Harmonizing KPMP / HuBMAP Data: Developing Novel Common Coordinate Framework User Interfaces

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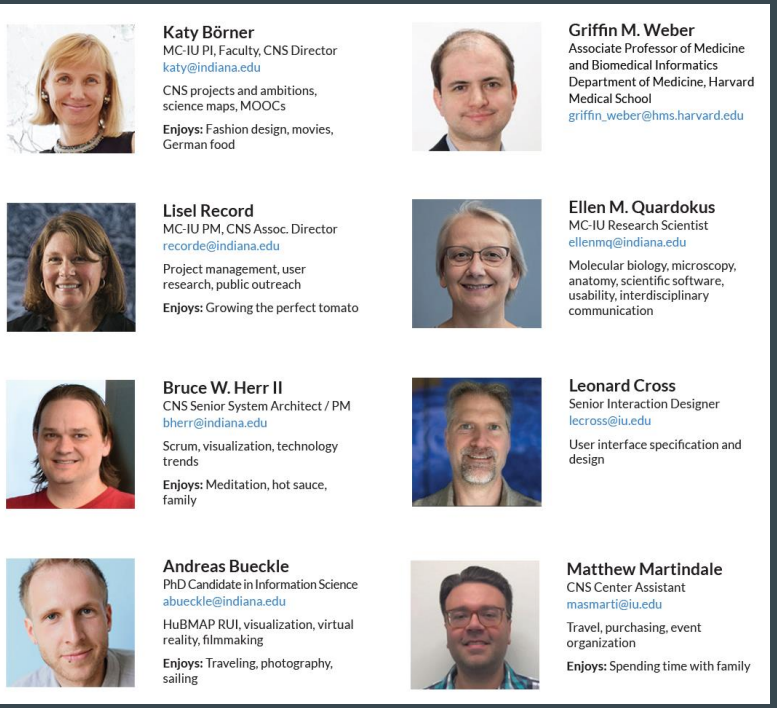
KPMP Virtual Meeting

March 17, 2020



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

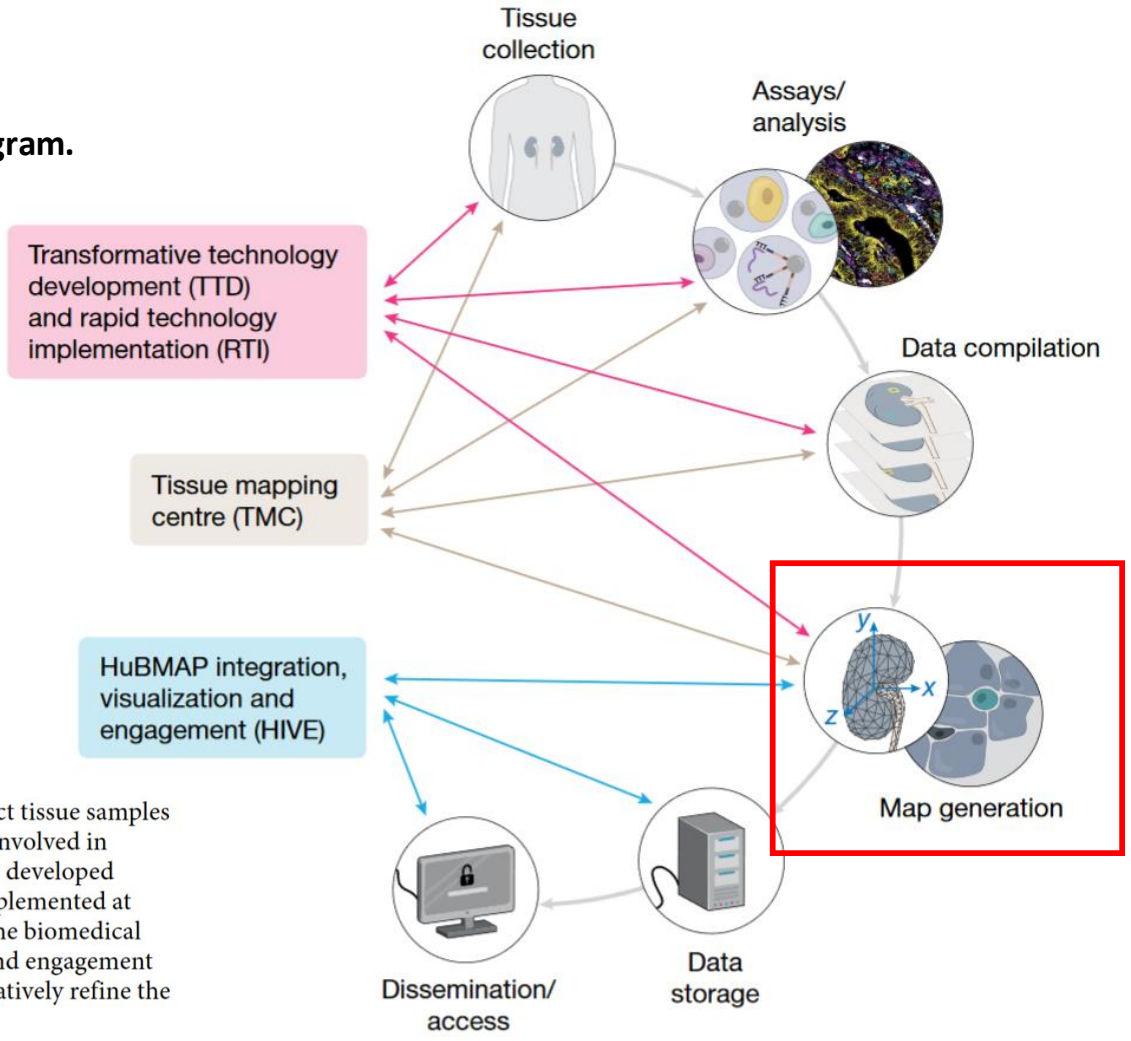


Fig. 1 | The HubMAP consortium. The TMCs will collect tissue samples and generate spatially resolved, single-cell data. Groups involved in TTD and RTI initiatives will develop emerging and more developed technologies, respectively; in later years, these will be implemented at scale. Data from all groups 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.

Landmarks are

- **Anatomical structures**
- **Biomolecular markers**

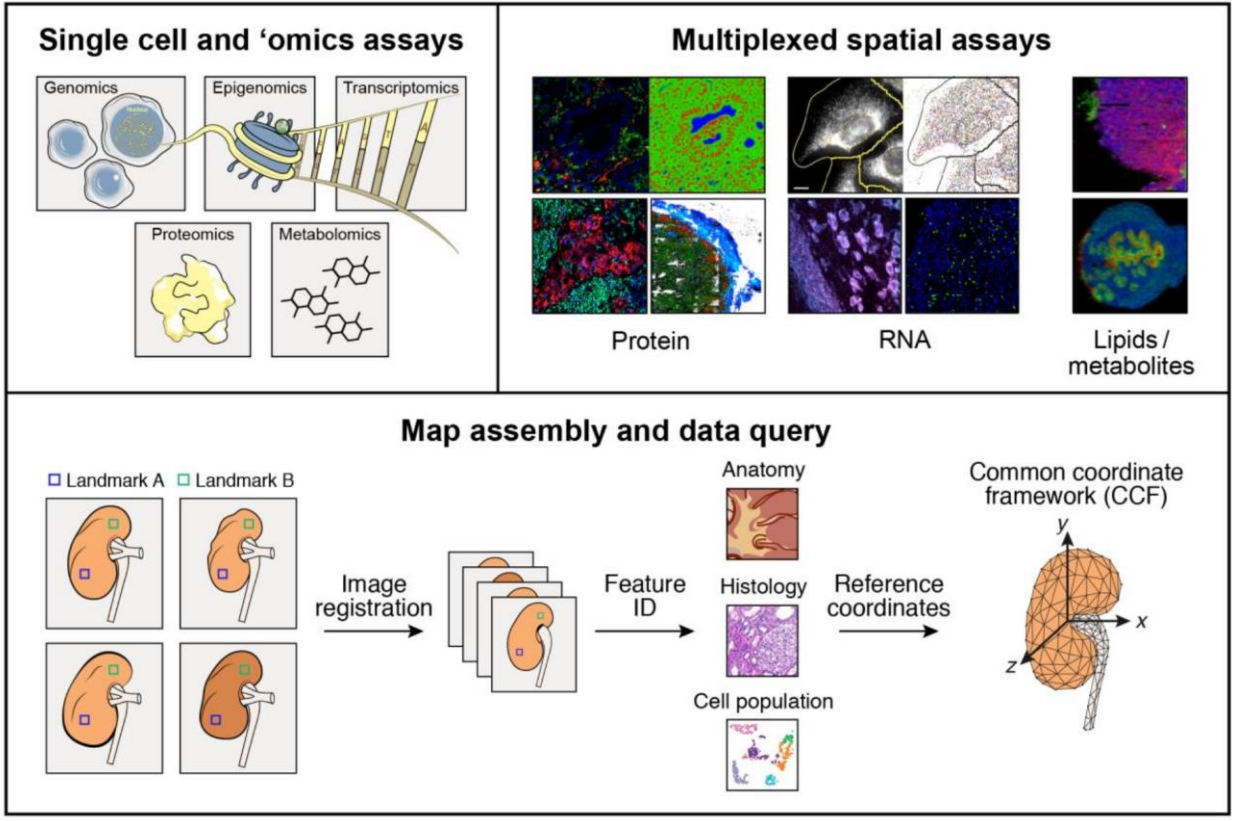
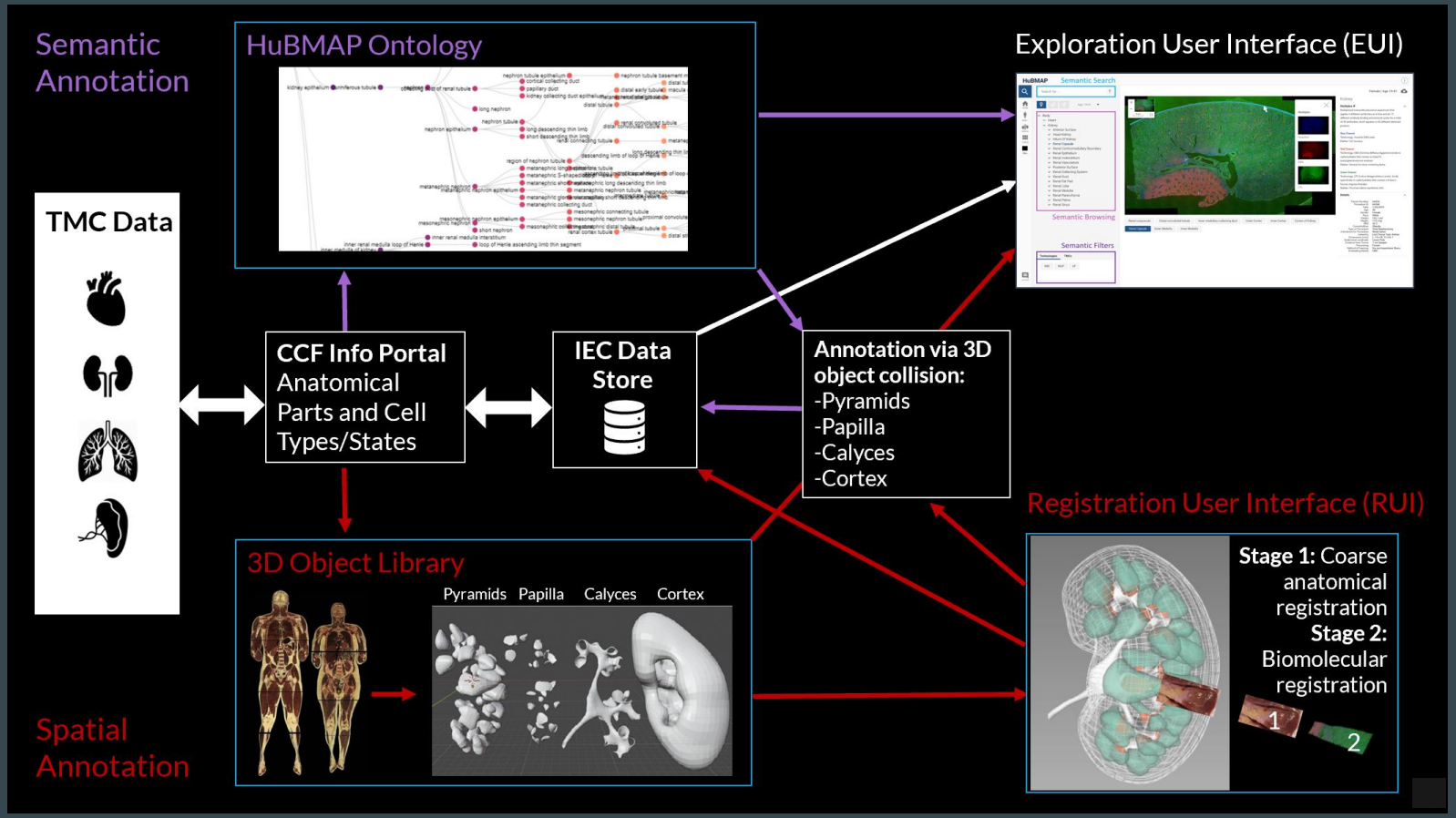


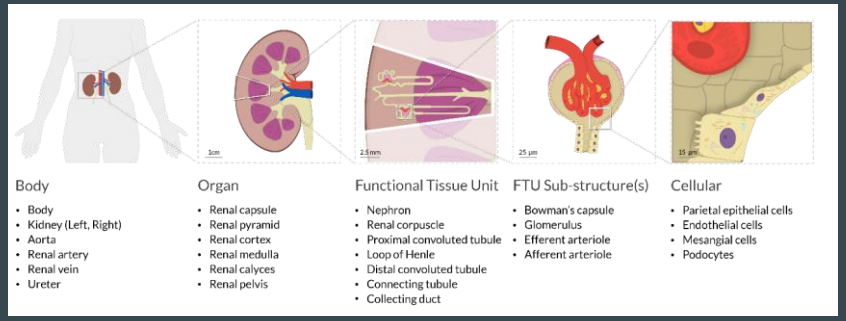
Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic,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

MC-IU: CCF Registration to CCF Exploration Workflow

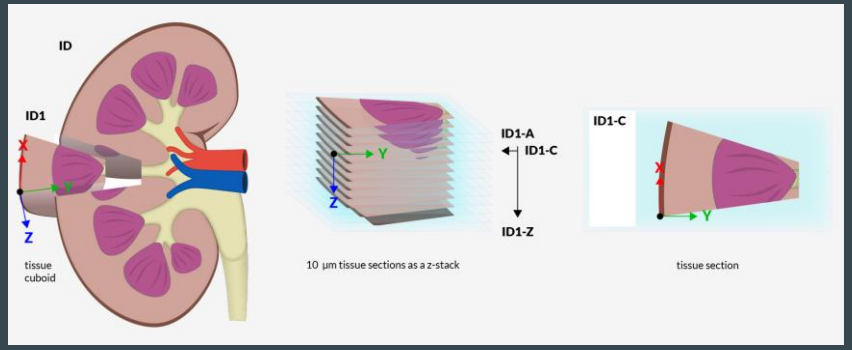


MC-IU: Common Coordinate Framework (CCF)

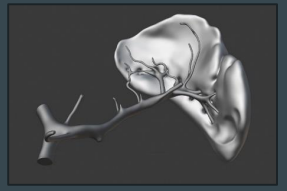
A common coordinate framework (CCF) is a conceptual and computational framework for the storage, analysis, and (visual) exploration of spatially and semantically indexed data---across individuals, technologies, labs.



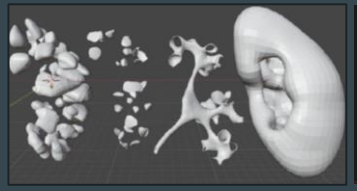
Semantic zoom from whole human body, to organ, to functional tissue units (FTUs), to single-cell level.

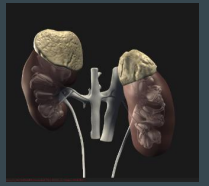


Three-step spatial registration of single cells in relation to reference organs.



VH Spleen





VH Kidney

MC-IU: CCF Relevant Metadata

HuBMAP

HuBMAP CCF Information Portal

This portal links to information that is critical for constructing Common Coordinate Frameworks (CCFs) for the National Institutes of Health Human Biomolecular Atlas Program (HuBMAP).

The information was provided by individual organ-specific Tissue Mapping Centers (TMCs), Transformative Technology Development (TTD), or Rapid Technology Implementation (RTI) efforts in close collaboration with the Mapping Component at Indiana University (MC-IU).

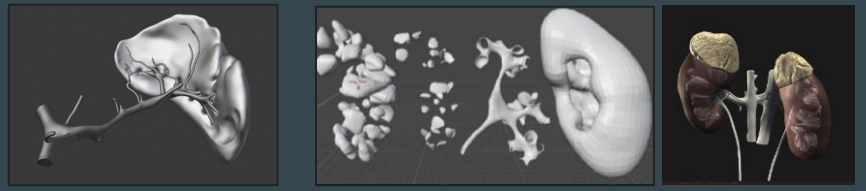
For questions, please contact MC-IU via infoccf@indiana.edu.

Organ	TMC	Technology
Kidney	TMC-Vanderbilt	MALDI Imaging Mass Spectrometry (MALDI IMS) LC-MS
Kidney	TTD-Purdue	nanoDESI IMS LC-MS
Kidney	TMC-UCSD	SNARE-seq2: snRNAseq SNARE-seq2: Chromatin Accessibility seq Bulk RNA-seq
Spleen	TMC-Caltech-UW	seq-FISH
Spleen	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell (sc) RNA-Seq 10x Genomics
Heart	TMC-Caltech-UW	seq-FISH
Lung	TMC-UCSD	Bulk RNA-seq SNARE-Seq2: snRNAseq SNARE-Seq2: Chromatin Accessibility seq
Large Intestine	TMC-Stanford	CODEX Bulk RNA-seq Bulk ATAC-seq Bulk Whole Genome Sequencing (WGS) Metabolomics/Lipidomics
Small Intestine	TMC-Stanford	CODEX snRNA-seq Bulk RNA-seq Bulk ATAC-seq scATAC-seq Bulk Whole Genome Sequencing (WGS) Metabolomics/Lipidomics
Small Intestine	TMC-Caltech-UW	SeqFISH
Bladder	TMC-UCSD	SNARE-seq2: Chromatin Accessibility seq
Ureters	TMC-UCSD	SNARE-seq2: Chromatin Accessibility seq
Thymus	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell (sc) RNA-Seq 10x Genomics
Lymph Nodes	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell (sc) RNA-Seq 10x Genomics

Information critical for CCF design but not yet captured in the data on Globus is documented in the CCF Info Portal.

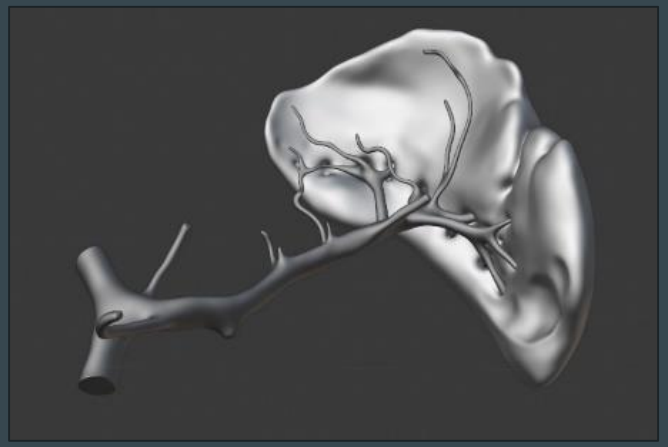
The CCF Info Portal also captures details for the CCF reference organs. Completed organs, approved by TMC organ experts:

- Kidney (left and right) for male and female Visible Human
- Spleen for male and female Visible Human



Anatomical and cell type data from the anatomical structures and cell types (ASCT) tables for the kidney and spleen have been linked to UBERON, Foundational Model of Anatomy (FMA), Kidney Tissue Anatomy Ontology (KTAO), and Cell Ontology (CL).

MC-IU: CCF Object Library



3D models by Kristen Browne, NIH. Rendering by MC-IU.

File Formats

Basic image/object: OME-Tiff (raster) and OBJ (vector)

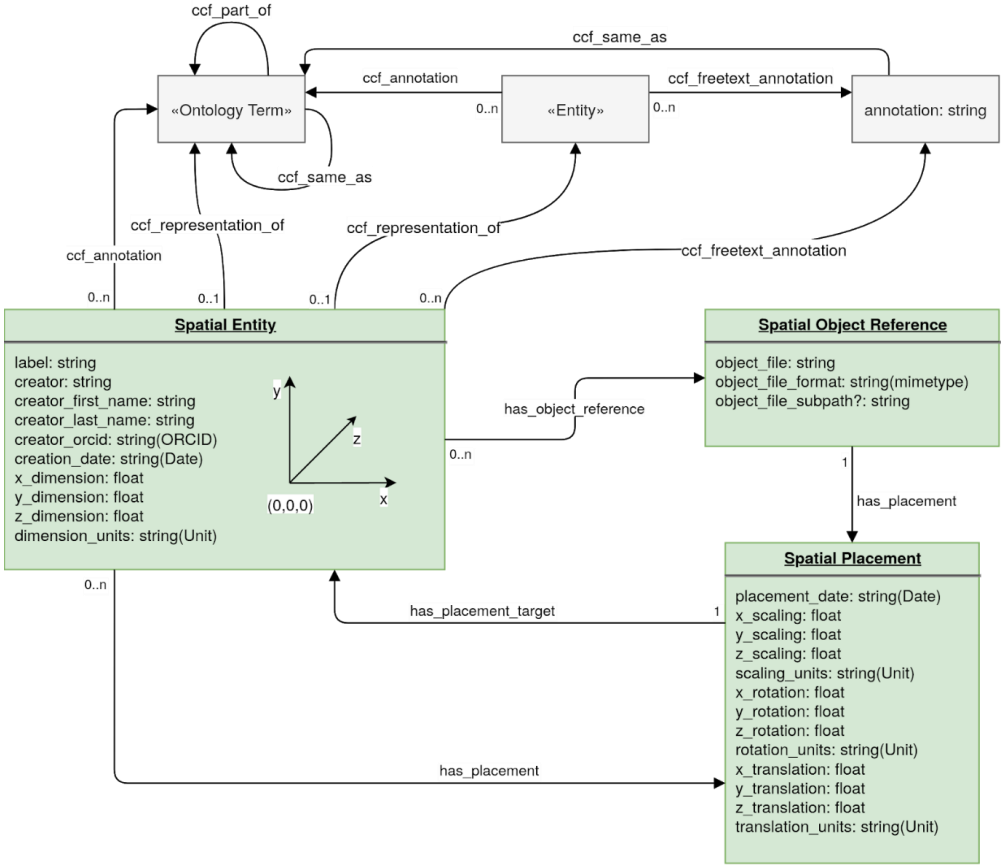
Regions: SVG annotations for 2D, OBJ regions in 3D (aligned with reference model for the organ)

Reference Organs

Kidney: Male and female kidneys from NLM VH
ImageVU 5/50/500 kidneys by Dec. 2019/Feb. 2020/June 2020

Lung: Lung D175 (June 2020)

MC-IU: ER Diagram of CCF Core Model

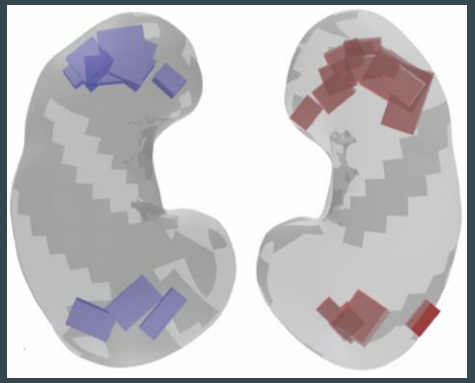


Current sources of ontology terms are: UBERON, Foundational Model of Anatomy (FMA), Kidney Tissue Anatomy Ontology (KTAO), and Cell Ontology (CL).

http://purl.org/ccf/latest/ccf.owl

- body
  - heart
  - kidney
    - renal pelvis
      - right renal pelvis
      - metanephric renal pelvis
      - mucosa of renal pelvis
      - kidney calyx
      - renal papilla
      - left renal pelvis
      - perihilar interstitium
      - kidney pelvis smooth muscle
      - kidney pelvis urothelium
    - renal parenchyma
      - cortex of kidney
    - kidney vasculature
      - kidney blood vessel

MC-IU: CCF Metadata Captured

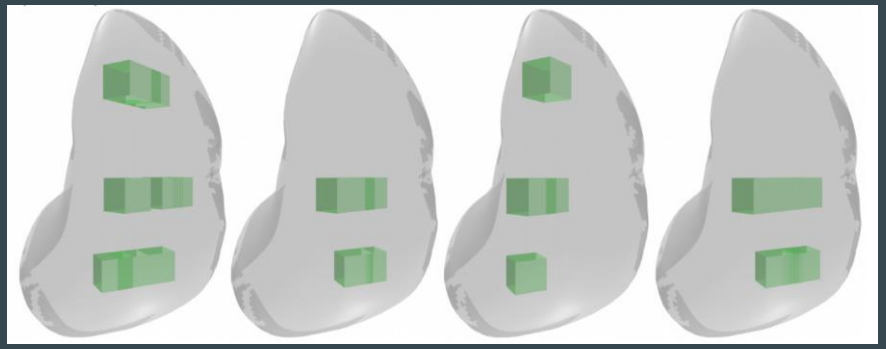


Kidney: right left

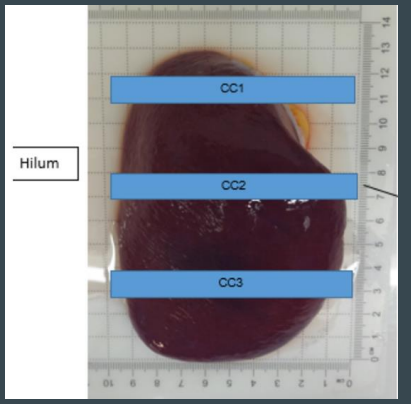
Kidney data by VU:
25 tissue cuboids were registered using the RUI. Data is on Globus.

Spleen data by UFL:
Data comes from 4 spleens. There exist 3 sampling sites (CC1-CC3).
Each CC is subdivided into 6 cuboids. 24 cuboids were registered.

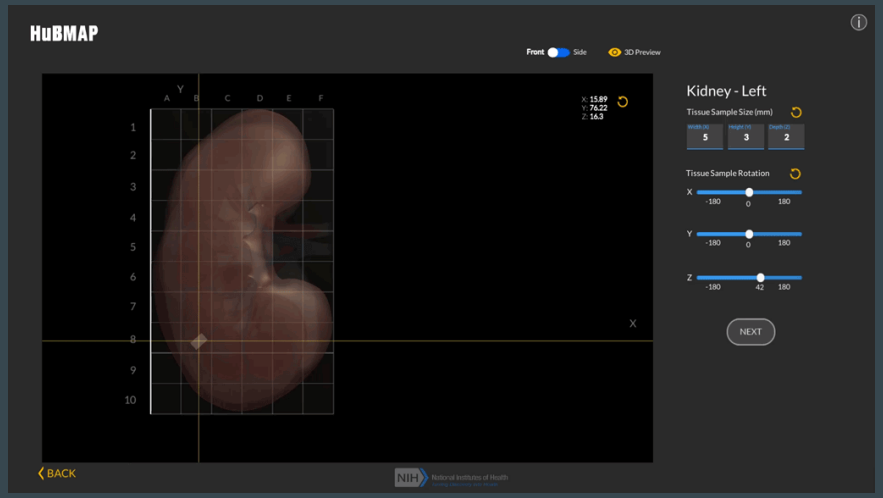
All 25 + 24 = 49 cuboid registrations were confirmed with TMC experts.

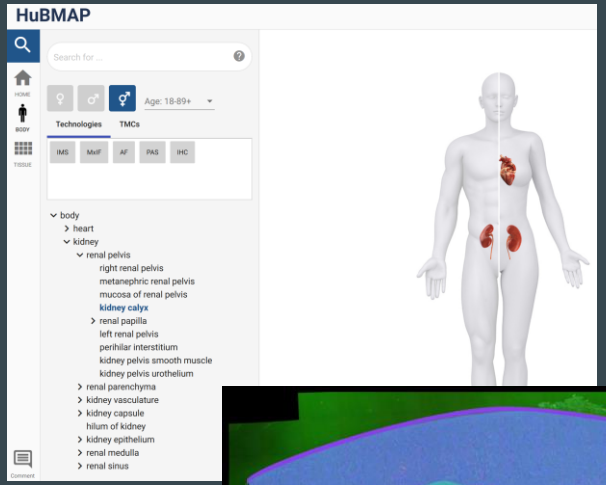


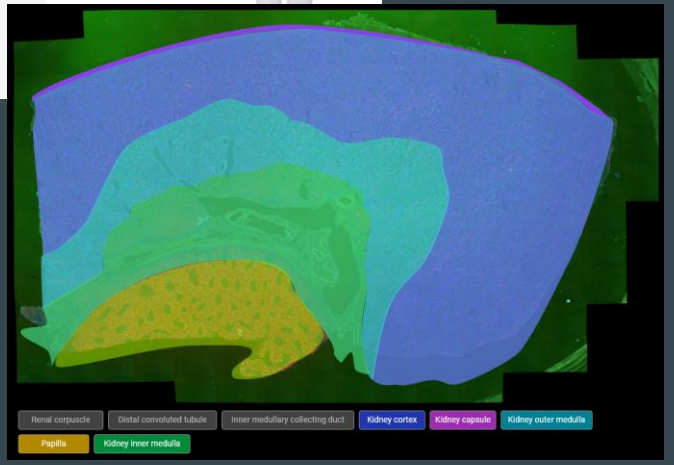
Spleen: UFL0001 UFL0002 UFL0003 UFL0004



MC-IU: CCF Registration UI (RUI) and Exploration UI (EUI)



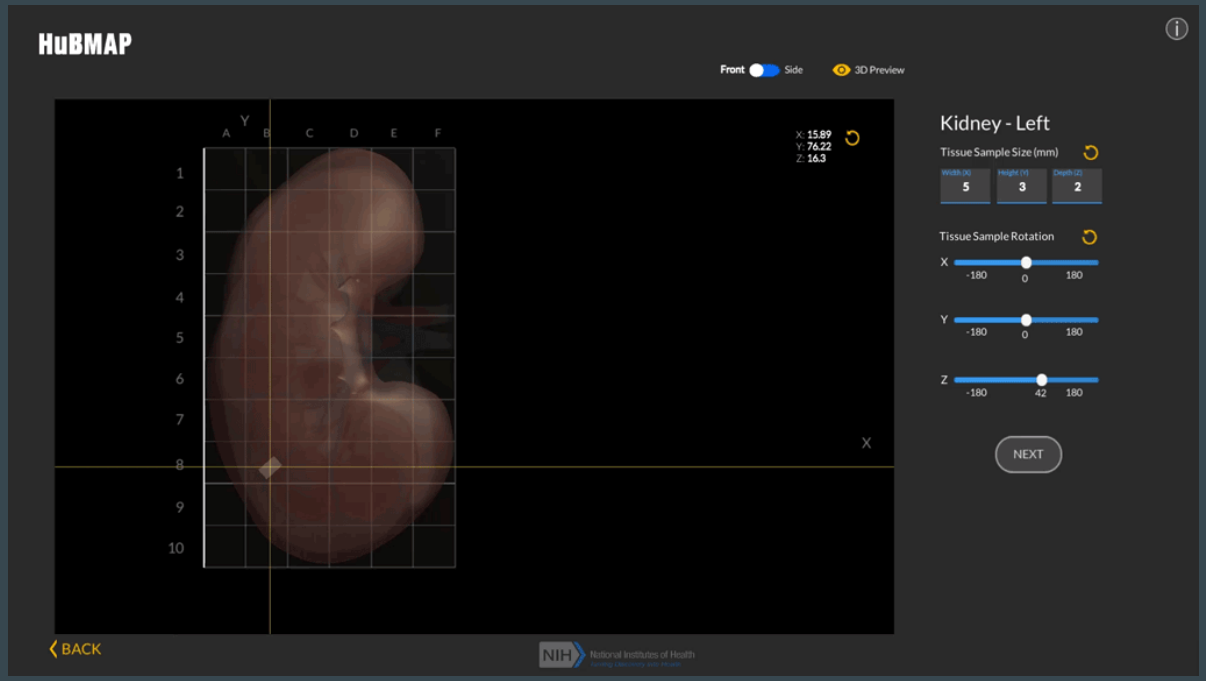




RUI was designed for experts that collect human tissue and need to document the tissue extraction site.
https://hubmapconsortium.github.io/ccf-3d-registration

EUI makes it possible to explore 2D/3D tissue samples semantically and spatially across multiple scales.
https://hubmapconsortium.github.io/ccf-ui/

CCF Registration UI (RUI) DEMO



Registration UI: https://hubmapconsortium.github.io/ccf-3d-registration
RUI Tutorial: https://www.youtube.com/watch?v=-ABy5IeCEk4
RUI Tech Demo: https://www.youtube.com/watch?v=E8GGcpPsohc
RUI Semantic Annotation Using Colission Dectection: https://www.youtube.com/watch?v=6SLqUBEJALE

Acknowledgements

HuBMAP Consortium (https://hubmapconsortium.org)

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NSF

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