

# Multi-Level, Multi-Modal CCF UIs for Data Providers and Users within the [Human BioMolecular Atlas Program \(HuBMAP\)](#)

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Y2/Q1 Demo Day, Stanford University

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# HIVE MC-IU Summary

## Y2 Q1 Progress Report

- A1.Q1.M1: Develop preliminary metadata specification for the CCF UIs and submit to TMCs for comments.
- A2.Q1.M1: Develop Tissue Registration UI v0.5.0
- A3.Q1.M1: Run User Studies on CCF UI v0.5.0
- A3.Q1.M2: Identify VHMOC Topics and Timeline; Record PI Interviews at HuBMAP meeting in September.
- A4.Q1.M1.a: Plan next CCF Workshop
- A5.Q1-M1.b: Collaborate with MC-NYGC on developing mapping tools to support Consortium data releases, TCs on integration of maps with the data portal, and IEC for the infrastructure needed for CCF and CCF UIs.

# Y1 Q3 Result – CCF Data & Metadata

MC-IU has released “HuBMAP Data and Metadata Formats for the Common Coordinate Framework (CCF) Exploration and Registration User Interfaces”

Shared with the HuBMAP consortium

<https://tiny.cc/ccf-data>

All questions and comments are welcome.

**WANTED: Comments**

## HuBMAP Data and Metadata Formats for the Common Coordinate Framework (CCF) Exploration and Registration User Interfaces

Authors: James Sluka, Bruce Herr II, Ellen Quardokus, Katy Borner, Andreas Bueckle, Leonard Cross, MC-IU, HIVE, HuBMAP

Version: 13 Sep. 2019

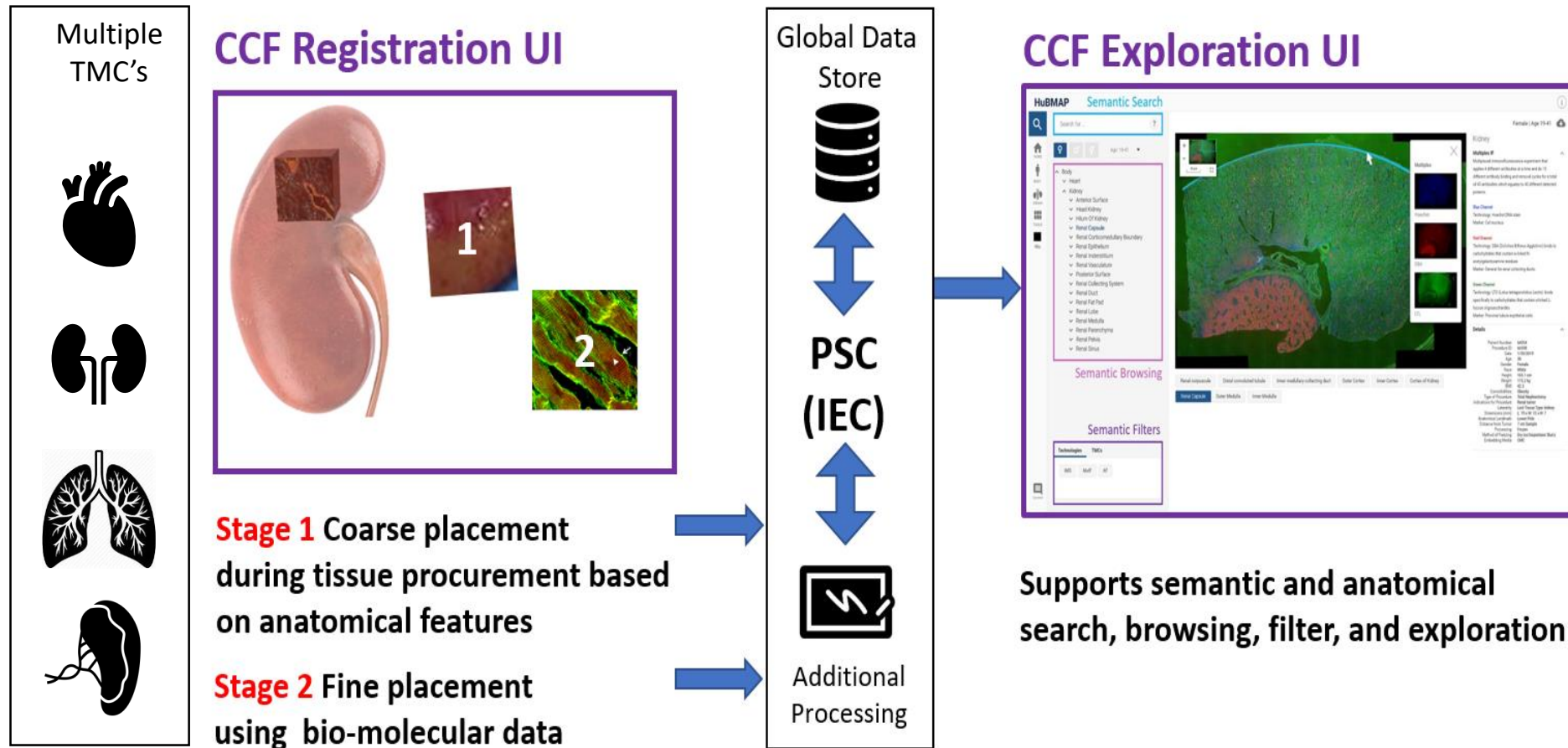
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### Introduction

Here we focus on the CCF required SUBSET of all data and metadata. We are primarily concerned with what data the CCF Registration User Interface (RUI) and the CCF Exploration UI (EUI) will need and what format that data will have. This specification is for the data and metadata formats for the EUI shown on the right side of the “CCF Data Store” Figure 1 below. In addition, we specify the data returned by the registration user interface (RUI), shown in the upper left of Figure 1.

# CCF Registration & Exploration UIs



# Y1 Q3 Result - CCF Exploration User Interface

**HuBMAP Semantic Search**

Search for ... ?

Female | Age 19-41

**Body**

- Heart
- Kidney**
  - Anterior Surface
  - Head Kidney
  - Hilum Of Kidney
  - Renal Capsule**
  - Renal Corticomedullary Boundary
  - Renal Epithelium
  - Renal Interstitium
  - Renal Vasculature
  - Posterior Surface
  - Renal Collecting System
  - Renal Duct
  - Renal Fat Pad
  - Renal Lobe
  - Renal Medulla
  - Renal Parenchyma
  - Renal Pelvis
  - Renal Sinus

**Semantic Browsing**

Renal corpuscule | Distal convoluted tubule | Inner medullary collecting duct | Outer Cortex | Inner Cortex | Cortex of Kidney

Renal Capsule | Outer Medulla | Inner Medulla

**Semantic Filters**

Technologies | TMCs

IMS | MxIF | AF

**Kidney**

**Multiplex IF**

Multiplex

Hoechst

DBA

LTL

**Blue Channel**

Technology: Hoechst DNA stain  
Marker: Cell nucleus

**Red Channel**

Technology: DBA (Dolichos Biflorus Agglutinin) binds to carbohydrates that contain a-linked N-acetylgalactosamine residues  
Marker: General for renal collecting ducts.

**Green Channel**

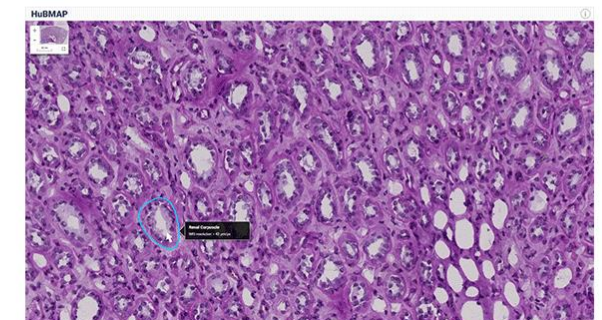
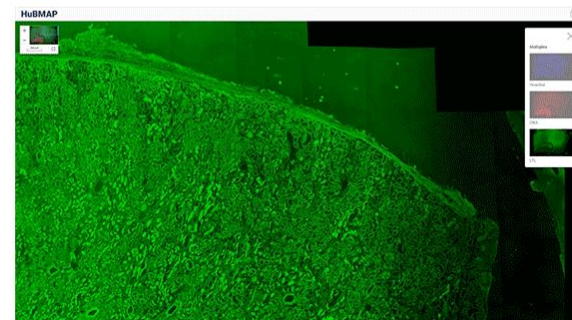
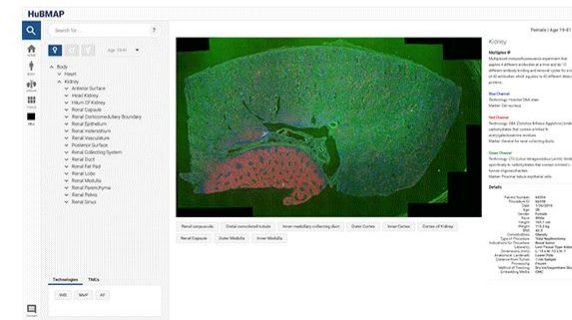
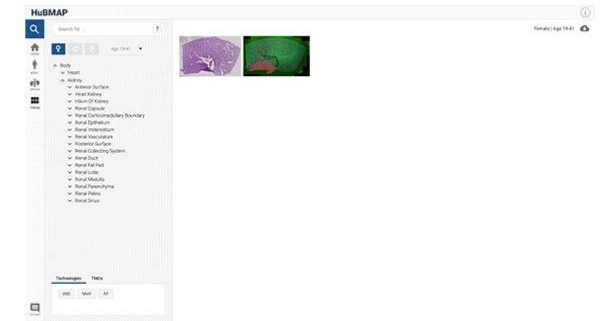
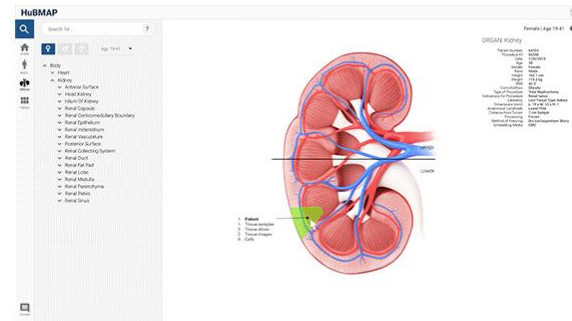
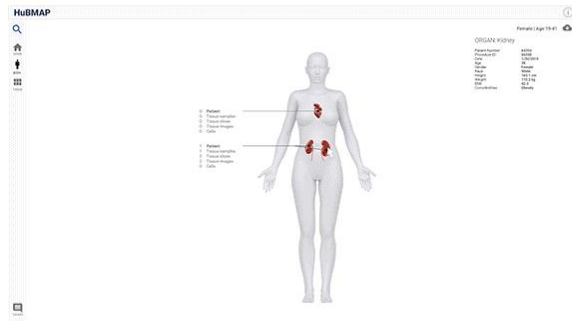
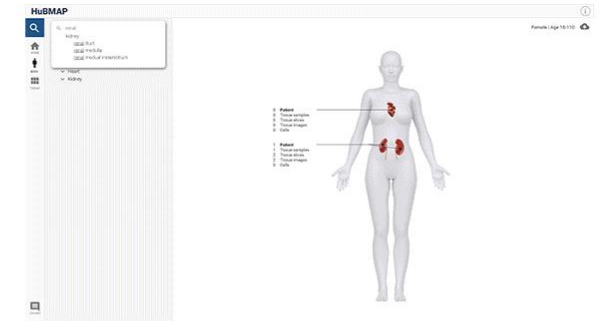
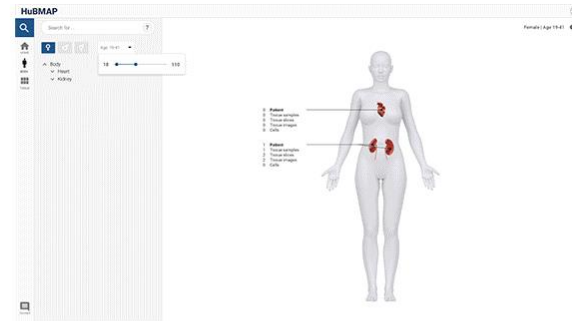
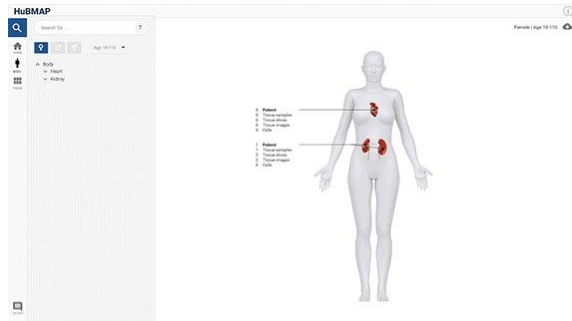
Technology: LTO (Lotus tetragonolobus Lectin) binds specifically to carbohydrates that contain a-linked L-fucose oligosaccharides  
Marker: Proximal tubule epithelial cells

**Details**

Patient Number:	64354
Procedure ID:	66598
Date:	1/30/2019
Age:	38
Gender:	Female
Race:	White
Height:	165.1 cm
Weight:	115.2 kg
BMI:	42.3
Comorbidities:	Obesity
Type of Procedure:	Total Nephrectomy
Indications for Procedure:	Renal tumor
Laterality:	Left Tissue Type: kidney
Dimensions (mm):	L: 19 x W: 13 x H: 7
Anatomical Landmark:	Lower Pole
Distance from Tumor:	7 cm Sample
Processing:	Frozen
Method of Freezing:	Dry ice/Isopentane Slurry
Embedding Media:	CMC

GitHub demo site: <https://hubmapconsortium.github.io/ccf-ui/>

# Y1 Q3 Result - CCF Exploration User Interface



# Y1 Q3 Result - CCF Exploration User Interface

MC-IU has released CCF user interface v0.5.0, a proof-of-concept version of the CCF UI.

The user interface supports:

- Visual browsing of tissue samples and metadata at the whole body, organ, tissue, and cell level.
- Filtering by metadata (age, gender, TMC, and technology), results are presented at all views.
- Submission of questions and comments on the CCF UI.
- Semantic search by ontology, results are presented at all levels.
- Data download at the whole body, organ, tissue, and cell level, i.e., link to <https://sampledata.hubmapconsortium.org>.

See also:

Recorded demo: [https://www.youtube.com/watch?v=rWMqKQc\\_00w&feature=youtu.be](https://www.youtube.com/watch?v=rWMqKQc_00w&feature=youtu.be)

GitHub link to code: <https://github.com/hubmapconsortium/ccf-ui>

GitHub demo site: <https://hubmapconsortium.github.io/ccf-ui/>

Original specs: <https://drive.google.com/open?id=1tqUzmVLxwqcGprtRlevfY86YvHHPEsDR>

# Y2 Q1 Result - CCF Registration User Interface

MC-IU has released the CCF Registration User Interface (RUI) v0.5.0 prototype

The user interface supports:

- Registration of tissue samples in human kidney
- Collection of alignment operator name, date, UUID, etc.
- Tissue slice dimensions
- Copy + paste of JSON file
- Usage via web browser

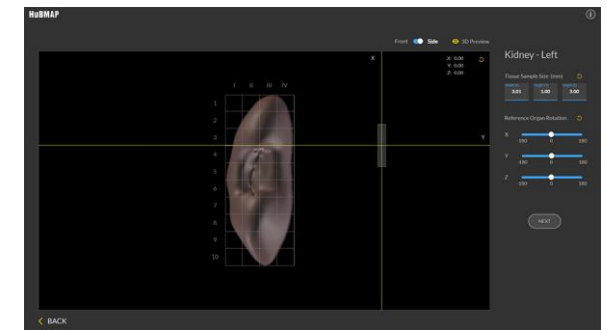
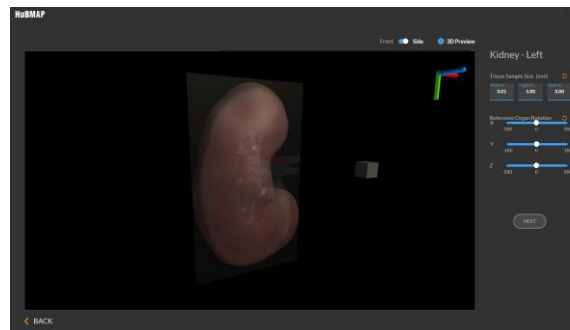
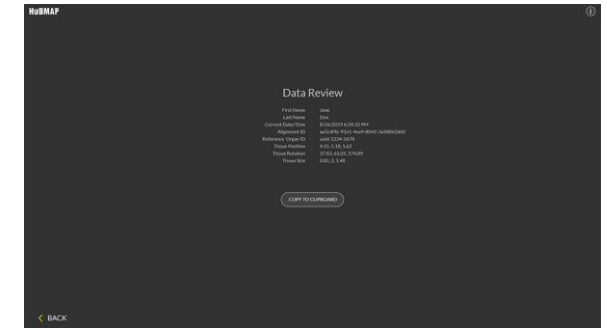
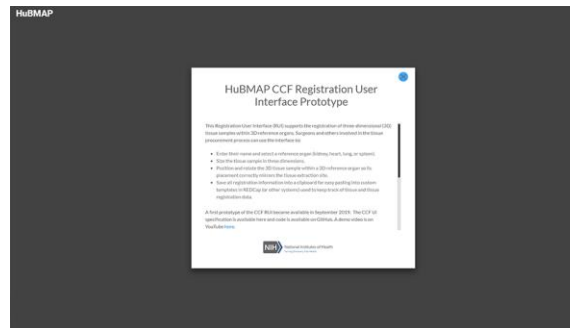
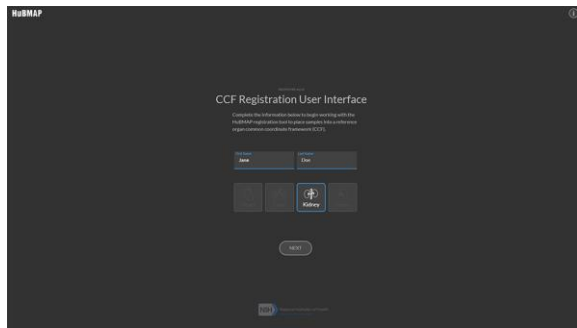


RUI Intro Page. Prototype built using Unity 3D.



# Y2 Q1 Result - CCF Registration User Interface

## RUI SCREENS

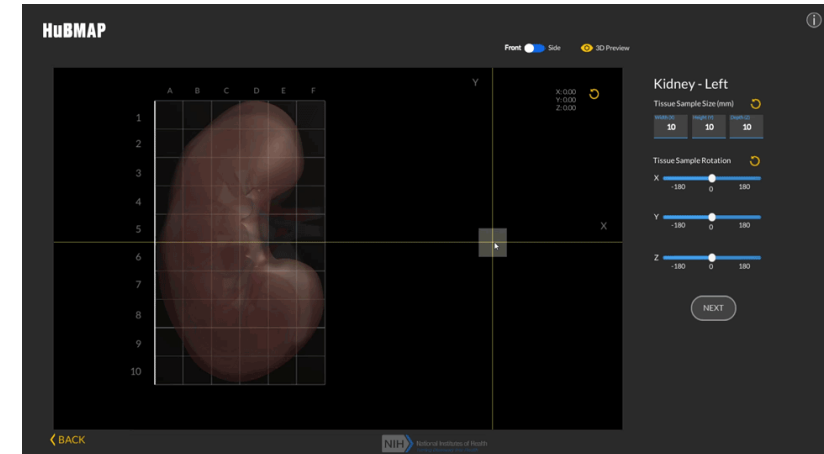


Link to RUI Prototype v0.5.0: <https://hubmapconsortium.github.io/ccf-3d-registration/>

# Y2 Q1 Result - CCF Registration User Interface

## USER STUDIES

Working with HuBMAP partners to gather UX insights we registered five (5) samples through the RUI prototype. Insights from the recorded Zoom sessions are helping us produce future refinements.

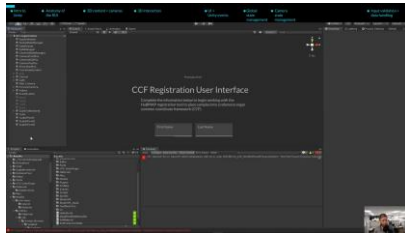


Participants:

- Jeff Spraggins, Research Assistant Professor (TMC-Vanderbilt)
- Elizabeth Neumann, Postdoctoral Researcher (Vanderbilt)
- Sanjay Jain, Associate Professor of Medicine (TMC-WUSTL)
- Bernard de Bono, MD PhD (SPARC) and Susan Tappan, Scientific Director (MBF Bioscience)

# Y2 Q1 Result - CCF Registration User Interface

## RESOURCES



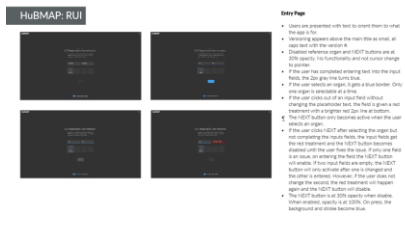
Recorded Unity Tech Demo

<https://www.youtube.com/watch?v=E8GGcpPsohc>



GitHub Prototype

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



Original Specs

<https://iu.box.com/s/zcgvlfbxbo9co0dxozeiye70qtx8uqzq>

# Visible Human MOOC Topics and Timeline

## Topics

1. Introduction to HuBMAP with interviews of lead PIs at Stanford U
2. New single-cell technologies and data processing pipelines
3. CCF ontologies and the CCF registration and exploration user interfaces
4. Biomolecular data harmonization and Seurat
5. HuBMAP Portal design and usage

## Timeline

- Sept 30: Identify VHMOC topics (see above 5) and develop a recording timeline
- Dec 31: Use Stanford U event to interview key experts
- March 31: Record other VHMOC content
- June 20: Deploy initial 5 videos in Visible Human MOOC as part of first HuBMAP Portal release

# Next Year's Deliverable in 1 slide

## **CCF Ontology**

- V1.0.0 Data format specifications for image data including specification of identified regions
- Patient, sample and technology metadata ontologies for kidney, heart, lung, and spleen in collaboration with TMCs

## **CCF User Interfaces**

- Go from Proof of Concept to fully-realized application
  - Support kidney, lung, heart and spleen data (need adequate standard organ models)
  - Integrate Tissue Registration UI data
  - Integrate expanded CCF Ontology
  - Connect to data/queries via IEC APIs and infrastructure
- Collaborate on a common Tissue Viewer with Nils' team at Harvard U
- Four 3-week sprints are scheduled starting Oct 21, 2019, Feb 17, Apr 21, and May 12, 2020.

# Collaborations

- Tissue viewer development with Nils' TC-Harvard (HuBMAP supplement)
- ImageVu large number of CT scans needed for the CCF (Vanderbilt supplement)
- Stage 2 biomolecular registration in RUI (KPMP GLUE grant pending)
- Jim Sluka is interacting with NIH projects: GenitoUrinary Development Molecular Anatomy Project (GUDMAP), Rebuilding a Kidney (RBK) and Kidney Precision Medicine Project (KPMP)
- Kristen Brown (Oliver Bodenreider) NLM, NIH: Segmented and annotated CT scans of VH organs
- Bernard deBono (SPARC): ApiNATOMY ontology & extending Registration UI to biopsy data
- Multiple experts at Allen: Adding a brain to the Exploration UI
- KitWare: Develops and distributes several software packages funded by the NIH and other US government entities, develops UIs for Allen Human Brain Atlas.

## **Barriers to collaboration:**

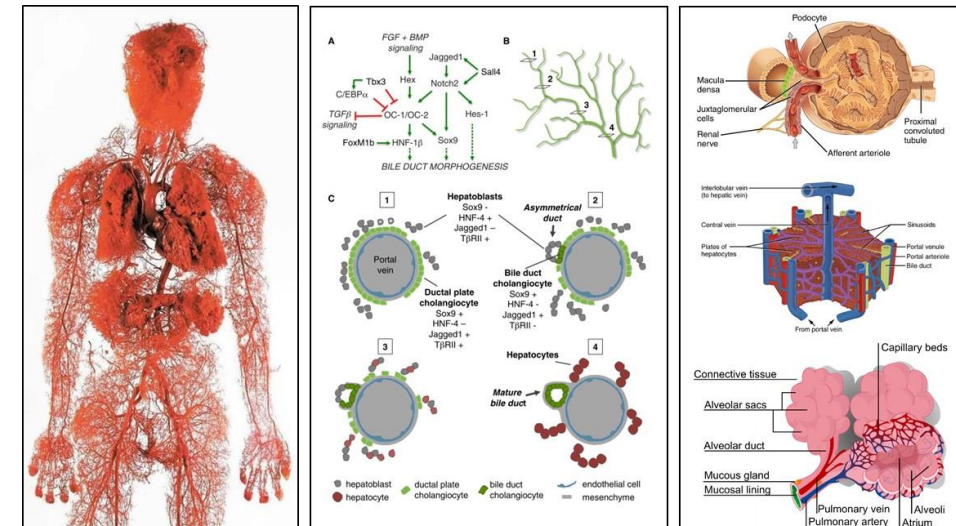
Need an official means to share data, documents, discussions with teams outside of HuBMAP.

# What should HuBMAP Do ?

- TMC-Vanderbilt uploaded new data with imaging MS, AF microscopy, PAS stained microscopy, Multiplexed IF microscopy, instrument metadata, CCF spatial metadata (via RUI), all spatial transform metadata files, all protocols ([protocols.io](https://protocols.io)), and clinical metadata. Let's use this data to test the entire pipeline—from **CCF Registration UI** to **CCF Exploration UI**.
- Sanjay Jain and Blue Lake recently shared single-cell data of different origin and representing two 2 different technologies (SPLIT-Seq and 10X). Rahul Satija use Seurat to harmonize the data. IEC should review data and harmonization workflow and consider supporting code like Seurat and alternatives.
- ASAP: Decide what will be in the 2020 HuBMAP Release.

# One Alternative CCF: Vascular CCF

- Instead of a 3D Cartesian coordinate system, one alternative is a "Vascular CCF", where the position of cells are described relative to the nearest blood vessel.
- This isn't a CCF of the vascular system. It is a CCF of the tissue surrounding vessels, using the vascular pathways as an axis of a coordinate system.
- Vessels are unique in that they:
  - reach with ~100 micrometers of every living cell to deliver oxygen
  - scale seamlessly from macro- to meso- to micro- levels
  - form the scaffolding of functional units in organs
  - can be identified histologically, gene expression, hypoxia levels, etc.
  - adapt to different body sizes and shapes
  - drive organogenesis (development of organs around vasculature)
  - used clinically to localize tissue, plan surgery, diagnose disease, etc.
- Next step: experiments to test whether it is possible to register cell location using a vascular CCF
- Thinking through a biological-based coordinate system helps us understand the benefits and limitations of a 3D Cartesian system.



- <https://www.pinterest.jp/pin/522699100479032485/>
- Si-Tayeb et al, Developmental Cell 2010
- Anatomy & Physiology, Connexions Web site. <http://cnx.org/content/col11496/1.6/>
- [https://en.wikipedia.org/wiki/Pulmonary\\_alveolus#/media/File:Alveolus\\_diagram.svg](https://en.wikipedia.org/wiki/Pulmonary_alveolus#/media/File:Alveolus_diagram.svg)



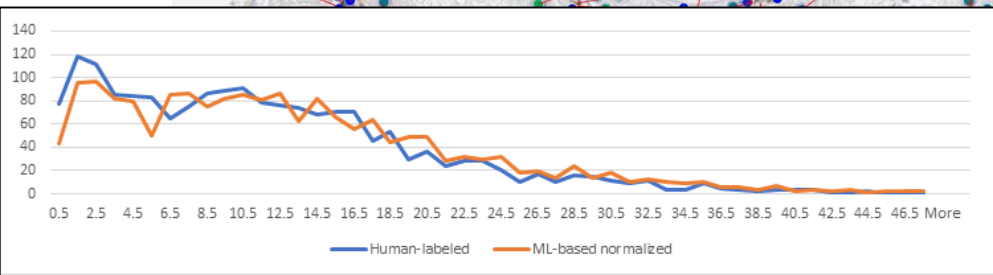
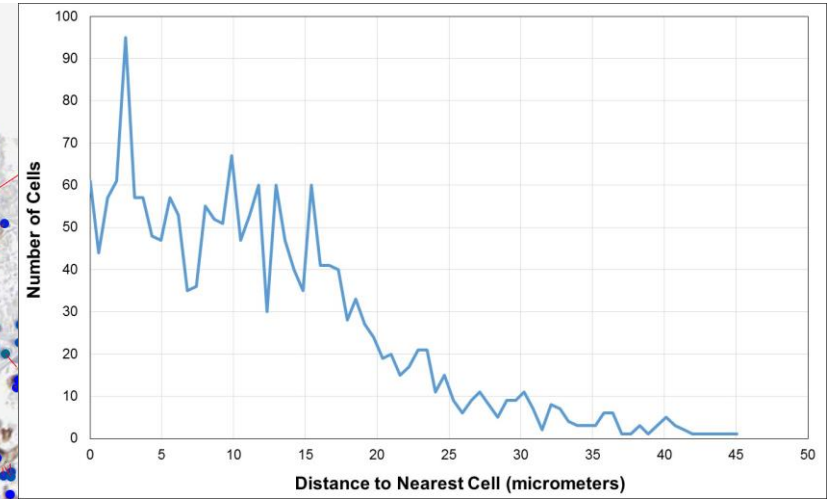
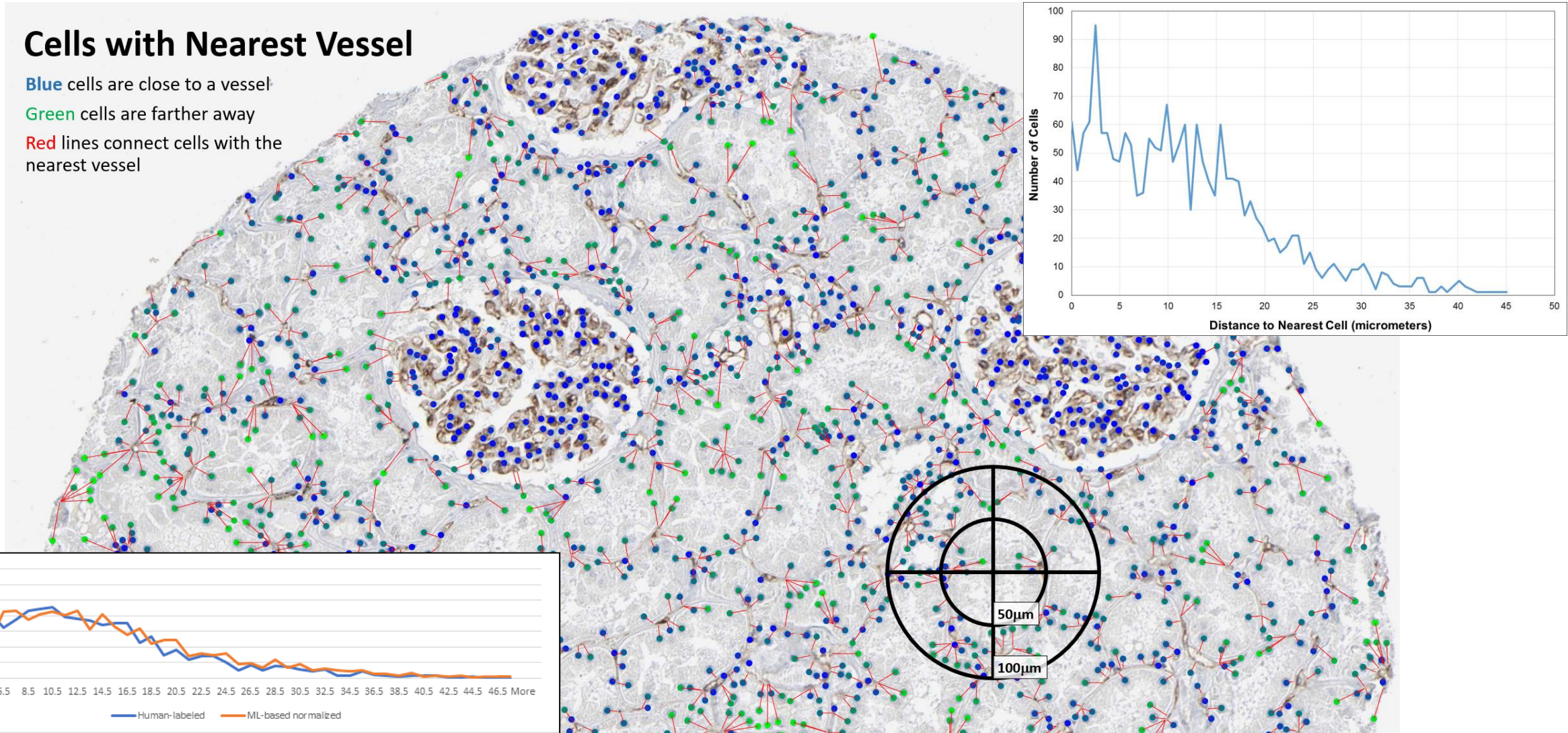
# Vascular CCF

Griffin Weber, Zorina Galis, Yingnan Ju  
Using data from the Human Protein Atlas

WANTED: Tissue Data

## Cells with Nearest Vessel

- Blue cells are close to a vessel
- Green cells are farther away
- Red lines connect cells with the nearest vessel



# Acknowledgments



<https://hubmapconsortium.org>

Plus, **patients** that agreed to volunteer healthy tissue and to use their data openly.



Jeffrey Spraggins  
TMC-Vanderbilt  
Vanderbilt University



Sanjay Jain  
TMC-UCSD  
Washington University, St. Louis



MC-IU HIVE Team at IU