

AUA
2024
San Antonio

MAY 3-6

Keynote:
The Human
Reference Atlas





Version 2.0

Human Reference Atlas

<https://humanatlas.io>



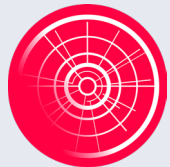


Keynote: The Human Reference Atlas



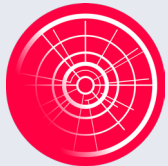
Bruce W. Herr II
Technical Director

*Cyberinfrastructure for Network Science Center
Department of Intelligent Systems Engineering
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

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

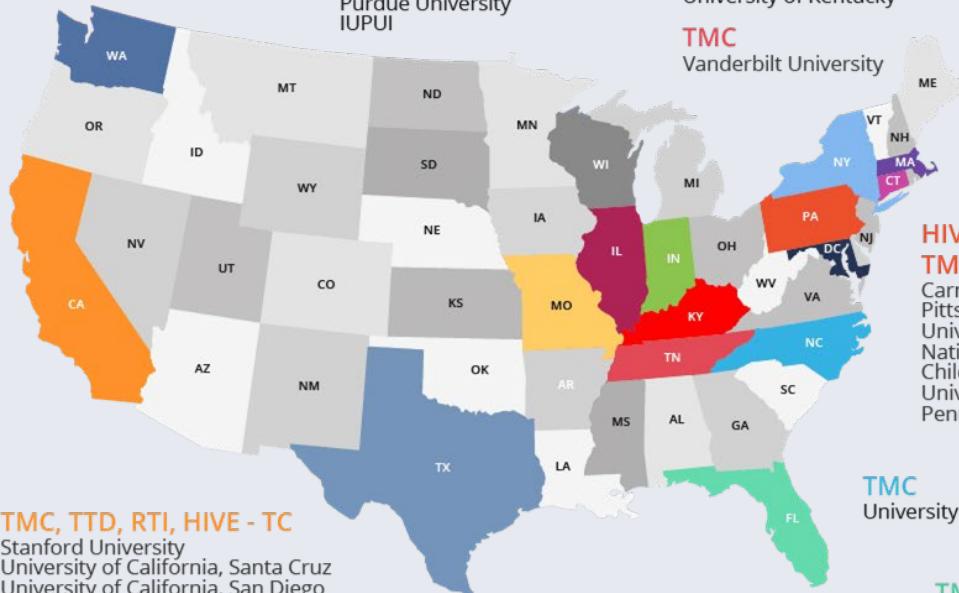
NIH Common Fund
Johns Hopkins University
Brigham and Women's Hospital

TMC, TTD

University of Connecticut
Yale University

HIVE - TC, TTD, RTI, TMC, DP

Harvard University
Harvard Medical School
Columbia University
Beth Israel Deaconess Medical Center



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

TMC

Texas Advanced Computing Center

TMC

University of North Carolina, Chapel Hill

HIVE - IEC, HIVE - TC, RTI, TMC, TTD, DP

Carnegie Mellon University
Pittsburgh Supercomputing Center
University of Pittsburgh
National Disease Research Interchange
Children's Hospital of Philadelphia
University of Pennsylvania
Pennsylvania State University

TMC, HIVE - TC

University of Florida

TMC

University of Zurich



TMC

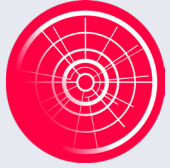
Delft University of Technology



HIVE - TC, TMC

European Bioinformatics Institute
Wellcome Sanger Institute





Early history of the HRA and HuBMAP

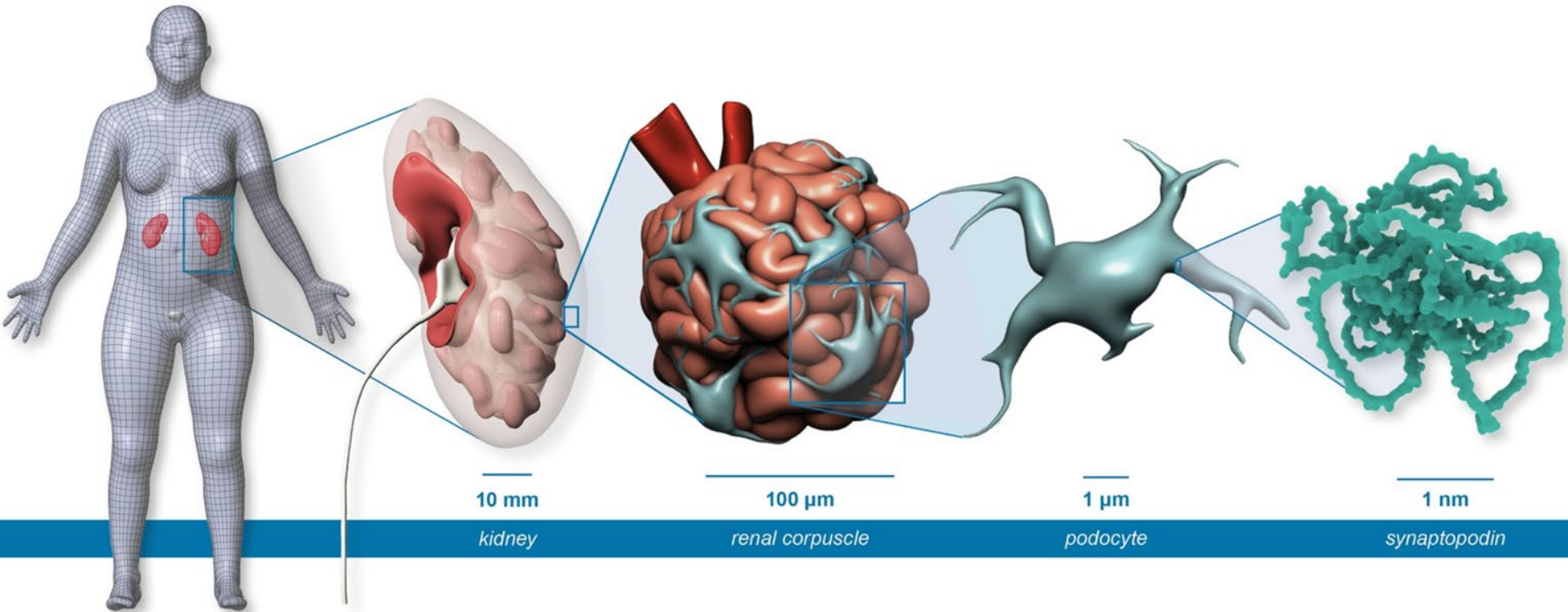
- HuBMAP started in 2018 with the goal of mapping the human body down to the cellular level
- The IU team started off with creating a common coordinate framework, that eventually evolved into the HRA
- In 2023, we published HRA v2.0
- We are now in the production phase of HuBMAP

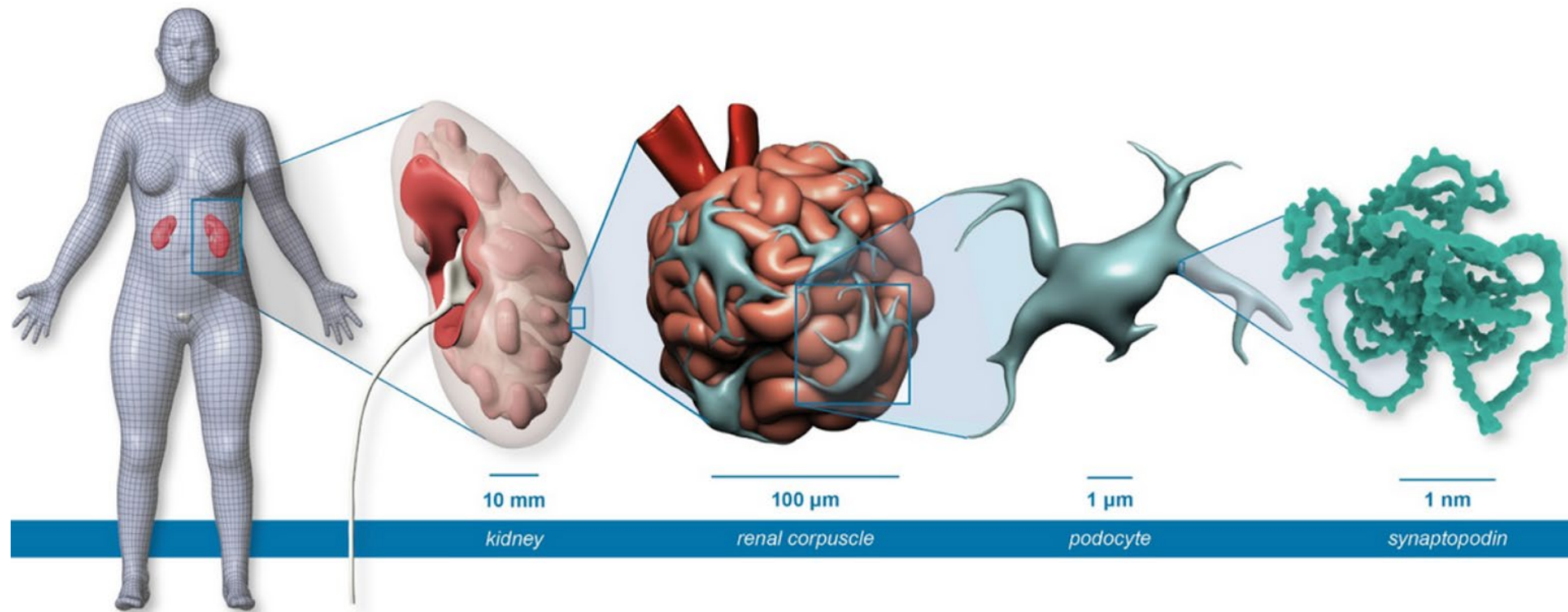


What is the HRA?

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, ..

Anatomical Structures

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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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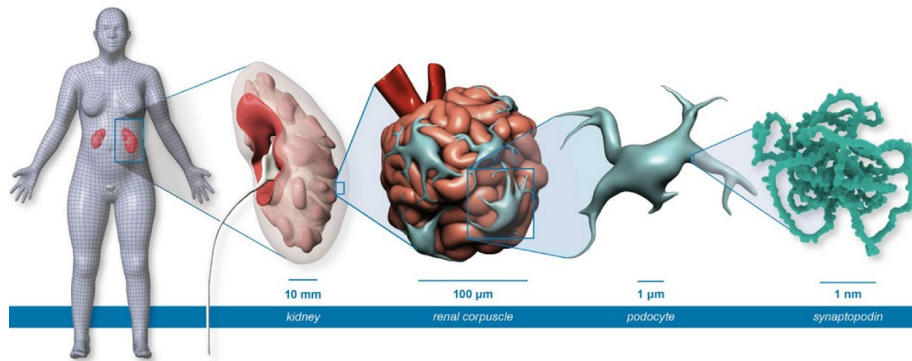
Vascular Geometry

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

Atlas++

HRApop (Experimental Data + Cell Summaries)

HRAlit (HRA-relevant Literature)



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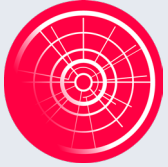
Vascular Geometry

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Atlas++

HRApop (Experimental Data + Cell Summaries)

HRAlit (HRA-relevant Literature)



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

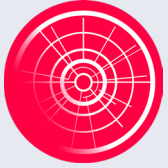
HRA User Stories

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, GTE_x, 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.

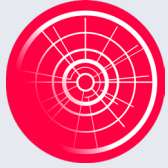
Feature	User Role	User Activities	Added Value
<i>Facilitate atlas construction by aligning new tissue blocks with existing data</i>			
US#1. Predict cell type populations	Programmers that support Researchers, Clinicians, Pathologists	Predict and explore the likely cell type populations for a RUI-registered 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

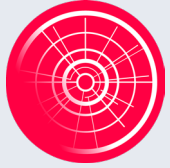
- Anatomical Structures
- Functional Tissue Units
- Cell Types
- Biomarkers



Human Reference Atlas

Connecting and empowering people

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



Human Reference Atlas

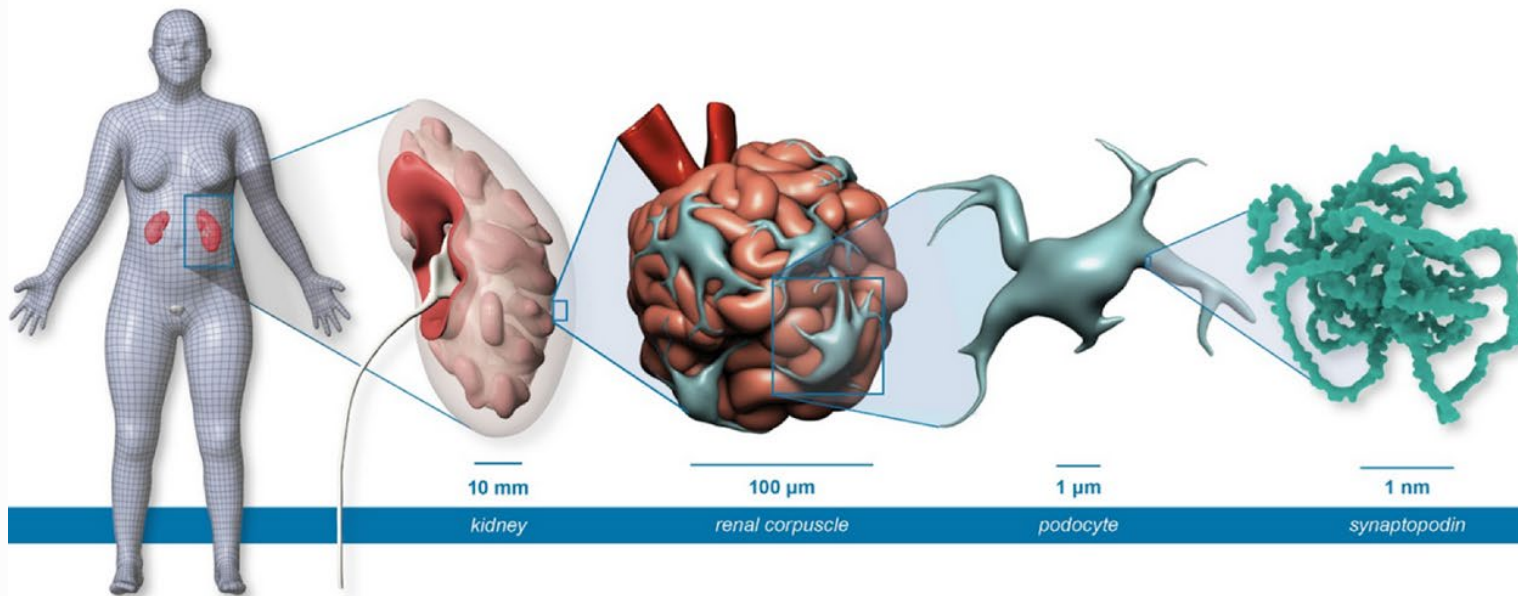
Relevance to Urology

- 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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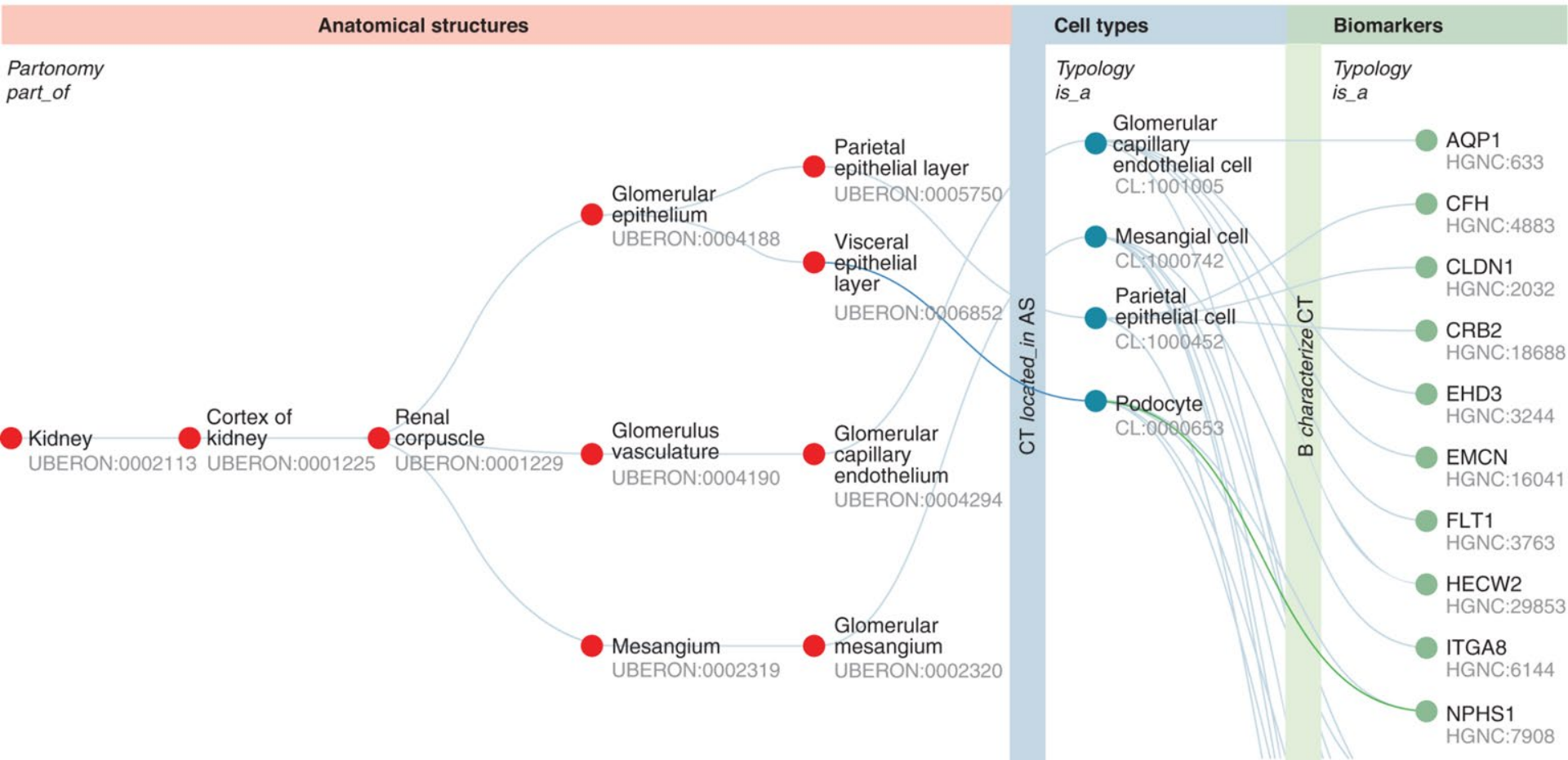
Atlas

3D Reference Organs

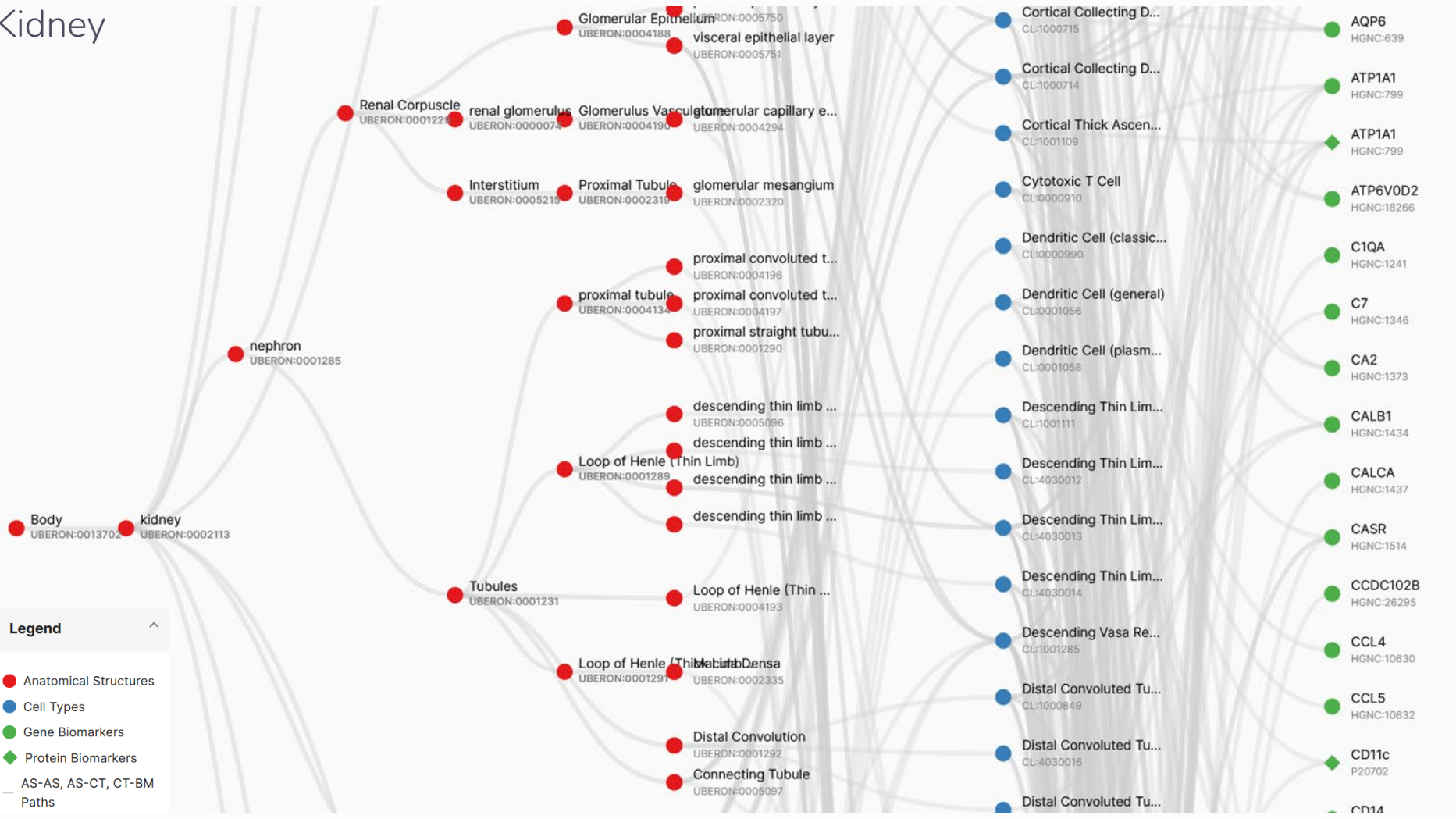
2D FTU
Illustrations

Organ Mapping Antibody Panels

ASCT+B Table Framework



Kidney

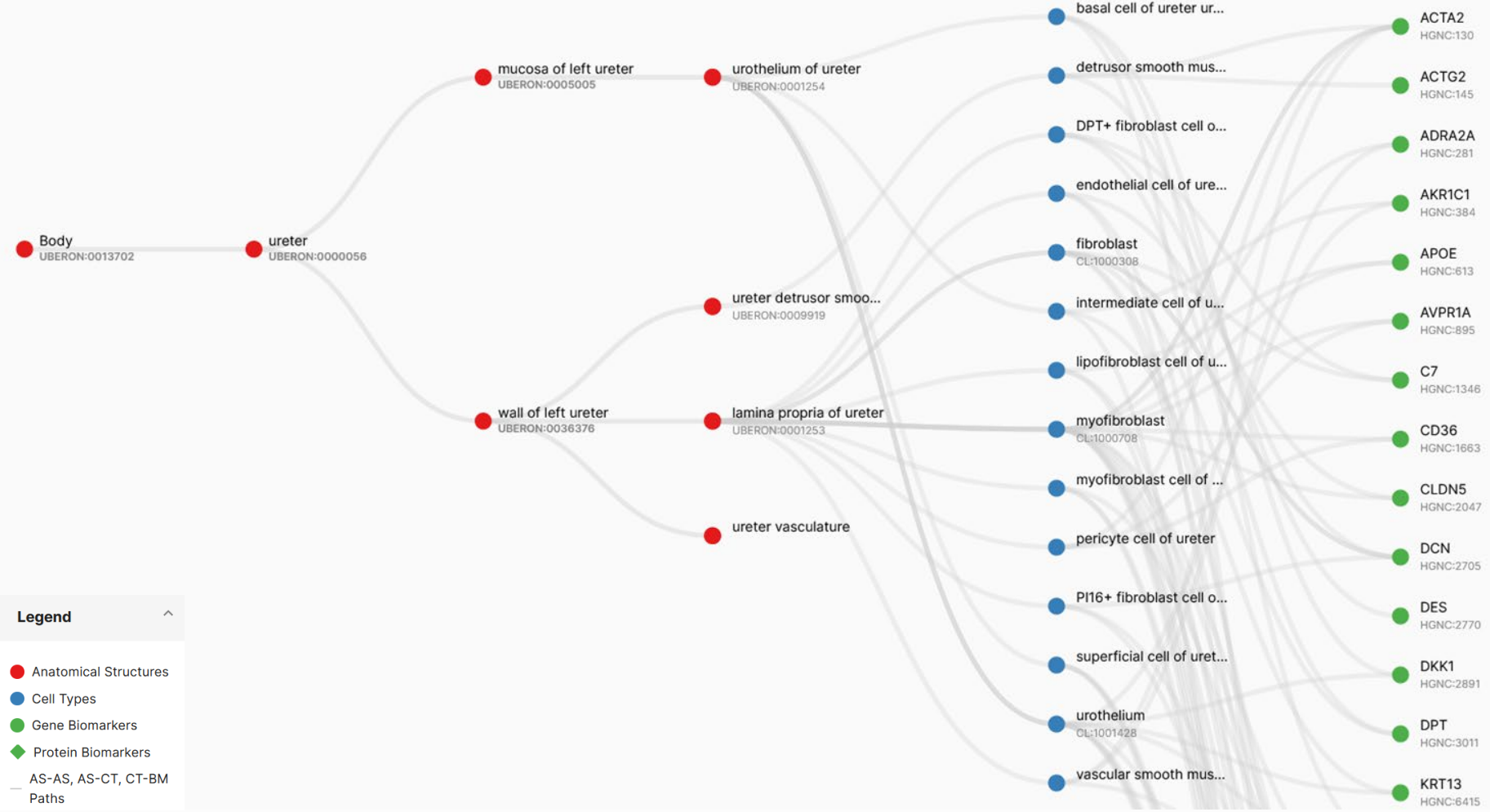


Legend

- Anatomical Structures
- Cell Types
- Gene Biomarkers
- ◆ Protein Biomarkers
- AS-AS, AS-CT, CT-BM
- Paths

Cell Type	Gene Biomarker
Cortical Collecting D...	AQP6
Cortical Collecting D...	ATP1A1
Cortical Thick Ascen...	ATP1A1
Cytotoxic T Cell	ATP6V0D2
Dendritic Cell (classic...	C1QA
Dendritic Cell (general)	C7
Dendritic Cell (plasm...	CA2
Descending Thin Lim...	CALB1
Descending Thin Lim...	CALCA
Descending Thin Lim...	CASR
Descending Thin Lim...	CCDC102B
Descending Vasa Re...	CCL4
Distal Convoluted Tu...	CCL5
Distal Convoluted Tu...	CD11c
Distal Convoluted Tu...	CD14

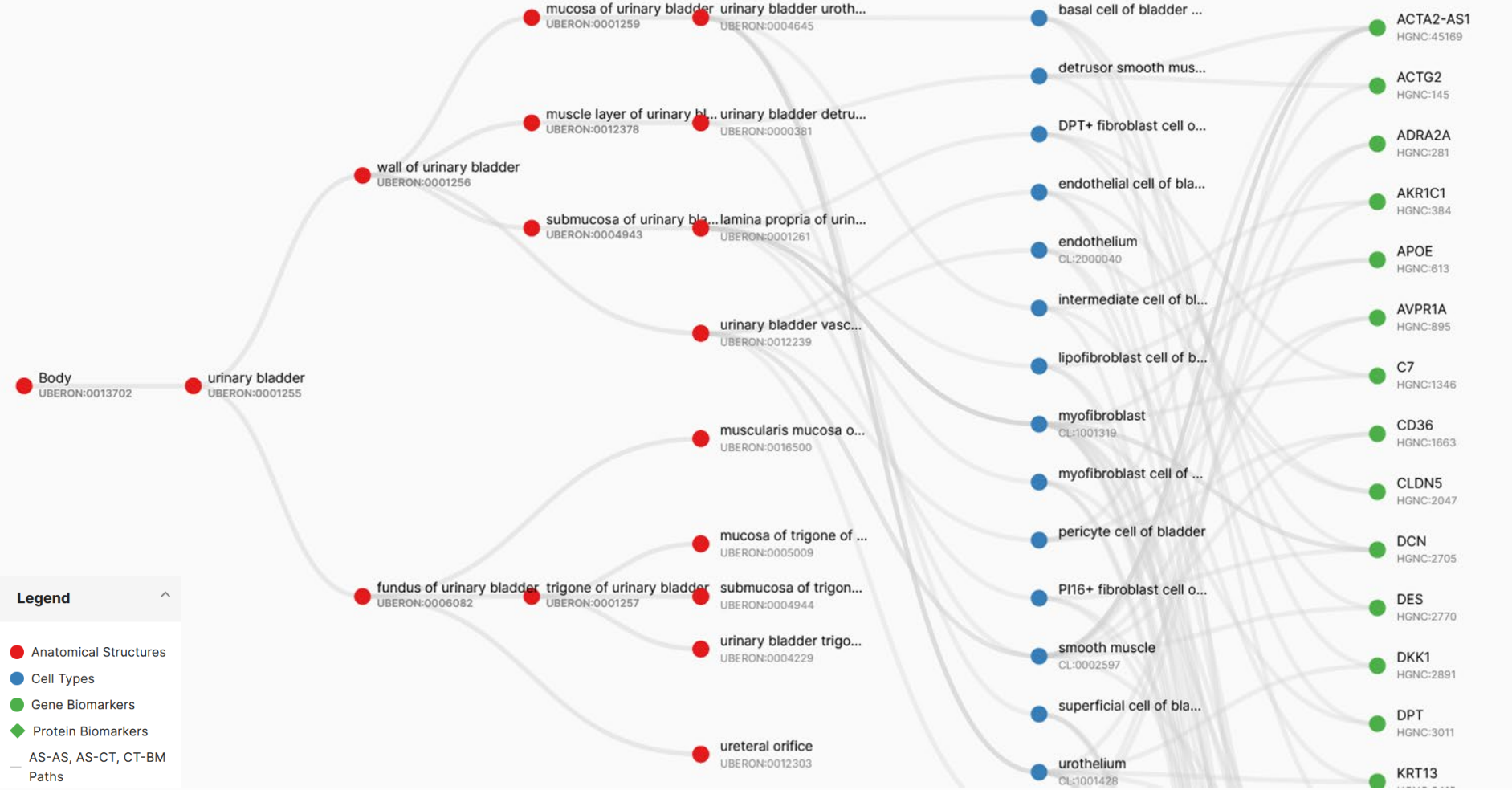
Ureter



Legend ^

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Urinary Bladder

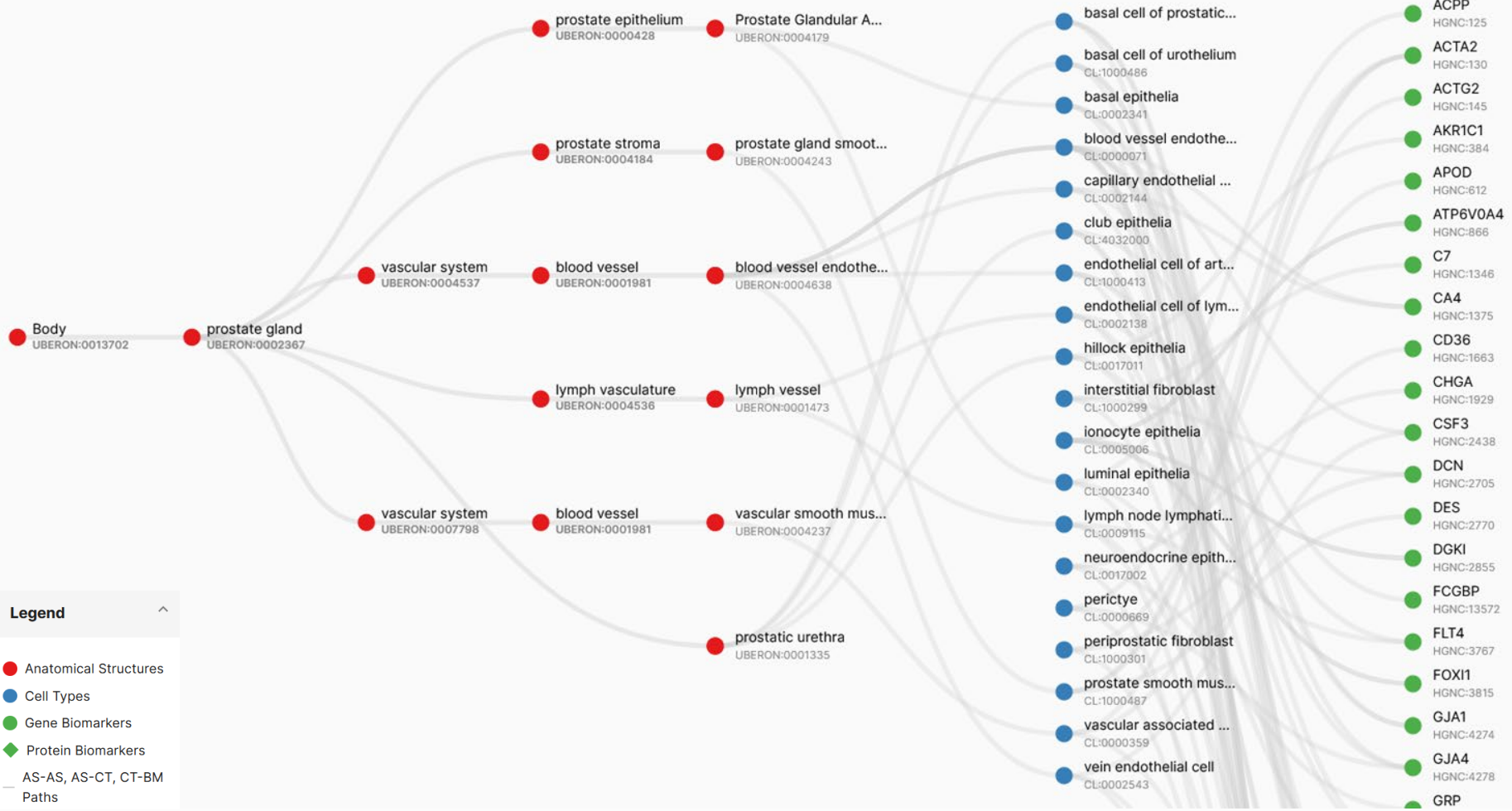


Legend ^

- Anatomical Structures
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- basal cell of bladder ...
- detrusor smooth mus...
- DPT+ fibroblast cell o...
- endothelial cell of bla...
- endothelium
CL:2000040
- intermediate cell of bl...
- lipofibroblast cell of b...
- myofibroblast
CL:1001319
- myofibroblast cell of ...
- pericyte cell of bladder
- P116+ fibroblast cell o...
- smooth muscle
CL:0002597
- superficial cell of bla...
- urothelium
CL:1001428
- ACTA2-AS1
HGNC:45169
- ACTG2
HGNC:145
- ADRA2A
HGNC:281
- AKR1C1
HGNC:384
- APOE
HGNC:613
- AVPR1A
HGNC:895
- C7
HGNC:1346
- CD36
HGNC:1663
- CLDN5
HGNC:2047
- DCN
HGNC:2705
- DES
HGNC:2770
- DKK1
HGNC:2891
- DPT
HGNC:3011
- KRT13

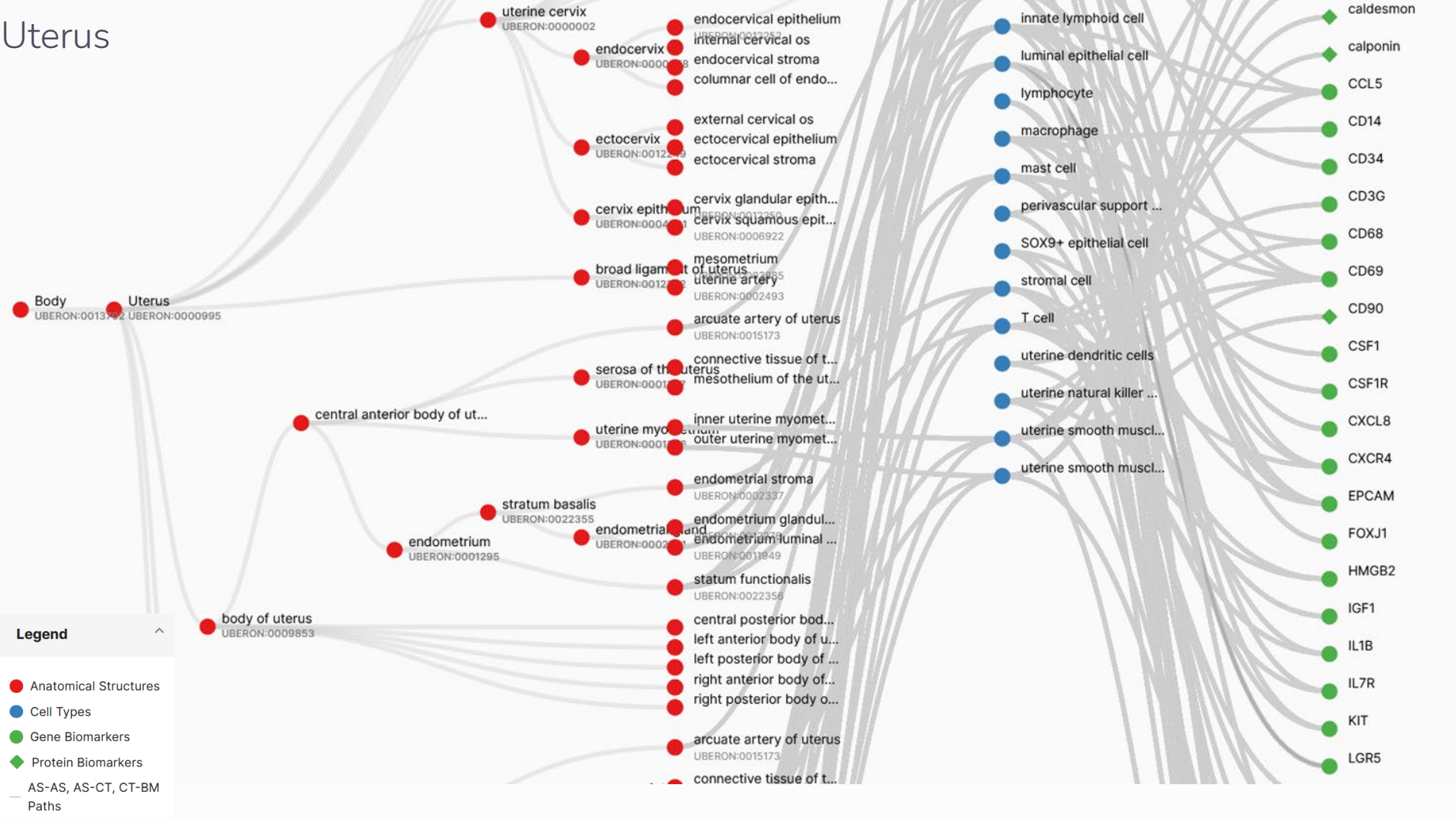
Prostate

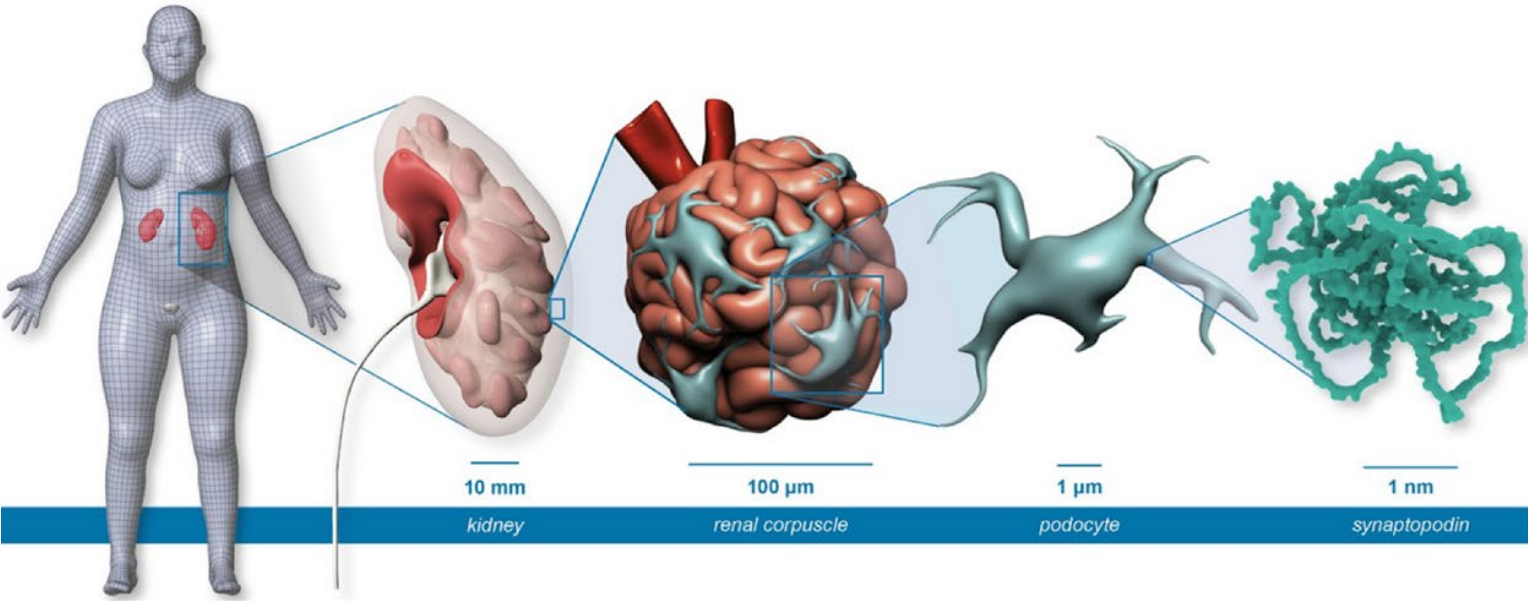


Legend ^

- Anatomical Structures
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Uterus





Anatomical Structures

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Genes, Proteins, ..

Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

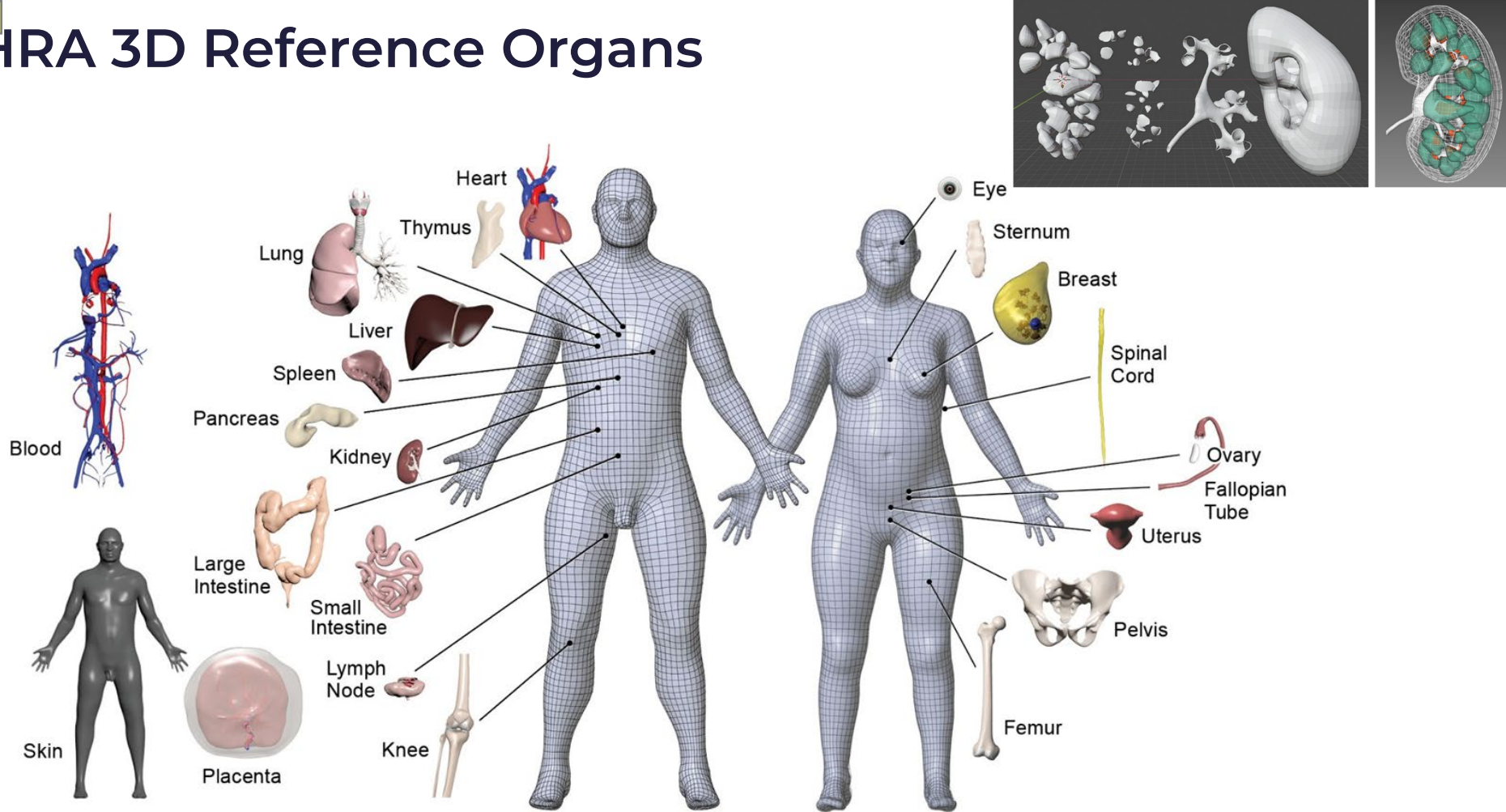
Atlas

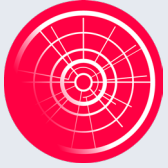
3D Reference Organs

2D FTU
Illustrations

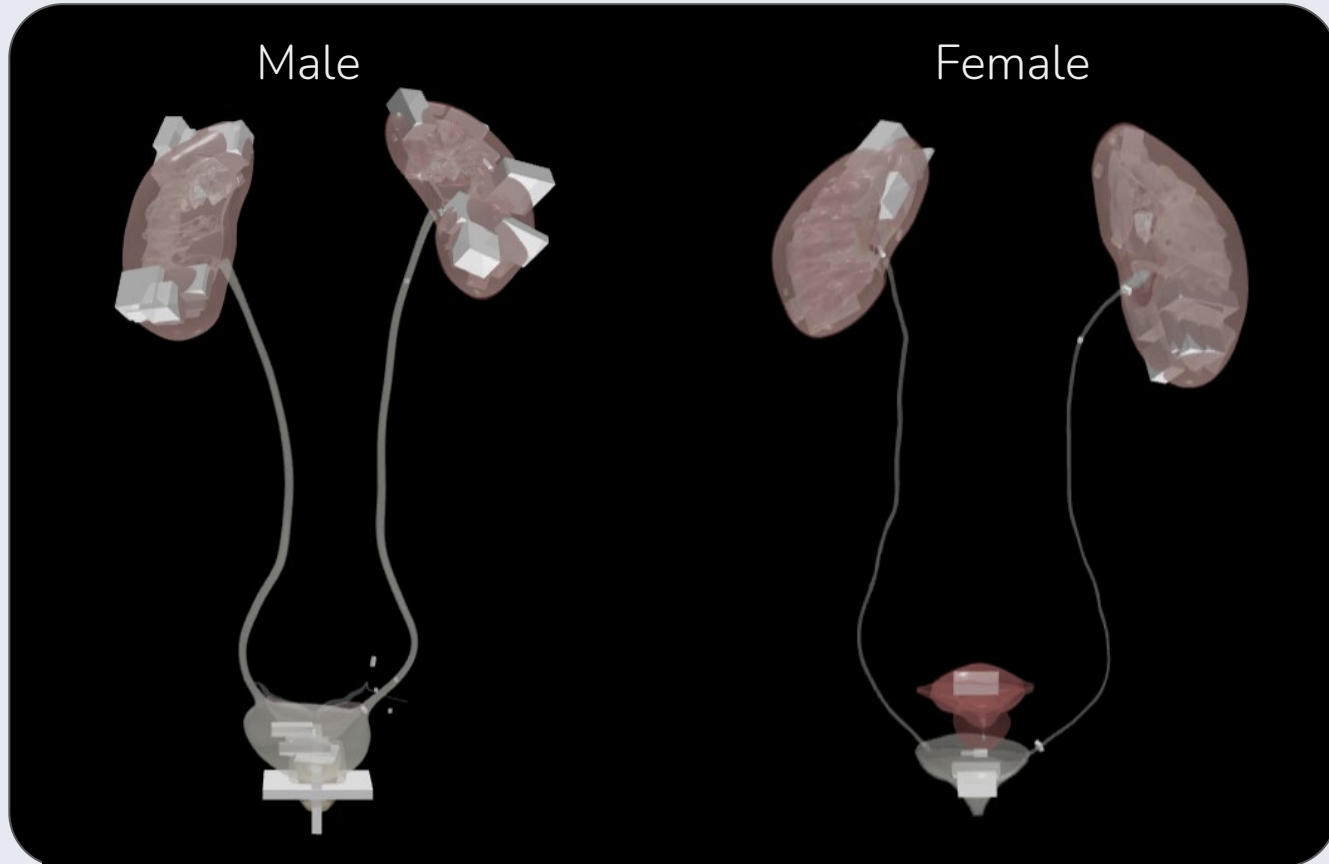
Organ Mapping Antibody Panels

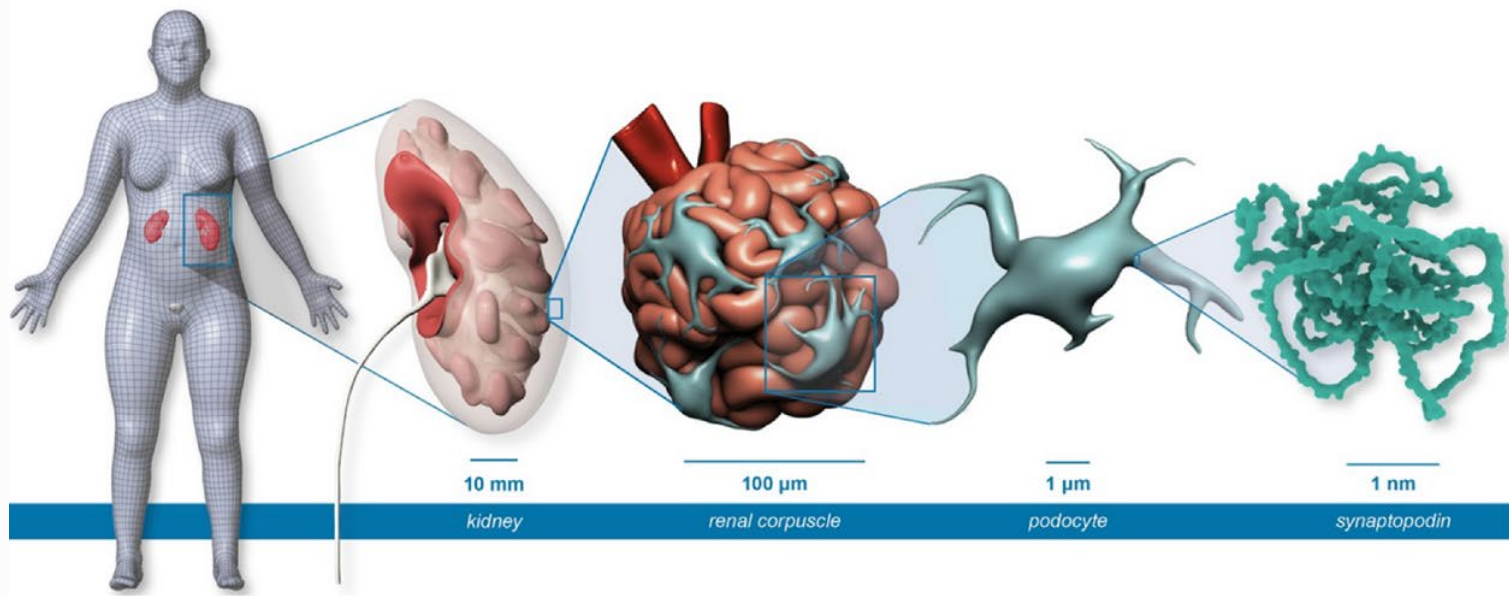
HRA 3D Reference Organs





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





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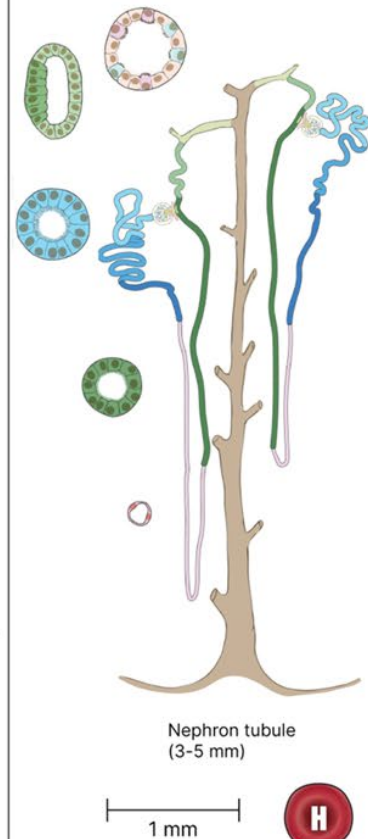
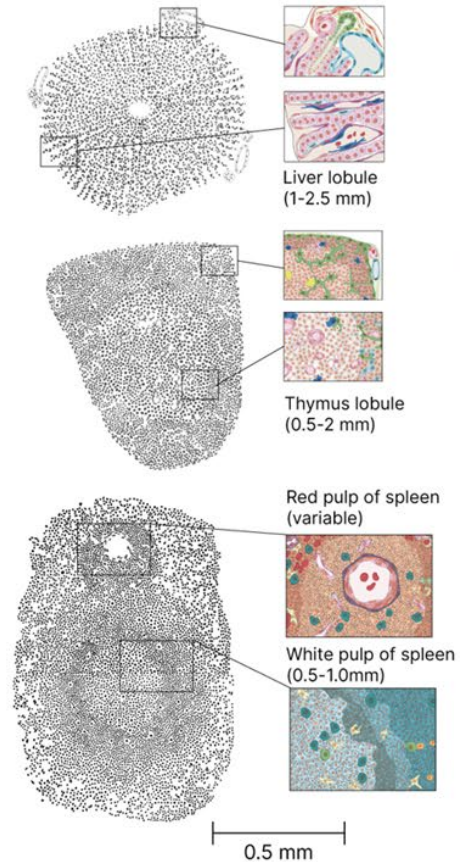
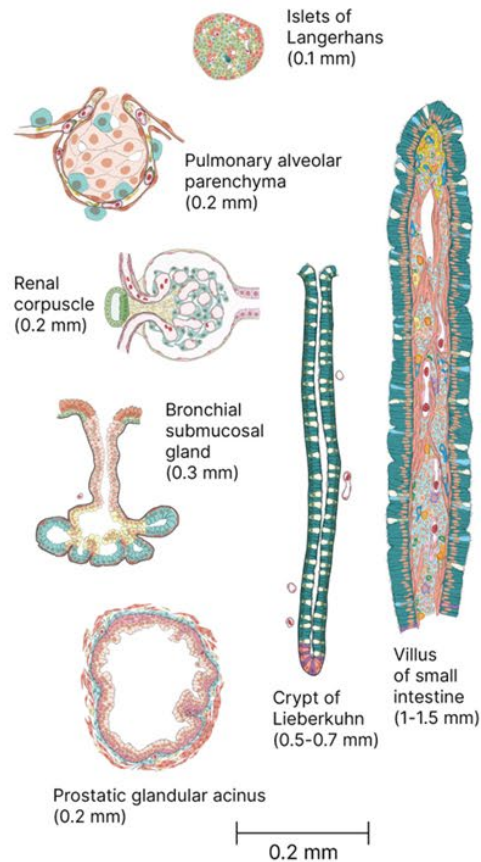
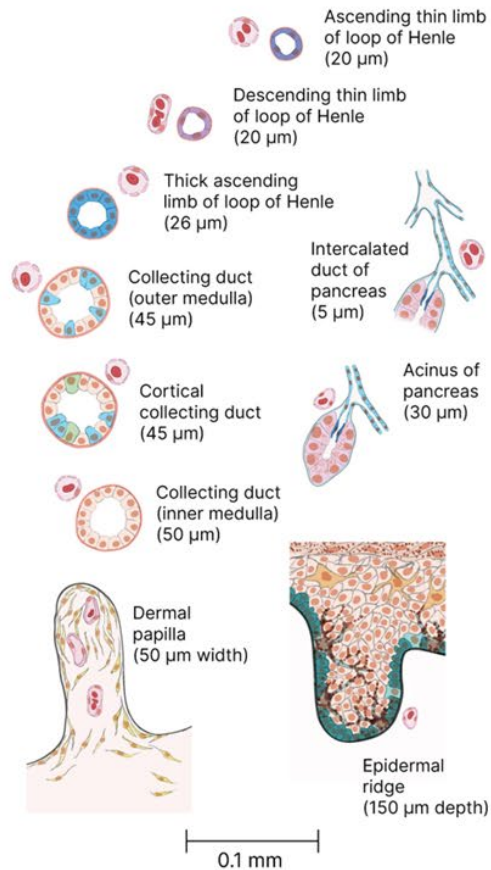
Atlas

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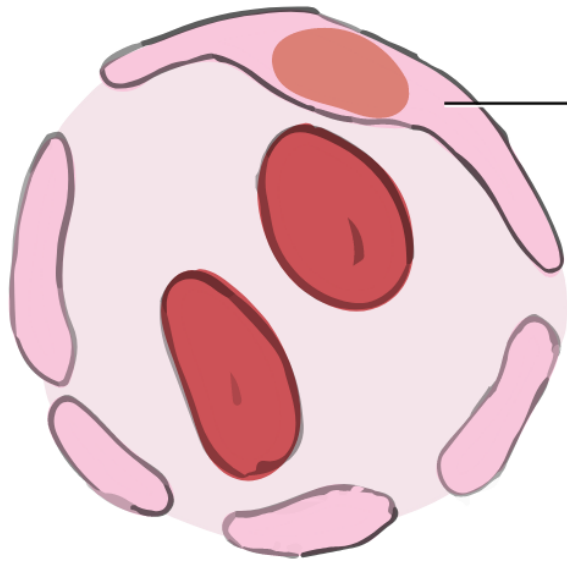
2D FTU
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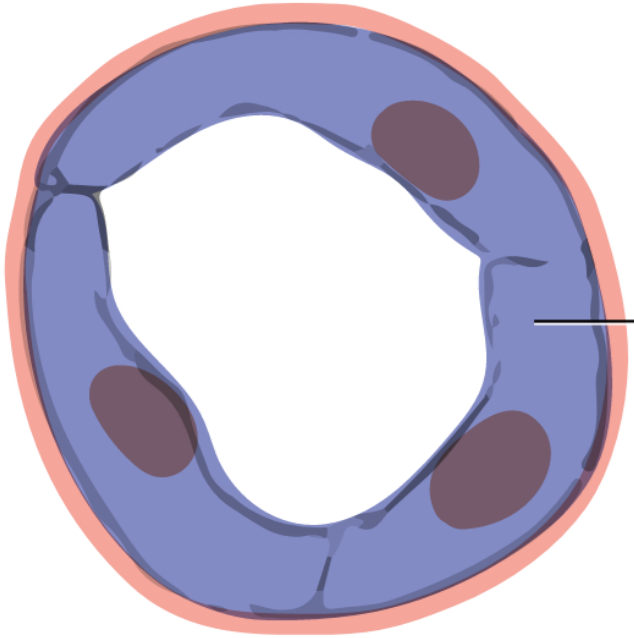
HRA Functional Tissue Units (FTUs)



Kidney - Ascending Thin Loop Of Henle



Ascending vasa recta

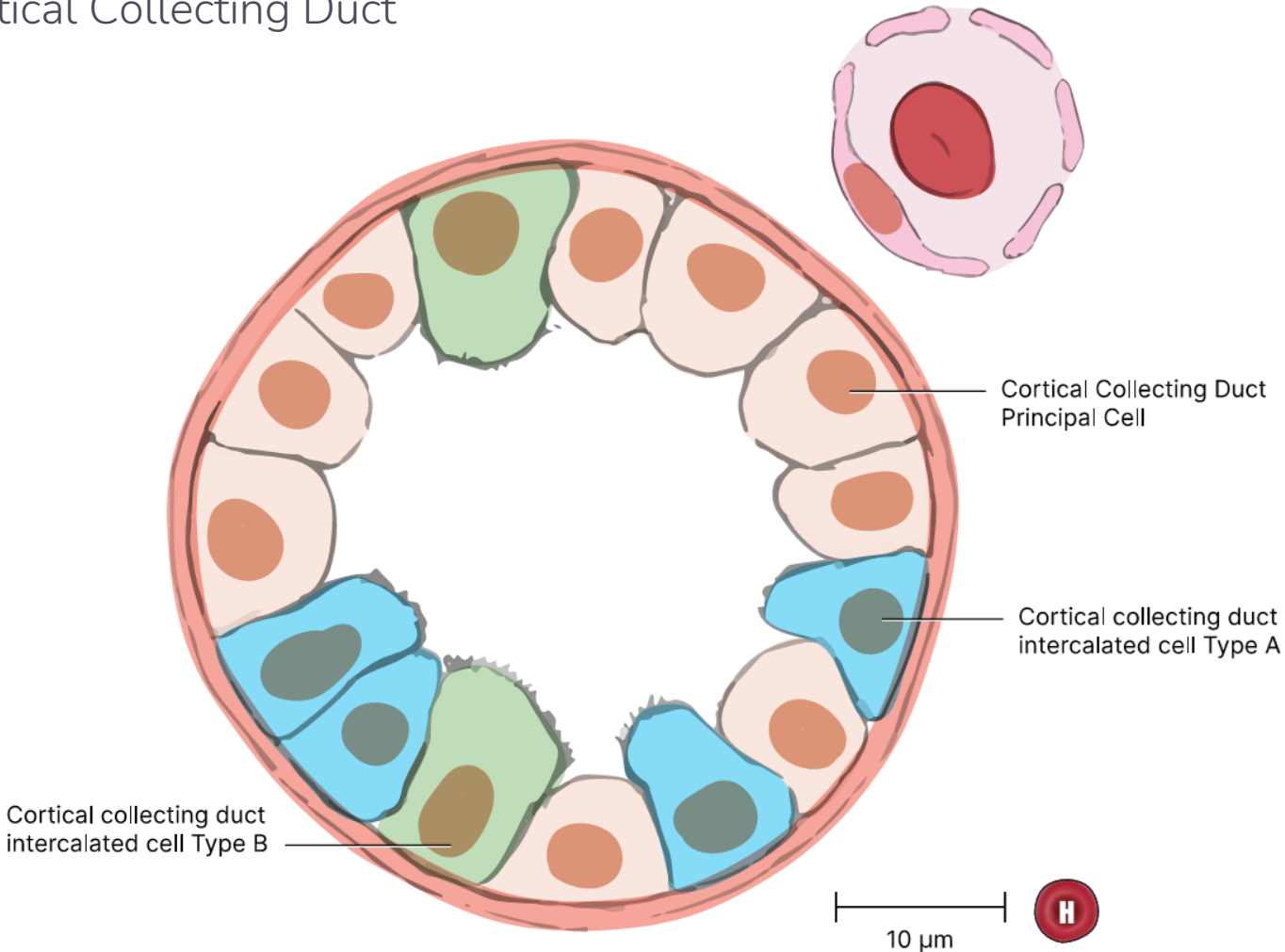


Ascending thin limb cell

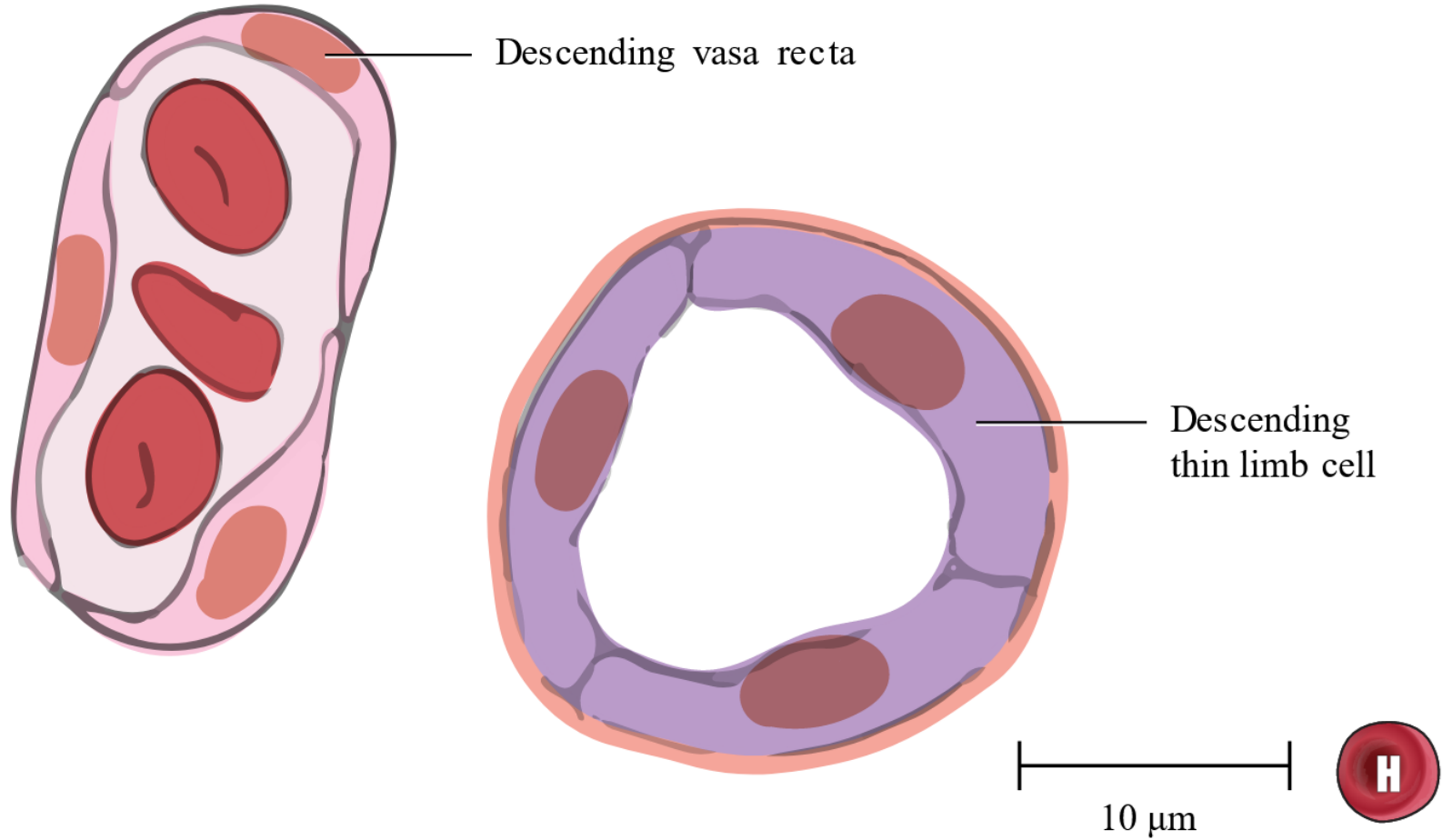
10 μ m



Kidney - Cortical Collecting Duct



Kidney - Descending Thin Loop Of Henle



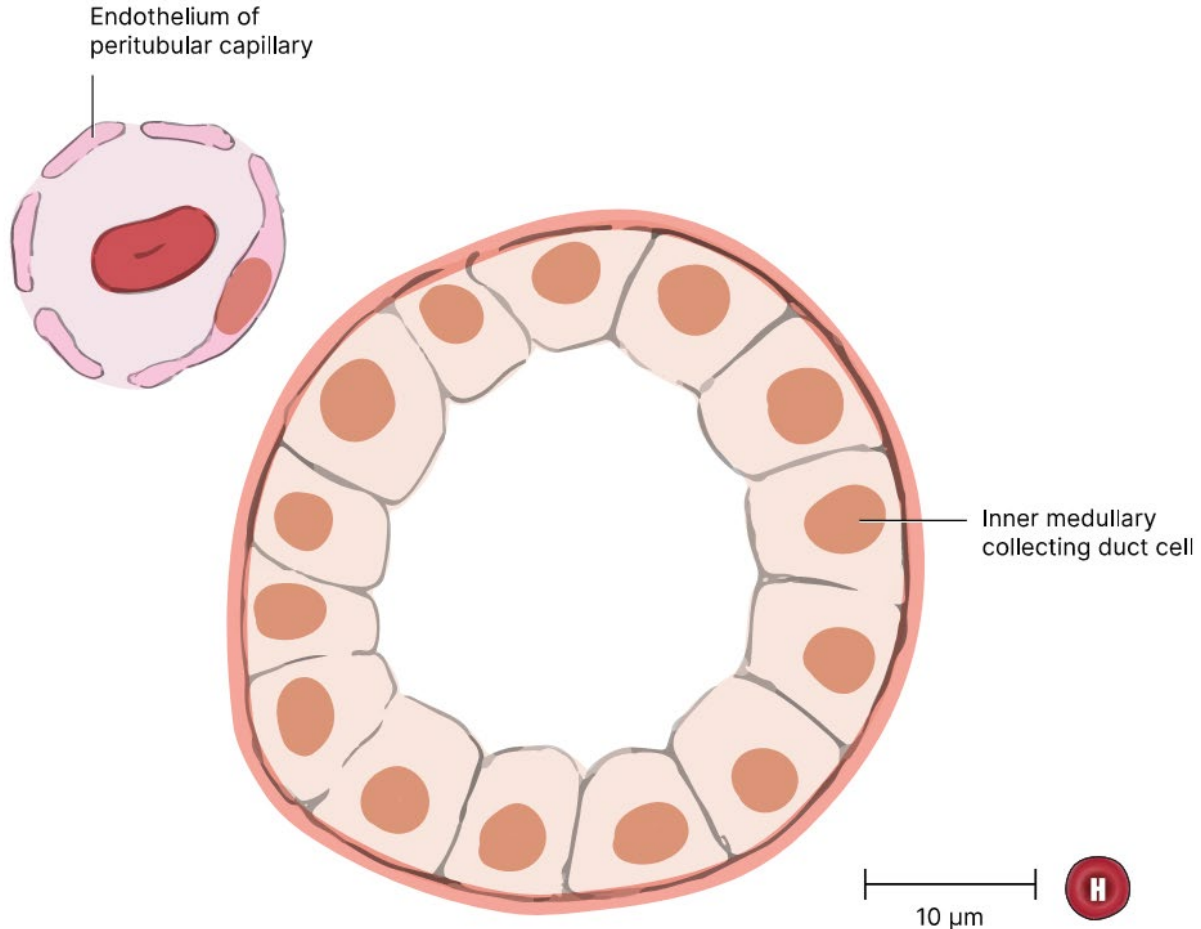
Descending vasa recta

Descending thin limb cell

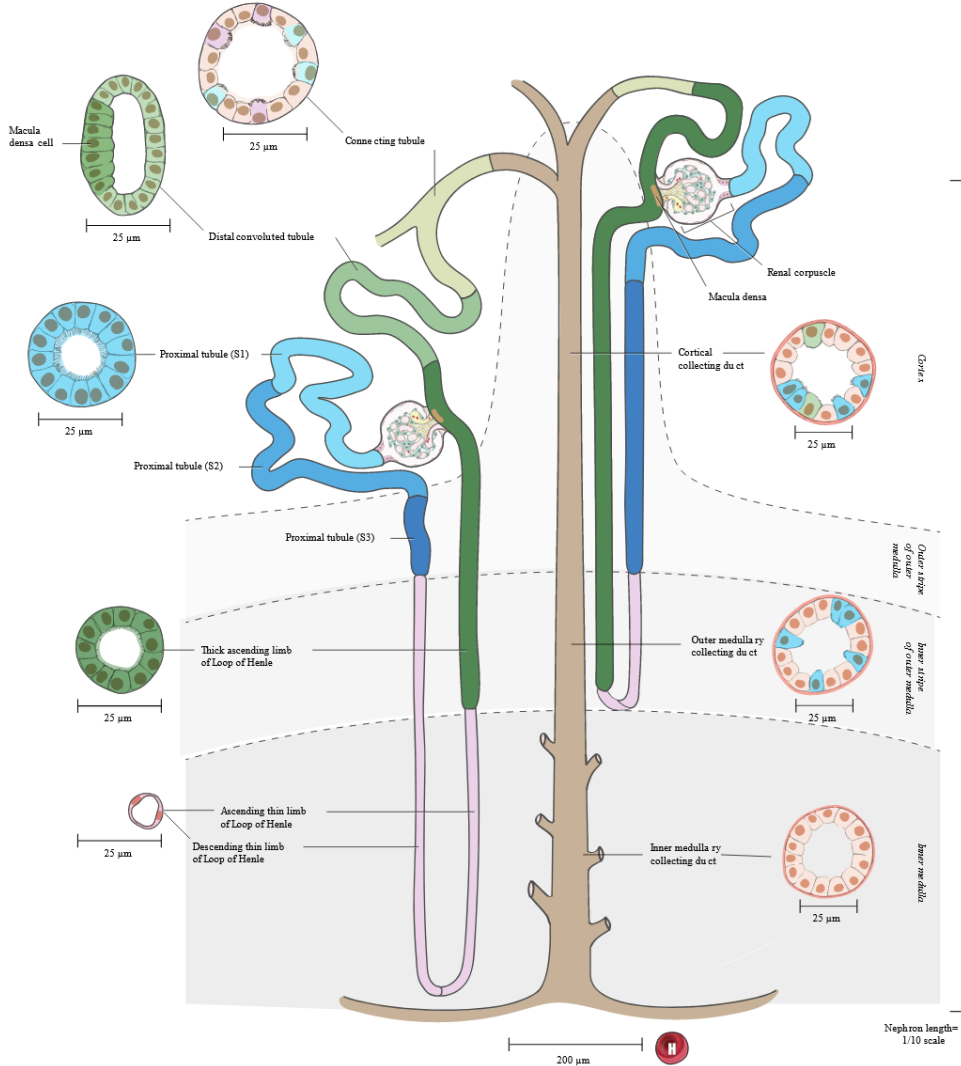
10 μm



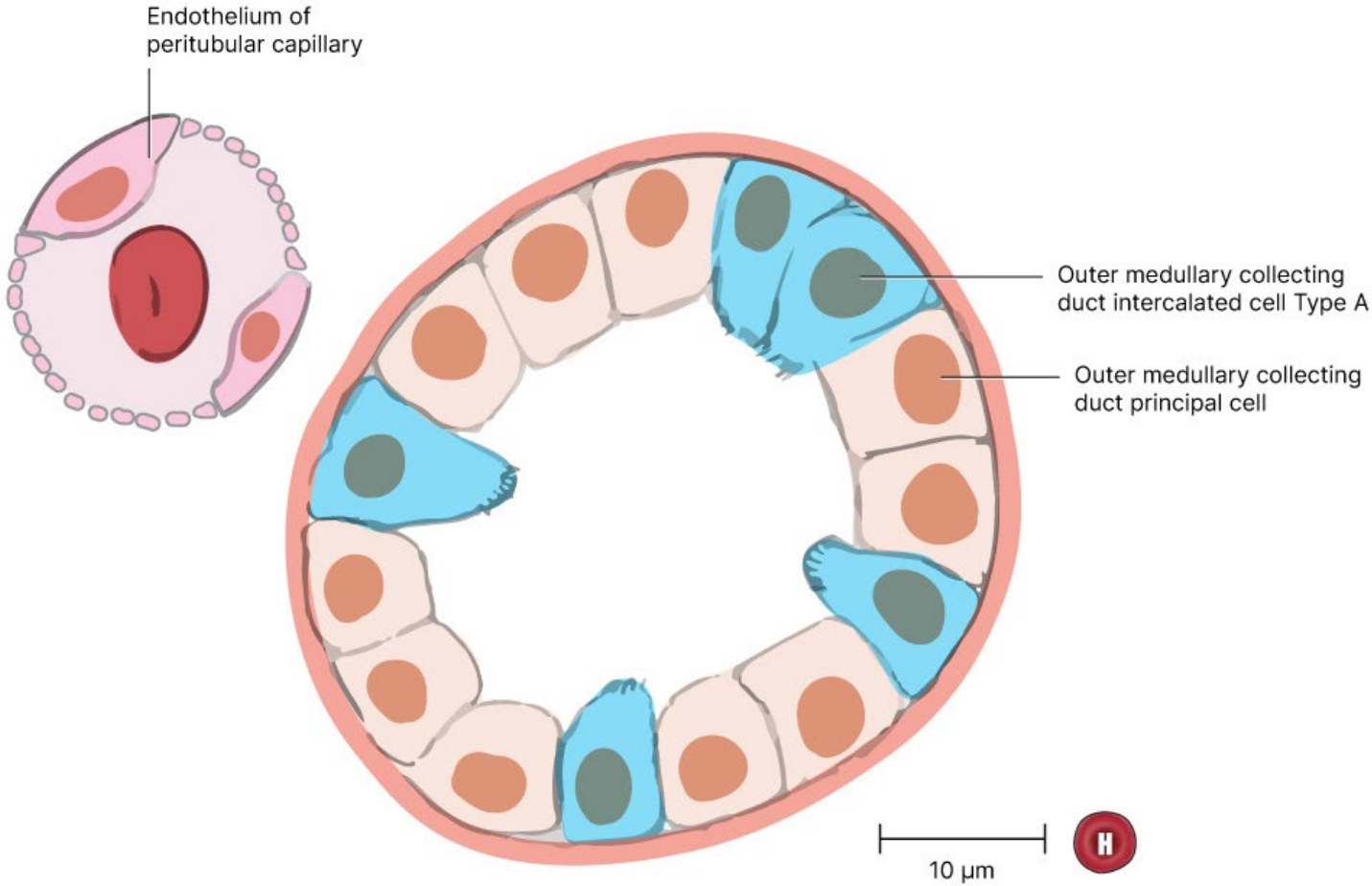
Kidney - Inner Medullary Collecting Duct



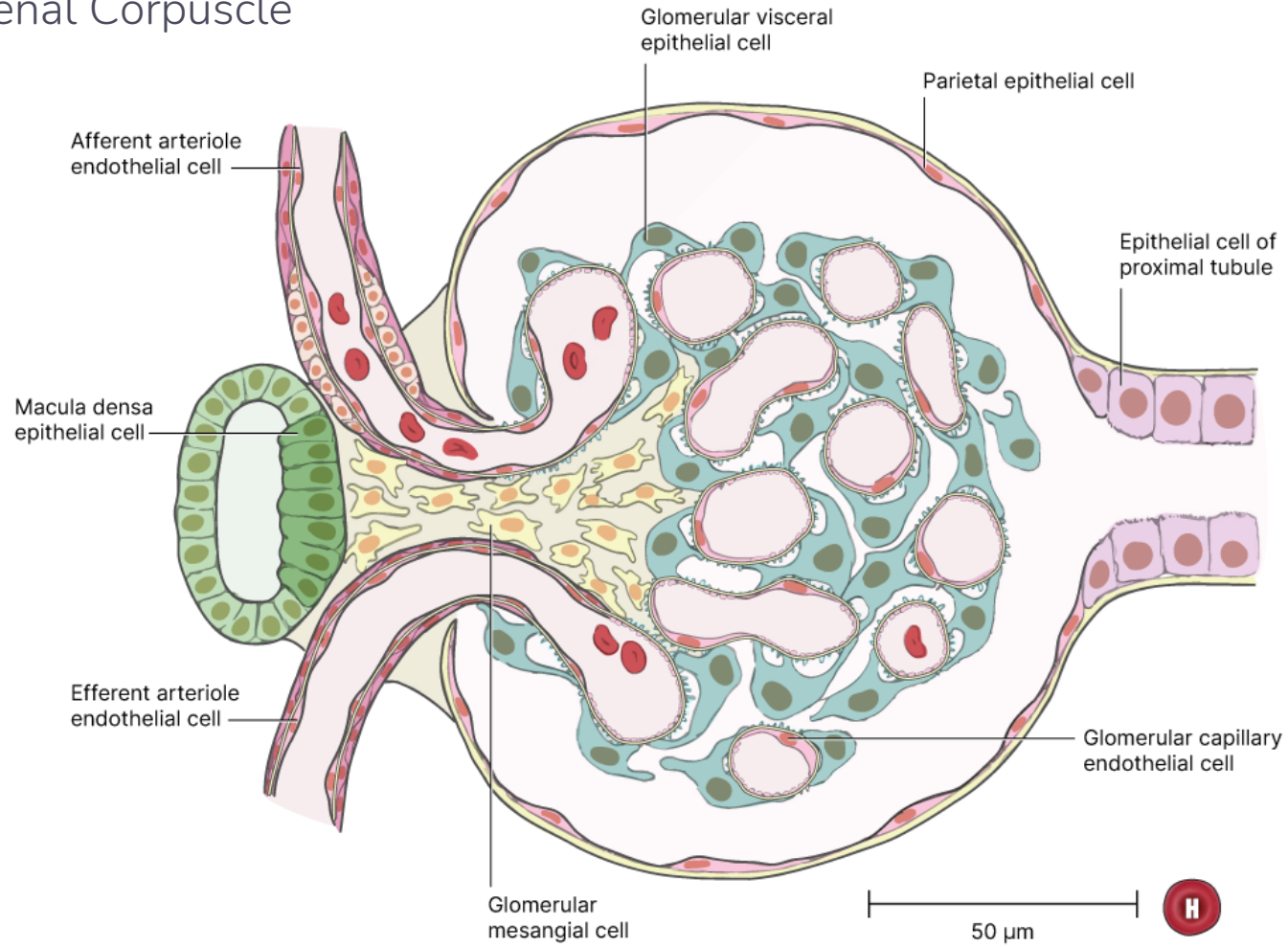
Kidney - Nephron



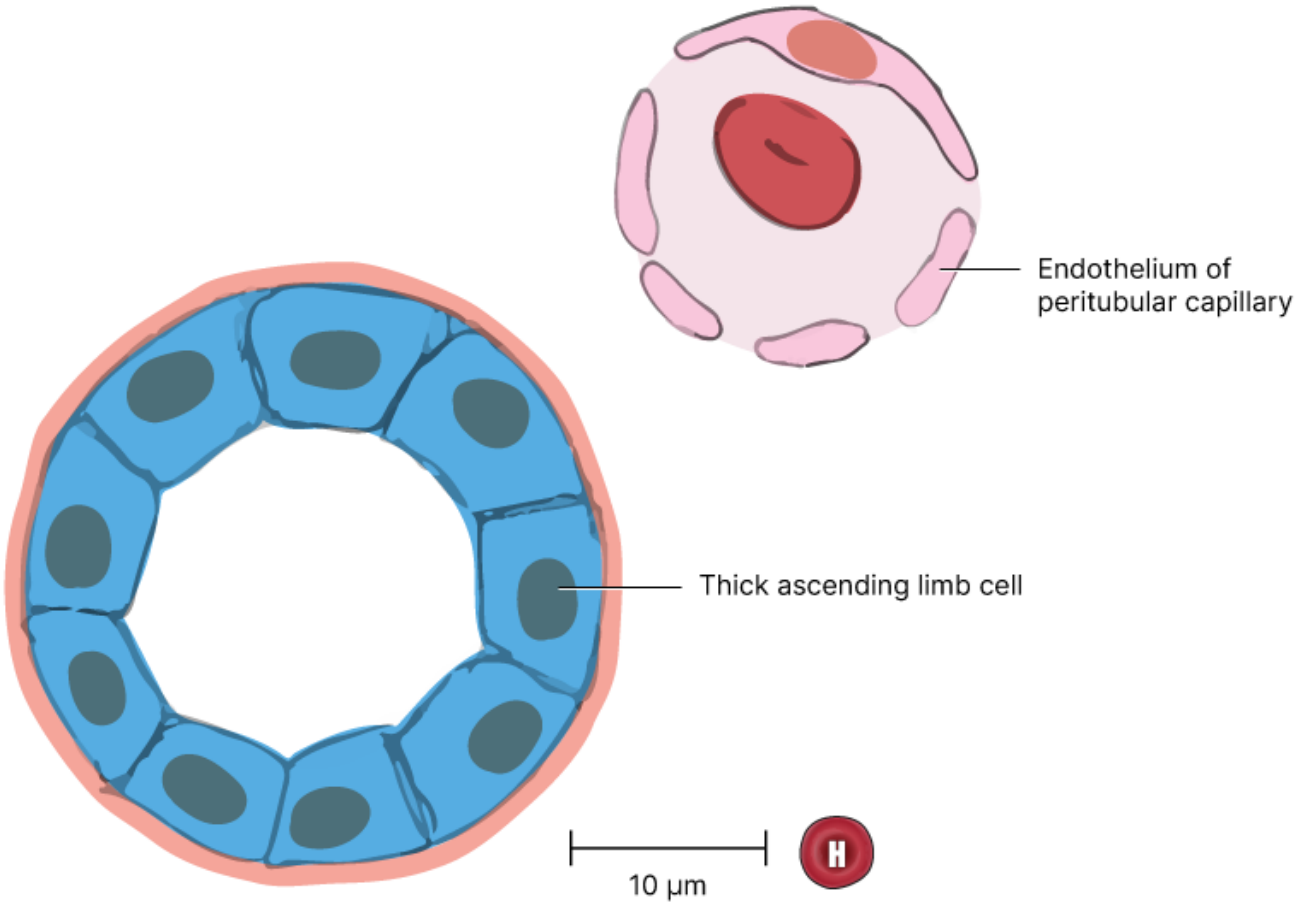
Kidney - Outer Medullary Collecting Duct



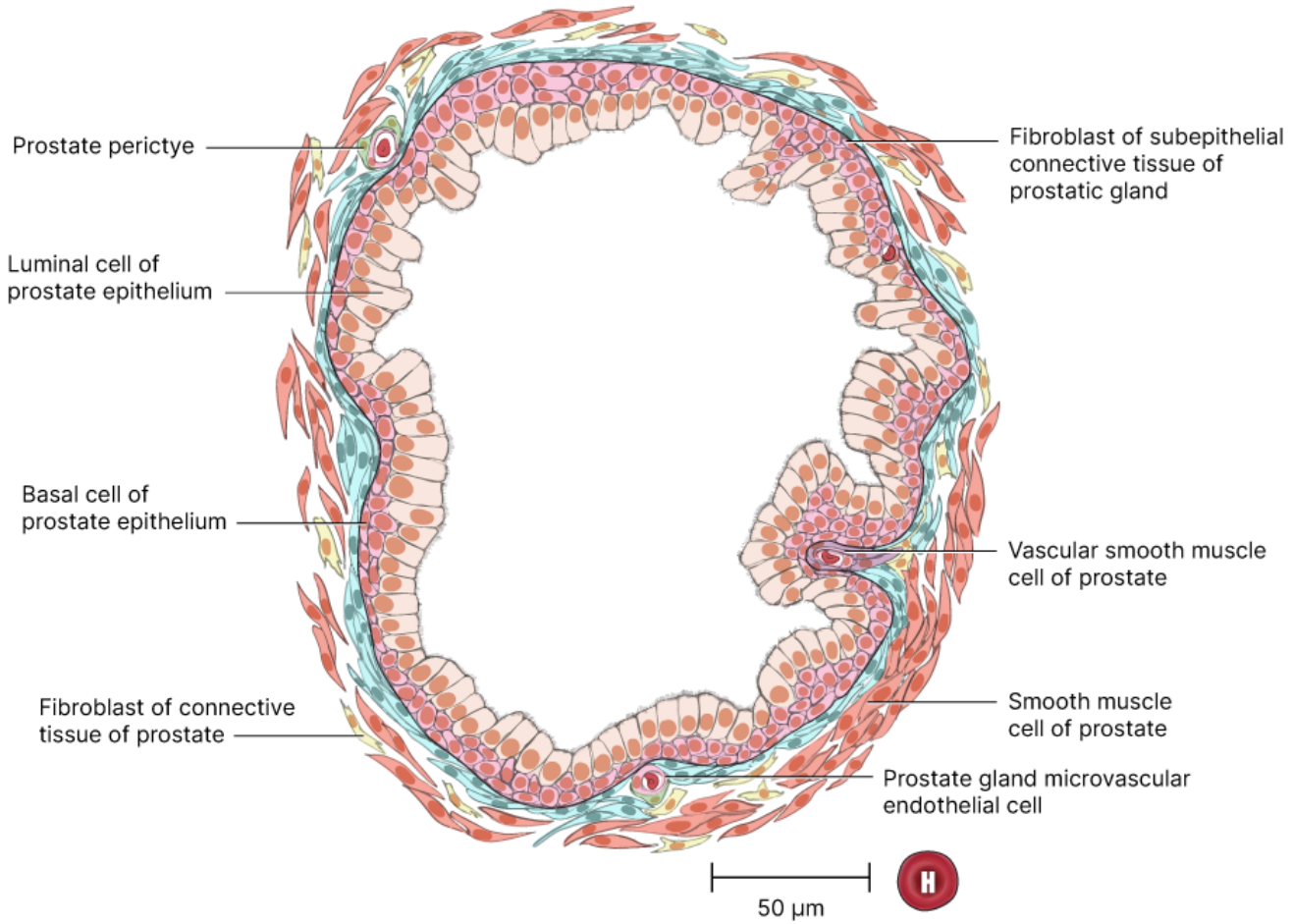
Kidney - Renal Corpuscle

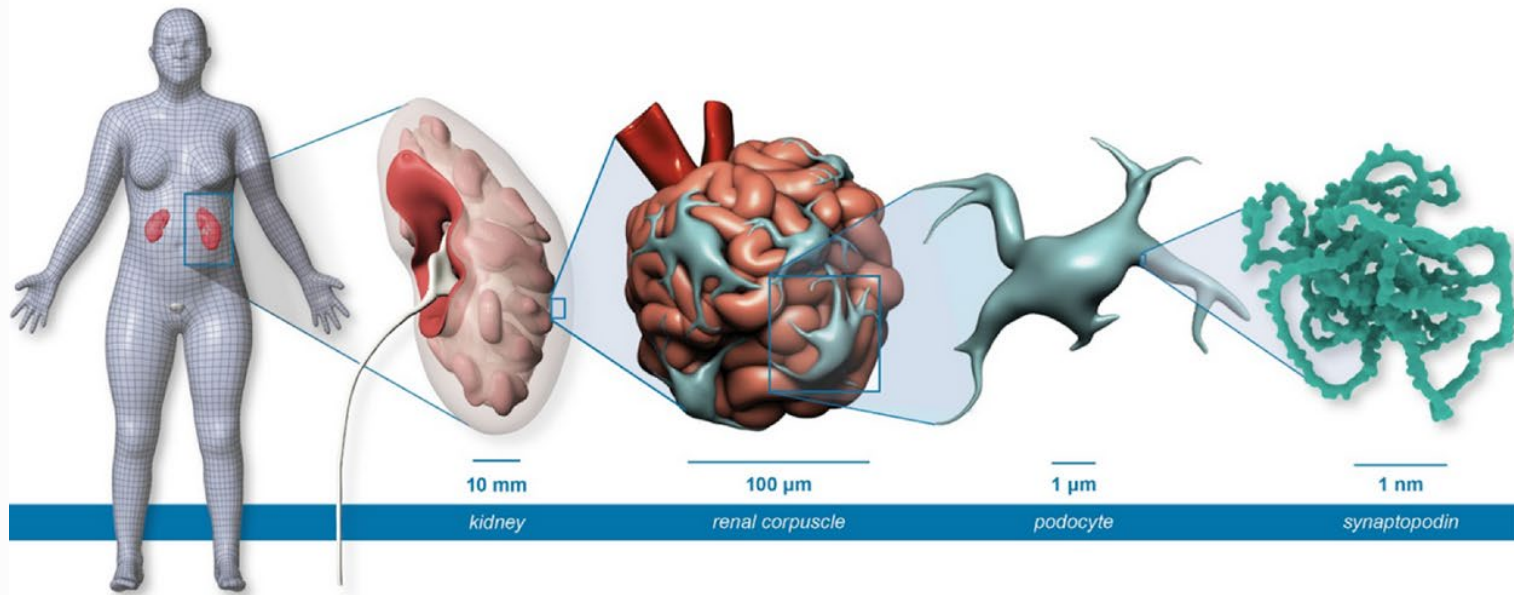


Kidney - Thick Ascending Loop Of Henle



Prostate - Glandular Acinus





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Tissue Units

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Genes, Proteins, ..

Conceptual

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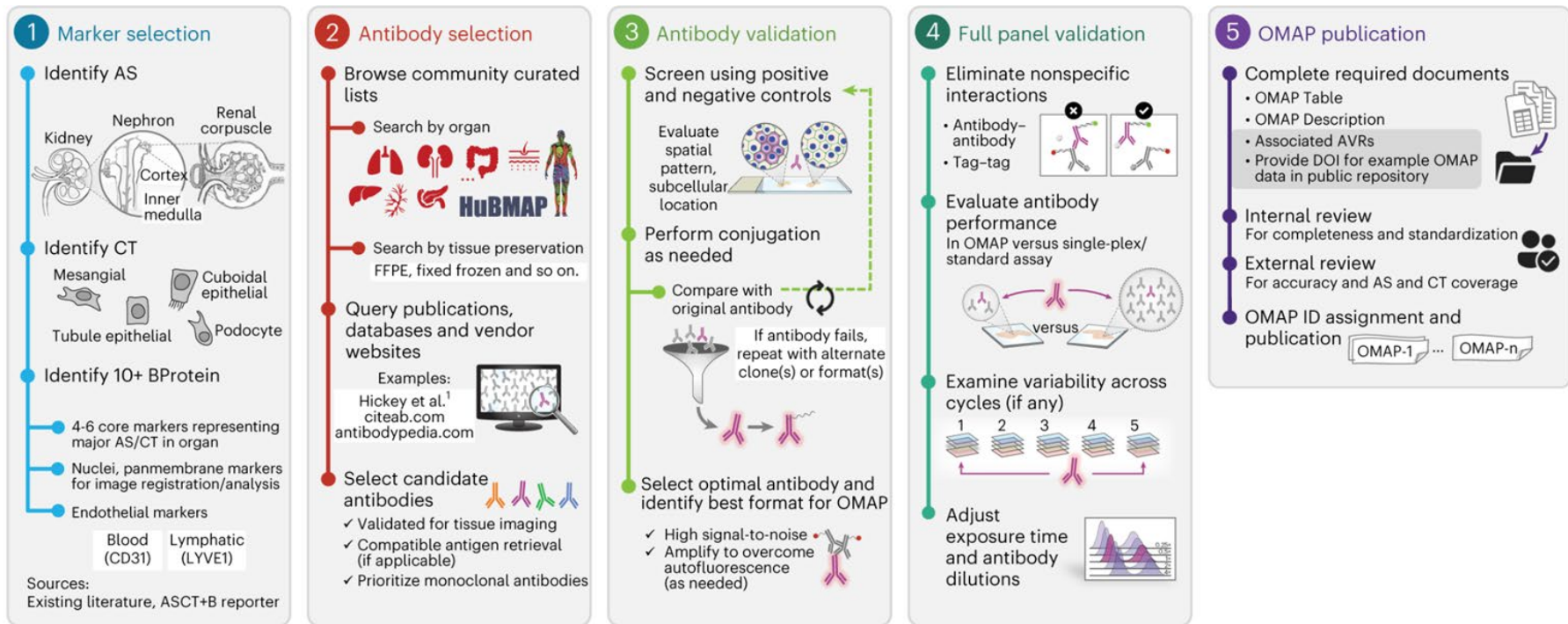
Atlas

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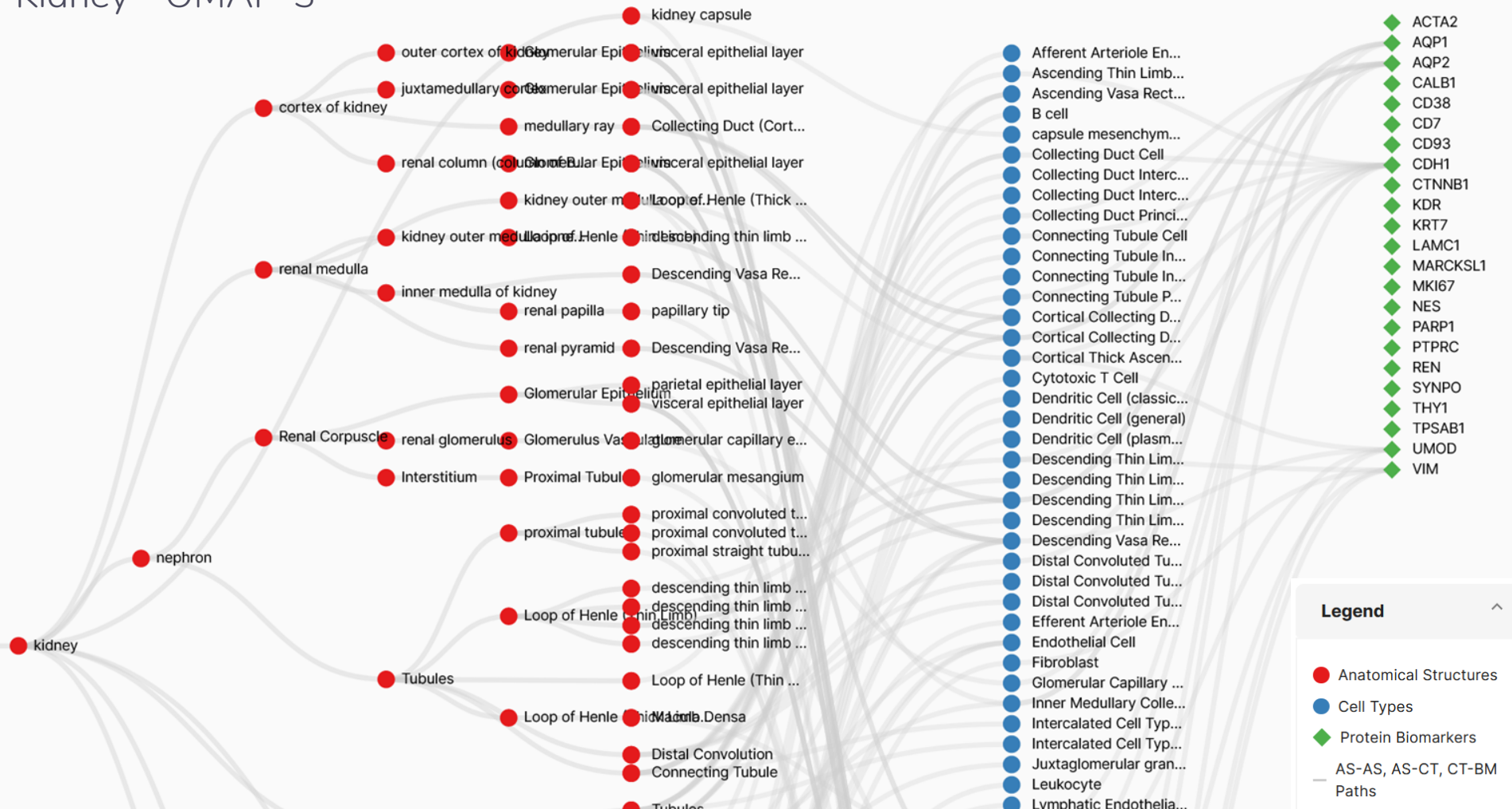
2D FTU
Illustrations

Organ Mapping Antibody Panels

OMAPs are wet-bench validated collection of antibodies that are designed to work together in multiplex antibody imaging technologies (CODEX/Phenocycler, CellDive, SIMS, etc.) primarily for identifying specific classes of cell types or tissue regions/layers.

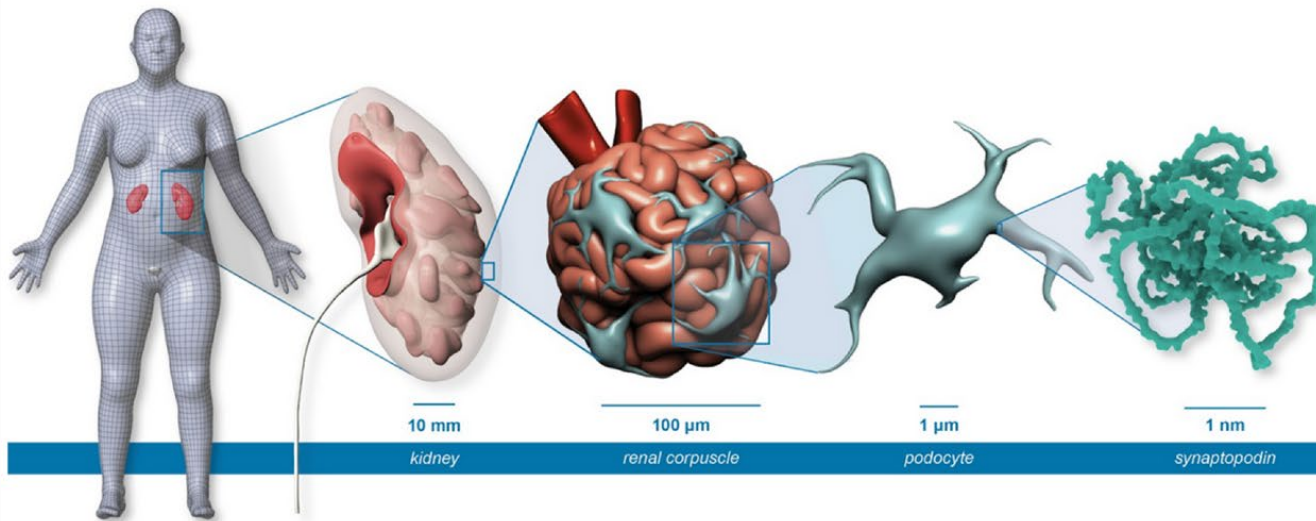


Kidney - OMAP-3



Legend

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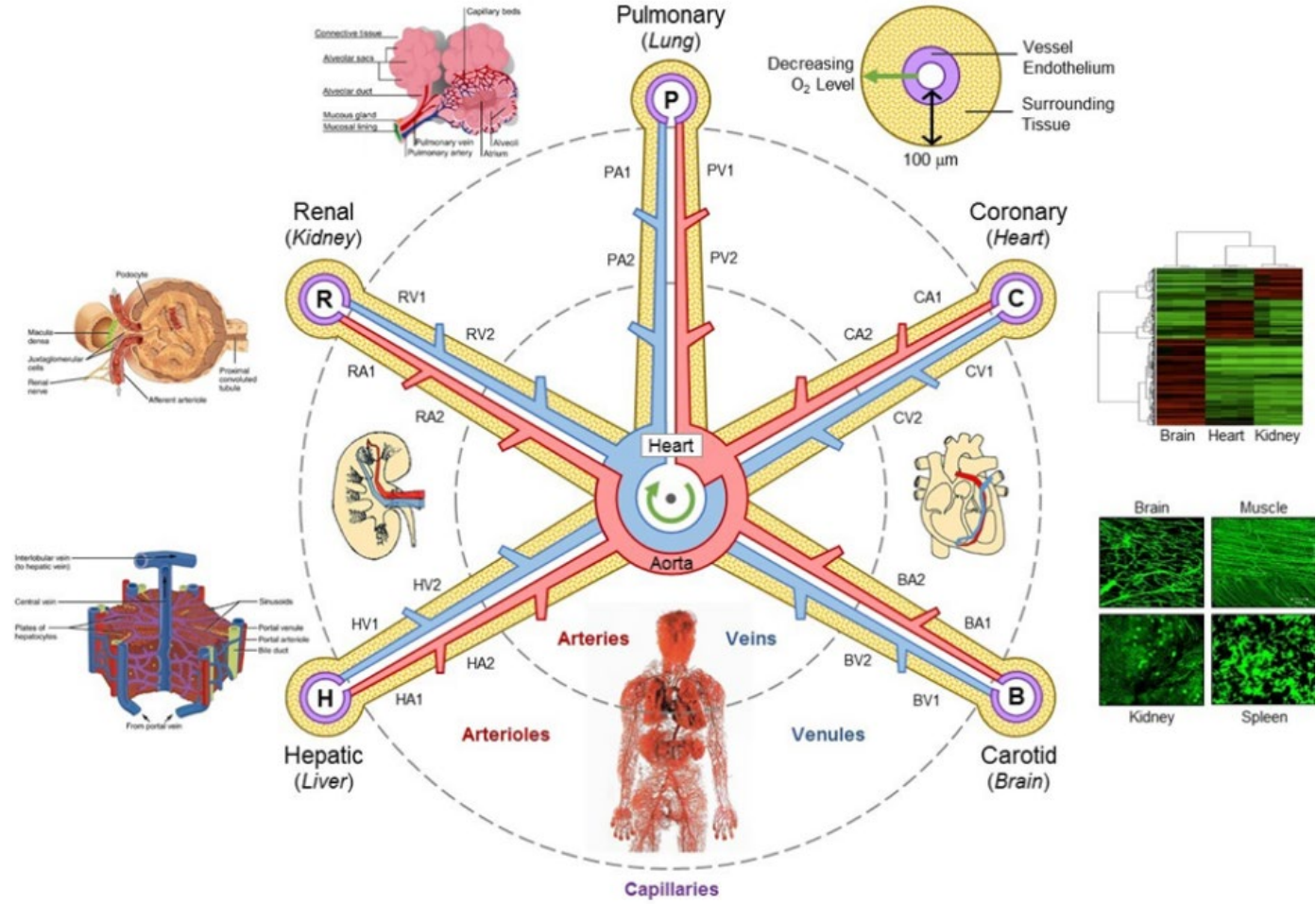
3D Reference Organs

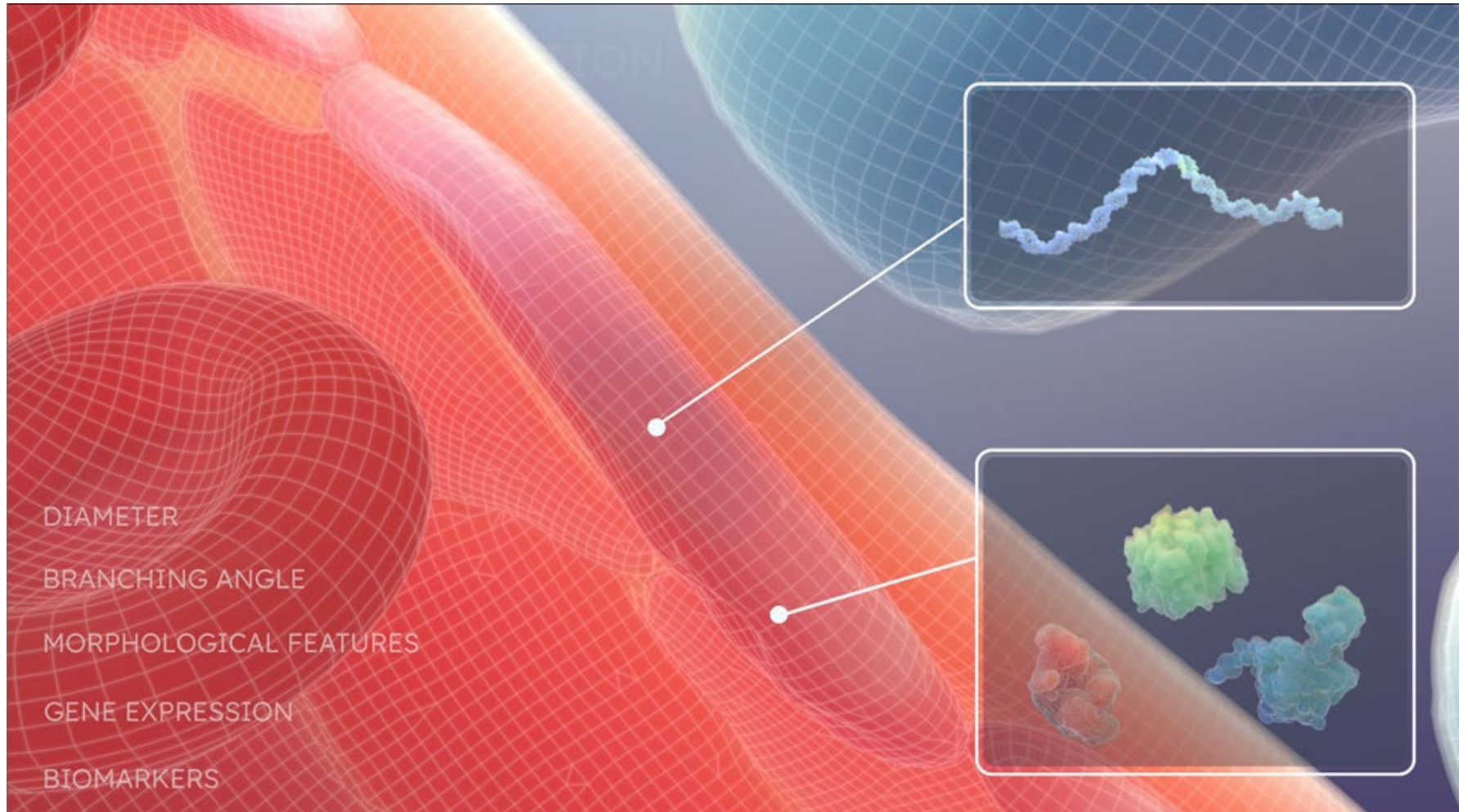
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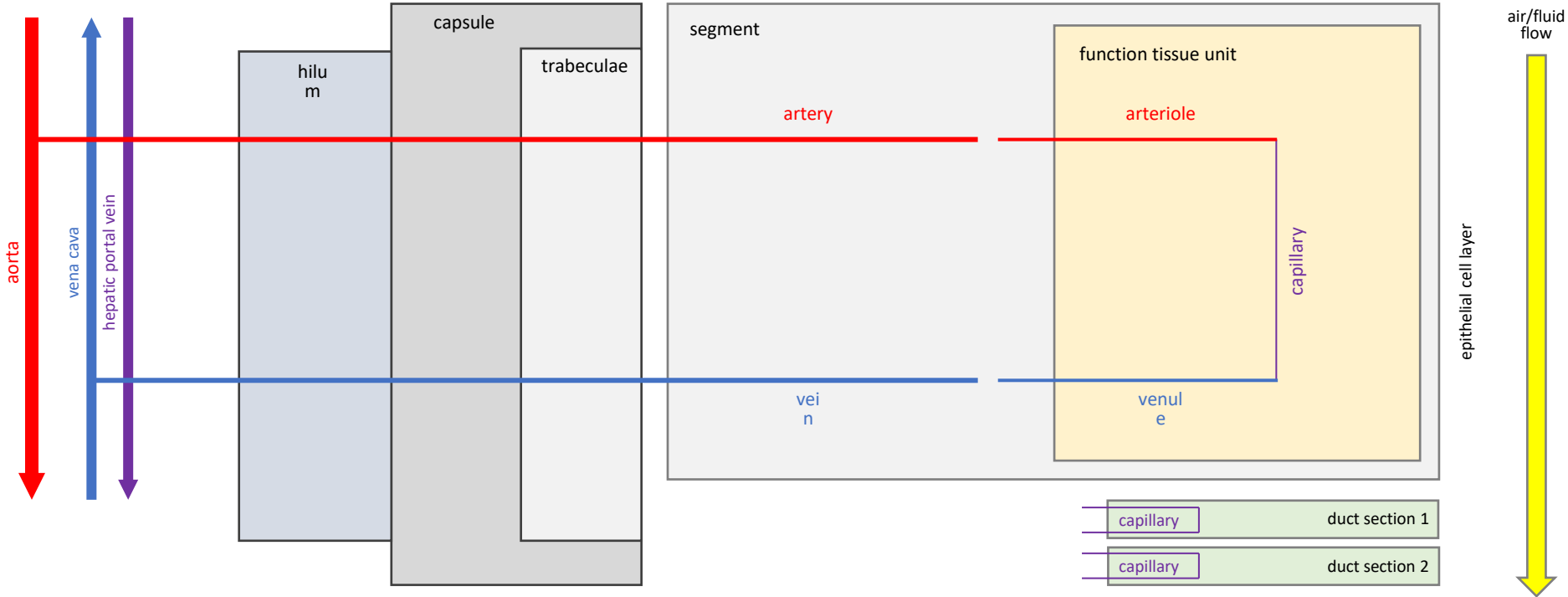
Vascular Geometry

Vasculature Common Coordinate Framework

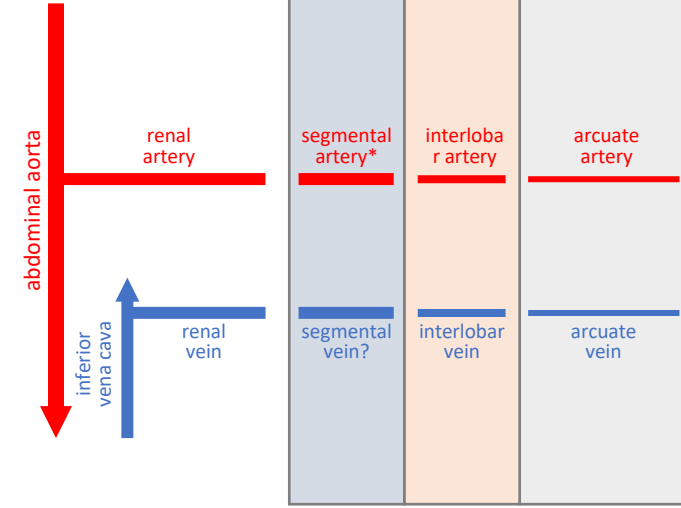




Template



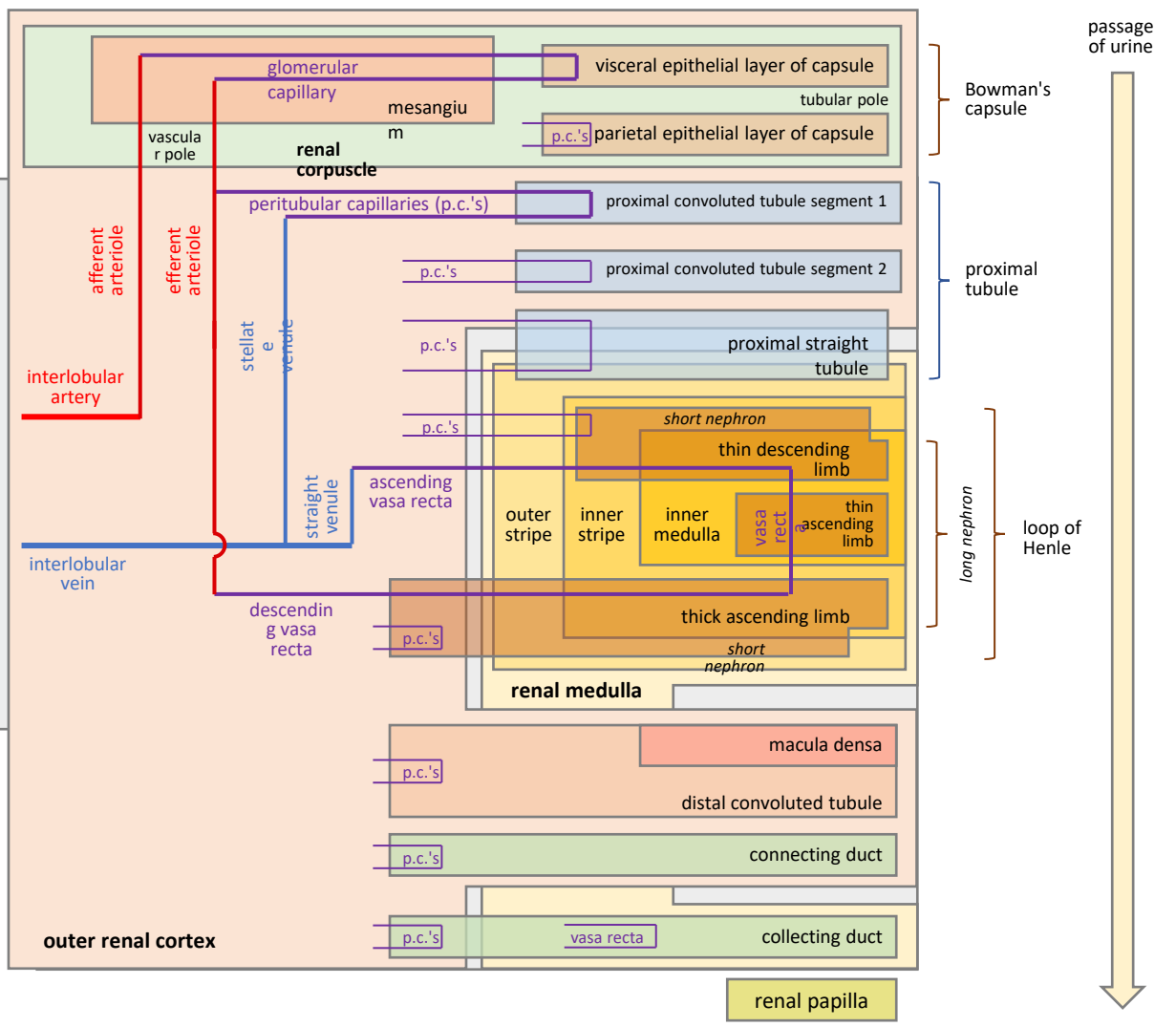
Vascular Geometry for kidney



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

renal cortex

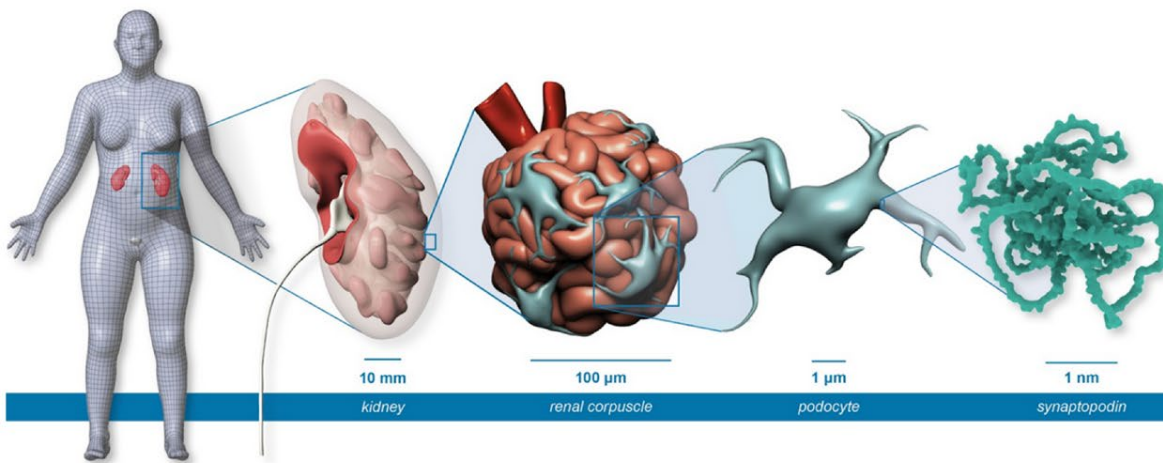


interlobular artery interlobular vein

stellate venule straight venule

ascending vasa recta descending vasa recta

vasa recta



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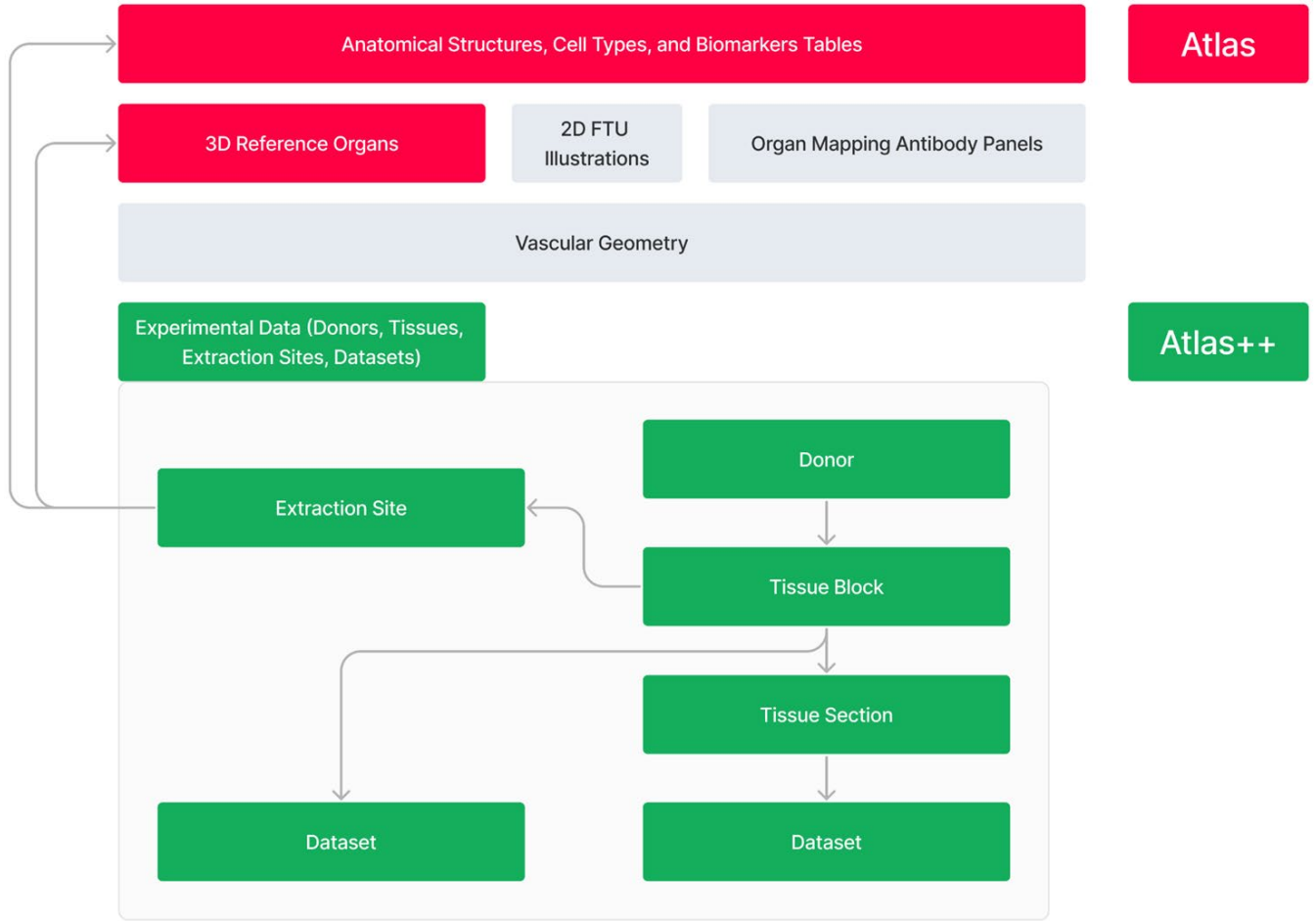
Organ Mapping Antibody Panels

Vascular Geometry

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

Atlas++

Experimental Dataset Framework

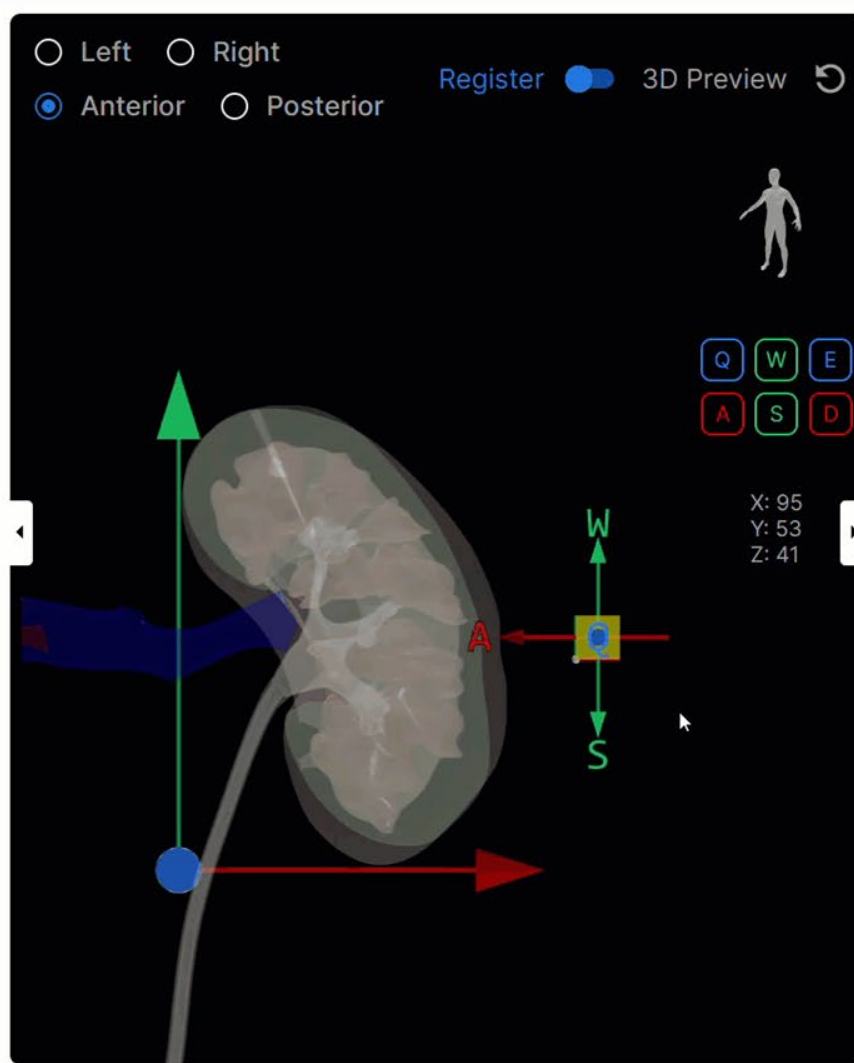


Anatomical Structures

- 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)
<input type="text" value="10"/>	<input type="text" value="10"/>	<input type="text" value="10"/>

Tissue Sections

Thickness	# Sections
<input type="text"/>	<input type="text"/>

Tissue Block Rotation

X	<input type="range" value="0"/>	0
Y	<input type="range" value="0"/>	0
Z	<input type="range" value="0"/>	0

Anatomical Structure Tags

Add Anatomical Structures ...

Assigned Added

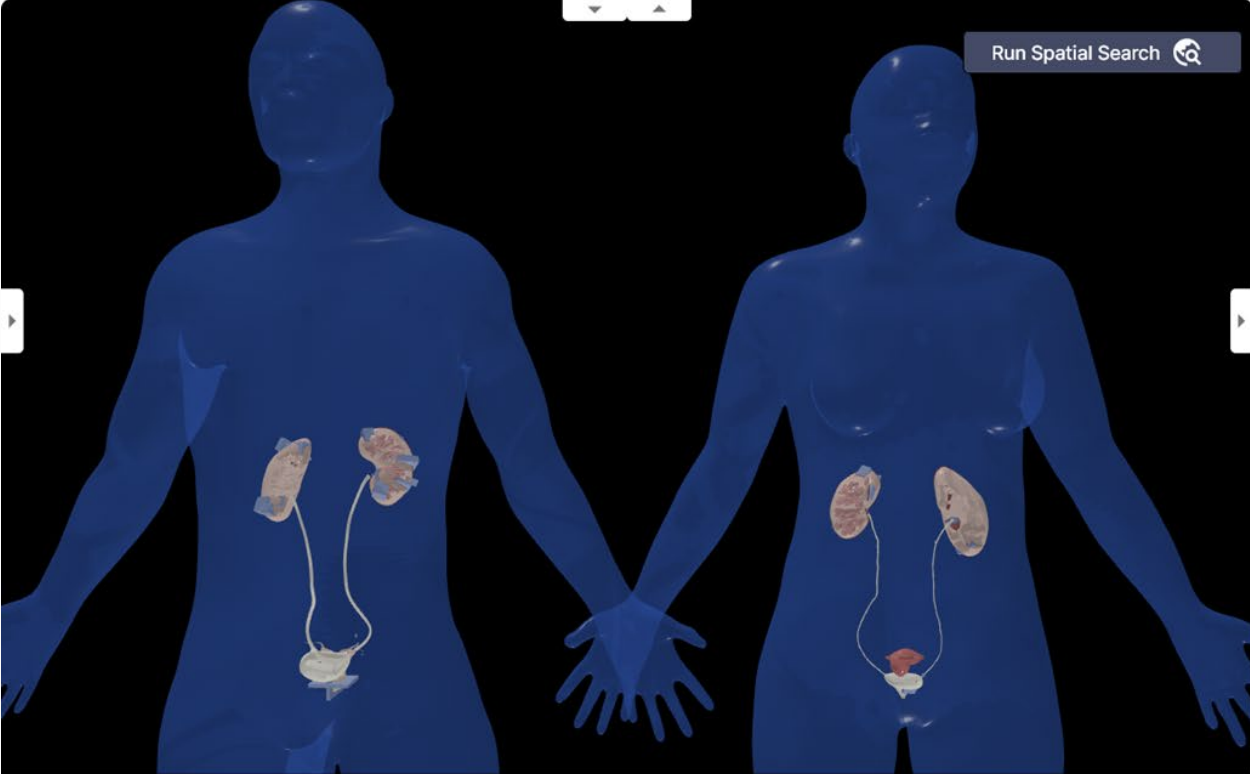
HRA-mapped Data: kidney, ureter, bladder, prostate, and uterus

HuBMAP HRA EXPLORATION

Navigation bar with icons and counts for various organs:

- Blood Vasculature: 0
- Brain: 0
- Eye, L: 0
- Eye, R: 0
- Fallopian Tube, L: 0
- Fallopian Tube, R: 0
- Heart: 0
- Kidney, L: 66
- Kidney, R: 57
- Knee, L: 0
- Knee, R: 0
- Large Intestine: 0

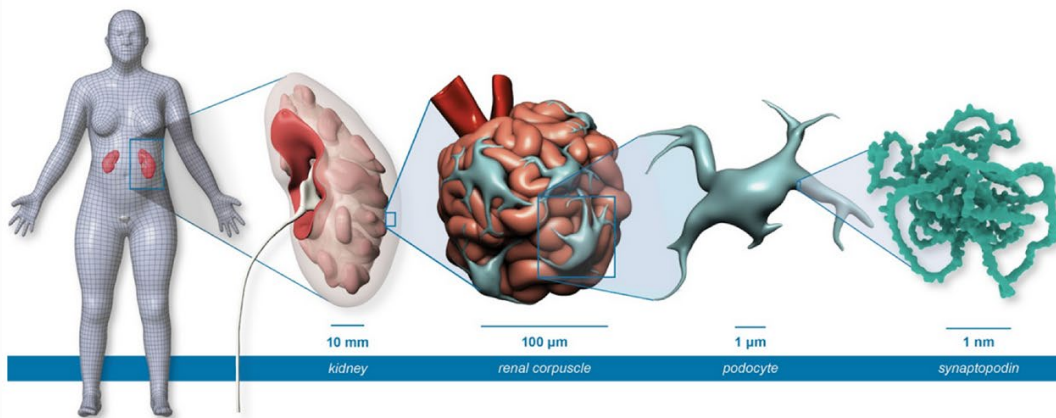
Utility icons: Full screen, Dark mode, Refresh, and Information.



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

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



Anatomical Structures

Functional
Tissue Units

Cell Types

Biomarkers
Genes, Proteins, ..

Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

Atlas

3D Reference Organs

2D FTU
Illustrations

Organ Mapping Antibody Panels

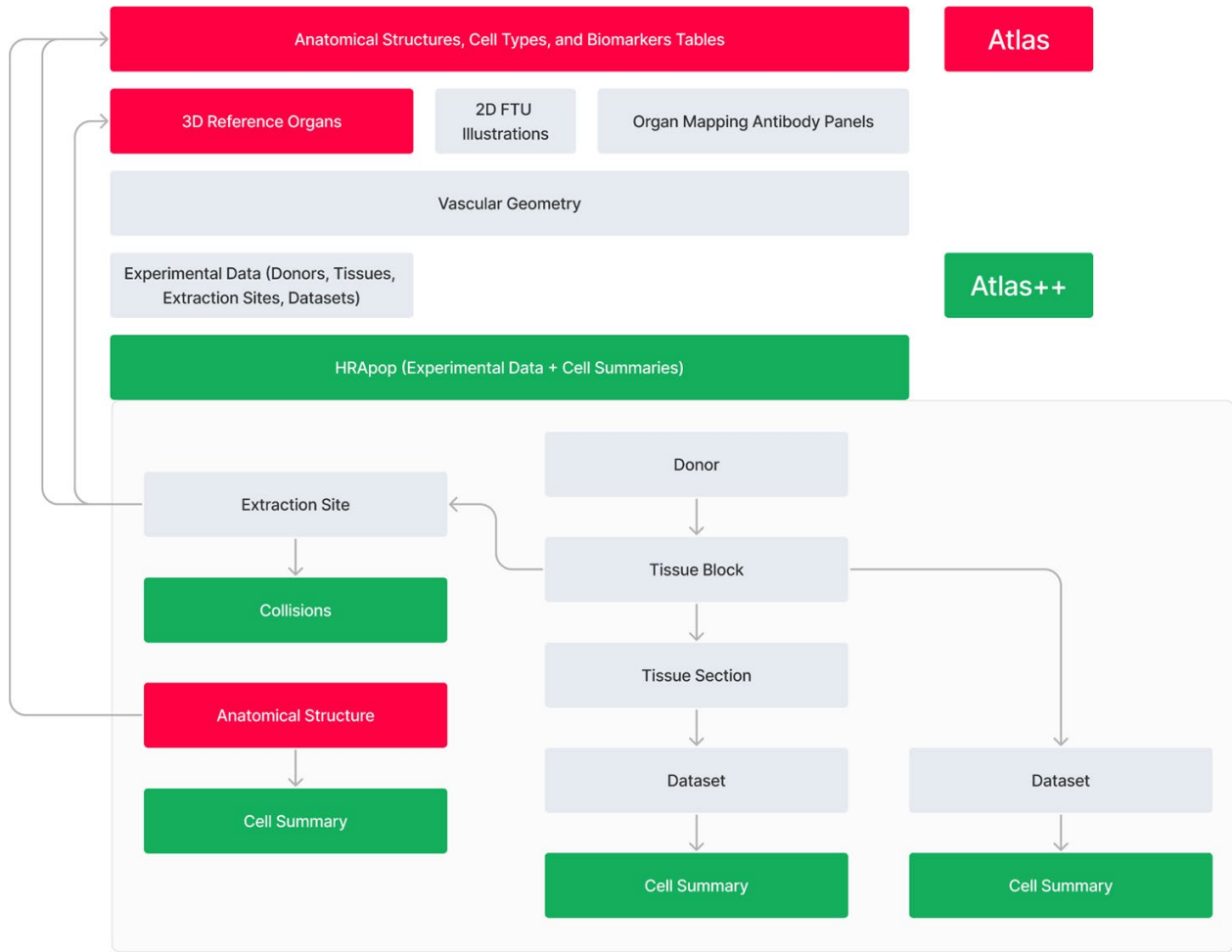
Vascular Geometry

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

Atlas++

HRApop (Experimental Data + Cell Summaries)

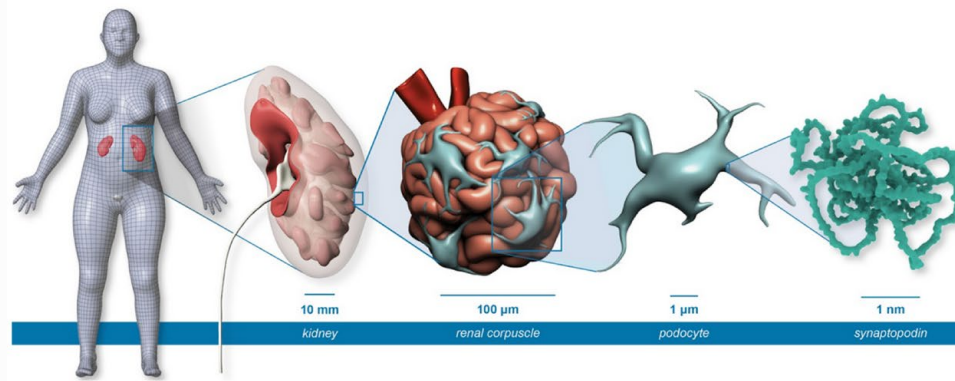
HRApop Framework





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



Anatomical Structures

Functional
Tissue Units

Cell Types

Biomarkers
Genes, Proteins, ..

Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

Atlas

3D Reference Organs

2D FTU
Illustrations

Organ Mapping Antibody Panels

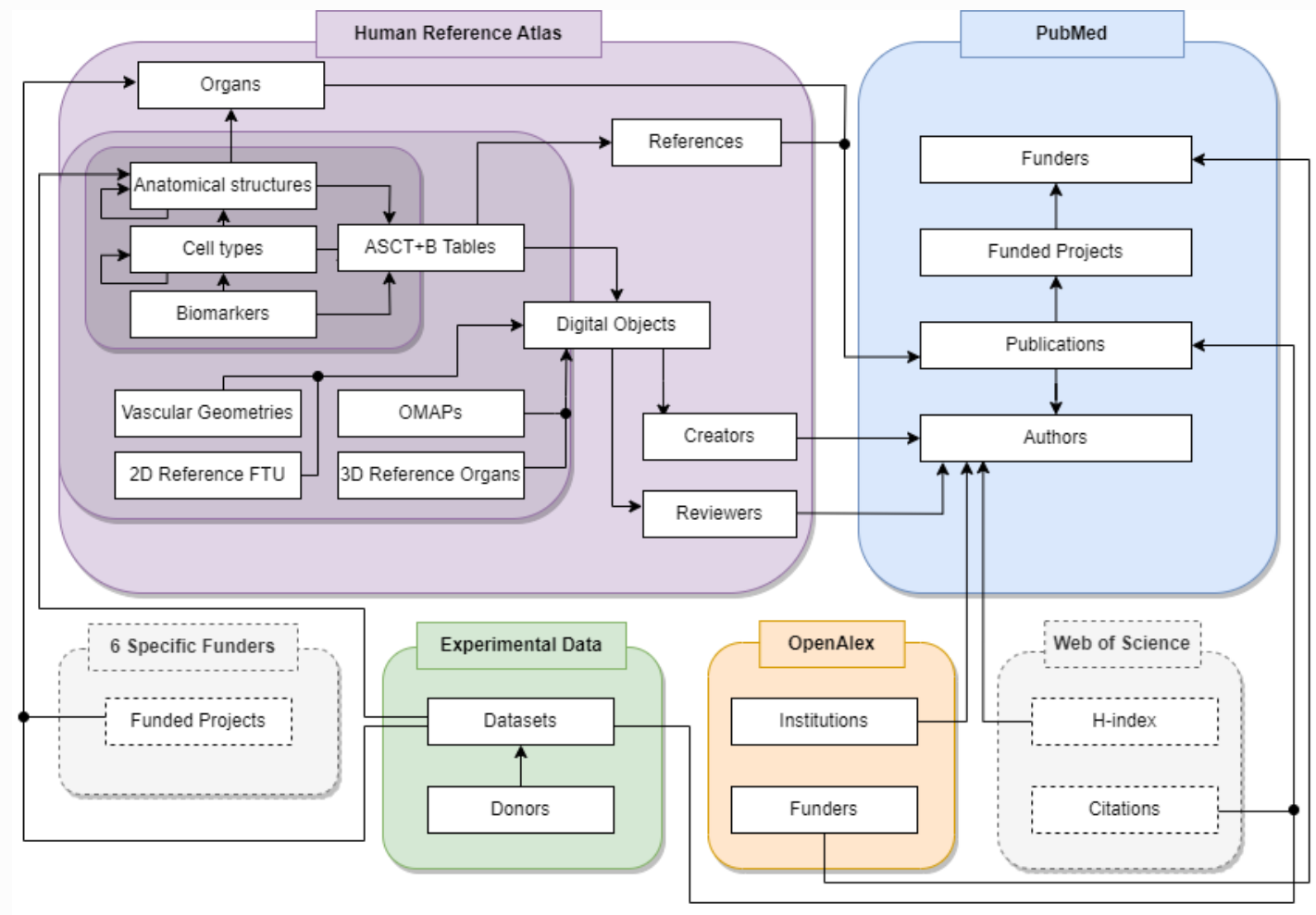
Vascular Geometry

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

Atlas++

HRApop (Experimental Data + Cell Summaries)

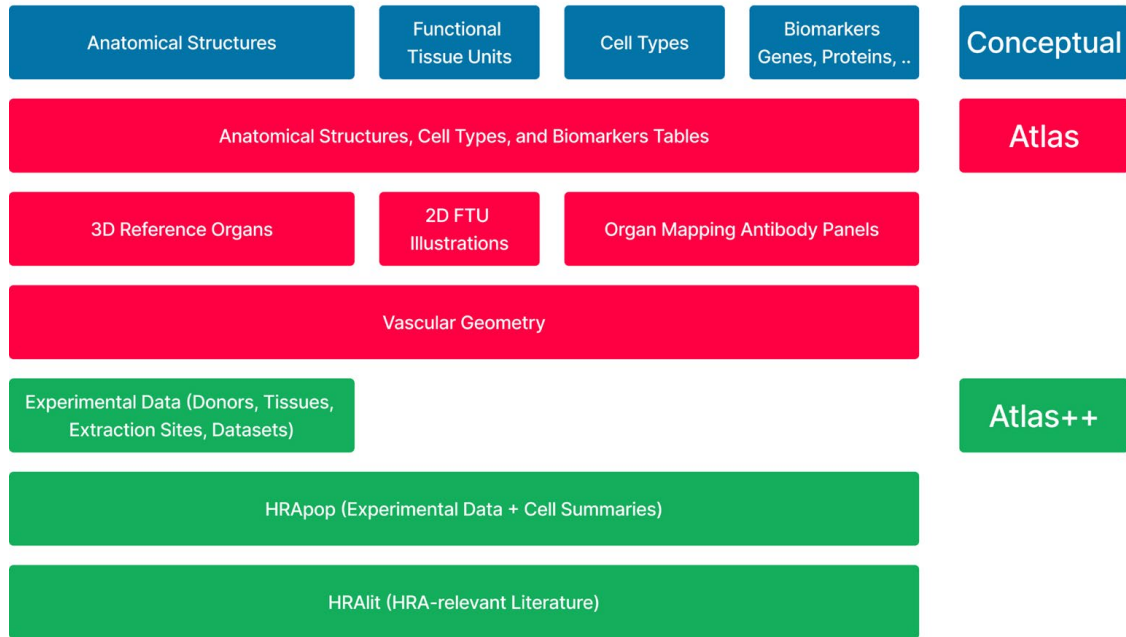
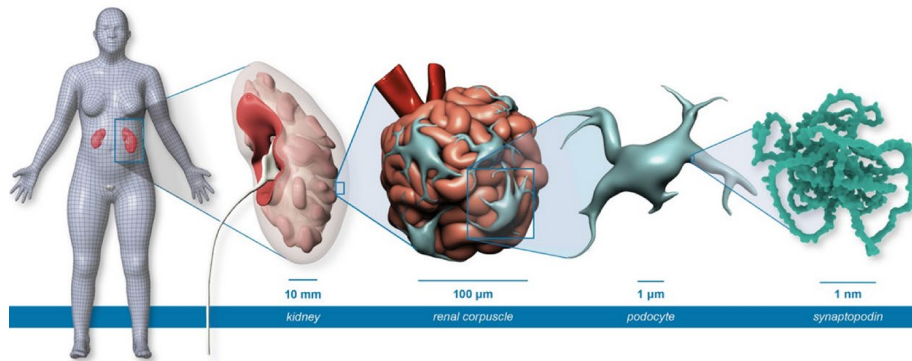
HRAlit (HRA-relevant Literature)





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

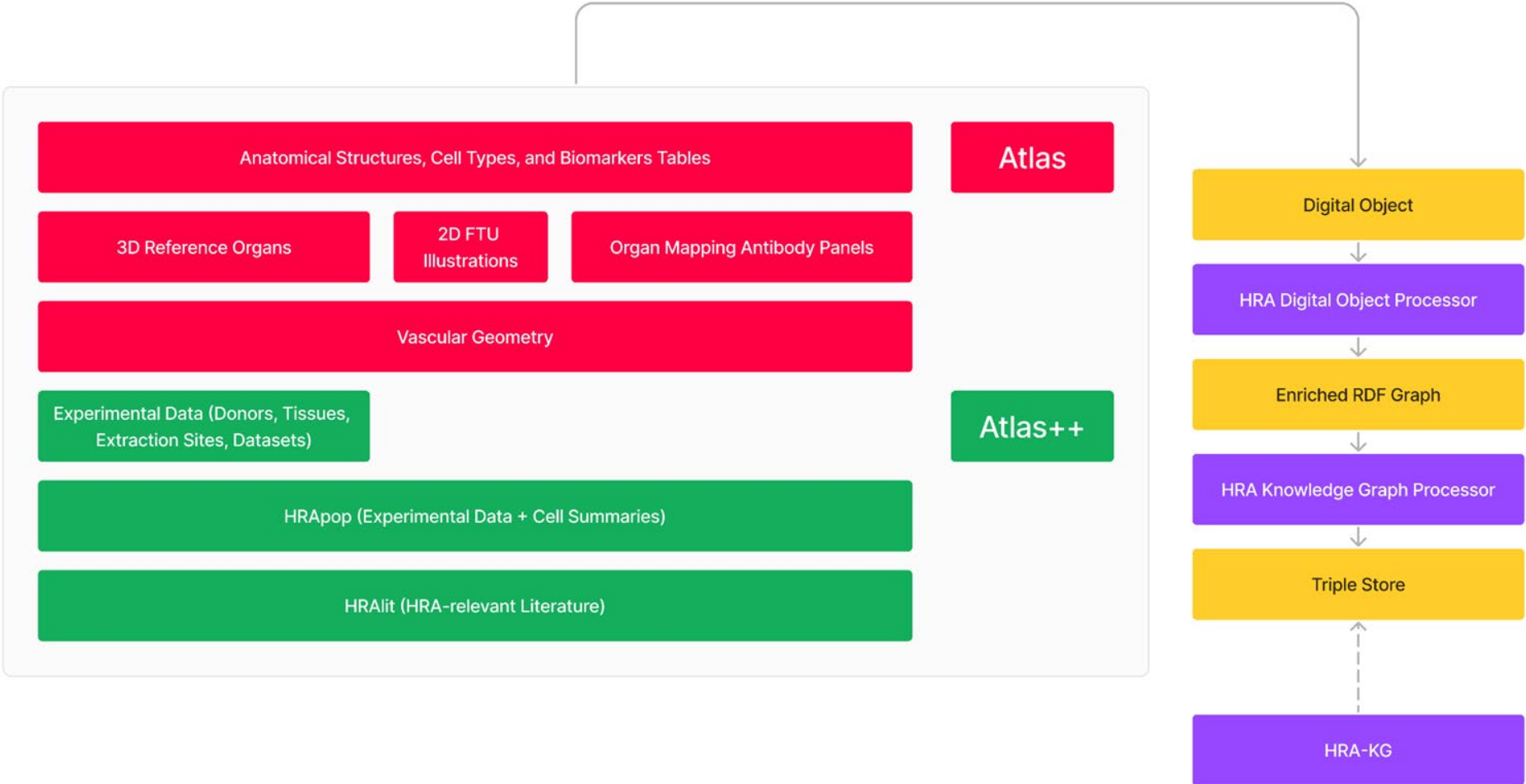
Organ	#Publications	#Experts	#Institutions	#Funded Projects	#Funders
kidney	762,095	59,910	8,899	97,041	1,485
prostate	174,800	23,131	5,078	34,219	907
ureter	62,702	3,921	1,564	3,294	144
urinary bladder	133,489	10,343	3,131	14,713	460
uterus	71,489	3,266	1,417	8,470	177
Total (sum, not unique)	1,204,575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



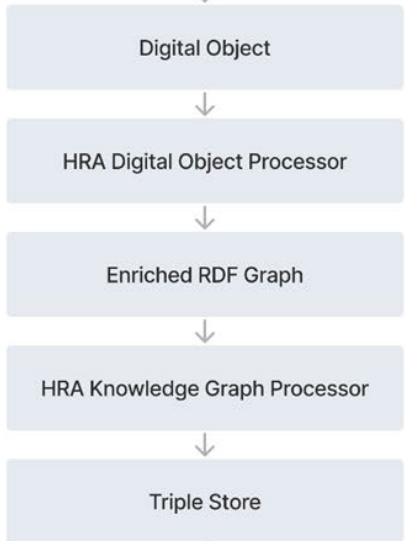
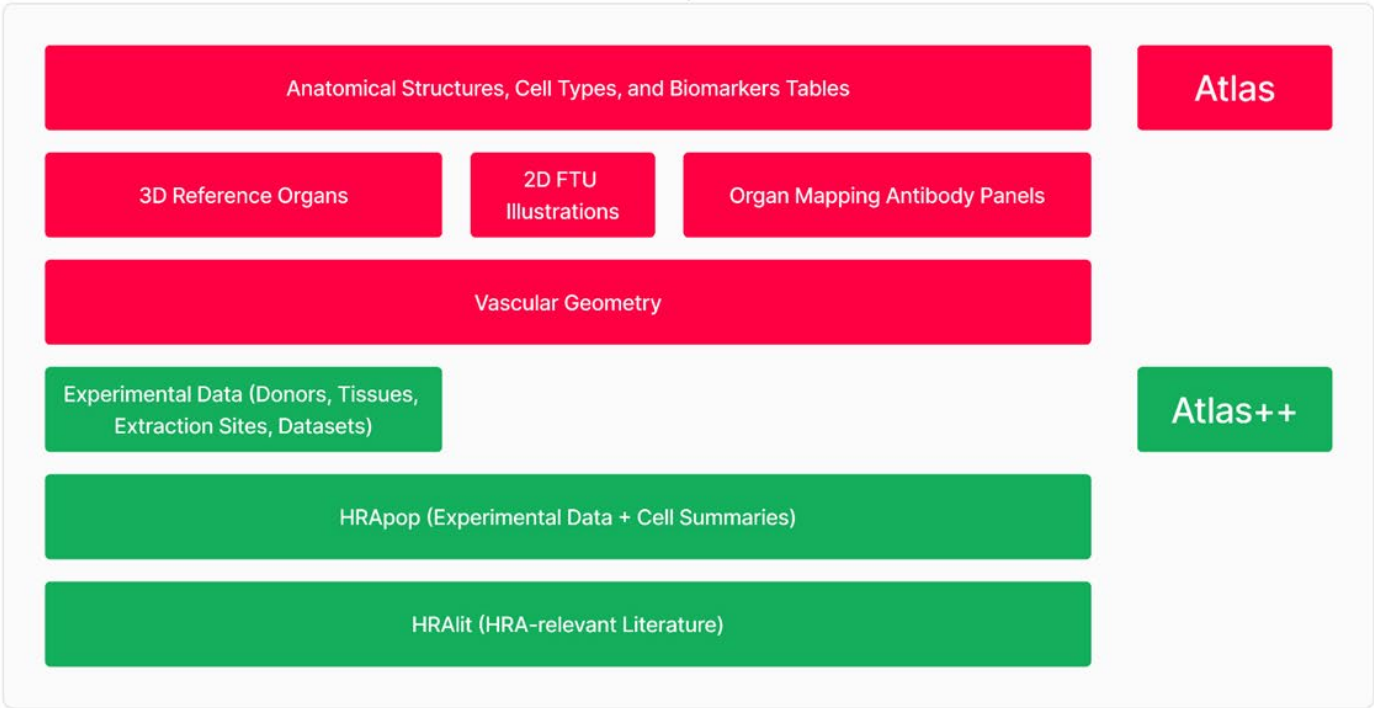
Using the HRA



HRA Knowledge Graph Framework



HRA API and Applications



ASCT+B Reporter User Interface

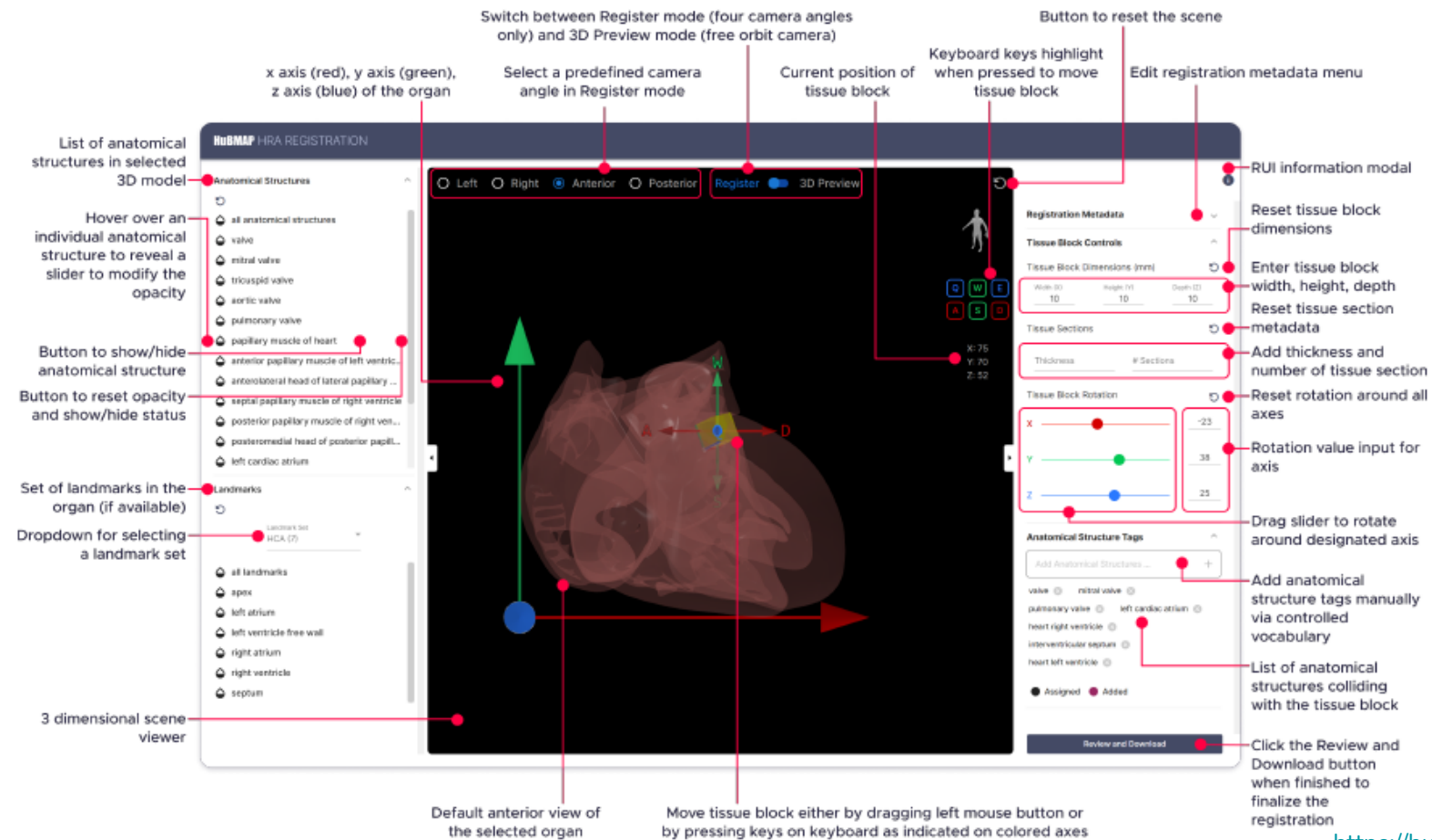
The image shows a screenshot of the ASCT+B Reporter User Interface. The interface is divided into several sections:

- Search and filter menu:** Located at the top left, it includes a search bar and filters for anatomical structures, cell types, and biomarkers.
- Legend:** A central panel on the left that allows users to filter the visualization by anatomical structures, cell types, gene biomarkers, and protein biomarkers. It also includes a section for Organ Mapping Antibody Panels (OMAPs).
- Tree visualization:** A large central area displaying a hierarchical tree of anatomical structures, cell types, and biomarkers. Nodes are color-coded and shaped according to the legend.
- Display settings:** A panel on the left side of the tree visualization that allows users to adjust various settings, including tree width, tree height, and biomarker display options.
- Information panels:** Pop-up windows that provide detailed information about selected nodes, including ontology IDs, IDs, and notes.
- Right side panel:** A panel on the right side of the interface that displays summary statistics and a message log of the visualization generation process.
- Navigation and utility buttons:** Buttons for refreshing the view, opening tables in Google Sheets, and accessing the playground view.

Annotations and callouts provide additional context for various UI elements:

- Search and filter menu for locating specific structures or reducing the tree visualization to specific anatomical structures, cell types, and biomarkers**
- Refresh view**
- Reveals a right side panel with indented list displaying organs in body partonomy**
- Open tables in Google Sheets**
- Playground view**
- Open right side panel to compare user-authored ASCT+B table with latest release table**
- View GitHub Repository and other information**
- Export the visualization in PNG, SVG, Vega Spec Graph Data, JSON-LD, and OWL (RDF/XML)**
- Message log of the visualization generation process**
- Summary statistics right 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**
- Anatomical structure nodes**
- Click the name of a node to open the information panel**
- Cell type nodes**
- Biomarker nodes**

Registration User Interface (RUI)



Exploration User Interface (EUI)

HRA EXPLORATION

Sex: Both Age: 1-110 BMI: 13-83

Filter for exploring tissue blocks of interest

List of reference organs for exploration

Number of tissue blocks per organ

Spatial search tool for filtering by location

Information modal for the interface

Show and hide lists for Anatomical Structures, Cell Types, and Biomarkers

AS CT B

Anatomical Structures list Tissue Blocks: 729

- brain: 11
- lymph node: 36
- eye: 43
- fallopian tube: 0
- heart: 159

Cell Types list Tissue Blocks: 729

- absorptive: 67
- adipocyte: 159
- adult endothelial progenitor cell: 39
- adventitial fibroblast: 39
- adventitial stromal cell: 67
- afferent arteriole endothelial cell: 121

Biomarkers list Tissue Blocks: 729

BG BL BM BP BF

Show and hide lists for specific biomarkers (genes, lipids, metabolites, proteins, proteoforms)

- a smooth muscle actin: 0
- A2M: 253
- ABC10-43608400015.1: 0
- ABCA1: 11
- ABCA13: 11
- ABCA3: 42
- ABCA4: 11
- ABCA8: 11
- ABCG9: 402
- ABCG2: 0
- ABCG2: 11
- ABI3BP: 11
- ABLIM1: 31
- AC002066.1: 0

Number of tissue blocks that collide with this anatomical structure

Number of tissue blocks that have this CT in colliding AS in ASCT+B table

Number of tissue blocks that have this biomarker in colliding AS in ASCT+B table

3D scene viewer

body | cell | biomarker

Results based on current filters

- 18 Tissue Data Providers
- 307 Donors
- 729 Tissue Blocks
- 892 Tissue Sections
- 3213 Tissue Datasets

Donor card in the expanded view

Tissue block card with information on number of tissue sections

Tissue section card

Dataset cards for viewing relevant portals, publications, or other resources

Male, Age 72, BMI 27.4
Entered 4/9/2021, Liz McDonough, RTI-Gener...

Registered 9/10/2021, Liz McDonough, RTI-G...
28 x 11 x 7 millimeter, 0.3 millimeter, 26 Secti...
0 26

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Registered 1/12/2021, Liz McDonough, RTL...
28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Cell Publication

Interactive FTU Explorer

Name of the selected Functional Tissue Unit: renal corpuscle

2D Illustration viewer: Shows a detailed anatomical diagram of a renal corpuscle with various cell types labeled: Afferent arteriole endothelial cell, Macula densa epithelial cell, Efferent arteriole endothelial cell, Glomerular visceral epithelial cell, Parietal epithelial cell, Epithelial cell proximal tubule, Glomerular mesangial cell, and Glomerular capillary endothelial cell. A 50 µm scale bar is present.

Cell types by biomarkers tables:
Cell Types by Gene Biomarkers

Gene Biomarkers	Protein Biomarkers	Lipid Biomarkers
Cell Type	Cell Count	AAGS AKT3 ALS2...
glomerular capillary endothelial cell	34,400	
glomerular mesangial cell	9,900	
glomerular visceral epithelial cell	34,700	
parietal epithelial cell	26,600	

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.

Biomarker Expression Mean in FTU: 0.0 to 1.0 scale. Percentage of Cells in FTU: 0%, 50%, 100%.

Source Data:
1. Single cell transcriptional and chromatin accessibility profiling redefine cellular heterogeneity in the adult human kidney [Sriniva-se et al. Three Healthy Human Kidney Tissue](#)

Functional Tissue Units available for exploration: FTU Library (Kidney, Liver, Lung, Pancreas, Prostate Gland, Skin, Small Intestine, Spleen, Thymus)

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

Collapse and expand Functional Tissue Unit listings within organs: Illustration, Download, Embed, Contact, HRA Portal

View the selected illustration digital object metadata page: Illustration

Download the selected illustration in various formats: Download

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

Direct link to experimental data: Contact

Contact form for Human Reference Atlas team: Contact

Open the Human Reference Atlas Portal: HRA Portal

Cell Distance Visualizations

Access documentation

Submit bug reports or feature requests to the Vitesse team

Vitesse pronunciation by IPA Reader

Demos showcasing core features

Use tutorials

Vitesse Python package

Vitesse R package

Blog posts

Vitesse GitHub repository

Switch between light mode and dark mode

Return to the Vitesse landing page

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

The screenshot shows the Vitesse software interface. The main window displays a 2D spatial viewer with a dark background and numerous colored cells. Red lines connect each cell to its closest endothelial cell. A legend on the right side lists various cell types with corresponding color swatches. A histogram at the bottom right shows the distribution of distances between different cell types and the nearest vasculature. The histogram has a y-axis labeled 'Number of Cells' ranging from 0 to 1000 and an x-axis labeled 'Distance (µm)' ranging from 0 to 400. A red dot on the x-axis at approximately 150 µm indicates a specific distance value.

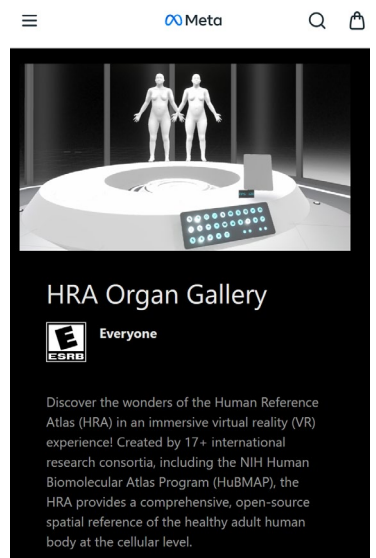
If you are interested to explore cell-cell, cell-FTU distance distributions, please share your data in this format:

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



Grab the cylinder to move, rotate, and scale the selected organ in high resolution by using the left and right VR controllers

Male and female body provide context for selected organ

Currently selected organ appears outlined in its position in the body

Application is used while sitting and user can exit application by pressing menu button on controller

The organ selected on the keyboard appears in the cylinder with all registered tissue blocks

Reset the organ to the original position, rotation, and scale

Select the sex of the organ (if applicable)

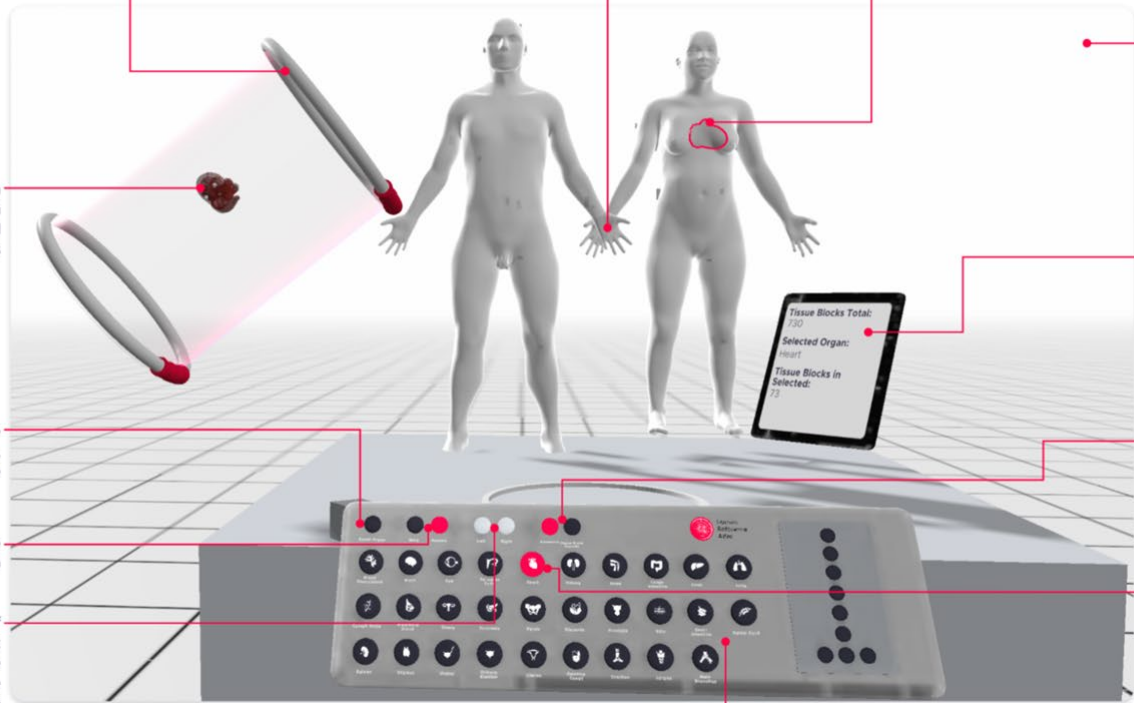
Select the laterality of the organ (if applicable): Gray means the selection is not possible for the current organ

Organ selection keyboard: Select an organ to view in 3D high-resolution

Details on the number of tissue blocks for all organs, the name of the currently selected organ, and the number of tissue blocks in that organ

Switch to change between using controllers for movement and manipulating tissue blocks

A red organ icon on the keyboard indicates an organ selected for further inspection



HRA API: Run an API Query

HRA-API Workflow 3: Run an API Query

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

The screenshot shows the HRA API v1.x Routes interface. The selected route is GET /v1/sparql, which runs a SPARQL query. The REQUEST section includes a text input for the SPARQL query (with an example: SELECT * WHERE { ?sub ?pred ?obj . } LIMIT 10), a token input, and a format dropdown menu. The RESPONSE section shows a successful operation with a 200 status code and an example JSON response: [{" }].

Select a response code to view example response and schema doc

Example response tab Schema documentation tab for the response

FILL EXAMPLE CLEAR TRY

Run the API query
Reset parameters
Fill parameters with example options

The background features several overlapping, semi-transparent, blue and green particle-like shapes. These shapes are irregular and resemble biological cells or molecular structures. They are filled with numerous small, colorful speckles in shades of red, green, and blue, giving them a textured, almost crystalline appearance. The overall aesthetic is clean and scientific.

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, GTE_x, GUDMAP, HCA, HuBMAP, Human Tumor Atlas Network (HTAN), KPMP, LungMAP, (Re)building the Kidney (RBK), and SenNet.

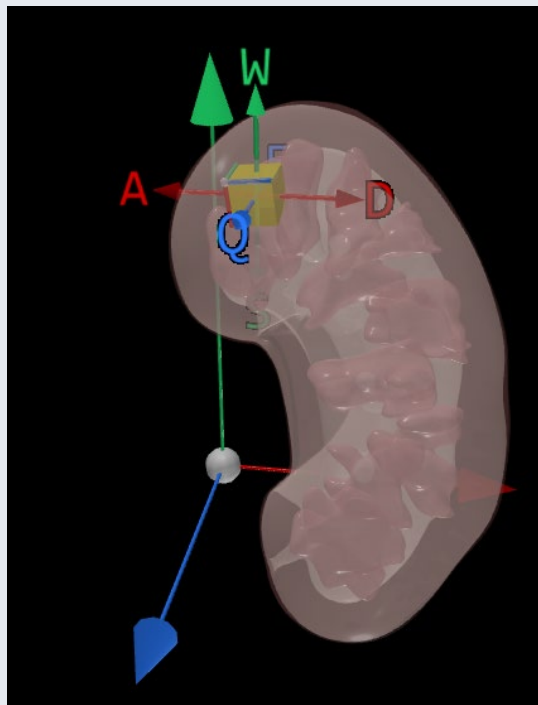
In addition, six programmers from different human atlas projects were surveyed.

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 Convolved 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

HRA EXPLORATION

Filter for exploring tissue blocks of interest: Sex: Both, Age: 1-110, BMI: 13-83

List of reference organs for exploration: Heart, Kidney, L

Spatial search tool for filtering by location: Run Spatial Search

Information modal for the interface: body | cell | biomarker

Show and hide lists for Anatomical Structures, Cell Types, and Biomarkers: AS, CT, B

Anatomical Structures list: Anatomical Structures (AS) Tissue Blocks: 729

- brain: 11
- lymph node: 36
- eye: 43
- fallopian tube: 0
- heart: 159

Number of tissue blocks that collide with this anatomical structure

Cell Types list: Cell Types (CT) Tissue Blocks: 729

- absorptive: 67
- adipocyte: 159
- adult endothelial progenitor cell: 39
- adventitial fibroblast: 39
- adventitial stromal cell: 67
- afferent arteriole endothelial cell: 121

Number of tissue blocks that have this CT in colliding AS in ASCT+B table

Biomarkers list: Biomarkers Tissue Blocks: 729

- BG: 0
- BL: 0
- BM: 0
- BP: 0
- BF: 0

Show and hide lists for specific biomarkers (genes, lipids, metabolites, proteins, proteoforms): BG, BL, BM, BP, BF

- a smooth muscle actin: 0
- A2M: 253
- ABC10-4360B400015.1: 0
- ABCA1: 11
- ABCA13: 11
- ABCA3: 42
- ABCA4: 11
- ABCA8: 11
- ABGGG: 402
- ABCG2: 0
- ABCG2: 11
- ABI3BP: 11
- ABLIM1: 31
- AC00206R.1: 0

Number of tissue blocks that have this biomarker in colliding AS in ASCT+B table

Number of tissue blocks per organ: 159

3D scene viewer

Results based on current filters: 19 Tissue Data Providers, 307 Donors, 729 Tissue Blocks, 892 Tissue Sections, 3213 Tissue Datasets

Donor card in the expanded view: Male, Age 72, BMI 27.4, Entered 4/9/2021, Liz McDonough, RTI-Gener...

Tissue block card with information on number of tissue sections: Registered 9/10/2021, Liz McDonough, RTI-G... 28 x 11 x 7 millimeter, 0.3 millimeter, block

Tissue section card: Registered 1/12/2021, Liz McDonough, RTI... 28 x 11 x 0.3 millimeter, 0.3 millimeter, block

Dataset cards for viewing relevant portals, publications, or other resources: Cell publication Dive

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

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

Name of the selected Functional Tissue Unit: renal corpuscle

2D Illustration viewer: Shows a detailed anatomical diagram of a renal corpuscle with labels for various cell types: Afferent arteriole endothelial cell, Macula densa epithelia cell, Efferent arteriole endothelial cell, Glomerular visceral epithelial cell, Parietal epithelial cell, Epithelial cell proximal tubule, Glomerular capillary endothelial cell, and Glomerular mesangial cell. A 50 µm scale bar is provided.

Cell types by biomarkers tables:
Cell Types by Gene Biomarkers

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

Expand the table view: Tabs to view tables for gene, protein, & lipids. Cell types, cell counts, & associated biomarker columns. Legend for cell types and biomarkers table: Hover over the information icons to reveal additional legend details.

Functional Tissue Units available for exploration: FTU Library (renal corpuscle selected)

- 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 corpuscle (selected)
 - thick ascending limb of loop of Henle
- Large Intestine
 - crypt of Lieberkuhn of large intestine
- Liver
 - liver lobule
- Lung
 - bronchus submucosal gland
 - alveolus of lung
- Pancreas
 - intercalated duct of pancreas
 - islet of Langerhans
 - pancreatic acinus
- Prostate Gland
 - prostate glandular acinus
- Skin
 - papillary layer of dermis
 - epidermal ridge of digit
- Small Intestine
 - intestinal villus
- Spleen
 - red pulp of spleen
 - white pulp of spleen
- Thymus
 - thymus lobule

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: Illustration

Download the selected illustration in various formats: Download

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

Direct link to experimental data: 1. Single cell transcriptional and chromatin accessibility profiling redefine cellular heterogeneity in the adult human kidney [scRNA-seq of Three Healthy Human Kidney Tissue](#)

Contact form for Human Reference Atlas team: Contact

Open the Human Reference Atlas Portal: HRA Portal

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

US#5. Provide cell distance distribution visualizations

Access documentation

Submit bug reports or feature requests to the Vitesse team

Vitesse pronunciation by IPA Reader

Demos showcasing core features

Use tutorials

Vitesse Python package

Blog posts

Vitesse GitHub repository

Open the Vitesse App

Vitesse R package

Switch between light mode and dark mode

Return to the Vitesse landing page

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

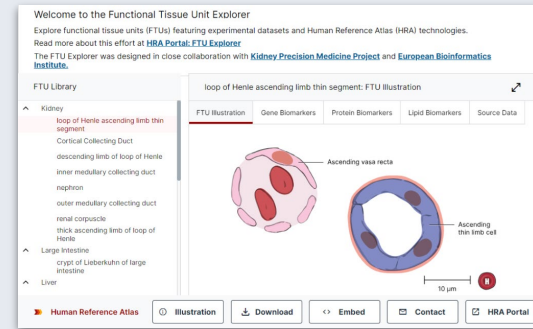
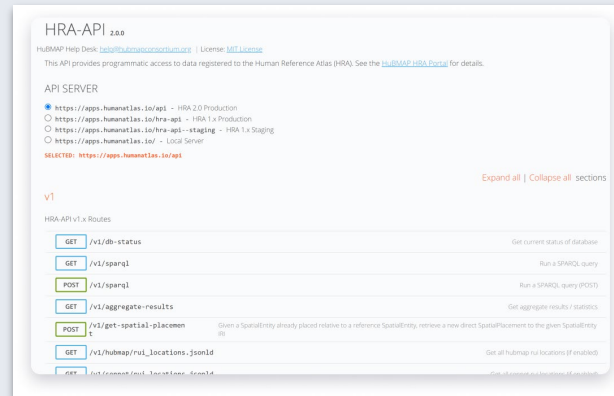
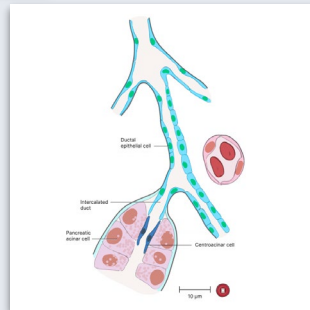
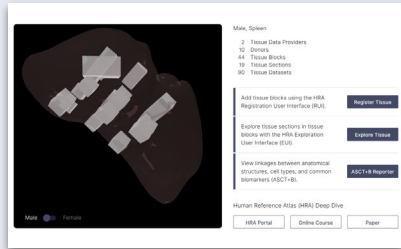
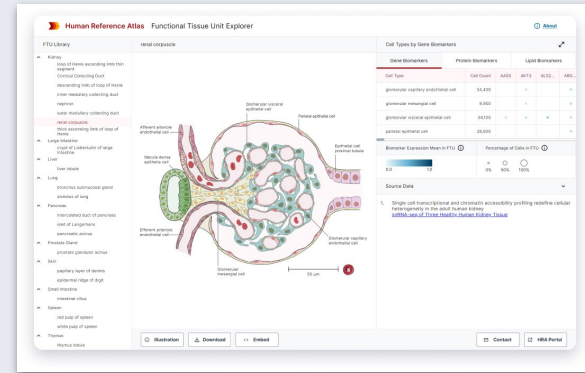
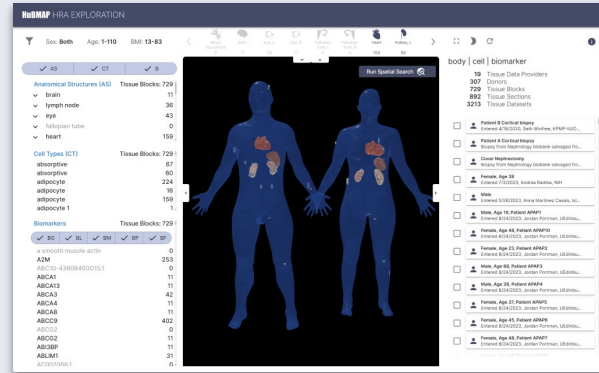
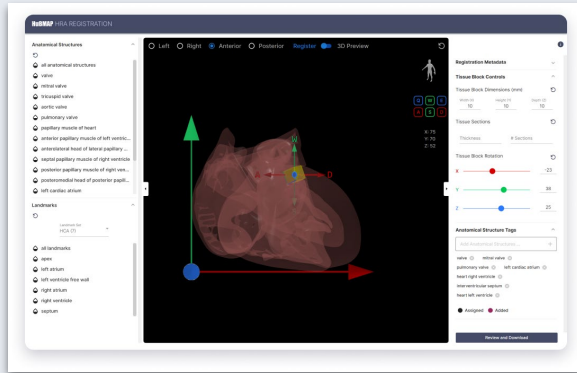
Legend showing colors for cell types and links from these cells to endothelial cells

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

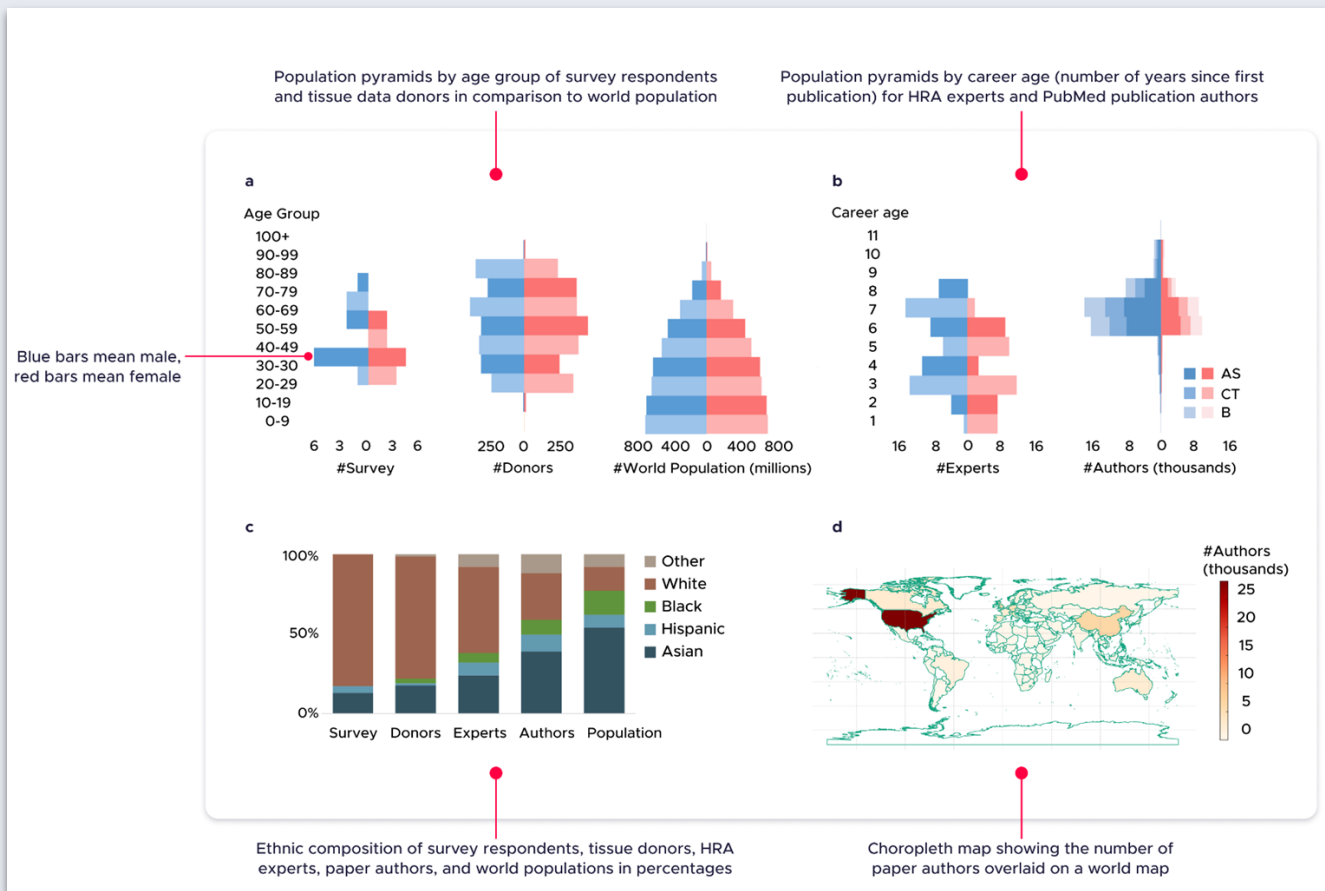
Coming June 14th on humanatlas.io

US#6. Develop lightweight atlas components



Coming June 14th on humanatlas.io

US#7. Implement dashboard for HRA



Ethnic composition of survey respondents, tissue donors, HRA experts, paper authors, and world populations in percentages

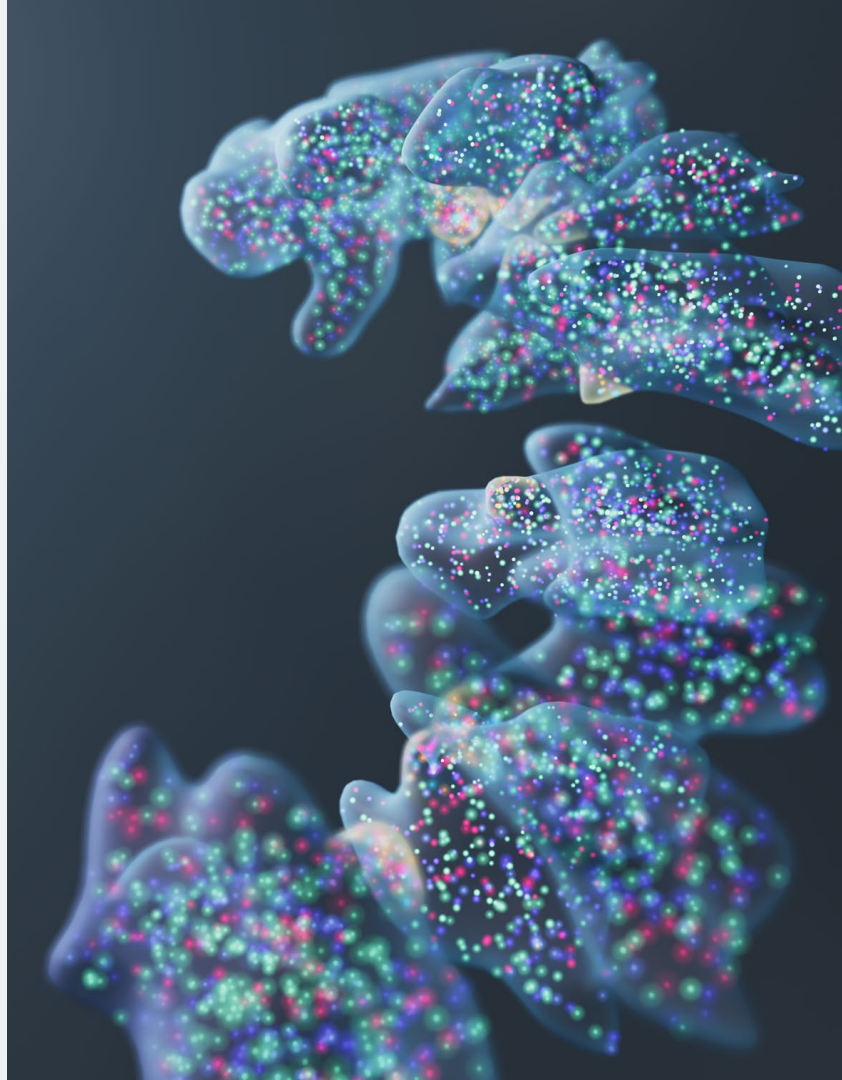
Choropleth map showing the number of paper authors overlaid on a world map



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

Connecting people is key to our success. Here are some of our great collaborators (apologies to those I missed!)

Principal Investigator,
Co-Principal Investigators,
and Consultants



Katy Börner
MC-IU PI
CNS Director

Mark Musen
Professor of Medicine
(Biomedical Informatics) and
of Biomedical Data Science

Helen Parkinson
Oncologist

David Van Valen
Assistant Professor of
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Fusheng Wang
Associate Professor of
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and Computer Science

Griffin Weber
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Full Time Staff



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Andreas Bueckle
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Josef Hardi
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(Machine Learning)

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Libby Maier
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Lisel Record
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Nancy Ruschman
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More information about the Human Reference Atlas is available at:

<https://humanatlas.io>



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Thank you!

Resources at:

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

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