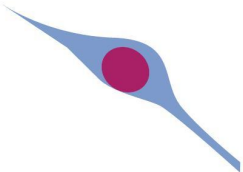
2020-08-22

Modification Date

2020-08-22

Visualization





Visual resource

Vascular Common Coordinate Framework

Vascular Common Coordinate Framework 3D Visualization

Region 10 / Donor 4 Virtual H&E Image Preview

UV Damage

- ✦ DDB2
- ✦ P53

Immune Cells

- Macrophage (CD68+)
- T reg (FOXP3)
- T killer (CD8)
- T helper (CD4)

Proliferation

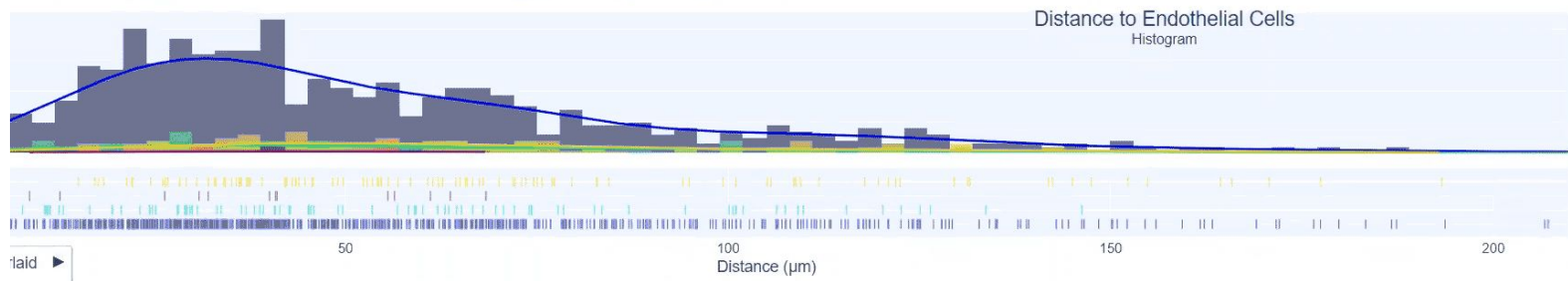
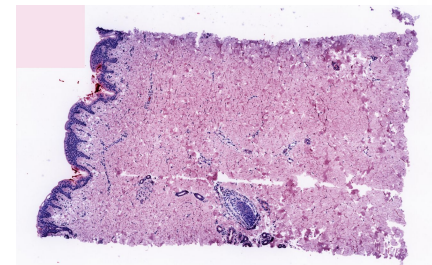
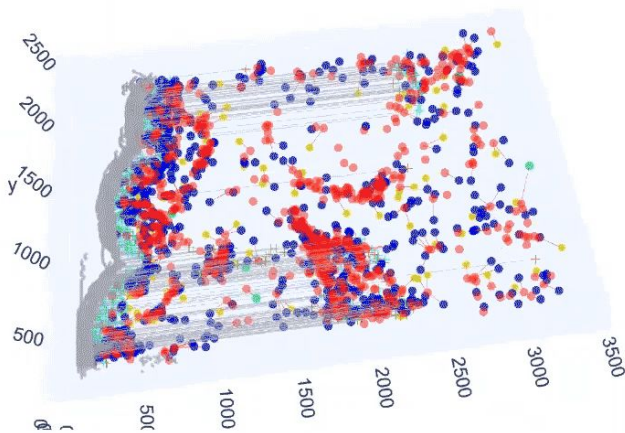
- ✦ Ki67

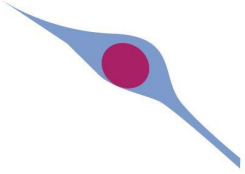
Endothelial & Skin

- Endothelial cell
- Skin surface

Link

- Distance-Endothelial cell
- Distance-Skin surface





Call to action

- All 3D/2D files are open source, available for download
- Take the free [Visible Human MOOC tutorial](#) to learn more
- Explore the [HuBMAP Data Portal](#) and [CCF Portals](#), including the visualization tools
- Contribute to and the [ASCT+B tables](#) for research on anatomical structures, cell types and biomarkers, and their hierarchical relationships
- Register tissues blocks in the RUI
- Become an SMEs/external reviewers of 3D models and FTUs
 - Expert in an human anatomy organ system
 - Work with medical artist to edit and create 3D organs and FTU illustrations

Contact us

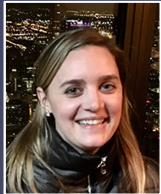
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