

AUA
2024 MAY 3-6
San Antonio

Keynote:
The Human
Reference Atlas





Version 2.0

Human Reference Atlas

<https://humanatlas.io>



Keynote: The Human Reference Atlas



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Technical Director

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Luddy School of Informatics, Computing, and Engineering
Indiana University, Bloomington, IN, USA



Human Reference Atlas Collaborators

- HuBMAP
- SenNet
- GTEx
- KPMP
- GUDMAP
- 13+ other consortia
- 250+ subject matter experts
- Funded by NIH and CIFAR
- Supported by HCA // Human Cell Atlas



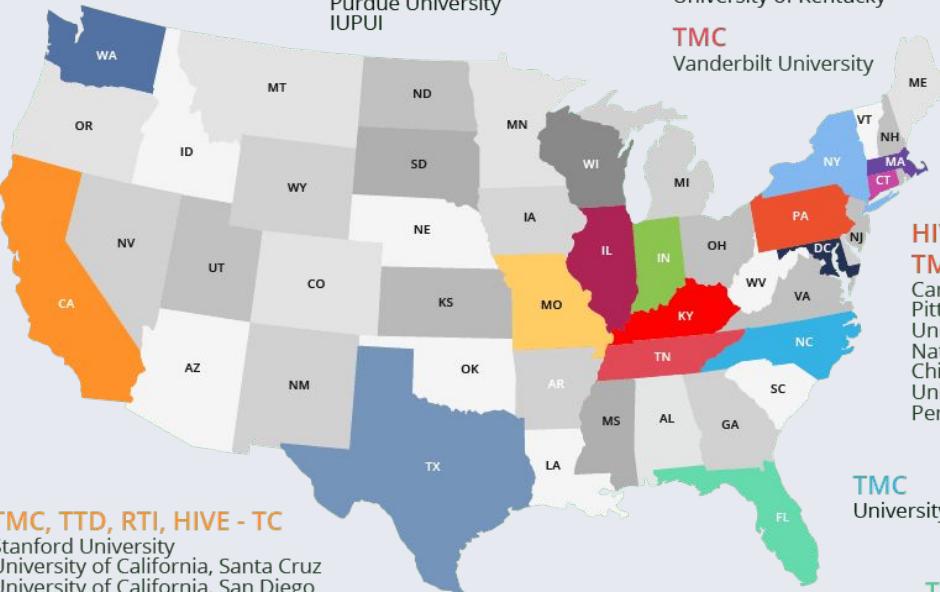
HuBMAP Contributing Sites

TMC, TTD

Pacific Northwest National Lab
Seattle Children's Hospital

TMC

Washington University, St. Louis



TMC, TTD, RTI, HIVE - TC

Stanford University
University of California, Santa Cruz
University of California, San Diego
City of Hope National Medical Center
Scripps Research

RTI, TTD, DP

Northwestern University
University of Illinois, Chicago
Lurie Children's Hospital of Chicago

HIVE - Mapping, TTD

Indiana University, Bloomington
Purdue University
IUPUI

HIVE - Mapping, RTI, TMC

New York Genome Center
University of Rochester Medical Center
General Electric Global Research Center

HIVE - TC

University of Kentucky

TMC

Vanderbilt University

NIH, TMC, DP

NIH Common Fund
Johns Hopkins University
Brigham and Women's Hospital



TMC

University of Zurich



TMC

Delft University of Technology



HIVE - TC, TMC

European Bioinformatics Institute
Wellcome Sanger Institute



Early history of the HRA and HuBMAP

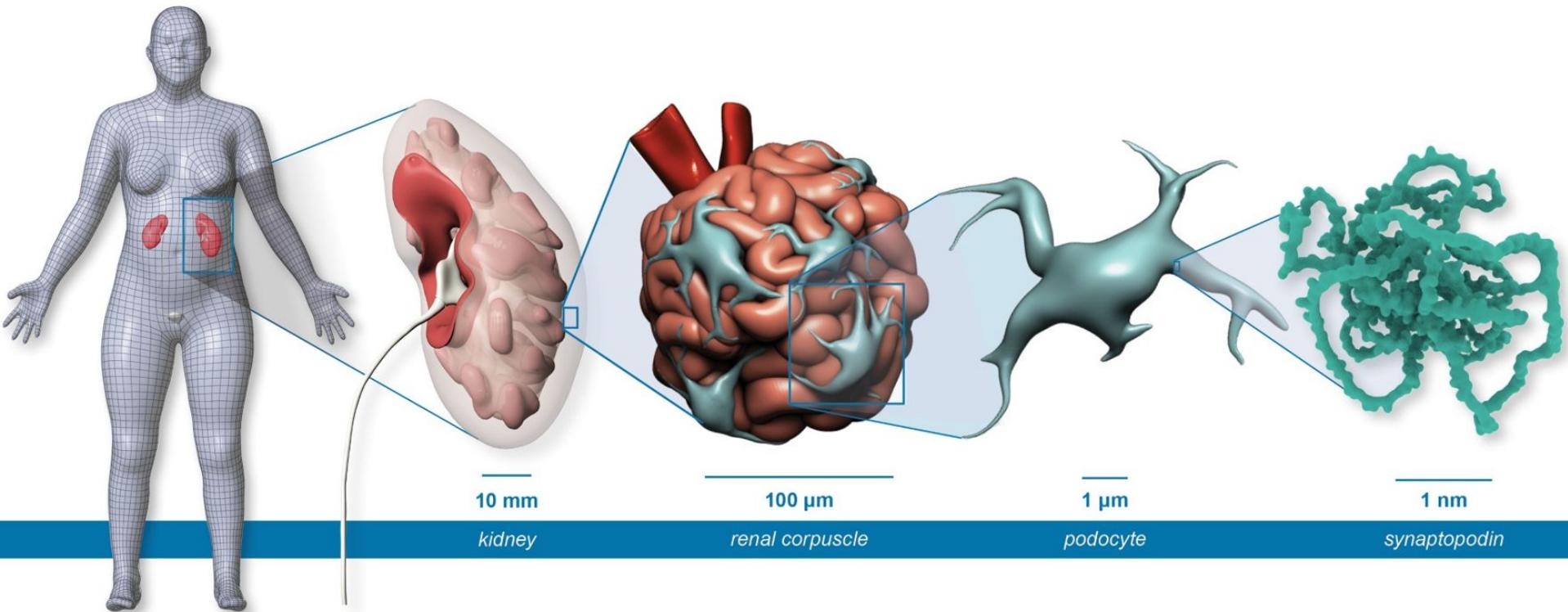
- HuBMAP started in 2018 with the goal of mapping the human body down to the cellular level
- The IU team started off with creating a common coordinate framework, that eventually evolved into the HRA
- In 2023, we published HRA v2.0
- We are now in the production phase of HuBMAP

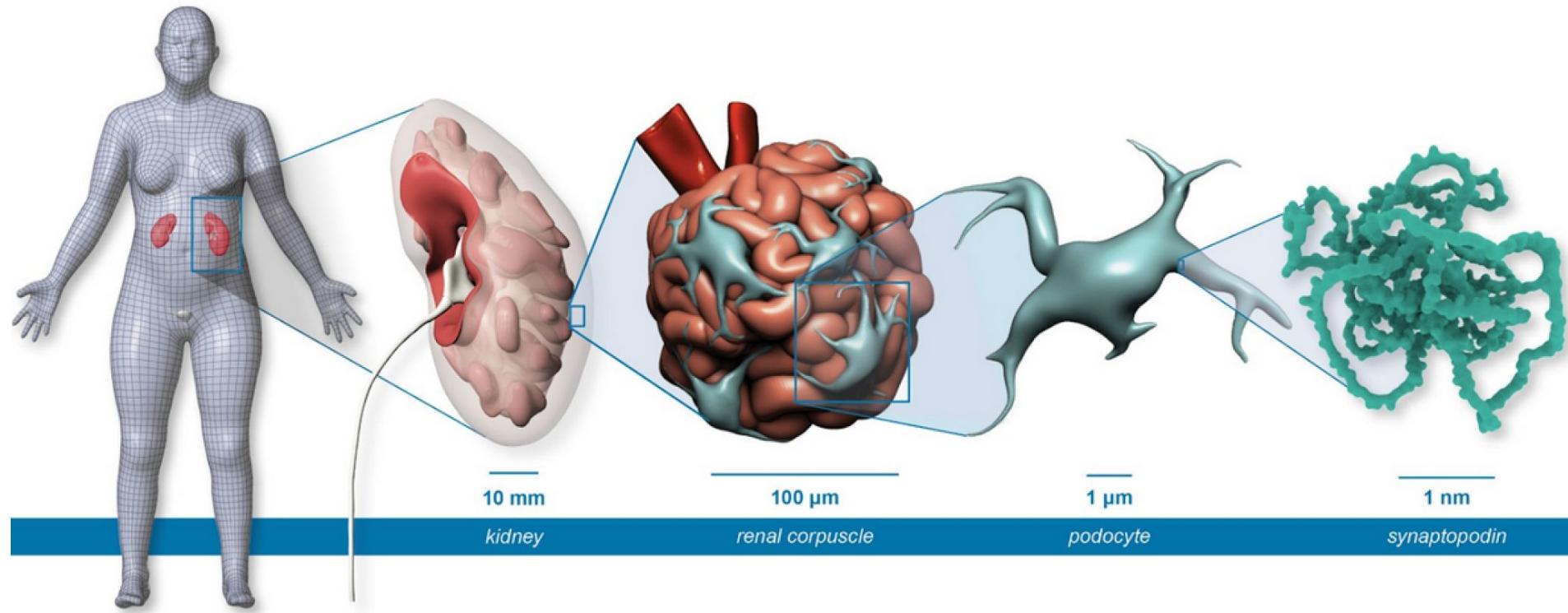
What is the HRA?



Human Reference Atlas (HRA)

A comprehensive, ontologically aligned, high-resolution, three-dimensional, multiscale atlas of anatomical structures and cells in the healthy human body





Anatomical Structures

Functional
Tissue Units

Cell Types

Biomarkers
Genes, Proteins, ..

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Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

Atlas

3D Reference Organs

2D FTU
Illustrations

Organ Mapping Antibody Panels

Vascular Geometry

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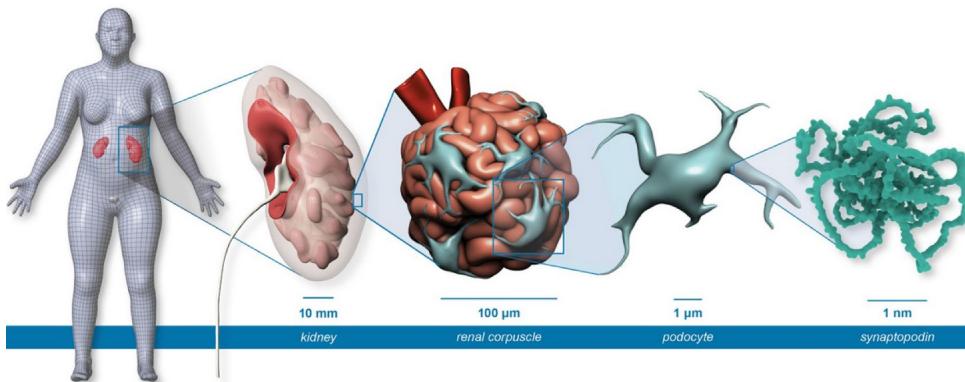
Vascular Geometry

Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

Atlas++

Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

HRAlit (HRA-relevant Literature)



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Human Reference Atlas

User Stories guide the HRA development and keep it grounded in providing value

User stories are centered around

- **Construction** - Facilitate atlas construction by aligning new tissue blocks with existing data
- **Usage** - Use the atlas to gain insights into changes that occur at all levels in the body with aging or disease
- **Sustainability** - Ensure atlas sustainability with processes that encourage collaboration and guide future development

HRA User Stories

More than 30 one-on-one interviews were conducted with atlas architects, i.e., experts who serve as principal investigators or are otherwise intimately involved in the construction of the latest generation of human atlases, including BICCN, GTEx, GUDMAP, HCA, HuBMAP, Human Tumor Atlas Network (HTAN), KPMP, LungMAP, (Re)building the Kidney (RBK), and SenNet.

In addition, six programmers from different human atlas projects were surveyed.

Table on right shows feature summary, target user roles, user activities, and added value for seven user stories that drive HRA development.

Feature	User Role	User Activities	Added Value
<i>Facilitate atlas construction by aligning new tissue blocks with existing data</i>			
US#1. Predict cell type populations	Programmers that support Researchers, Clinicians, Pathologists	Predict and explore the likely cell type populations for a RUI-registered tissue block.	Improve cell type annotation through information on what cell type populations exist in what anatomical structures.
US#2. Predict spatial origin of tissue samples	Programmers that support Researchers, Clinicians	Predict and explore the likely 3D location in the human body for a given tissue block with known cell type population.	Compensate for the absence of spatial origin information in many single cell datasets.
<i>Use the atlas to gain insights into changes that occur at all levels in the body with aging or disease</i>			
US#3. Compare reference tissue with aging/diseased tissue	Researchers, Clinicians	Compare tissue blocks, cell types, and biomarker expression levels between healthy reference tissue and aging/diseased tissue.	Understand and communicate changes in tissue structure and function with age or disease.
US#4. Compare reference Functional Tissue Units with aging/diseased FTUs	Researchers, Clinicians	Compare FTUs in terms of cell types and mean biomarker expression levels for healthy reference tissue and aging/diseased tissue.	Understand and communicate changes in FTU structure and function with age or disease
US#5. Provide cell distance distribution visualizations	Researchers, Pathologists	Compute, visualize, and explore distance distributions between different cells, cell types, and anatomical structures (e.g., FTUs), and cell types and morphological features (e.g., the edge of an organ).	Add granularity to our understanding of how disease develops (e.g., how tumor cells grow or metastasize) in support of targeted therapies.
<i>Ensure atlas sustainability with processes that encourage collaboration and guide future development</i>			
US#6. Develop lightweight atlas components	Programmers that support Researchers and Clinicians	Implement usable and useful HRA components (interfaces and APIs) into other portals in the growing ecosystem of human atlases.	Facilitate collaboration and data/code reuse between the HRA and other portals in support of FAIR data principles.
US#7. Implement dashboard for HRA	Researchers, Clinicians, Funders	Track the evolution and usage of the HRA using data, code, and portal usage statistics in aggregate and divided by portal (e.g., HubMAP or SenNet) or PEDP survey results.	Enable evidence-based decision-making by providing insights into the atlas' construction and usage (e.g., gaps in data, application areas, user demographics, equitable access).



Human Reference Atlas

Naming and connecting across scales

- Anatomical Structures
- Functional Tissue Units
- Cell Types
- Biomarkers



Human Reference Atlas

Connecting and empowering people

- Subject Matter Experts
- Ontologists
- Programmers
- Experimentalists
- Researchers, Clinicians, and Pathologists



Human Reference Atlas

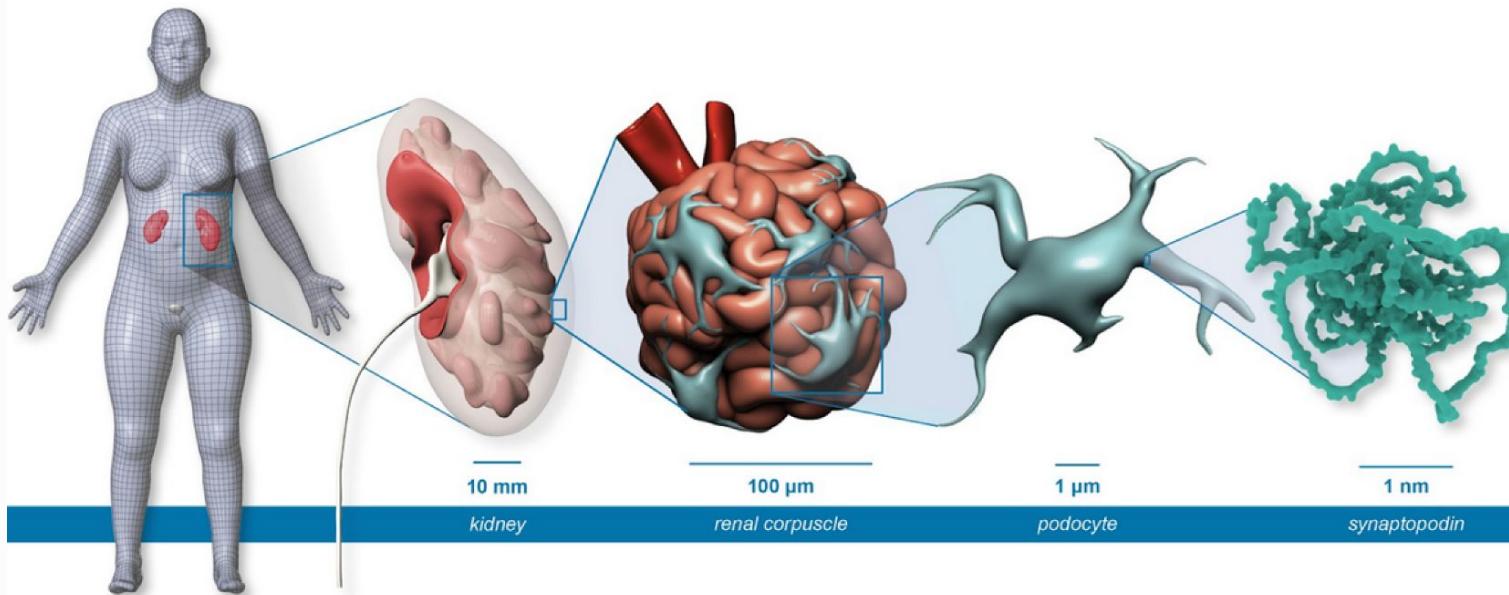
Relevance to Urology

- Measure what's healthy to compare to what's unhealthy
- Knowledge and data resource
- Open data and code, reproducible workflows, lightweight user interface components

NOTE: Not ready for clinical practice

Tour of the HRA





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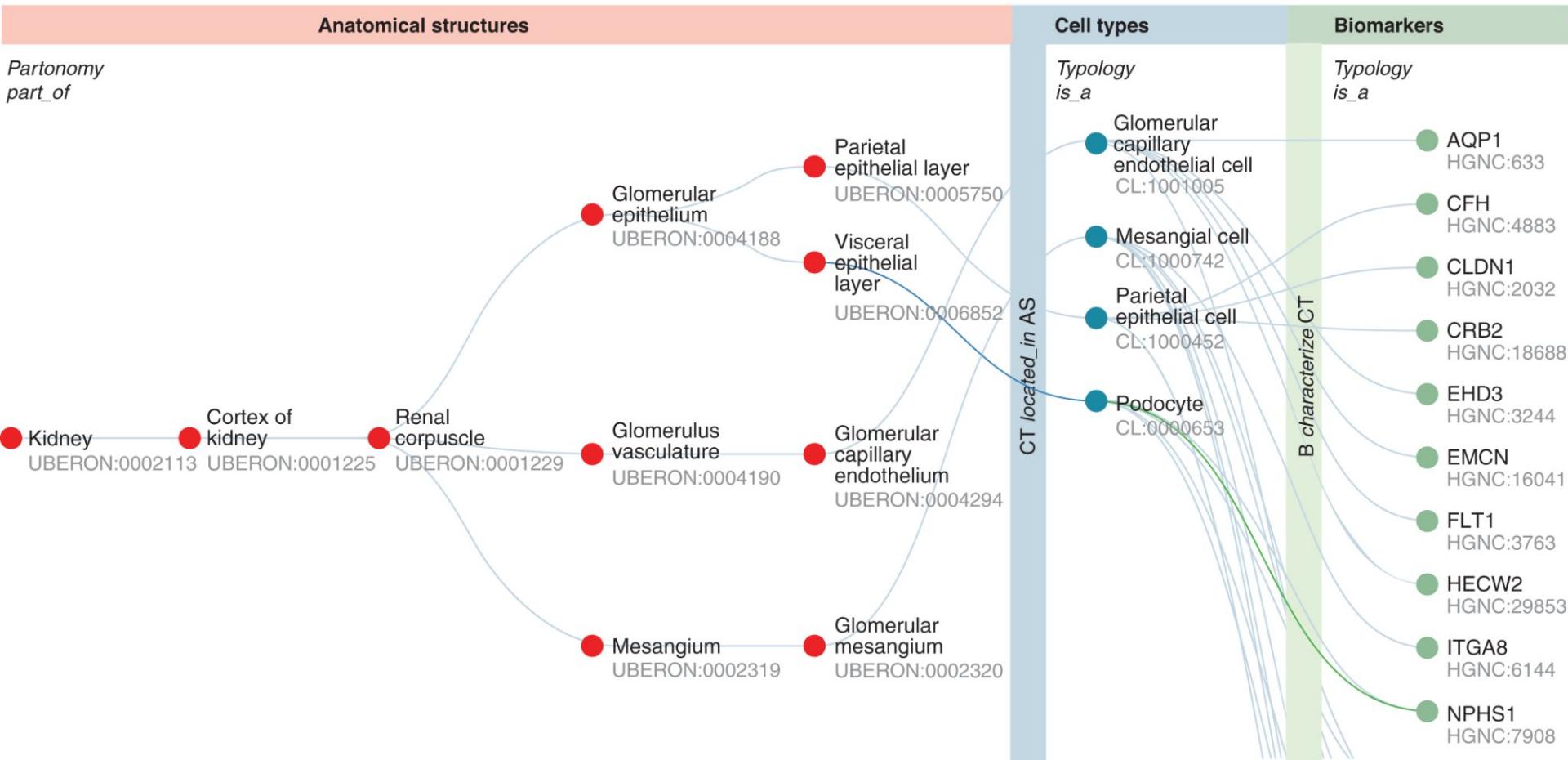
Atlas

3D Reference Organs

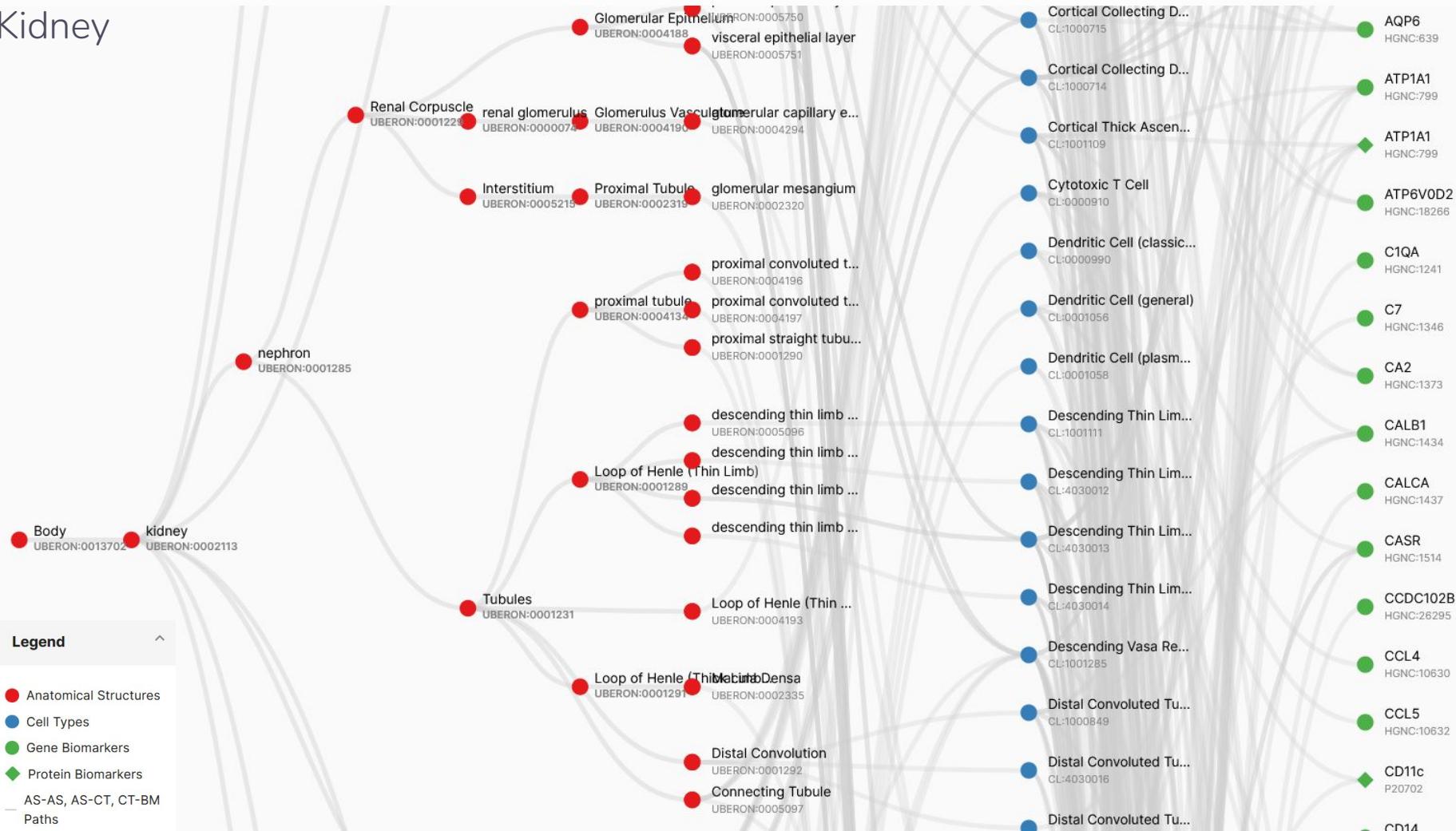
2D FTU
Illustrations

Organ Mapping Antibody Panels

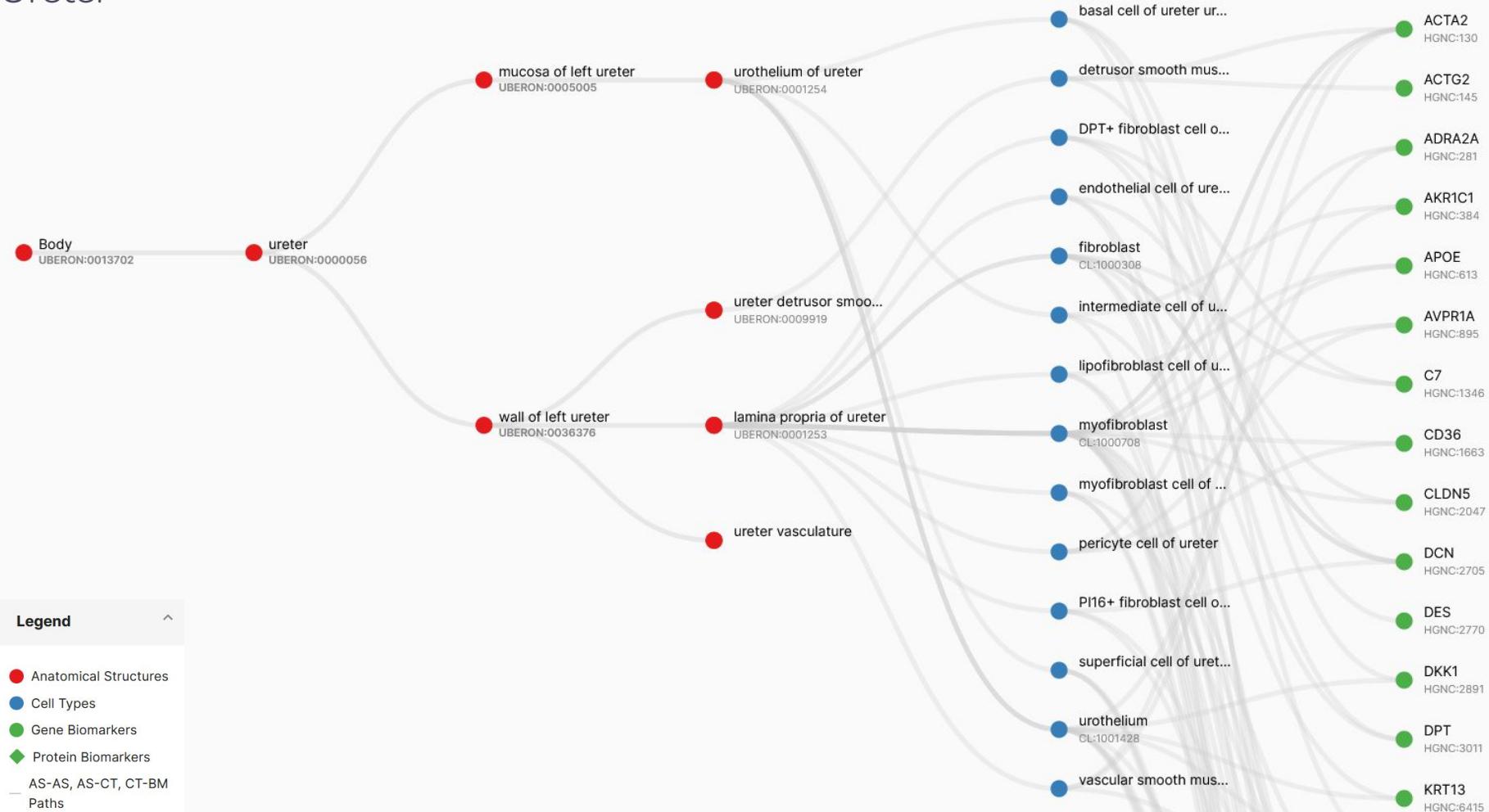
ASCT+B Table Framework



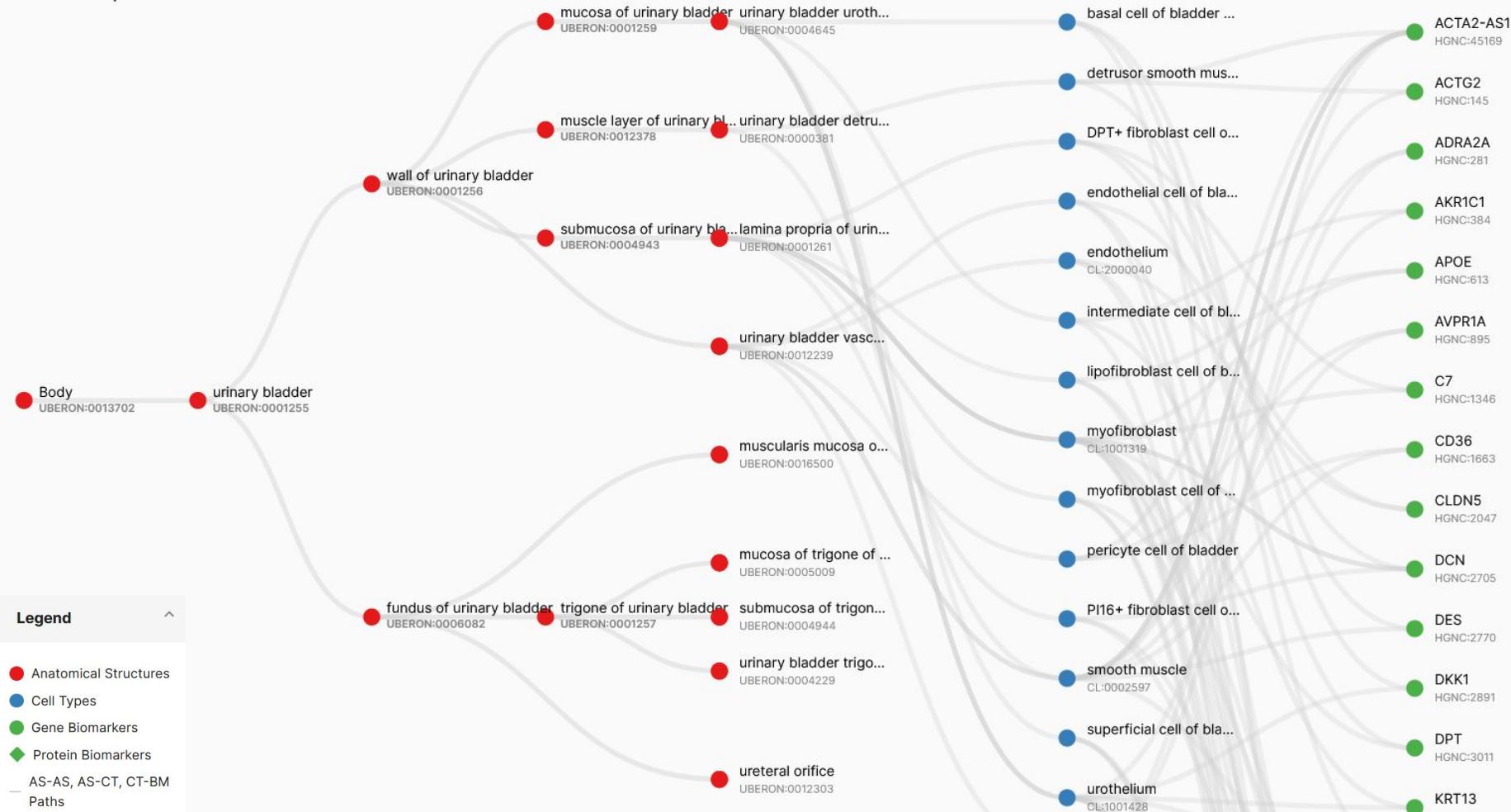
Kidney



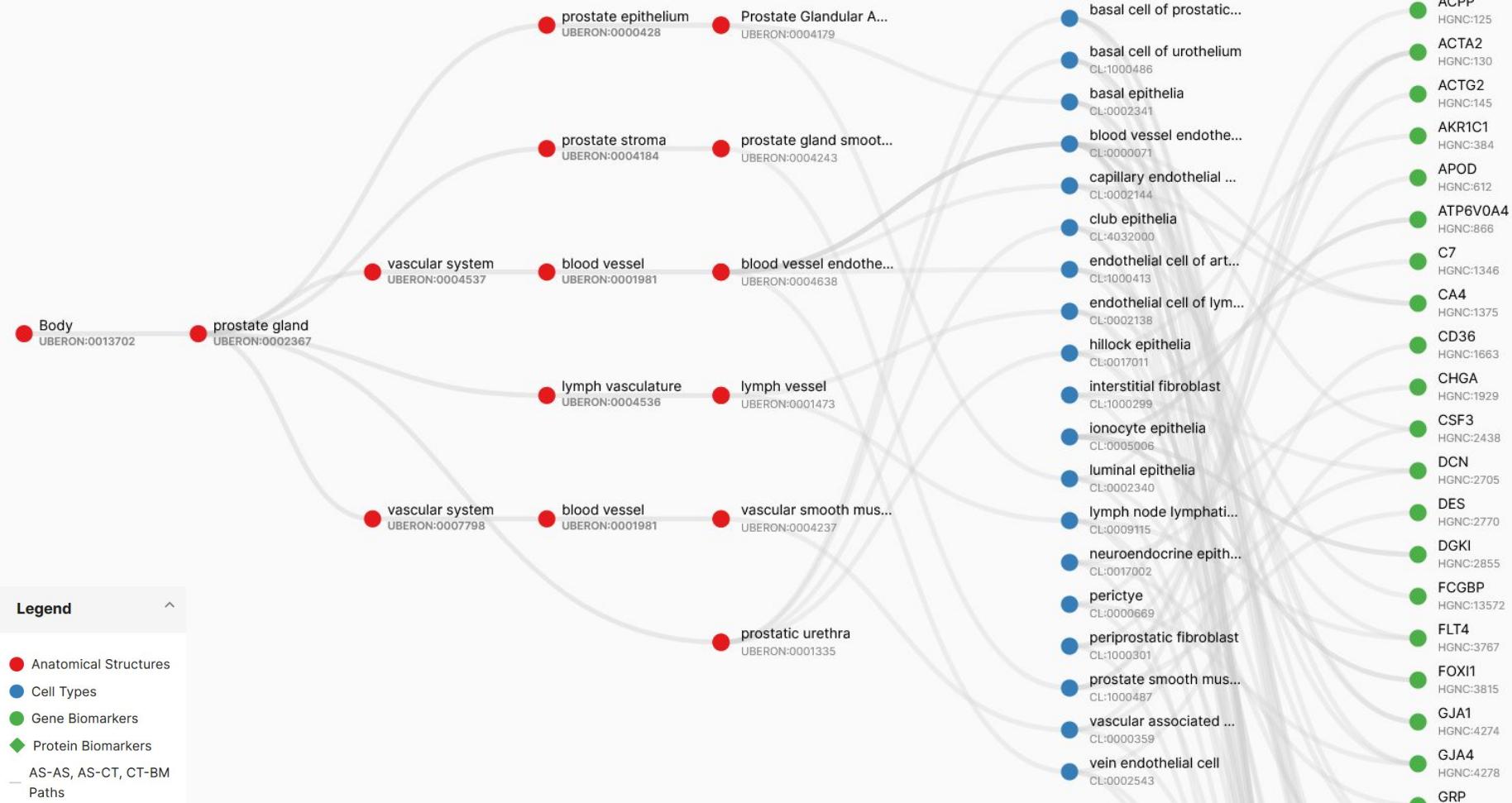
Ureter



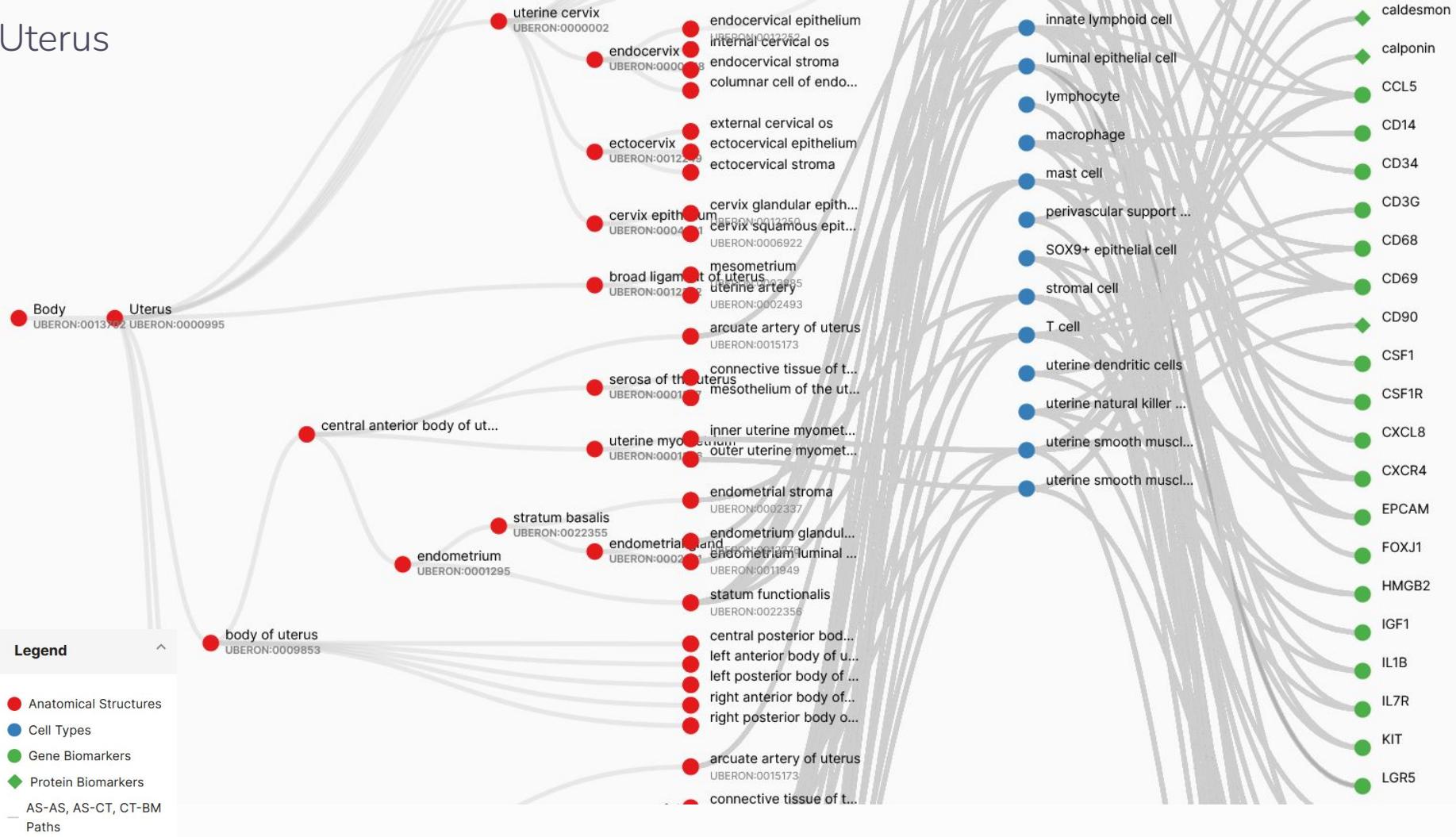
Urinary Bladder

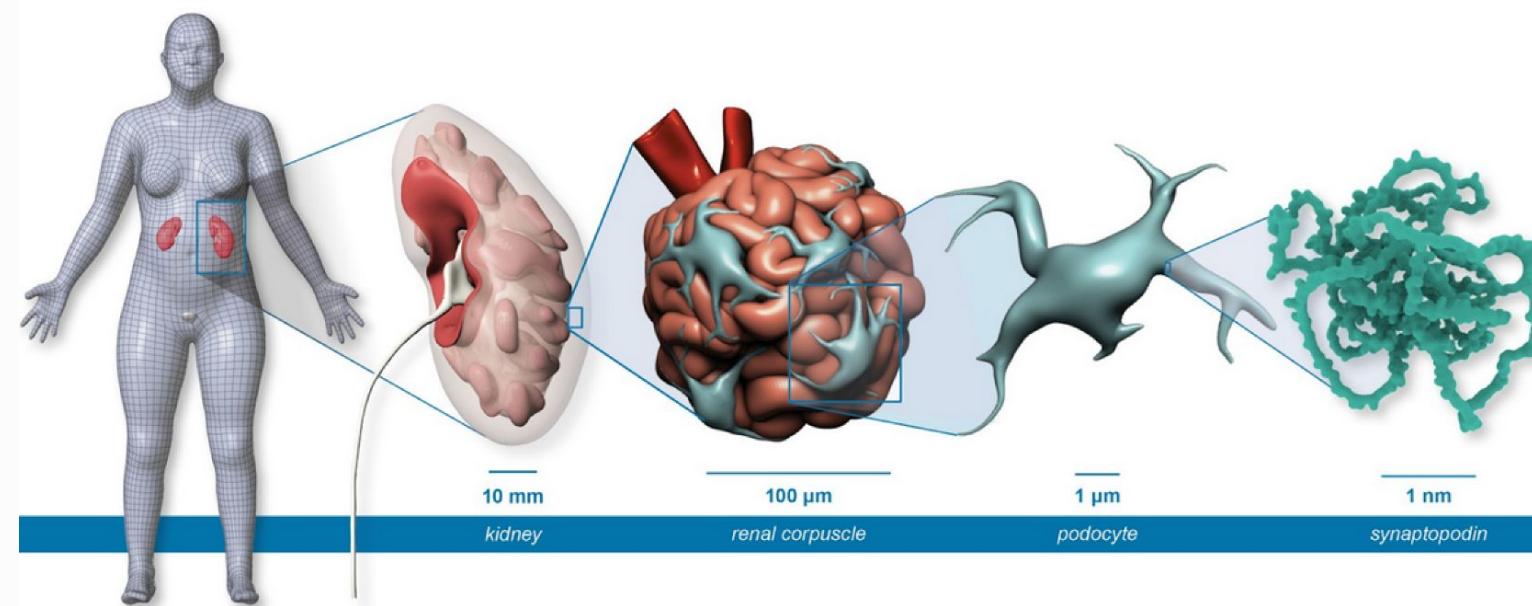


Prostate



Uterus





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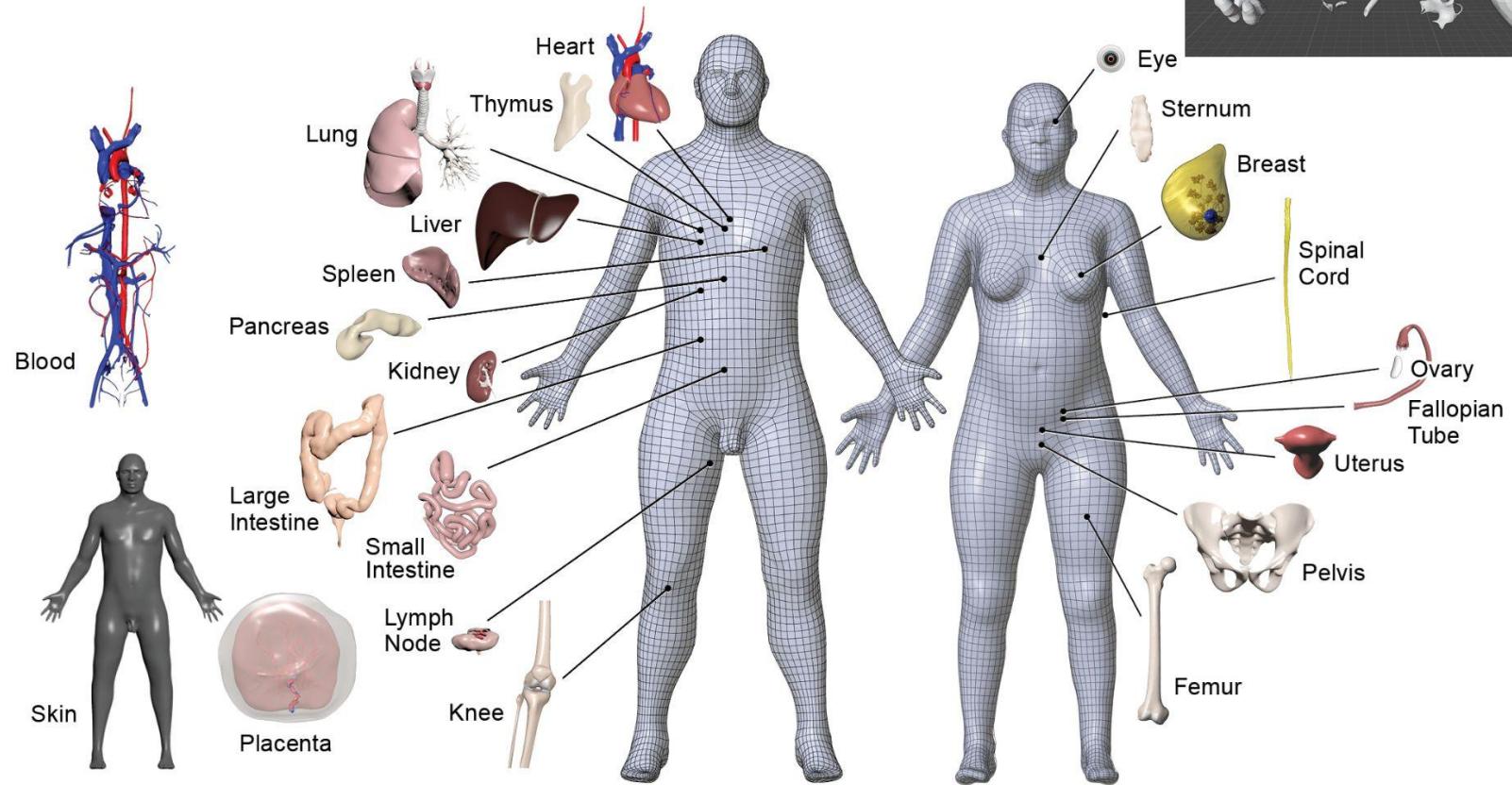
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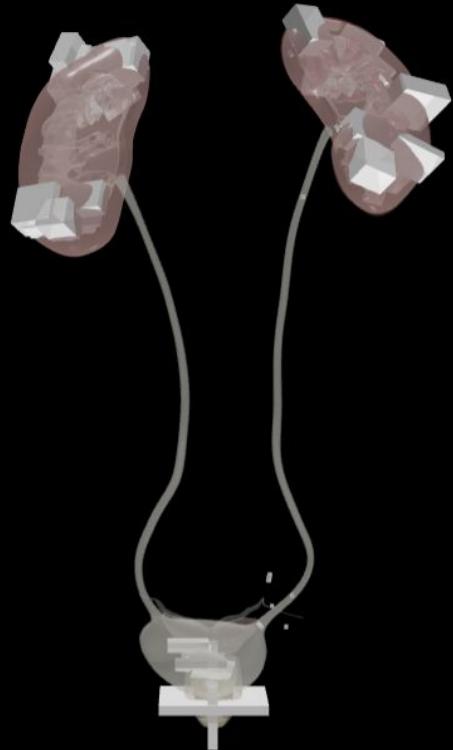
HRA 3D Reference Organs





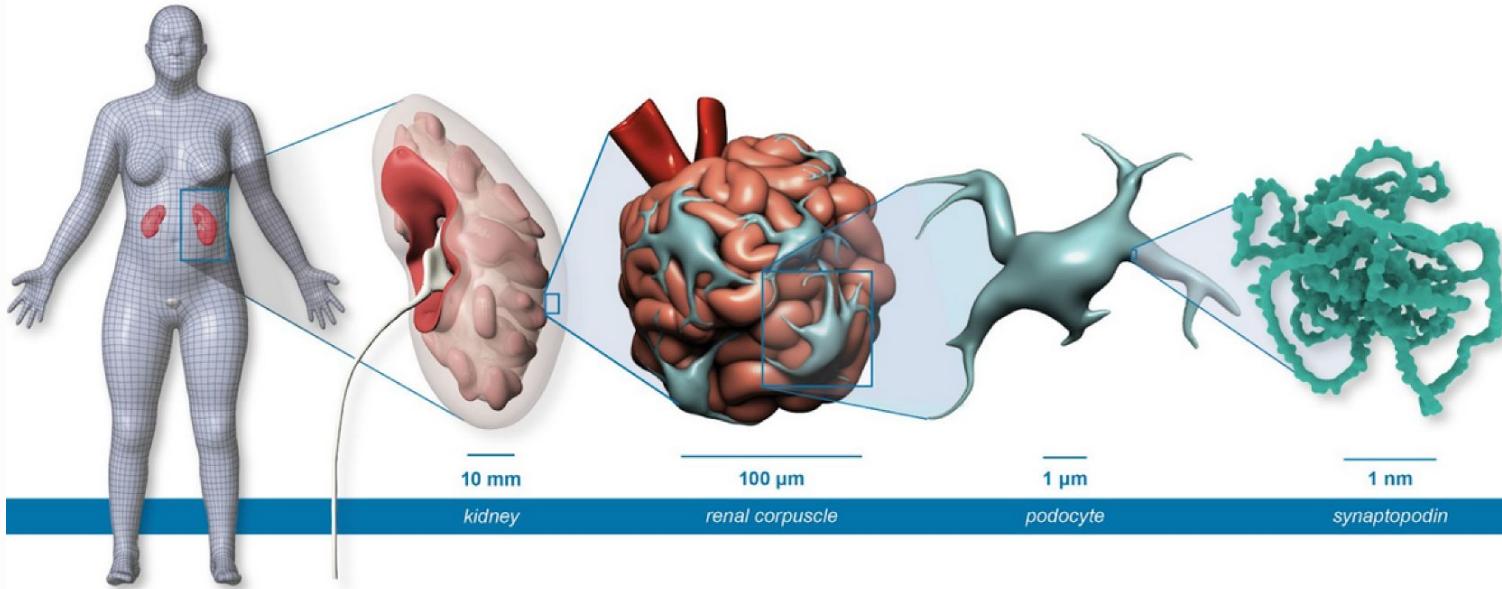
HRA 3D Reference Organs: kidney, ureter, bladder, prostate, and uterus

Male



Female





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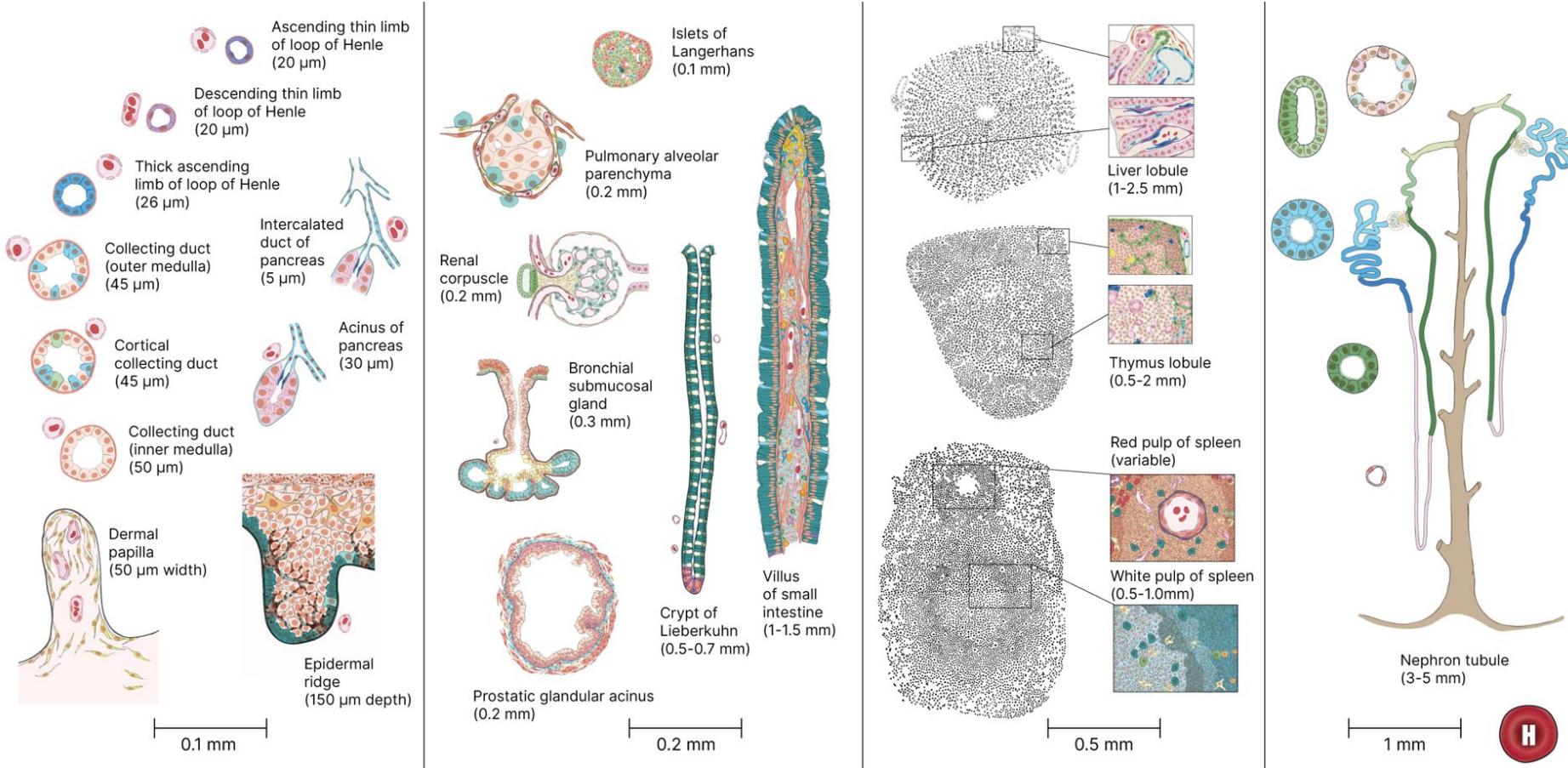
Atlas

3D Reference Organs

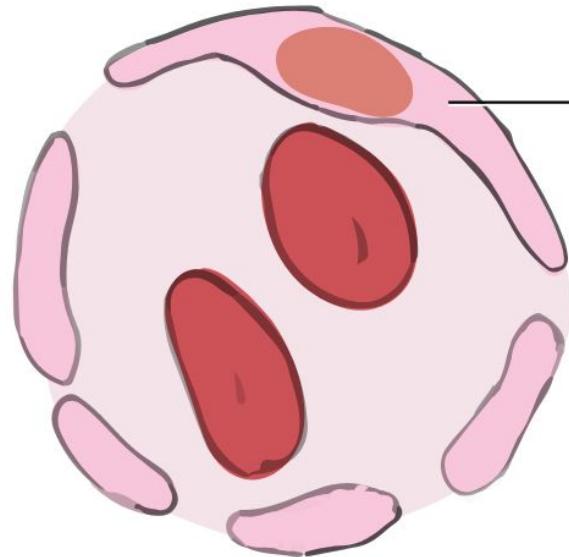
2D FTU
Illustrations

Organ Mapping Antibody Panels

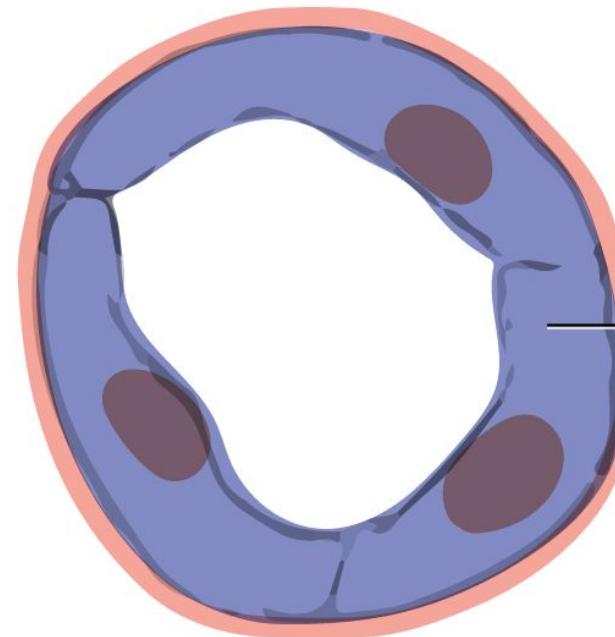
HRA Functional Tissue Units (FTUs)



Kidney - Ascending Thin Loop Of Henle



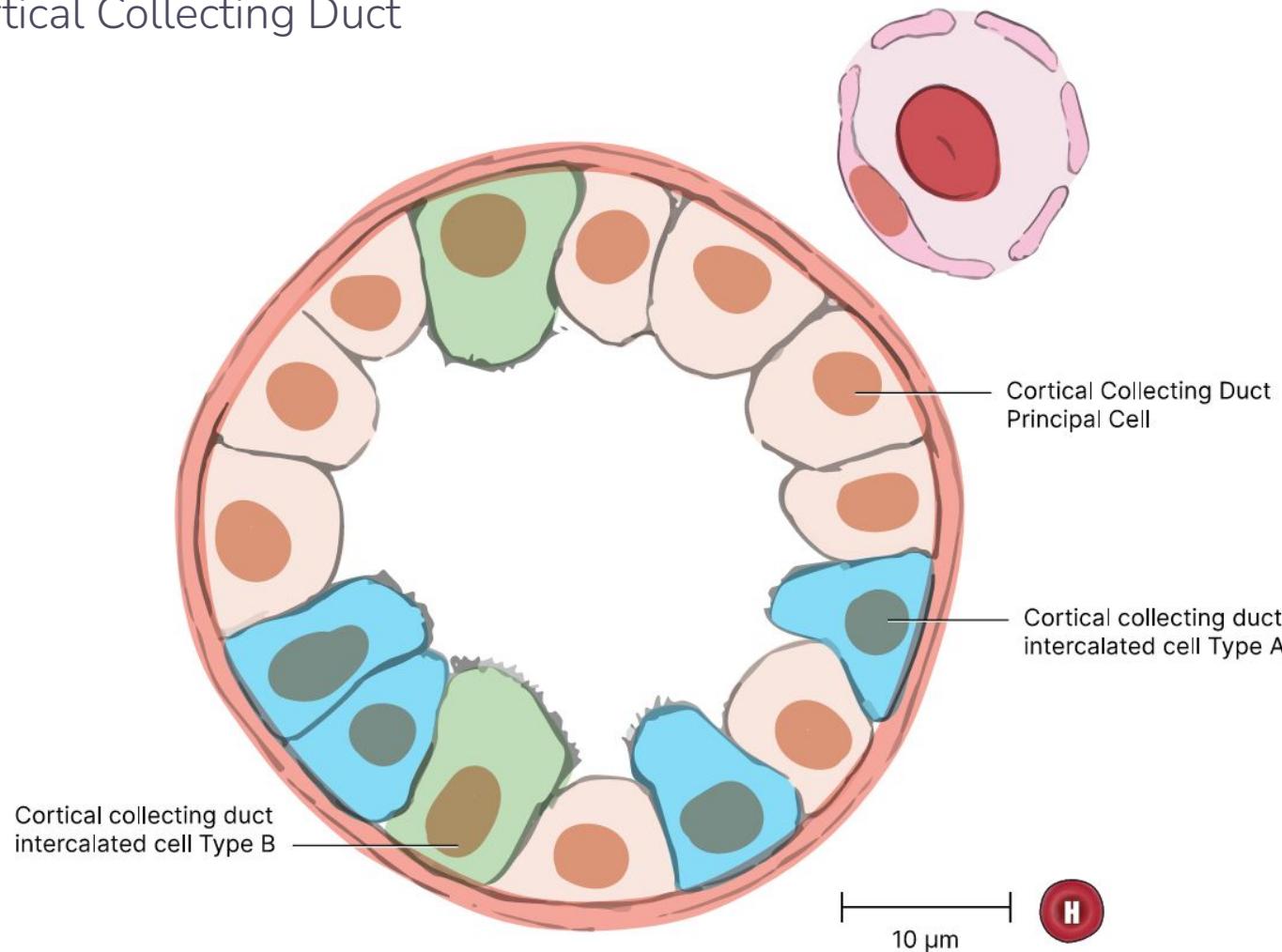
Ascending vasa recta



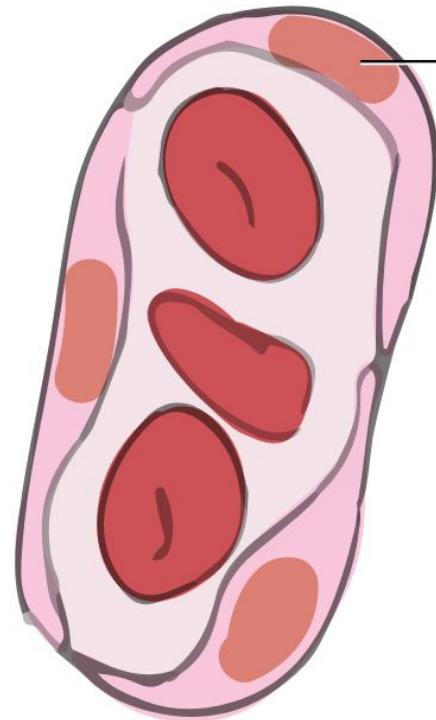
Ascending
thin limb cell



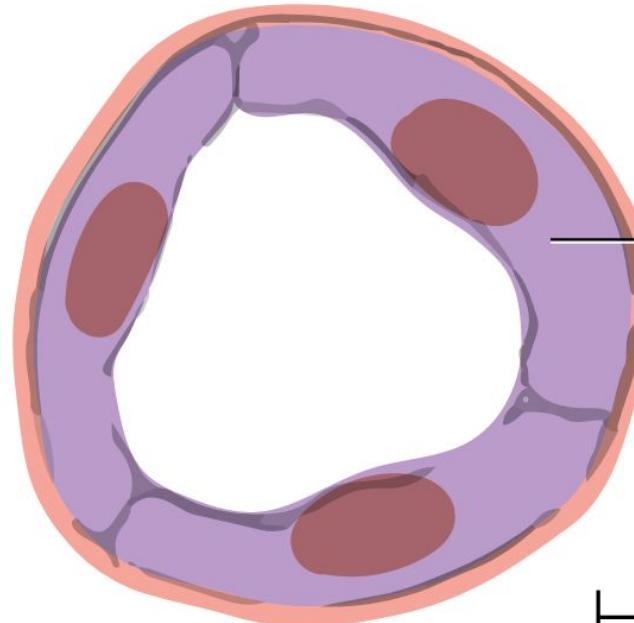
Kidney - Cortical Collecting Duct



Kidney - Descending Thin Loop Of Henle



Descending vasa recta

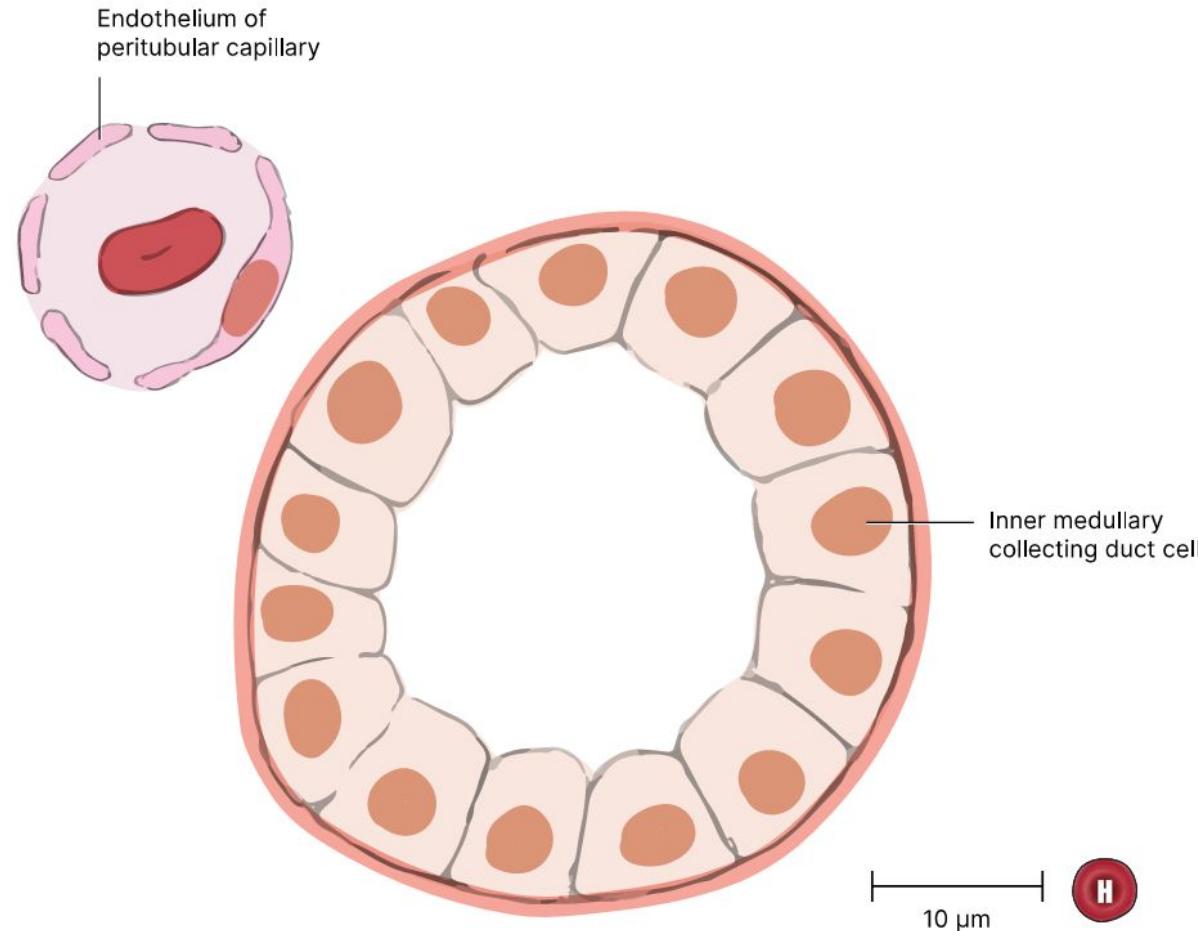


Descending
thin limb cell

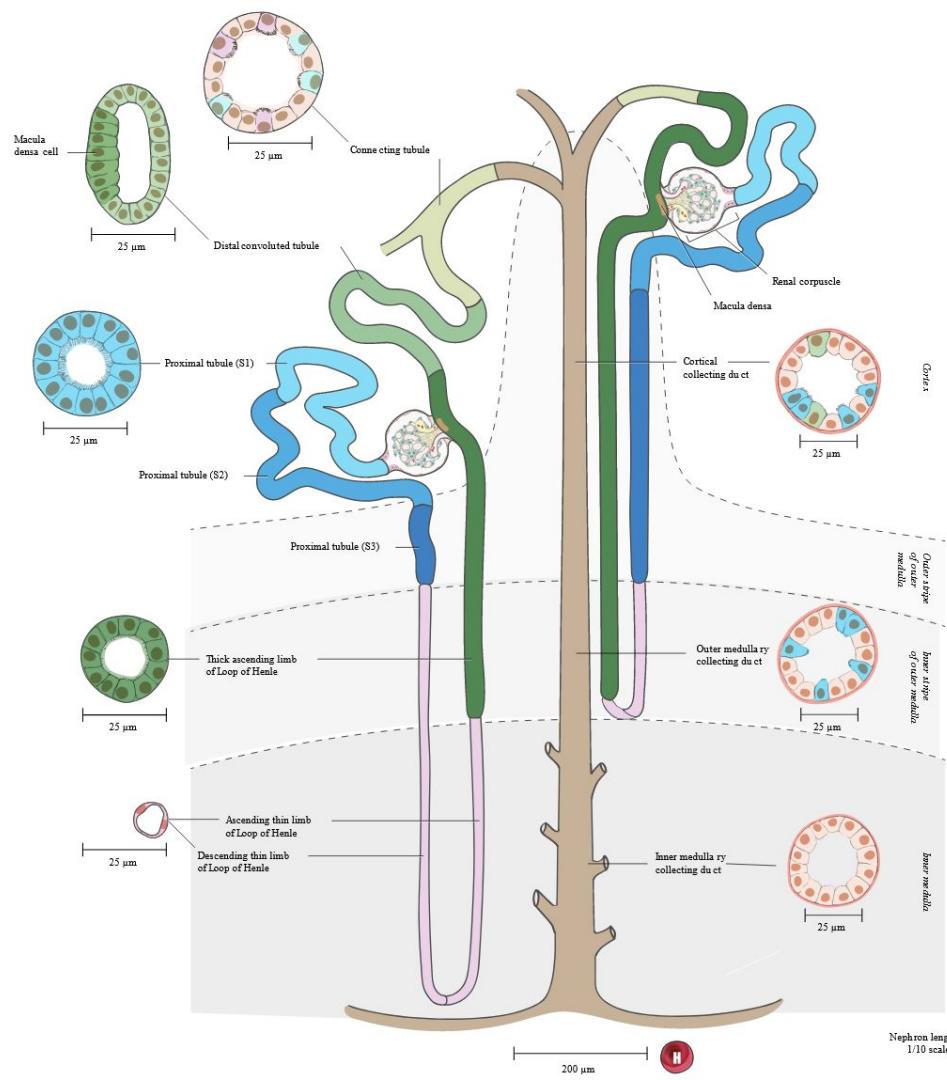
10 μm



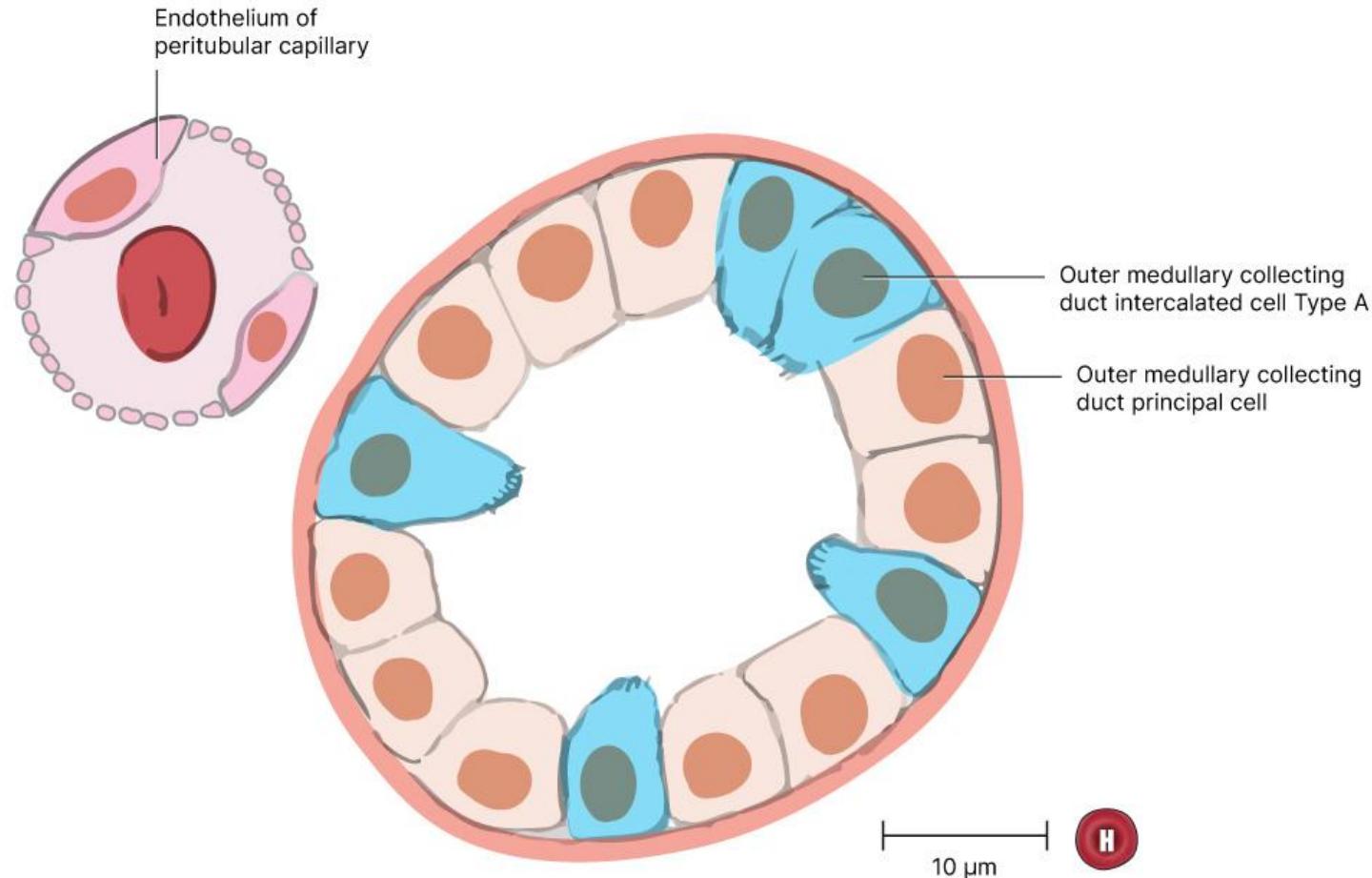
Kidney - Inner Medullary Collecting Duct



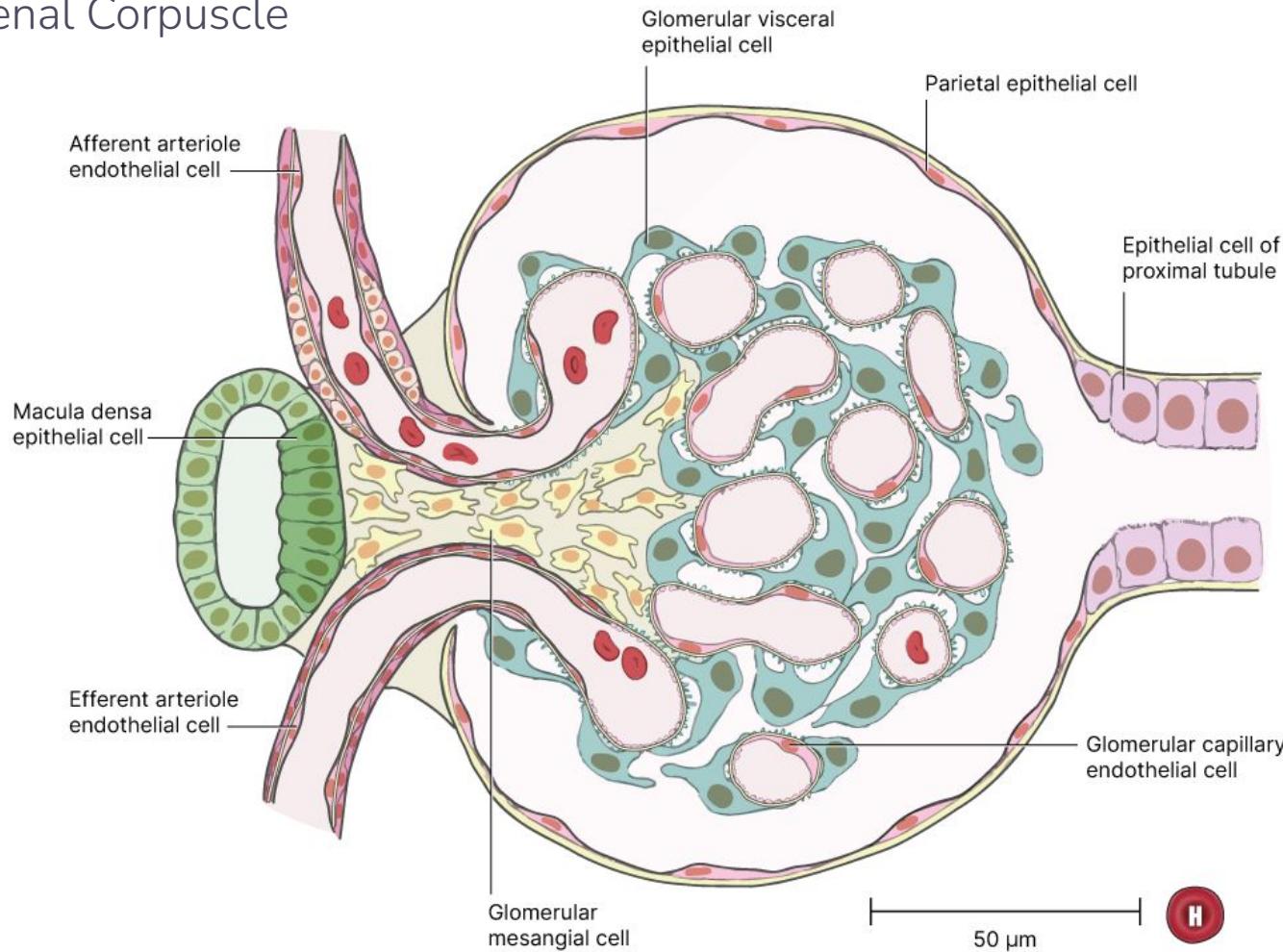
Kidney - Nephron



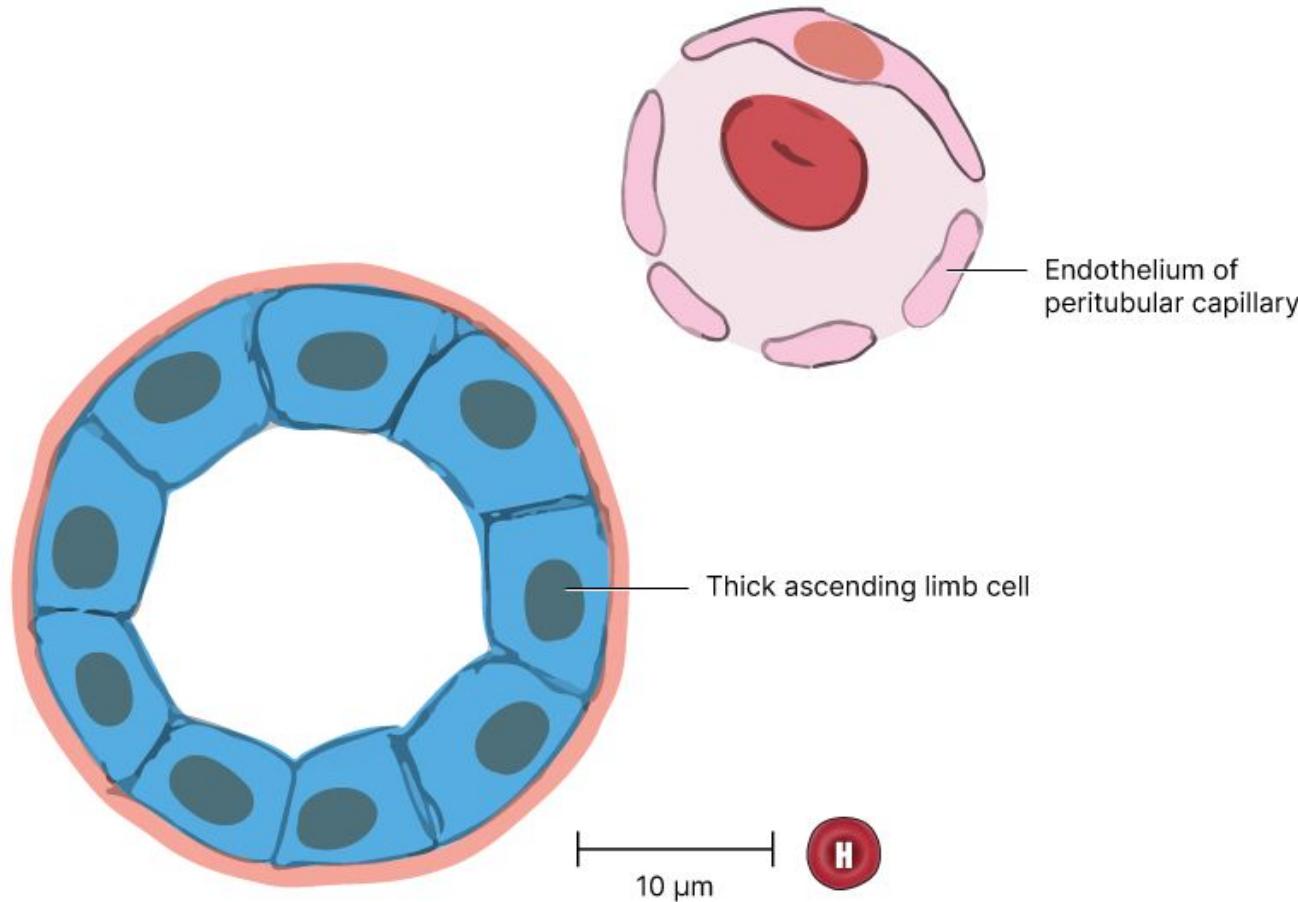
Kidney - Outer Medullary Collecting Duct



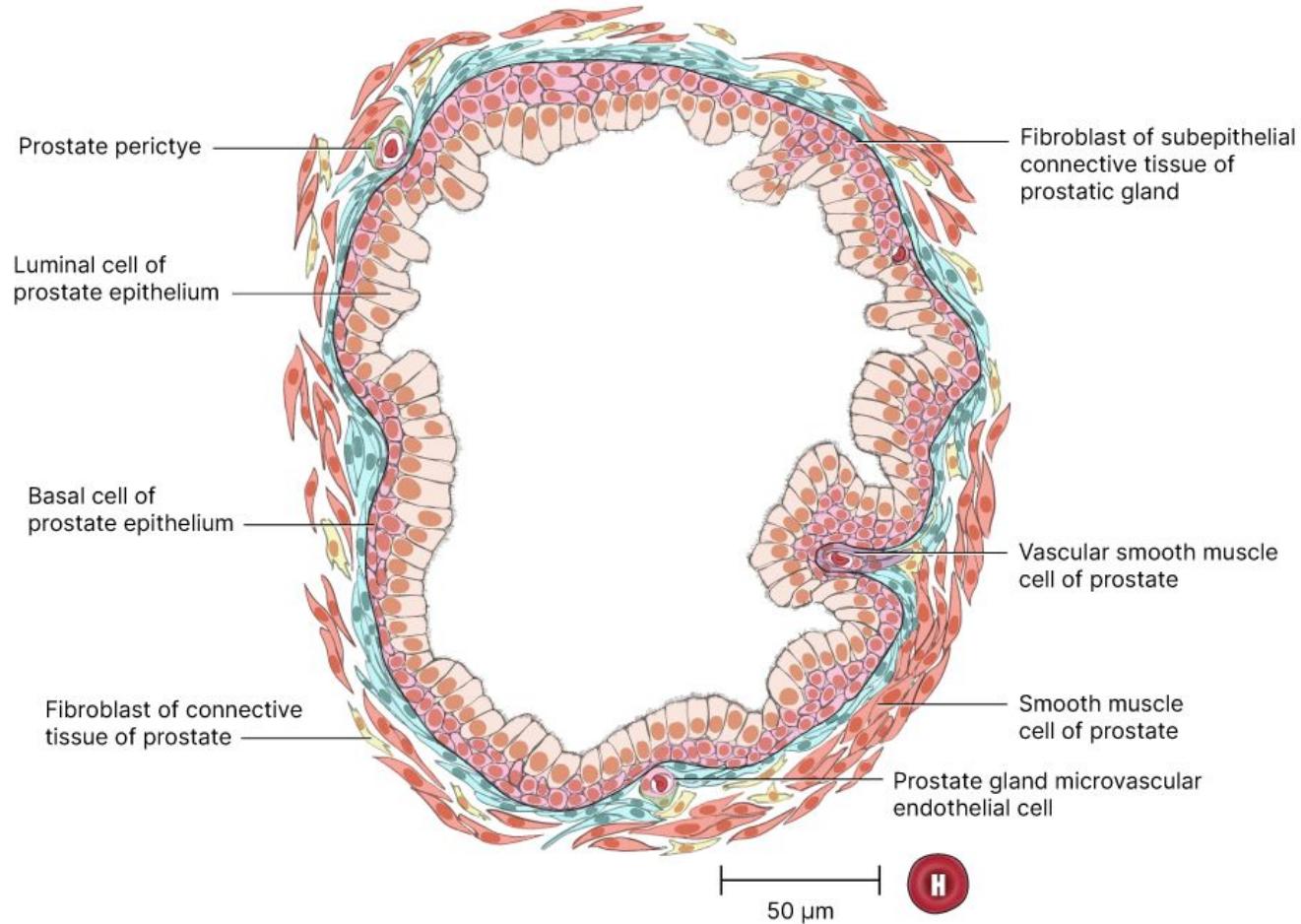
Kidney - Renal Corpuscle

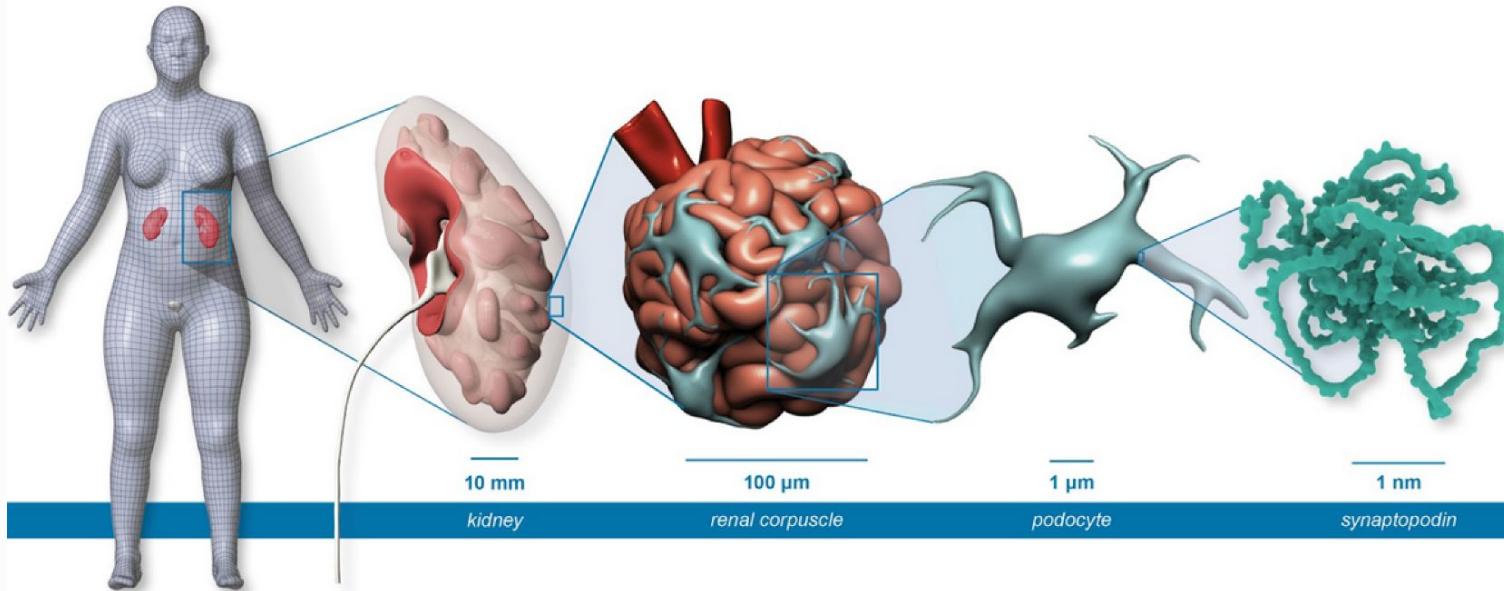


Kidney - Thick Ascending Loop Of Henle



Prostate - Glandular Aculus





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Functional
Tissue Units

Cell Types

Biomarkers
Genes, Proteins, ..

Conceptual

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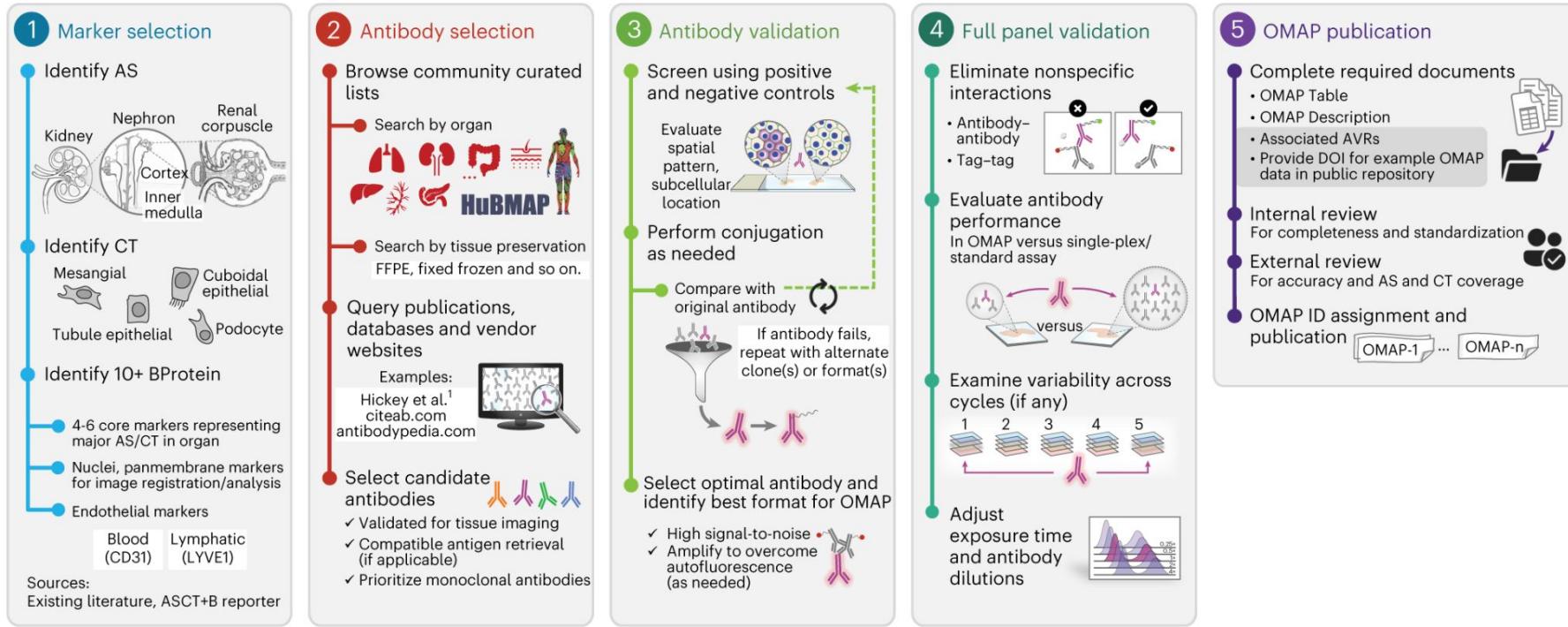
Atlas

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2D FTU
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OMAP Framework



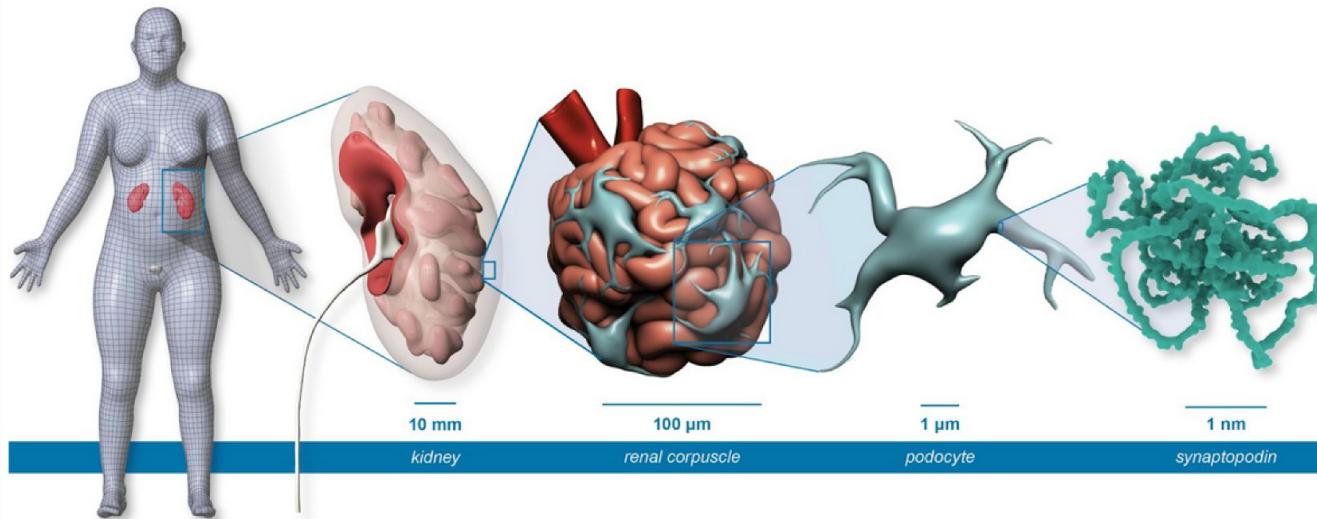
Required metadata for multiplexed antibody-based imaging and standardization across related mapping efforts

	① Target	② Antibody information	③ Methodology	④ OMAP-specific	⑤ Publication
OMAP	• • •	• • • • • • • •	• • • •	• • •	• • •
AVR	• • •	• • • • • • •	• • • •	•	• •
ASCT+B	• •			•	•

Uniprot ID, Target name, HGNC ID, Host, Isotype, Clonality, Vendor, RRID, Catalog no., Recombinant, Lot number, Dilution or concentration or Organ/tissue, Preservation method, Protocol DOI, Imaging method, Conjugate, Cycle number, Fluorescent reporter, Core panel, Rationale, Author ORCID, Reviewer ORCID, Dataset DOI

Kidney - OMAP-3





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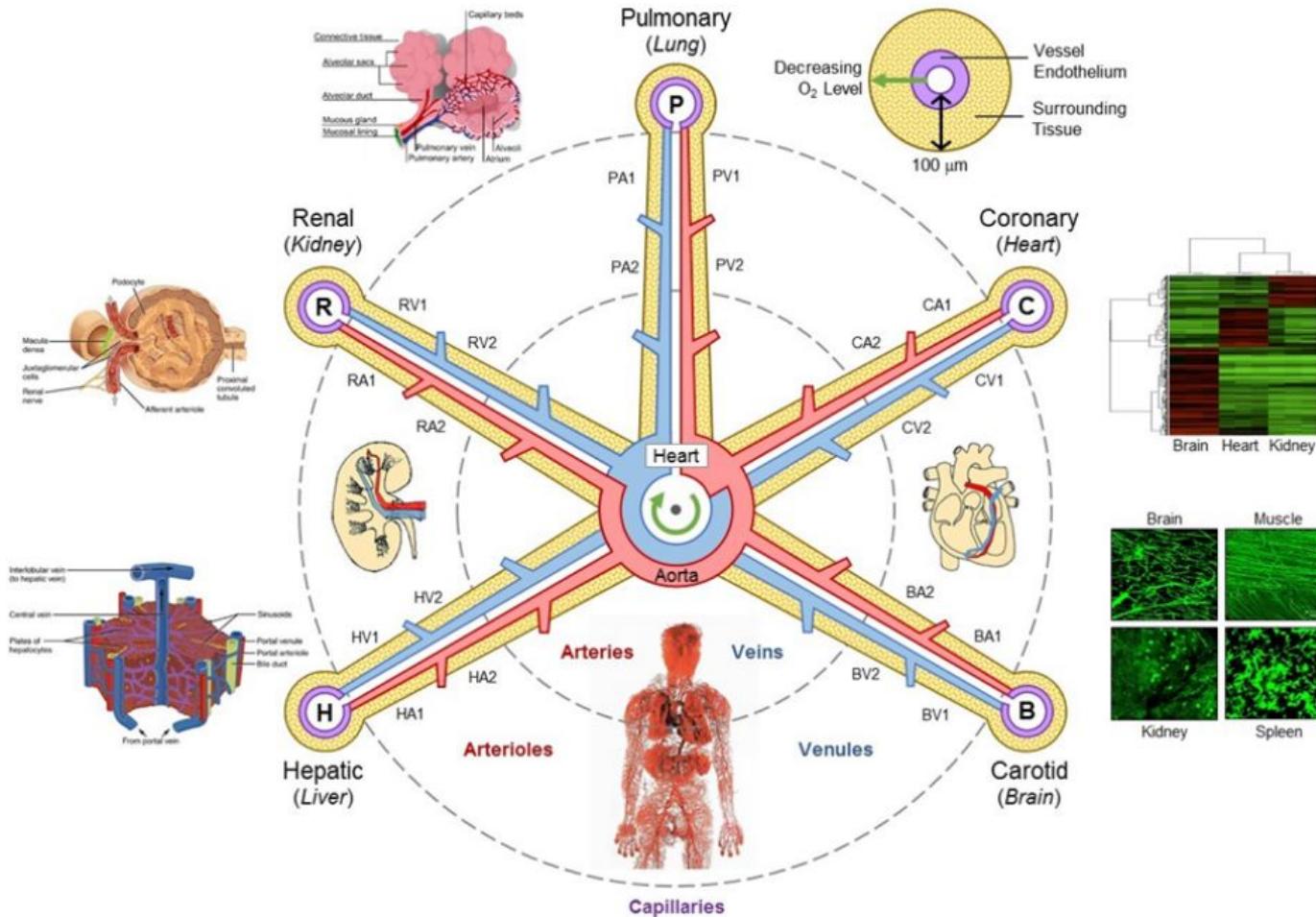
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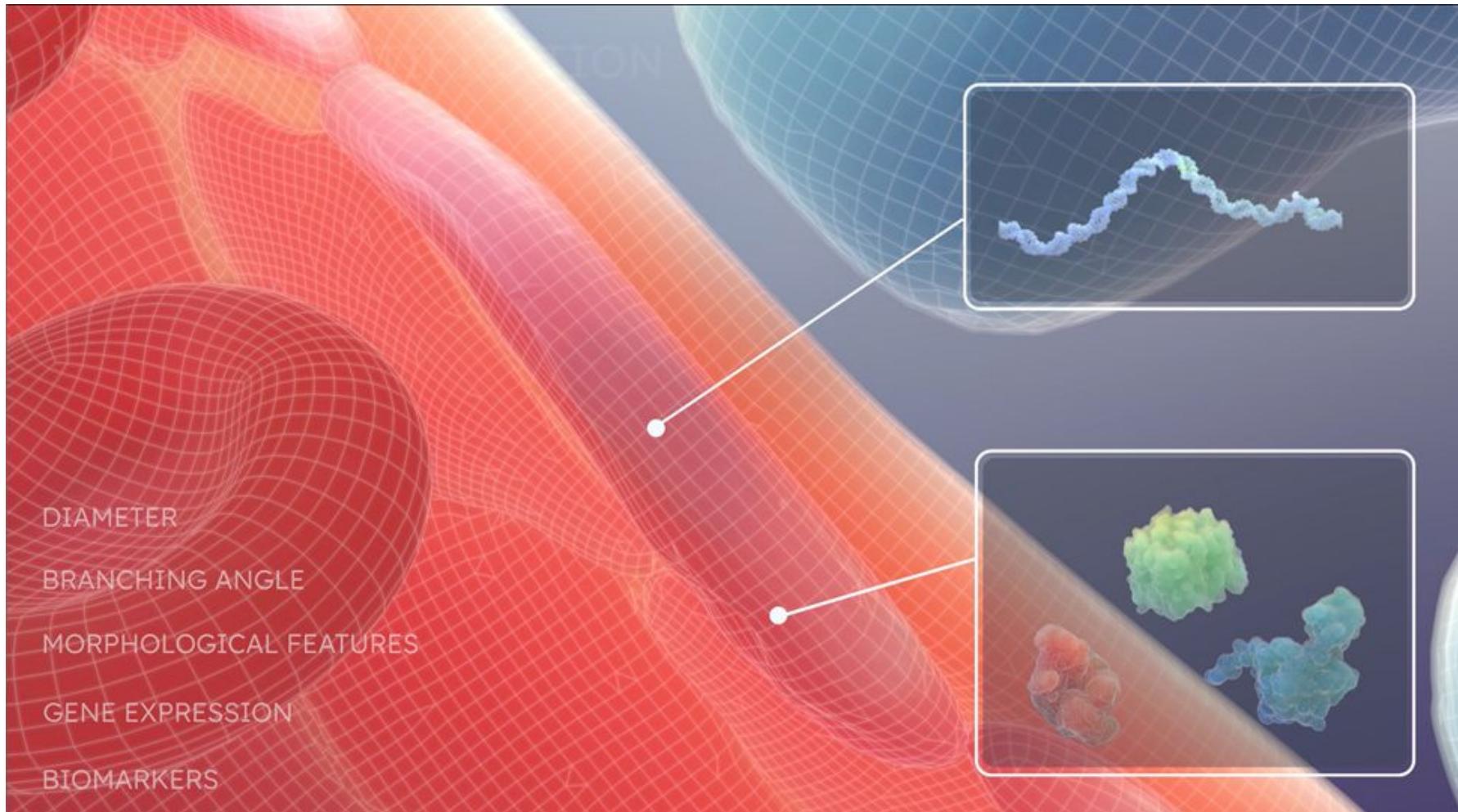
Organ Mapping Antibody Panels

Vascular Geometry

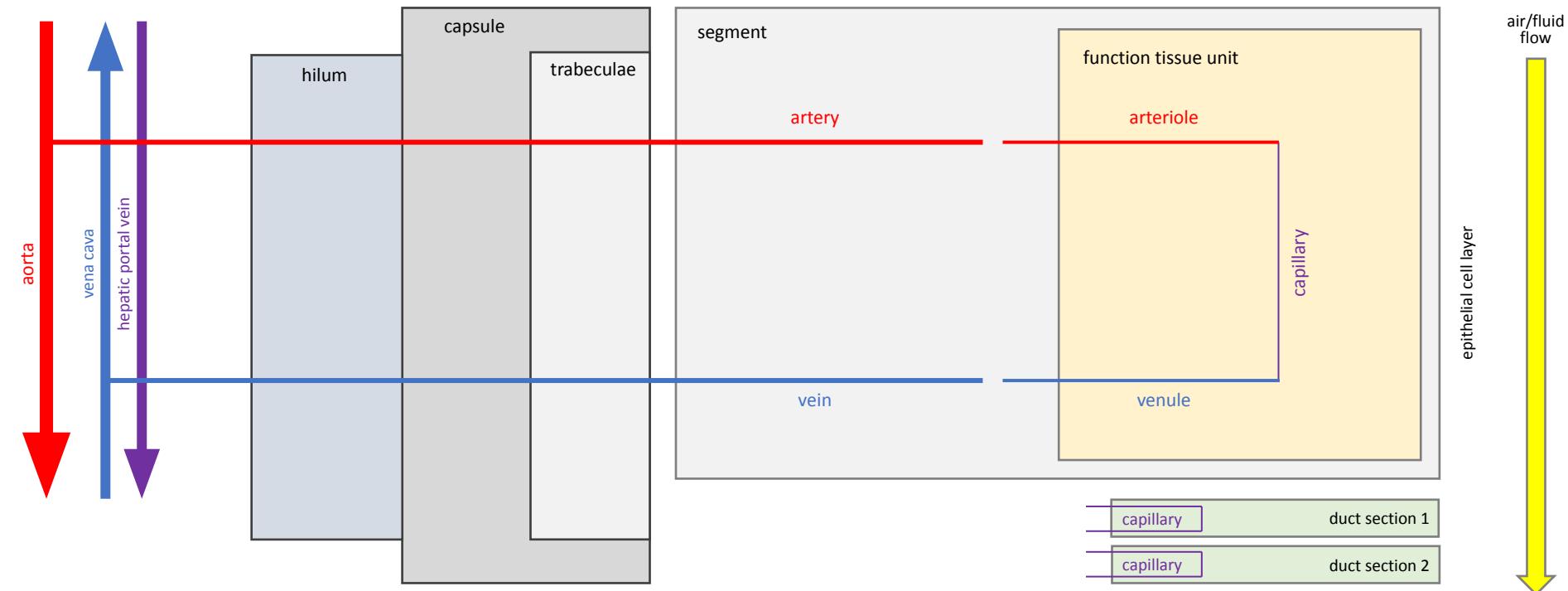
Vasculature Common Coordinate Framework



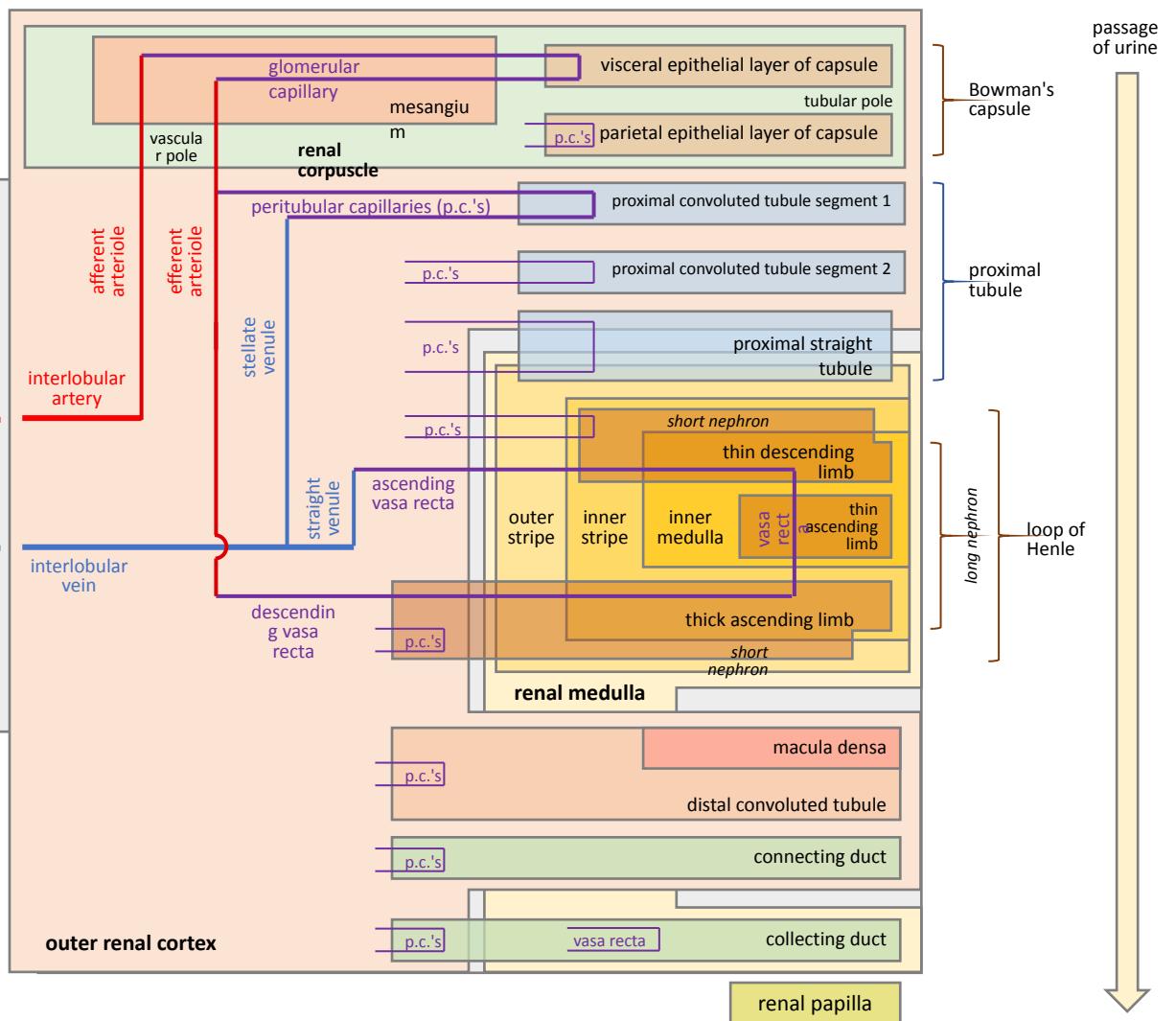
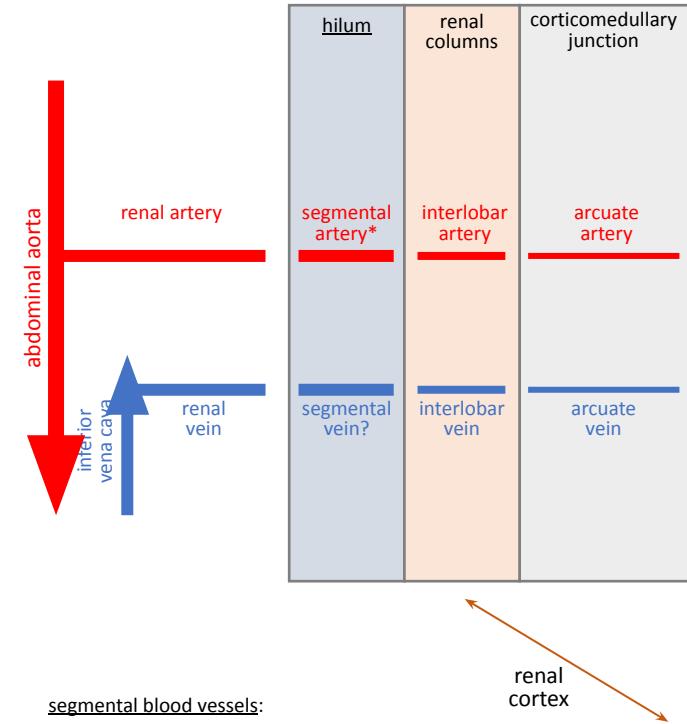
VCCF Video: https://youtu.be/zQeMgxo8n_U



Template

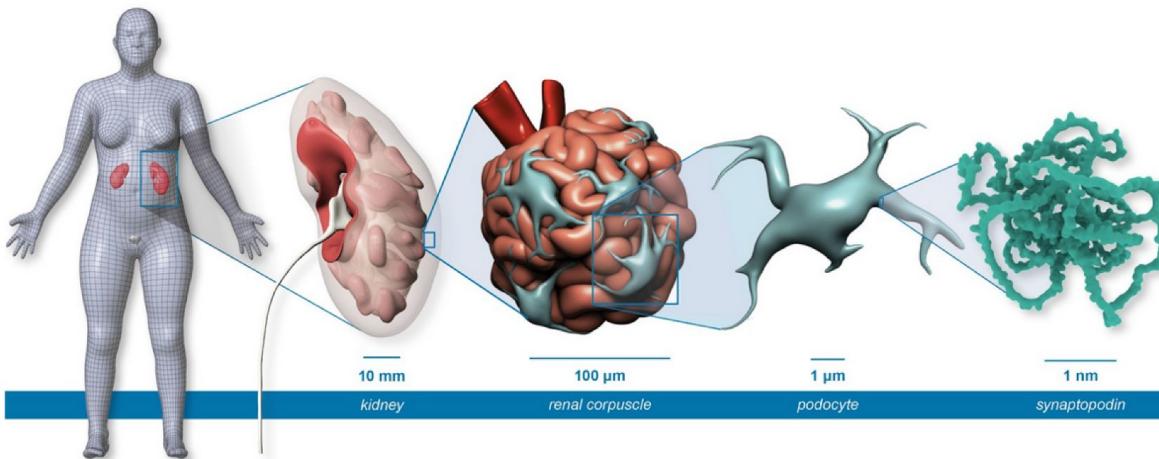


Vascular Geometry for kidney



segmental blood vessels:

- inferior segmental renal artery
- anterior inferior segmental renal artery
- anterior superior segmental renal artery
- posterior segmental renal artery
- superior segmental renal artery



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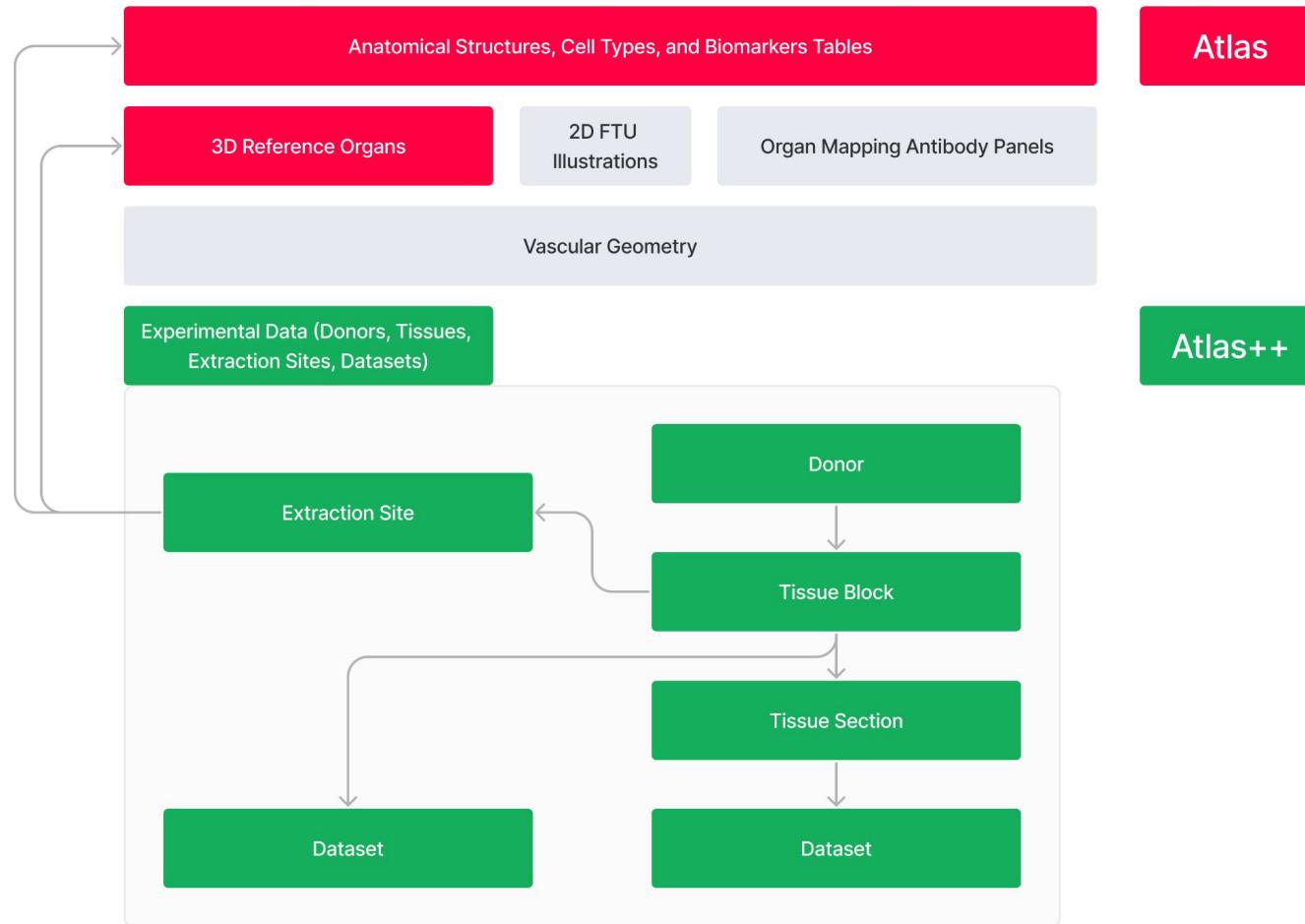
Organ Mapping Antibody Panels

Vascular Geometry

Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

Atlas++

Experimental Dataset Framework

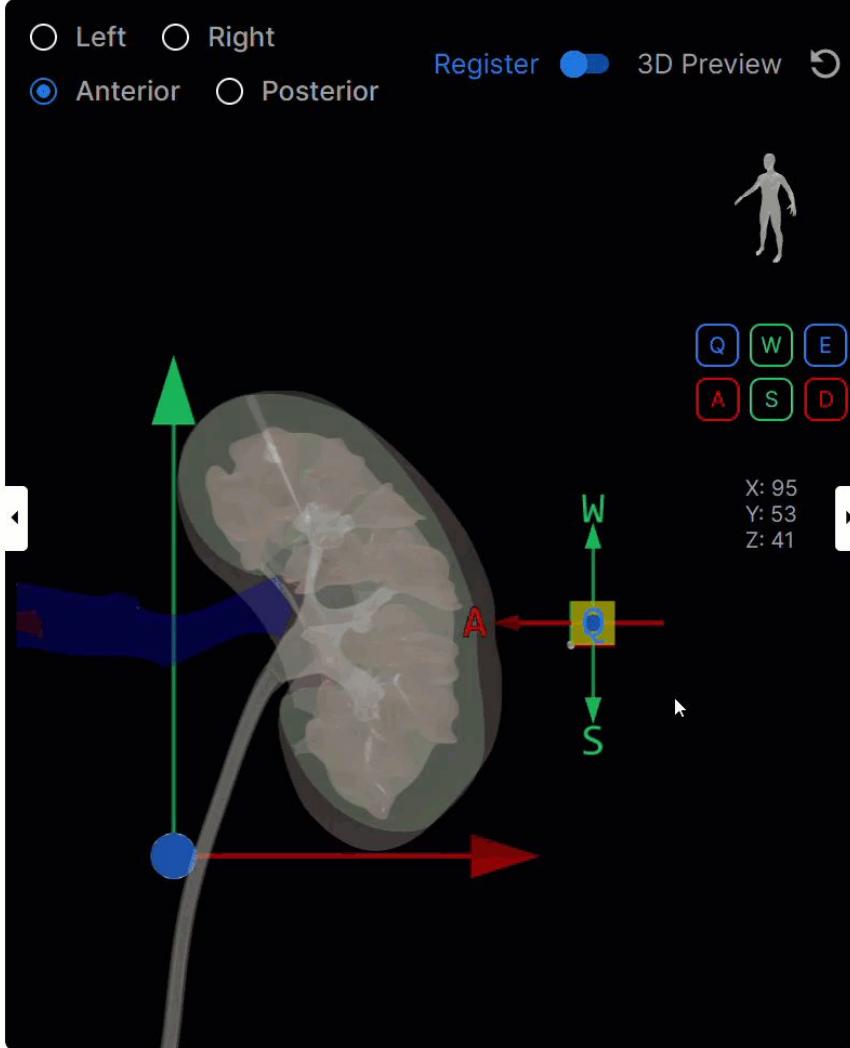


Anatomical Structures

- Left
 - Right
 - Anterior
 - Posterior
- Register 3D Preview
- all anatomical structures
 - kidney capsule
 - hilum of kidney
 - cortex of kidney
 - renal column
 - outer cortex of kidney
 - renal medulla
 - renal papilla
 - renal pyramid

Landmarks

- all landmarks
- bisection line
- left renal artery
- left renal pelvis
- left renal vein
- left ureter
- major calyces
- minor calyces



Tissue Block Controls

Tissue Block Dimensions (mm)

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

Tissue Sections

Thickness # Sections

Tissue Block Rotation

X

Y

Z

Anatomical Structure Tags

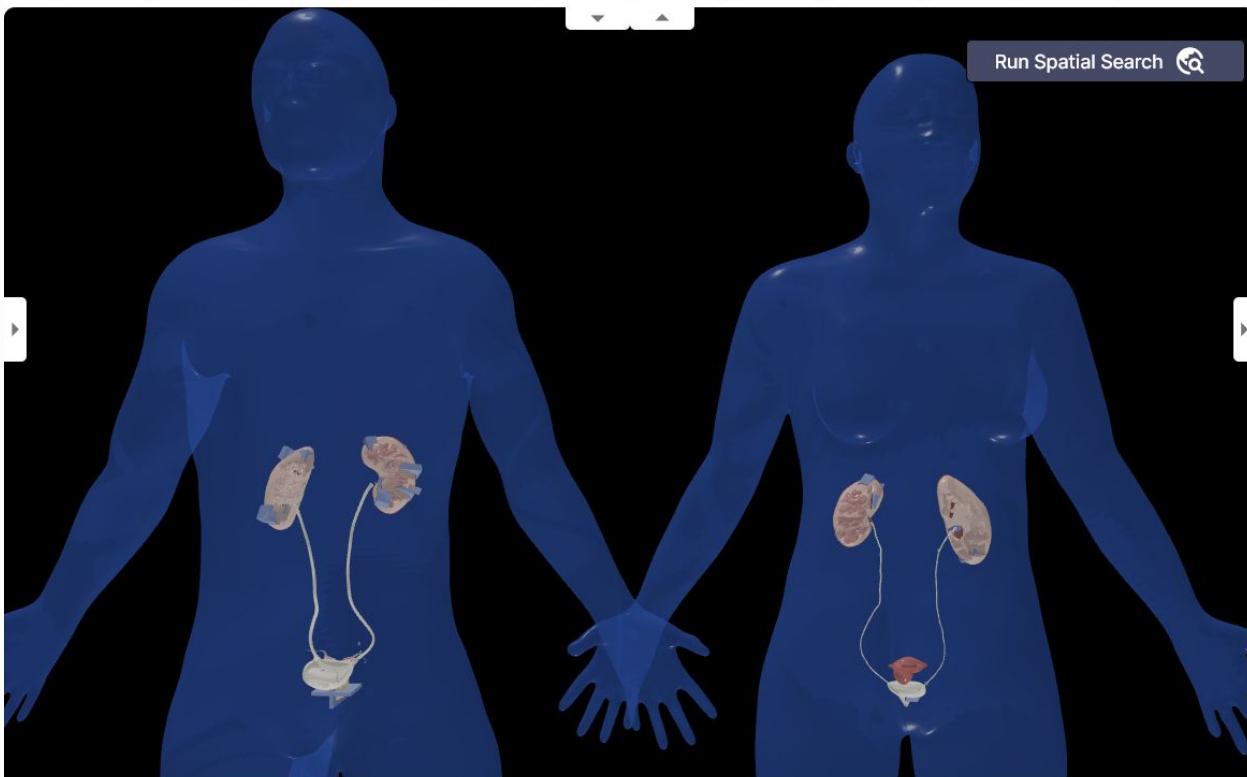
Add Anatomical Structures ...

Assigned Added

Review and Download

HRA-mapped Data: kidney, ureter, bladder, prostate, and uterus

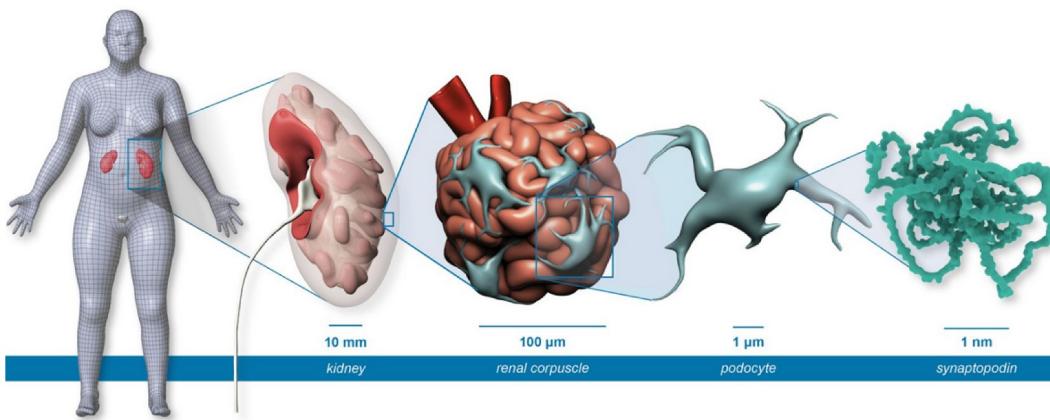
HuBMAP HRA EXPLORATION



kidney, ureter, urinary bladder, prostate, uterus | cell | biomarker

5 Tissue Data Providers
98 Donors
161 Tissue Blocks
131 Extraction Sites
400 Tissue Sections
1184 Tissue Datasets

- | | |
|--------------------------|---|
| <input type="checkbox"/> | Patient B Cortical biopsy
Entered 4/18/2020, Seth Winfree, KPMP-IU/O... |
| <input type="checkbox"/> | Patient A Cortical biopsy
Biopsy from Nephrology biobank-salvaged fro... |
| <input type="checkbox"/> | Cover Nephrectomy
Biopsy from Nephrology biobank-salvaged fro... |
| <input type="checkbox"/> | Male, Age 42, Donor ID D46
Entered 8/10/2023, John Lafin, UT Southwest... |
| <input type="checkbox"/> | Male, Age 25, Donor ID D38
Entered 8/10/2023, John Lafin, UT Southwest... |
| <input type="checkbox"/> | Male, Age 18, Donor ID D20
Entered 8/10/2023, John Lafin, UT Southwest... |
| <input type="checkbox"/> | Male, Age 36, Donor ID D80
Entered 8/10/2023, John Lafin, UT Southwest... |
| <input type="checkbox"/> | Male, Age 18, Donor ID D20 |



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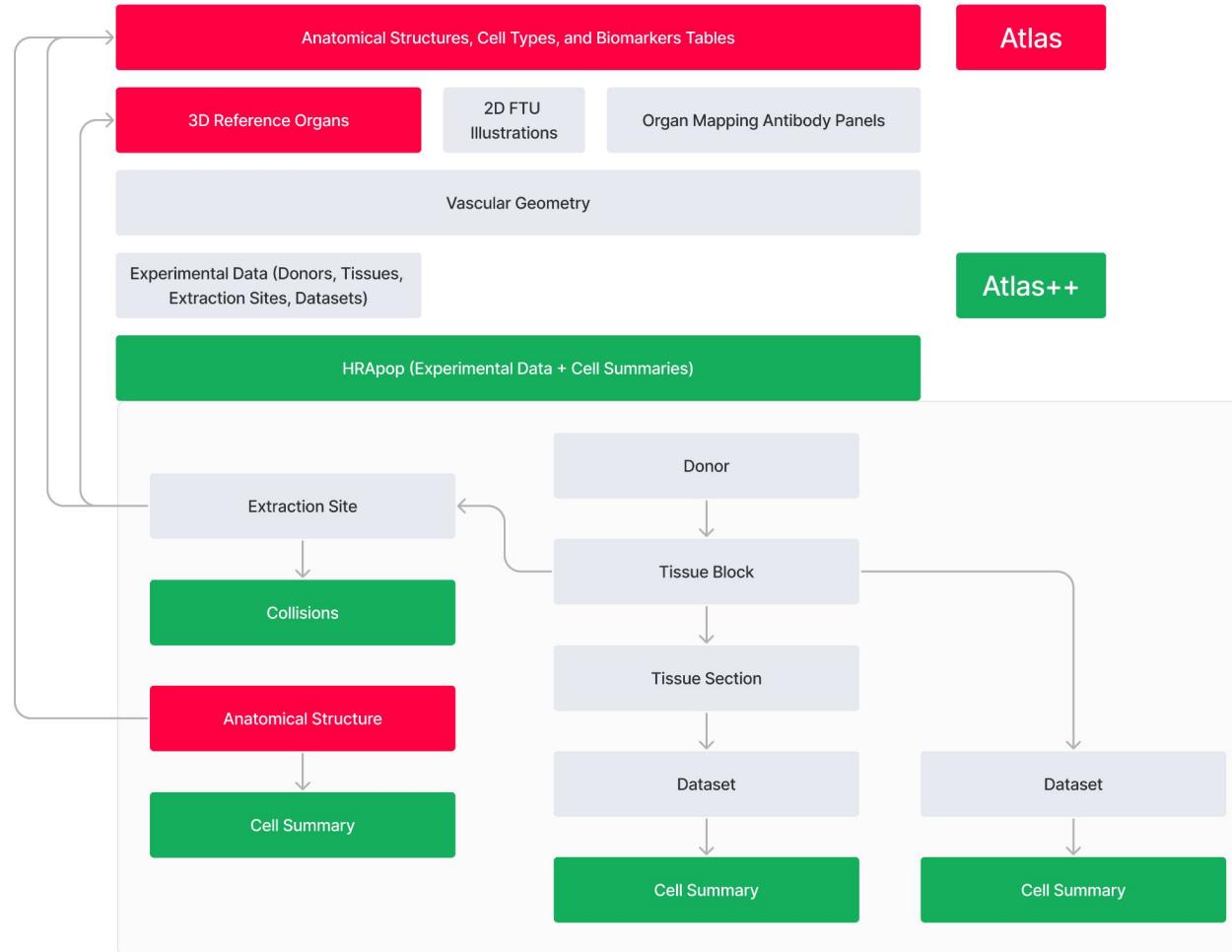
Vascular Geometry

Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

Atlas++

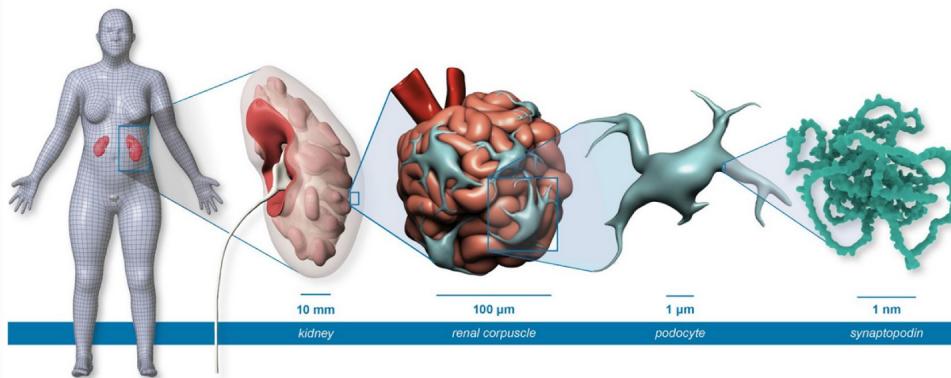
HRApop (Experimental Data + Cell Summaries)

HRApop Framework



HRApop data: kidney, ureter, bladder, prostate, and uterus

Organ	Datasets with H5AD file	ASCT+B and 3D Reference Organs			Cell Type Annotation Tools		
		#AS in 3D (male + female)	#AS	#CT	#CT in Azimuth	#CT in CellTypist	#CT in popV
kidney	207	116	61	70	58	34	0
prostate gland	34	18	13	19	0	0	13
urinary bladder	0	15	16	15	0	0	14
ureter	0	4	7	14	0	0	0
uterus	23	10	61	18	0	0	13
Total (sum, not unique)	264	159	151	122	58	34	40



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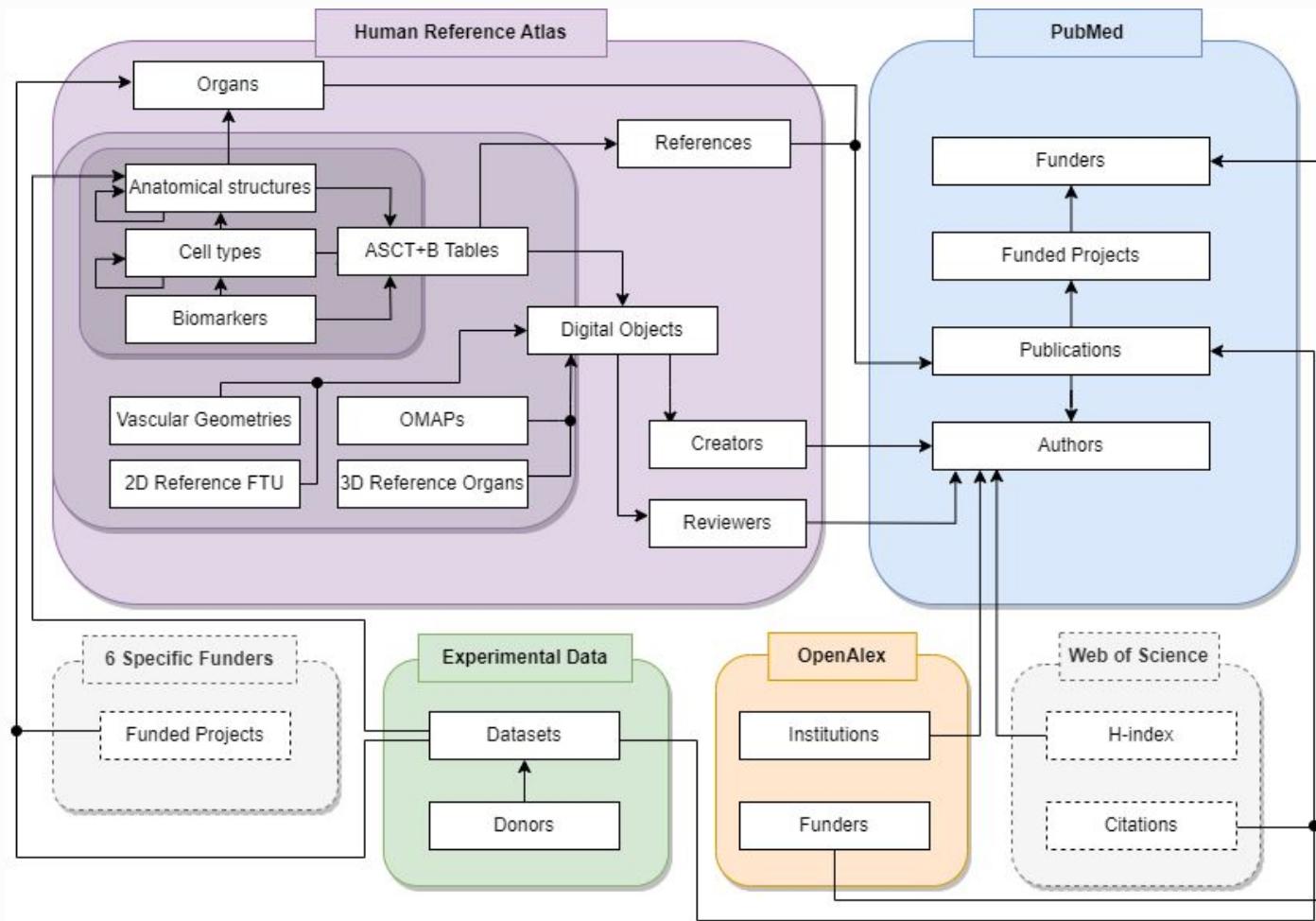
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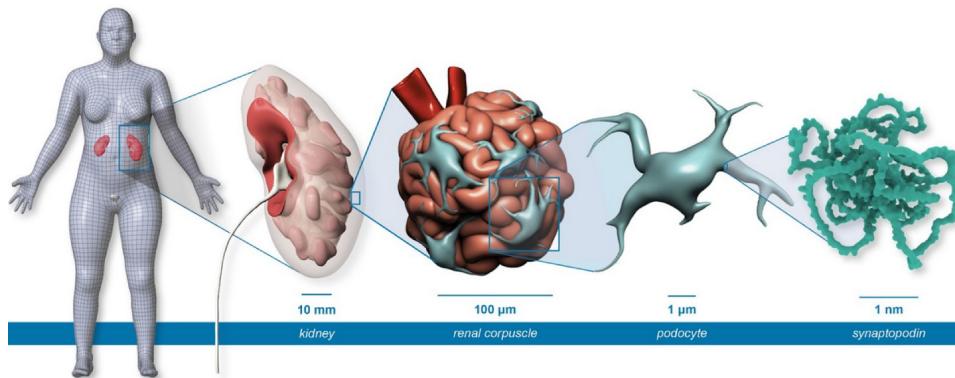
HRAlit (HRA-relevant Literature)

HRAlit Framework



HRAlit data: kidney, ureter, bladder, prostate, and uterus

Organ	#Publications	#Experts	#Institutions	#Funded Projects	#Funders
kidney	762,095	59,910	8,899	97,041	1,485
prostate	174,800	23,131	5,078	34,219	907
ureter	62,702	3,921	1,564	3,294	144
urinary bladder	133,489	10,343	3,131	14,713	460
uterus	71,489	3,266	1,417	8,470	177
Total (sum, not unique)	1,204,575	100,571	20,089	157,737	3,173



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Vascular Geometry

Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

Atlas++

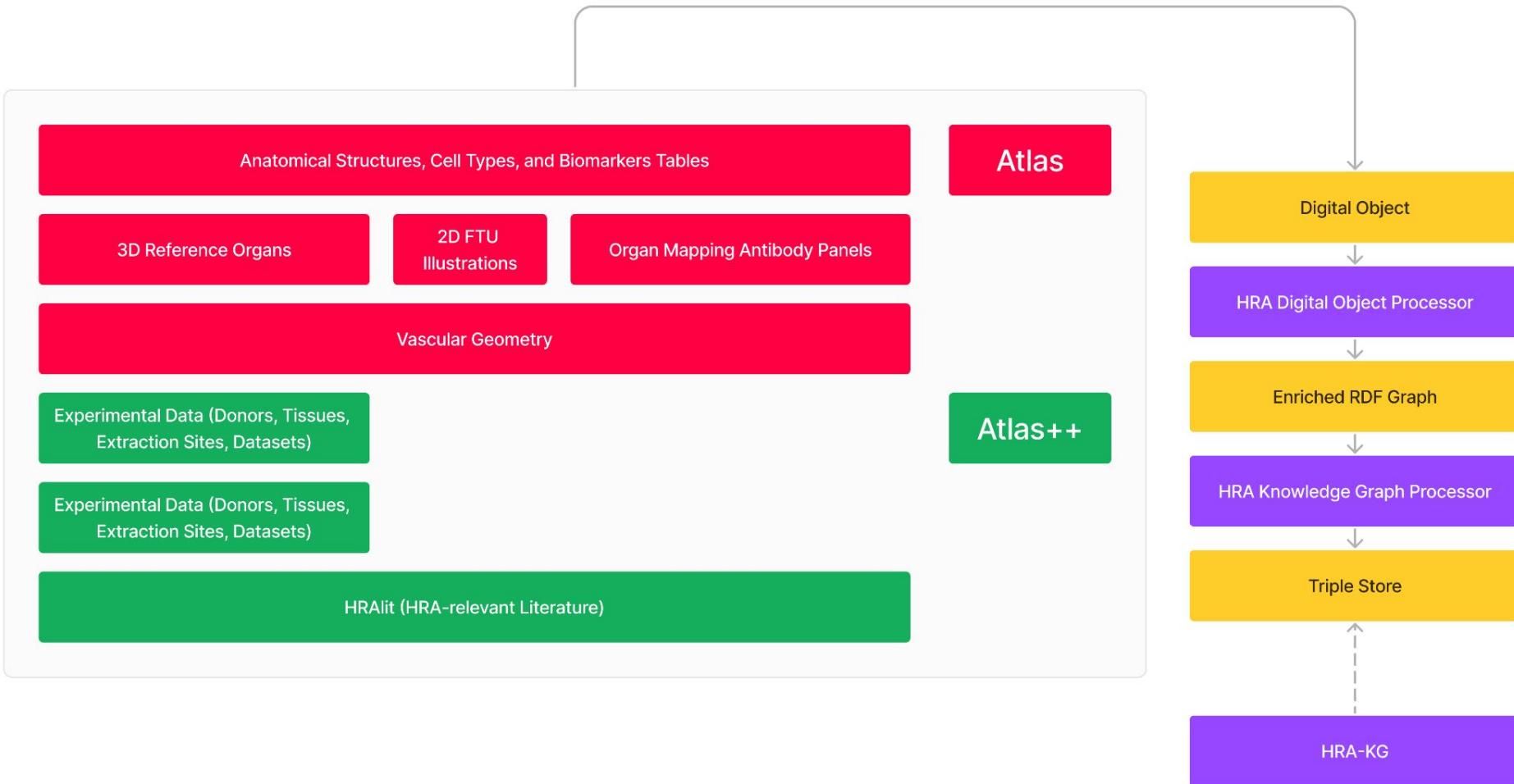
Experimental Data (Donors, Tissues,
Extraction Sites, Datasets)

HRAlit (HRA-relevant Literature)

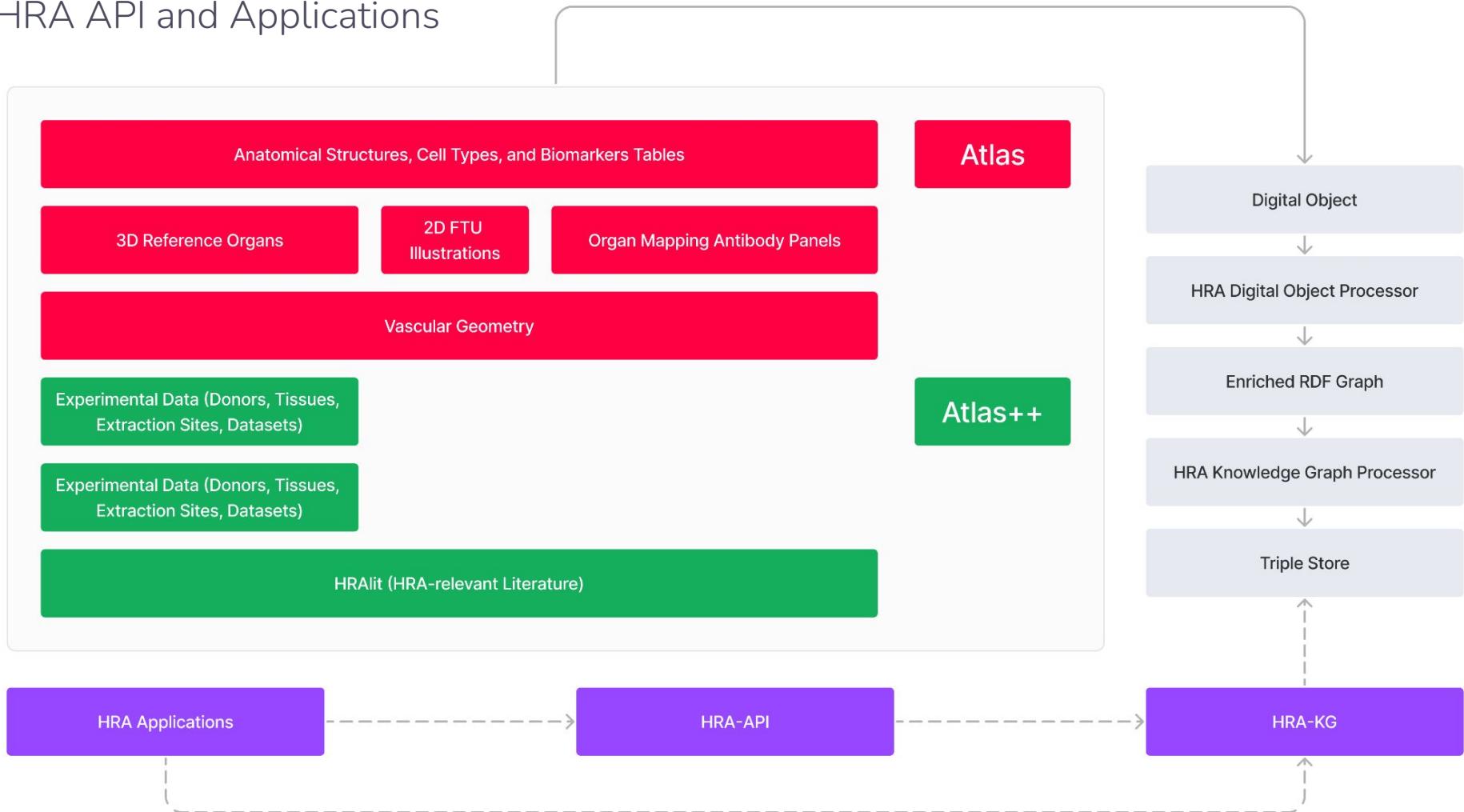
Using the HRA



HRA Knowledge Graph Framework



HRA API and Applications



ASCT+B Reporter User Interface

The screenshot illustrates the ASCT+B Reporter User Interface, featuring a central network visualization and several interactive panels.

Left Side Panel:

- Search and filter menu for locating specific structures or reducing the tree visualization to specific anatomical structures, cell types, and biomarkers.
- Collapse the legend and display settings in the left side panel.
- Return to the ASCT+B Reporter home page.
- Tree visualization legend for color and node shape.
- Display settings for OMAP Tables.
- Display settings for cell types.
- Display settings for the tree visualization.
- Display settings for biomarkers.
- Top of legend and display settings left side panel.
- Hovering over a node reveals more information.
- Email questions and feedback to the Human Reference Atlas team.

Central Network Visualization:

- Select organs displayed in the tree visualization (e.g., ASCT+B-Liver).
- Refresh view.
- Open tables in Google Sheets.
- Playground view.
- Compare.
- Reset.
- Export.
- Front.
- View GitHub Repository and other information.
- Message log of the visualization generation process.
- Summary statistics right side panel.

Information Panels:

- Anatomical structure nodes (e.g., central axis, digital nerve).
- Cell type nodes (e.g., endothelial cell).
- Biomarker nodes (e.g., CD31, CD34).

Bottom Labels:

- Anatomical structure nodes.
- Cell type nodes.
- Biomarker nodes.

<https://humanatlas.io/overview-tools>

Registration User Interface (RUI)

The screenshot illustrates the HubMAP HRA Registration User Interface (RUI) for 3D registration of anatomical structures. The interface includes a central 3D viewer, a left sidebar for anatomical structures, and a right sidebar for registration metadata.

Central 3D Viewer:

- Default anterior view of the selected organ.
- Move tissue block either by dragging left mouse button or by pressing keys on keyboard as indicated on colored axes (red, green, blue).

Top Bar:

- Switch between Register mode (four camera angles only) and 3D Preview mode (free orbit camera).
- Select a predefined camera angle in Register mode (Left, Right, Anterior, Posterior).
- Current position of tissue block (X: 76, Y: 70, Z: 52).
- Keyboard keys highlight when pressed to move tissue block.
- Button to reset the scene.

Left Sidebar: HubMAP HRA REGISTRATION

- List of anatomical structures in selected 3D model.
- Hover over an individual anatomical structure to reveal a slider to modify the opacity.
- Button to show/hide anatomical structure.
- Button to reset opacity and show/hide status.
- Set of landmarks in the organ (if available).
- Dropdown for selecting a landmark set (e.g., Landmark set HCA (1)).
- 3 dimensional scene viewer.

Right Sidebar: Registration Metadata

- RUI information modal.
- Reset tissue block dimensions.
- Enter tissue block width, height, depth.
- Reset tissue section metadata.
- Add thickness and number of tissue section.
- Reset rotation around all axes.
- Rotation value input for axis.
- Drag slider to rotate around designated axis.
- Add anatomical structure tags manually via controlled vocabulary.
- List of anatomical structures colliding with the tissue block.
- Click the Review and Download button when finished to finalize the registration.

Bottom Buttons:

- Review and Download.

Exploration User Interface (EUI)

The screenshot illustrates the HRA Exploration interface, designed for exploring tissue blocks across various anatomical structures, cell types, and biomarkers.

Filter for exploring tissue blocks of interest: Located at the top left, this section includes dropdown menus for Sex (Both), Age (1-110), and BMI (13-83). It also features checkboxes for Anatomical Structures (AS), Cell Types (CT), and Biomarkers (B).

List of reference organs for exploration: A sidebar on the right lists reference organs with their corresponding tissue block counts: Skin (2), Brain (11), Lung (28), Eye (17), Fallopian Tube (1), Heart (159), and Kidney, L (66).

Number of tissue blocks per organ: A red callout points to the count of 159 tissue blocks associated with the Heart organ.

Spatial search tool for filtering by location: A search bar labeled "Run Spatial Search" is positioned above the 3D scene viewer.

Information modal for the interface: A modal window provides information about the current filters applied: body | cell | biomarker.

Results based on current filters: The main results panel displays three categories of data:

- Tissue Data Providers**: 19 entries, including 307 Donors, 729 Tissue Blocks, 892 Tissue Sections, and 3213 Tissue Datasets.
- Donor card in the expanded view**: A detailed card for a male donor, Liz McDonough, registered on 9/10/2021, showing details like age (72), BMI (27.4), and entry date (4/9/2021).
- Tissue block card with information on number of tissue sections**: A card for a tissue block registered on 1/12/2021, showing dimensions (28 x 11 x 0.3 millimeter) and section count (26).
- Tissue section card**: A card for a tissue section registered on 1/12/2021, showing dimensions (28 x 11 x 0.3 millimeter) and section count (26).
- Dataset cards for viewing relevant portals, publications, or other resources**: Cards for "Cell Dive" and "Publication" datasets, each listing multiple registered entries.

Anatomical Structures list: Shows a tree view of anatomical structures and their tissue block counts. For example, the heart has 159 tissue blocks.

Number of tissue blocks that collide with this anatomical structure: A red callout points to the count of 159 tissue blocks associated with the heart.

Cell Types list: Shows a list of cell types and their tissue block counts. For example, adipocyte has 159 tissue blocks.

Number of tissue blocks that have this CT in colliding AS in ASCT+B table: A red callout points to the count of 159 tissue blocks associated with the adipocyte cell type.

Biomarkers list: Shows a list of biomarkers and their tissue block counts. For example, a smooth muscle actin has 0 tissue blocks.

Show and hide lists for specific biomarkers (genes, lipids, metabolites, proteins, proteoforms): A red callout points to the list of biomarkers.

Number of tissue blocks that have this biomarker in colliding AS in ASCT+B table: A red callout points to the count of 0 tissue blocks associated with a smooth muscle actin.

3D scene viewer: The central feature of the interface, displaying two blue human silhouettes with internal tissue blocks highlighted in orange.

<https://humanatlas.io/overview-tools>

Interactive FTU Explorer

Name of the selected Functional Tissue Unit

Functional Tissue Units available for exploration

Select to display the medical illustration, cell type, biomarker data, and data sources

Collapse and expand Functional Tissue Unit listings within organs

View the selected illustration digital object metadata page

Download the selected illustration in various formats

Get the FTU Explorer web component via the HRA-UI GitHub Repository

Direct link to experimental data

Expand the table view

Tabs to view tables for gene, protein, & lipids

Cell types, cell counts, & associated biomarker columns

Hover for details on ontology IDs and expression values

Legend for cell types and biomarkers table: Hover over the information icons to reveal additional legend details

Higher opacity means higher mean biomarker expression levels

Publication in which experimental data was published and linked to source data

Contact form for Human Reference Atlas team

Open the Human Reference Atlas Portal

<https://humanatlas.io/overview-tools>

Human Reference Atlas Functional Tissue Unit Explorer

FTU Library

- Kidney
 - loop of Henle ascending limb thin segment
 - Cortical Collecting Duct
 - descending limb of loop of Henle
 - inner medullary collecting duct
 - neprion
 - outer medullary collecting duct
 - renal corpuscle
 - thick ascending limb of loop of Henle
- Large intestine
- Colon
- Liver
- Lung
- Pancreas
- Prostate Gland
- Skin
- Sensory Insectile
- Spleen
- Thyroid

renal corpuscle

2D Illustration viewer

Cell types by biomarkers tables

Expand the table view

Cell Types by Gene Biomarkers

Gene Biomarkers	Protein Biomarkers	Lipid Biomarkers
DLL4	Cell Count	A2GZ
glomerular capillary endothelial cell	34,400	AKT2
glomerular mesangial cell	9,900	ALSO...
glomerular visceral epithelial cell	34,700	
parietal epithelial cell	36,600	

Biomarker Expression Mean in FTU

Percentage of Data in FTU

Source Data

Single cell transcriptional and chromatin accessibility profiling redefine cellular heterogeneity in the adult human kidney
scRNA-seq of Three Healthy Human Kidney Tissues

Illustration Download Embed

Contact HRA Portal

80 μm

Cell Distance Visualizations

The screenshot shows the Vitessce spatial viewer interface. On the left is a large 2D spatial viewer area displaying a dense network of red and purple points representing cells, with many lines connecting them to show distances. A legend below it identifies colors for different cell types and links. To the right of the viewer are two smaller panels: one titled "Spatial Layers" showing a zoomed-in view of the network, and another showing a histogram of distances between cells and vasculature. The top of the screen has a navigation bar with various links and icons.

- Access documentation
- Demos showcasing core features
- Open the Vitessce App
- Return to the Vitessce landing page
- Use tutorials
- Vitessce Python package
- Vitessce R package
- Submit bug reports or feature requests to the Vitessce team
- Blog posts
- Vitessce GitHub repository
- Vitessce pronunciation by IPA Reader
- Switch between light mode and dark mode
- The Spatial Layers panel displays more general cell type categorization of all cells: Categories may be switched on/off

Spatial View component:

- Visualizes all cells
- Connects each cell to its closest endothelial cell
- View the distributions of distances between different cell types
- View the nearest vasculature for the Vasculature Common Coordinate Framework (VCCF)

Hover over a cell to examine details

2D spatial viewer area

Legend showing colors for cell types and links from these cells to endothelial cells

Click on a cell type to filter

A separately generated histogram that displays the distributions of distances between different cell types and the nearest vasculature for the Vasculature Common Coordinate Framework

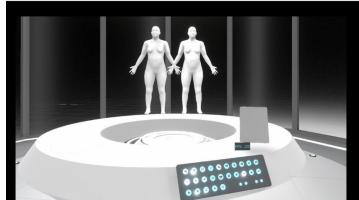
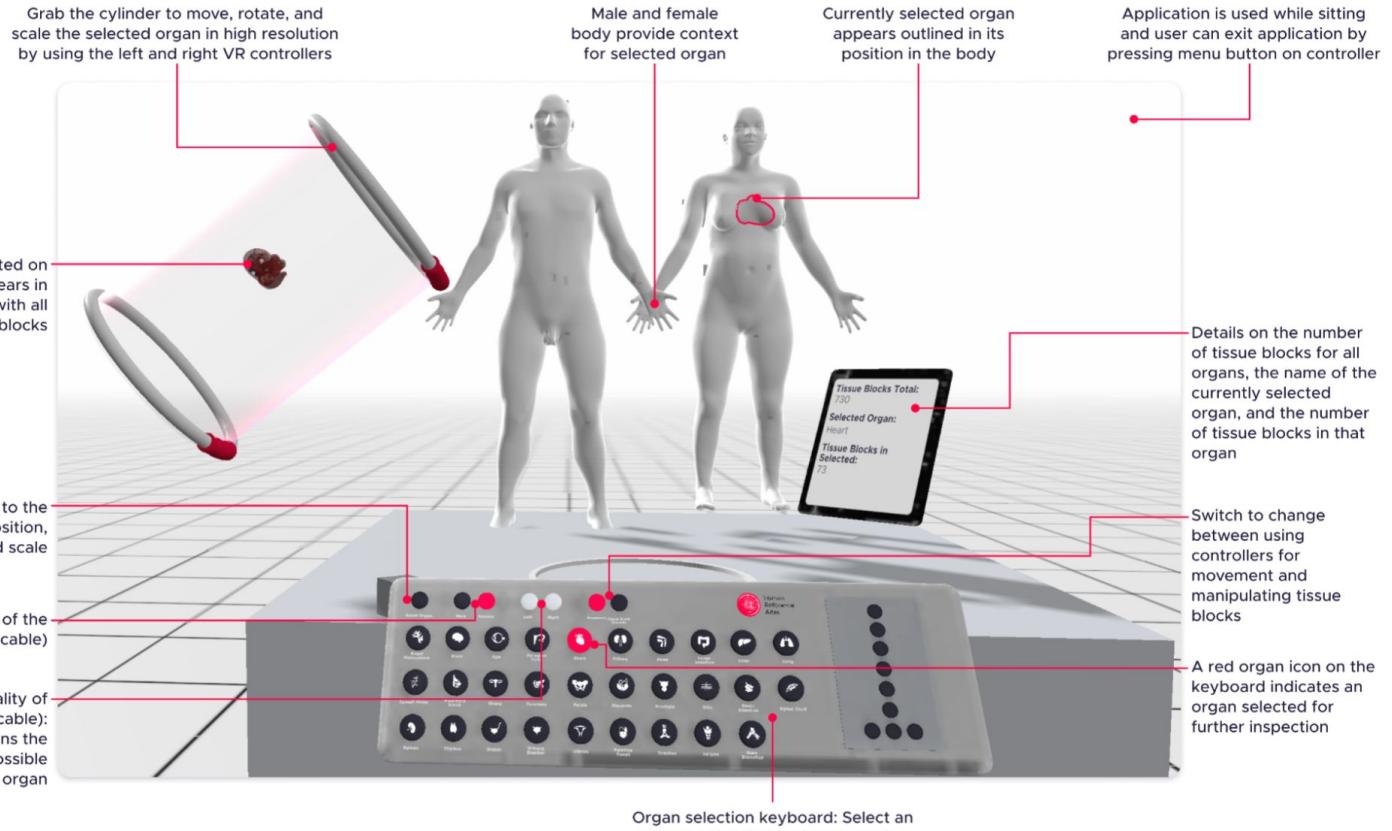
If you are interested to explore cell-cell, cell-FTU distance distributions, please share your data in this format:

x	y	z	Cell Type
555	756	4	Endothelial cell
765	231	3	B cell
356	235	7	T cell

With Yash Jain, MC-IU
yashjain@iu.edu.

Join zoom next meeting on March 25, 2024 at 4-5p ET. Email Nancy Ruschman, nruschma@indiana.edu if you don't see invite in your cal.

HRA Organ Gallery in VR



HRA Organ Gallery



Everyone

Discover the wonders of the Human Reference Atlas (HRA) in an immersive virtual reality (VR) experience! Created by 17+ international research consortia, including the NIH Human Biomolecular Atlas Program (HuBMAP), the HRA provides a comprehensive, open-source spatial reference of the healthy adult human body at the cellular level.

HRA API: Run an API Query

Input parameters for running an API query:
Fill in parameter values for the route

HRA-API Workflow 3: Run an API Query

v1

HRA-API v1.x Routes

REQUEST

QUERY-STRING PARAMETERS

- query string: SPARQL query to use
Examples: `SELECT * WHERE { ?sub ?pred ?obj. } LIMIT 10`
- token string: Authentication token to use for authenticated searches
- format: enum Allowed: application/json | application/ld+json | application/n-quads | application/n-triples | application/sparql-results+json | application/sparql-results+xml | application/trig | simple | stats | table | text/csv | text/n3 | text/tab-separated-values | text/turtle | tree
Override SPARQL response format (Note that not all formats are supported for all SPARQL query types)

API Server: <https://apps.humanatlas.io/api>
Authentication: Not Required

RESPONSE

Select a response code to view example response and schema doc

200 404

Successful operation. SPARQL responses vary by format/content negotiation.

EXAMPLE SCHEMA

```
[ { }, ]
```

Copy

Example response tab Schema documentation tab for the response

Run the API query

Reset parameters

Fill parameters with example options

<https://humanatlas.io/api>

HRA User Stories



HRA User Stories

More than 30 one-on-one interviews were conducted with atlas architects, i.e., experts who serve as principal investigators or are otherwise intimately involved in the construction of the latest generation of human atlases, including BICCN, GTEx, GUDMAP, HCA, HuBMAP, Human Tumor Atlas Network (HTAN), KPMP, LungMAP, (Re)building the Kidney (RBK), and SenNet.

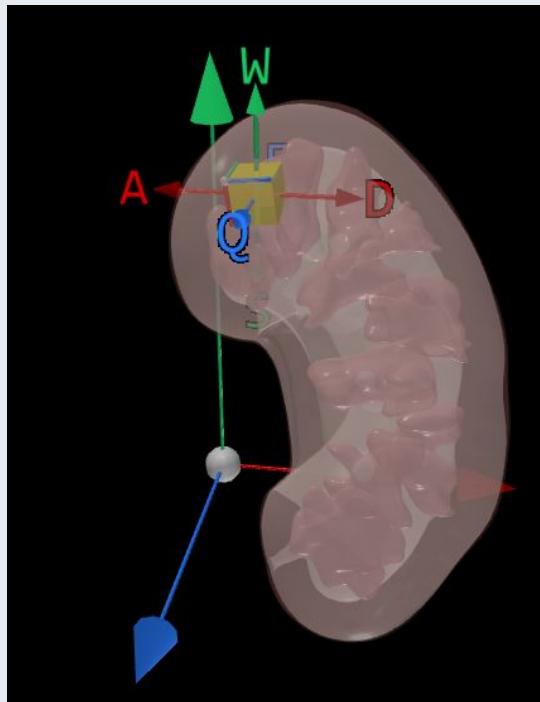
In addition, six programmers from different human atlas projects were surveyed.

Table on right shows feature summary, target user roles, user activities, and added value for seven user stories that drive HRA development.

Feature	User Role	User Activities	Added Value
<i>Facilitate atlas construction by aligning new tissue blocks with existing data</i>			
US#1. Predict cell type populations	Programmers that support Researchers, Clinicians, Pathologists	Predict and explore the likely cell type populations for a RUI-registered tissue block.	Improve cell type annotation through information on what cell type populations exist in what anatomical structures.
US#2. Predict spatial origin of tissue samples	Programmers that support Researchers, Clinicians	Predict and explore the likely 3D location in the human body for a given tissue block with known cell type population.	Compensate for the absence of spatial origin information in many single cell datasets.
<i>Use the atlas to gain insights into changes that occur at all levels in the body with aging or disease</i>			
US#3. Compare reference tissue with aging/diseased tissue	Researchers, Clinicians	Compare tissue blocks, cell types, and biomarker expression levels between healthy reference tissue and aging/diseased tissue.	Understand and communicate changes in tissue structure and function with age or disease.
US#4. Compare reference Functional Tissue Units with aging/diseased FTUs	Researchers, Clinicians	Compare FTUs in terms of cell types and mean biomarker expression levels for healthy reference tissue and aging/diseased tissue.	Understand and communicate changes in FTU structure and function with age or disease
US#5. Provide cell distance distribution visualizations	Researchers, Pathologists	Compute, visualize, and explore distance distributions between different cells, cell types, and anatomical structures (e.g., FTUs), and cell types and morphological features (e.g., the edge of an organ).	Add granularity to our understanding of how disease develops (e.g., how tumor cells grow or metastasize) in support of targeted therapies.
<i>Ensure atlas sustainability with processes that encourage collaboration and guide future development</i>			
US#6. Develop lightweight atlas components	Programmers that support Researchers and Clinicians	Implement usable and useful HRA components (interfaces and APIs) into other portals in the growing ecosystem of human atlases.	Facilitate collaboration and data/code reuse between the HRA and other portals in support of FAIR data principles.
US#7. Implement dashboard for HRA	Researchers, Clinicians, Funders	Track the evolution and usage of the HRA using data, code, and portal usage statistics in aggregate and divided by portal (e.g., HubMAP or SenNet) or PEDP survey results.	Enable evidence-based decision-making by providing insights into the atlas' construction and usage (e.g., gaps in data, application areas, user demographics, equitable access).

US#1. Predict cell type populations

Given a location in the body, what cell types and their distribution should I see?



% of Total	# Cells	Cell
17%	549,473	Cortical Thick Ascending Limb
15%	476,562	Inner Medullary Collecting Duct
8.0%	259,453	Proximal Tubule Epithelial Segment 1
7.4%	242,118	Distal Convoluted Tubule Type 1
6.3%	203,659	Ascending Thin Limb
6.0%	194,380	Connecting Tubule
5.7%	185,991	Descending Thin Limb Type 1
5.2%	168,763	Descending Thin Limb Type 2
4.7%	152,603	Proximal Tubule Epithelial Segment 3
3.9%	127,341	Medullary Thick Ascending Limb
2.9%	95,842	Fibroblast
2.7%	87,883	Cortical Collecting Duct Principal
2.1%	66,948	Macula Densa
1.8%	59,228	Medullary Fibroblast

<https://apps.humanatlas.io/us1/>

US#2. Predict spatial origin of tissue samples

Given a distribution of cells, where in the body might this have come from?

% of Total	# Cells	Cell
17%	549,473	Cortical Thick Ascending Limb
15%	476,562	Inner Medullary Collecting Duct
8.0%	259,453	Proximal Tubule Epithelial Segment 1
7.4%	242,118	Distal Convoluted Tubule Type 1
6.3%	203,659	Ascending Thin Limb
6.0%	194,380	Connecting Tubule
5.7%	185,991	Descending Thin Limb Type 1
5.2%	168,763	Descending Thin Limb Type 2
4.7%	152,603	Proximal Tubule Epithelial Segment 3
3.9%	127,341	Medullary Thick Ascending Limb
2.9%	95,842	Fibroblast
2.7%	87,883	Cortical Collecting Duct Principal
2.1%	66,948	Macula Densa
1.8%	59,228	Medullary Fibroblast



Similarity	Label
0.99	outer cortex of kidney
0.93	kidney pyramid
0.73	hilum of kidney
0.73	renal column
0.72	kidney capsule
0.50	renal papilla

Also, similar datasets and HRA extraction sites

<https://apps.humanatlas.io/us2/>

US#3. Compare reference tissue with aging/diseased tissue

The screenshot illustrates the Human Reference Atlas (HRA) Exploration interface. At the top, there's a header bar with a search icon, a user profile, and navigation icons. Below it is a toolbar with filters for Sex (Both), Age (1-110), and BMI (13-83). The main area features a 3D scene viewer with two human silhouettes. Tissue blocks are represented as colored shapes (e.g., red, orange, yellow) distributed across the body regions.

Filter for exploring tissue blocks of interest: A panel on the left lists categories: Anatomical Structures (AS), Cell Types (CT), and Biomarkers. Each category has a checkbox and a count of tissue blocks: AS (729), CT (729), and Biomarkers (729).

List of reference organs for exploration: A scrollable list of organs with their counts: brain (11), lymph node (36), eye (43), fallopian tube (0), heart (159).

Number of tissue blocks per organ: A list of organs with their counts: heart (159), kidney, L (86).

Spatial search tool for filtering by location: A search bar labeled "Run Spatial Search" with a magnifying glass icon.

Information modal for the interface: A modal window with an "i" icon containing information about the current filters: "Male, Age 72, BMI 27.4" and "Entered 4/9/2021, Liz McDonough, RTI-Gen...".

Results based on current filters: A list of results: 19 Tissue Data Providers, 307 Donors, 729 Tissue Blocks, 892 Tissue Sections, 3213 Tissue Datasets.

Donor card in the expanded view: A card for a donor: Male, Age 72, BMI 27.4, Entered 4/9/2021, Liz McDonough, RTI-Gen... with a registration date of 9/10/2021.

Tissue block card with information on number of tissue sections: A card for a tissue block: Registered 9/10/2021, Liz McDonough, RTI-Gen... 28 x 11 x 0.3 millimeter, 0.3 millimeter, 26 Secti...

Tissue section card: A card for a tissue section: Registered 1/12/2021, Liz McDonough, RTI-Gen... 28 x 11 x 0.3 millimeter, 0.3 millimeter, block.

Dataset cards for viewing relevant portals, publications, or other resources: A list of dataset cards: Cell Dive, Publication, and several entries for Liz McDonough, RTI-Gen... with registration dates from 1/12/2021 to 1/13/2021.

3D scene viewer: A central area showing two human silhouettes with colored tissue blocks overlaid.

<https://apps.humanatlas.io/eui/>

US#4. Compare reference FTUs with aging/diseased FTUs

This figure illustrates the Human Reference Atlas Functional Tissue Unit Explorer interface, showing how to compare reference FTUs with aging/diseased FTUs.

Functional Tissue Units available for exploration: A tree view of various organs and their subunits. Clicking on an organ or subunit expands its list of components. A red dot highlights the "renal corpuscle" under the "Kidney" section.

Name of the selected Functional Tissue Unit: Displays the name of the selected FTU, "renal corpuscle".

2D Illustration viewer: A detailed 2D illustration of a renal corpuscle. Labels include: Glomerular visceral epithelial cell, Parietal epithelial cell, Epithelial cell proximal tubule, Glomerular capillary endothelial cell, Glomerular mesangial cell, Macula densa epithelia cell, Afferent arteriole endothelial cell, Efferent arteriole endothelial cell. A scale bar indicates 50 μm.

Cell types by biomarkers tables: A table showing cell types by gene, protein, and lipid biomarkers. The table includes columns for Cell Type, Gene Biomarkers, Protein Biomarkers, and Lipid Biomarkers.

Cell Type	Gene Biomarkers	Protein Biomarkers	Lipid Biomarkers
glomerular capillary endothelial cell	34,400	AASS AKT3 ALS2...	
glomerular mesangial cell	9,900		
glomerular visceral epithelial cell	34,100		
parietal epithelial cell	26,600		

Expand the table view: A button to expand the table view for more details.

Tabs to view tables for gene, protein, & lipids: Tabs for viewing tables for gene, protein, and lipid biomarkers.

Cell types, cell counts, & associated biomarker columns: Columns for cell type, cell count, and associated biomarker values.

Hover for details on ontology IDs and expression values: A callout for hovering over the table cells.

Legend for cell types and biomarkers table: A legend for the cell types and biomarkers table, showing a color scale from 0.0 (blue) to 1.0 (red) for mean expression levels and a size scale for the percentage of cells in the FTU (0%, 50%, 100%).

Publication in which experimental data was published and linked to source data: A callout for the publication link at the bottom of the table.

Higher opacity means higher mean biomarker expression levels: A callout for the color intensity in the table cells.

Contact form for Human Reference Atlas team: A contact button for the Human Reference Atlas team.

Open the Human Reference Atlas Portal: A button to open the Human Reference Atlas Portal.

View the selected illustration digital object metadata page: A button to view the digital object metadata page for the selected illustration.

Download the selected illustration in various formats: A button to download the selected illustration in various formats.

Get the FTU Explorer web component via the HRA-UI GitHub Repository: A button to get the FTU Explorer web component via the HRA-UI GitHub Repository.

Direct link to experimental data: A button to directly link to experimental data.

Illustration, Download, Embed: Buttons for navigating the illustration viewer.

Contact, HRA Portal: Buttons for contacting the team and opening the portal.

<https://apps.humanatlas.io/ftu-explorer/>

US#5. Provide cell distance distribution visualizations

The screenshot shows the Vitessce spatial viewer interface. A large central area displays a 2D spatial viewer with a network of red lines connecting cells to their nearest endothelial neighbors. A legend below the viewer identifies cell types by color: Endothelial (blue), Endothelial_link (light blue), Endothelial_stromal (green), Endothelial_stromal_link (light green), Endothelial_stromal_stromal (yellow), Endothelial_stromal_stromal_link (light yellow), Endothelial_stromal_stromal_stromal (orange), Endothelial_stromal_stromal_stromal_link (light orange), Endothelial_stromal_stromal_stromal_stromal (purple), Endothelial_stromal_stromal_stromal_stromal_link (light purple), Endothelial_stromal_stromal_stromal_stromal_stromal (pink), Endothelial_stromal_stromal_stromal_stromal_stromal_link (light pink), Endothelial_stromal_stromal_stromal_stromal_stromal_stromal (grey), Endothelial_stromal_stromal_stromal_stromal_stromal_stromal_link (light grey), Endothelial_stromal_stromal_stromal_stromal_stromal_stromal_stromal (black), Endothelial_stromal_stromal_stromal_stromal_stromal_stromal_stromal_link (light black). A smaller inset window shows a zoomed-in view of the network. To the right is a histogram showing the distribution of distances between different cell types and the nearest vasculature for the Vasculature Common Coordinate Framework (VCCF).

Annotations:

- Access documentation
- Demos showcasing core features
- Open the Vitessce App
- Use tutorials
- Vitessce Python package
- Vitessce R package
- Submit bug reports or feature requests to the Vitessce team
- Vitessce pronunciation by IPA Reader
- Blog posts
- Vitessce GitHub repository
- Switch between light mode and dark mode
- Return to the Vitessce landing page
- Spatial View component:
 - Visualizes all cells
 - Connects each cell to its closest endothelial cell
 - View the distributions of distances between different cell types
 - View the nearest vasculature for the Vasculature Common Coordinate Framework (VCCF)
- Hover over a cell to examine details
- 2D spatial viewer area
- Legend showing colors for cell types and links from these cells to endothelial cells
- Click on a cell type to filter
- The Spatial Layers panel displays more general cell type categorization of all cells: Categories may be switched on/off
- A separately generated histogram that displays the distributions of distances between different cell types and the nearest vasculature for the Vasculature Common Coordinate Framework

Coming June 14th on humanatlas.io

US#6. Develop lightweight atlas components

The screenshot shows the NetMAP HRA Registration software interface. At the top, there's a navigation bar with tabs: Left, Right, Anterior, Posterior, Rightmost, and 3D Preview. Below the navigation bar is a section titled "Anatomical Structures" with a list of structures: all anatomical structures, atria, ventricle, mitral valve, tricuspid valve, aortic valve, pulmonary veins, papillary muscle of heart, anterior papillary muscle of left ventricle, anterolateral head of lateral papilla, anteromedial head of lateral papilla, posterior papillary muscle of right atrium, posteroanterior head of posterior papilla, and left cardiac atrium.

On the left side, there's a "Landmarks" section with a dropdown menu set to "Labeled landmarks" and a list of landmarks: all landmarks, atria, ventricle, left atrium, left ventricle free wall, right atrium, and right ventricle.

The central part of the interface features a 3D heart model with a coordinate system (red, green, blue axes) and a registration grid overlaid. A registration tool is active, indicated by a yellow dot on the grid and a red dot on the heart model. The registration parameters shown are:

- Tissue Block Dimensions (mm): X: 7.75, Y: 7.90, Z: 7.60
- Tissue Sections: 4 Sections
- Tissue Block Rotation (degrees): X: -23, Y: 30, Z: 25

On the right side, there's a "Registration Metrics" section with a "Tissue Block Controls" table and a "Tissue Block Rotation" table. The "Tissue Block Controls" table includes columns for Name, Metric, and Value. The "Tissue Block Rotation" table includes columns for Axis, Angle, and Value. At the bottom right, there's a "Review and Download" button.

The screenshot shows a 3D reconstruction of several tissue blocks within a dark, irregular boundary. A vertical sidebar on the right contains the following text:

Male, Gonen

- 2 Tissue Data Providers
- 10 Donors
- 44 Tissue Blocks
- 198 Tissue Sections
- 90 Tissue Datasets

100 tissue blocks using the HRAI registration open interface (HRI).

Extract tissue sections in tissue blocks with the HRAI Exploration User Interface (EUI).

View images through anatomical structures, cell types, and common biomarkers (ASC-B).

Register Tissue

Explore Tissue

ASCB Report

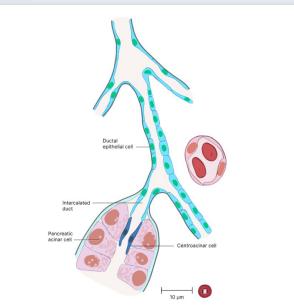
Human Reference Atlas (HRA) Deep Dive

HRA Portal

Online Course

Paper

MMB Female



HRA-API 2.0

HuBMAP Help Doc <https://hubmapconsortium.org> | License: [MIT License](#)

This API provides programmatic access to data registered to the Human Reference Atlas (HRA). See the [HuBMAP HRA Portal](#) for details.

API SERVER

- 🌐 <https://apps.humanatlas.io/api> - HRA 2.0 Production
- 🌐 <https://apps.humanatlas.io/hra-api> - HRA 1.x Production
- 🌐 <https://apps.humanatlas.io/hra-api--staging> - HRA 1.x Staging
- 🌐 <https://apps.humanatlas.io/> - Local Server

SELECTED: <https://apps.humanatlas.io/api>

[Expand all](#) | [Collapse all](#) sections

v1

HRA-API v1.x Routes

Method	Path	Description
GET	/v1/db-status	Get current status of database
GET	/v1/sparql	Run a SPARQL query
POST	/v1/sparql	Run a SPARQL query (POST)
GET	/v1/aggregate-results	Get aggregate results / statistics
POST	/v1/get-spatial-placements	Given a SpatialEntity already placed relative to a reference SpatialEntity, retrieve a new direct SpatialPlacements to the given SpatialEntity
GET	/v1/hubmap/rvi/locations.jsonld	Get all hubmap/rvi locations (if enabled)
GET	/v1/hubmap/rvi/locations.jsonld	Get all hubmap/rvi locations (if enabled)

Welcome to the Functional Tissue Unit Explorer

Explore functional tissue units (FTUs) featuring experimental datasets and Human Reference Atlas (HRA) technologies. Read more about this effort at [HRA Portal: FTU Explorer](#)

The FTU Explorer was designed in close collaboration with [Kidney Precision Medicine Project](#) and [European Bioinformatics Institute](#).

FTU Library

loop of Henle ascending limb thin segment: FTU Illustration

FTU Illustration Gene Biomarkers Protein Biomarkers Lipid Biomarkers Source Data

Ascending vasa recta

Ascending thin limb cell

10 μ m

Kidney

- loop of Henle ascending limb thin segment
- Cortical Collecting Duct
- descending limb of loop of Henle
- inner medullary collecting duct
- nephron
- outer medullary collecting duct
- renal capsule
- thick ascending limb of loop of Henle

Large Intestine

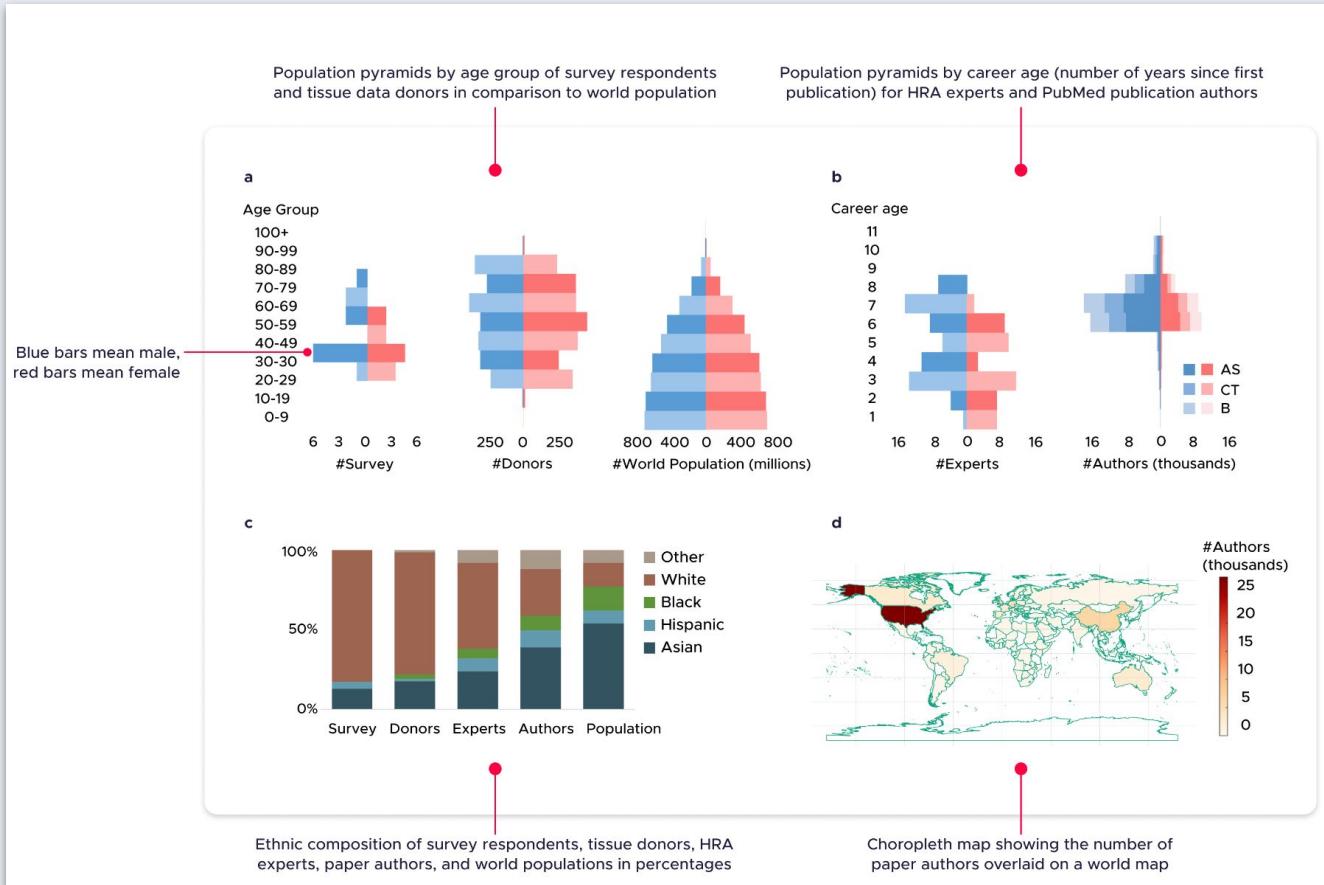
- crypt of Lieberkuhn of large intestine

Liver

Illustration Download Embed Contact HRA Portal

Coming June 14th on humanatlas.io

US#7. Implement dashboard for HRA



Coming June 14th on humanatlas.io

Wrapping it up



Future work

- Releases every 6 months (June and December)
- More data, more collaborations, more organs, continued advancement of US#1-7
- HRA in clinical settings



Current Team

Principal Investigator,
Co-Principal Investigators,
and Consultants



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MC-IU PI
CNS Director

Mark Musen
Professor of Medicine
(Biomedical Informatics) and
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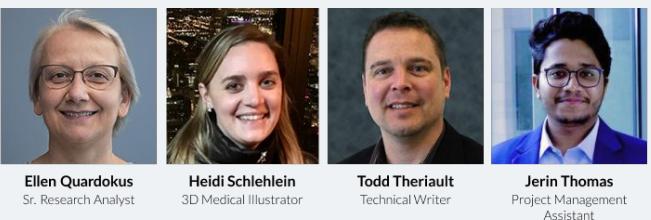
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Bhushan Sanjay
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Connecting people is key to our success. Here are some of
our great collaborators (apologies to those I missed!)



Ellen Quardokus
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Heidi Schlelein
3D Medical Illustrator

Todd Theriault
Technical Writer

Jerin Thomas
Project Management
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Thank you!

Resources at:

<https://humanatlas.io/events/AUA2024>

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