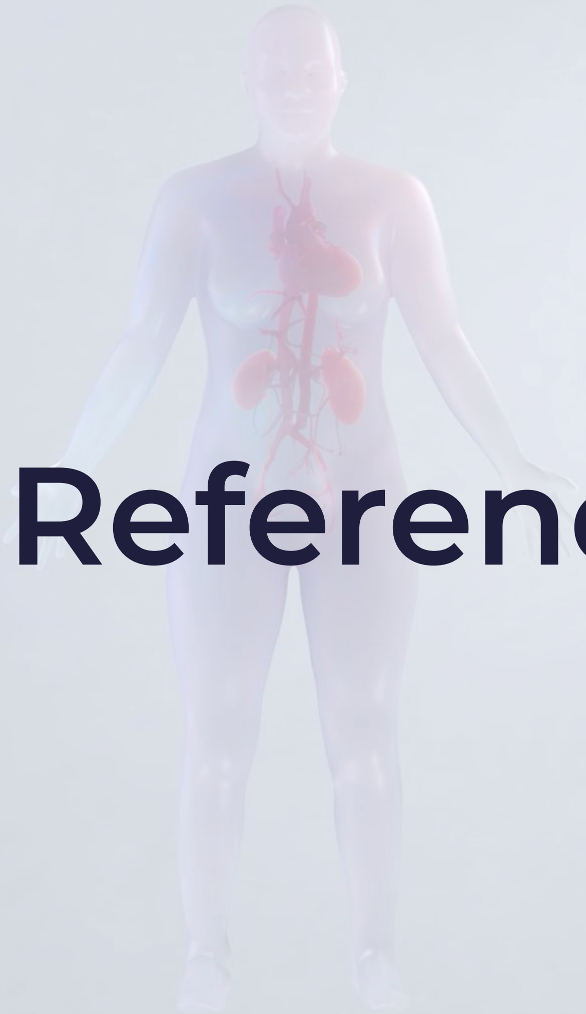
AUA 2024 MAY 3-6 San Antonio

Keynote: The Human Reference Atlas

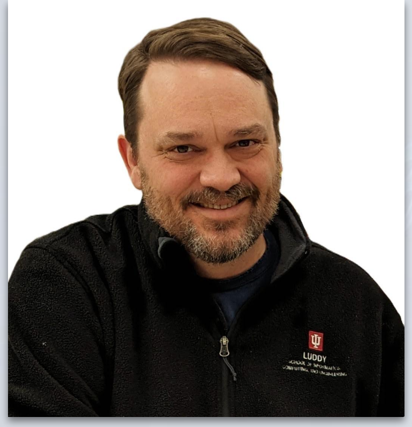
Version 2.0



Human Reference Atlas

https://humanatlas.io

Keynote: The Human Reference Atlas



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Technical Director

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Keynote | Basic Sciences Symposium | 2024 AUA Annual Meeting | San Antonio, TX | May 5, 2024

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

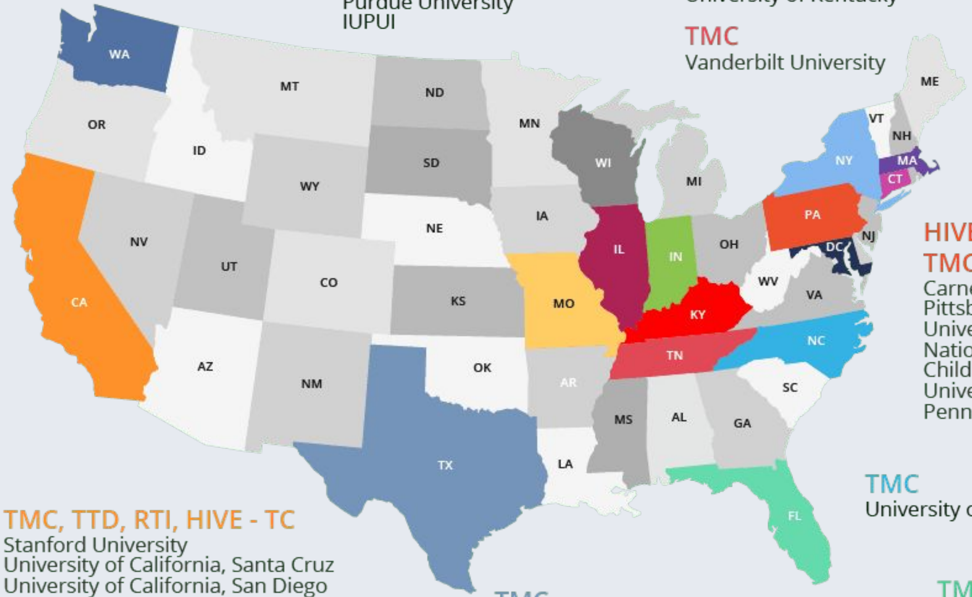
HIVE - TC
University of Kentucky

TMC
Vanderbilt University

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

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



TMC
University of Zurich

TMC
Delft University of Technology

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
University of North Carolina, Chapel Hill

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, HIVE - TC
University of Florida

HIVE - TC, TMC
European Bioinformatics Institute
Wellcome Sanger Institute

Source: https://hubmapconsortium.org/about/

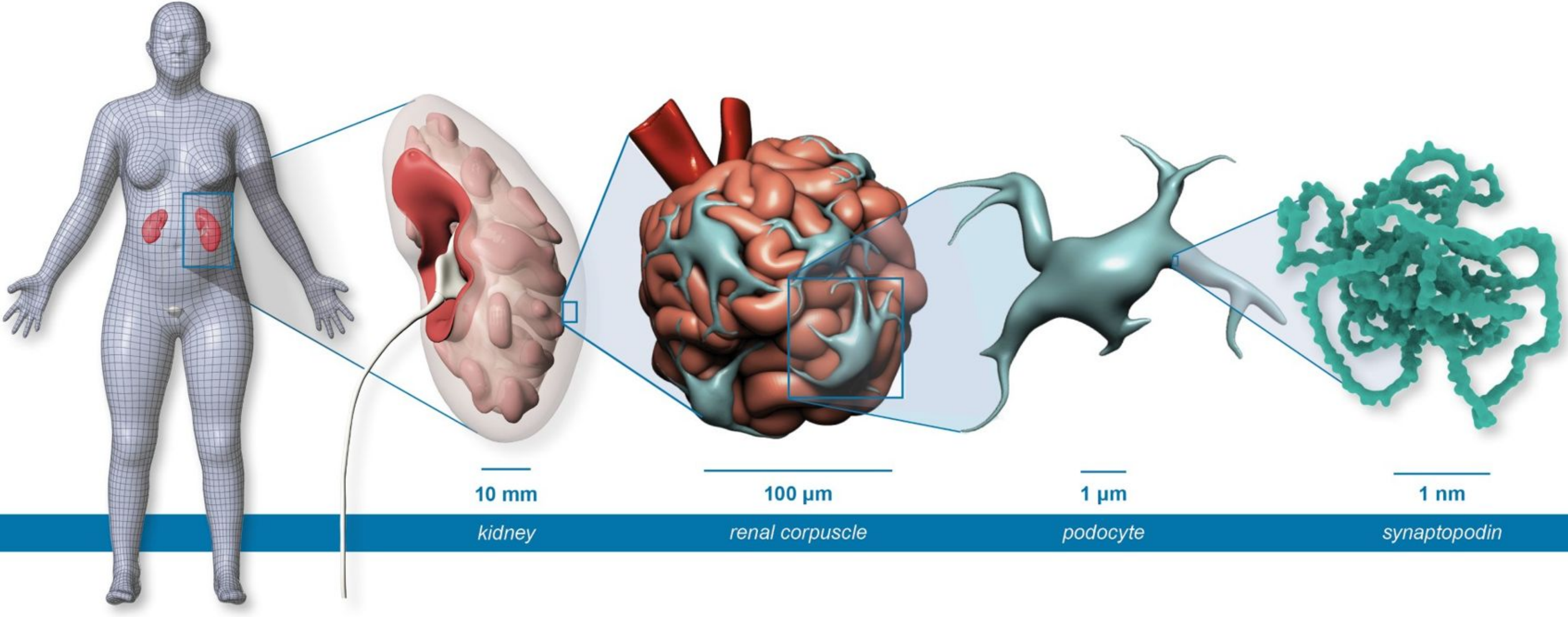
Early history of the HRA and HuBMAP

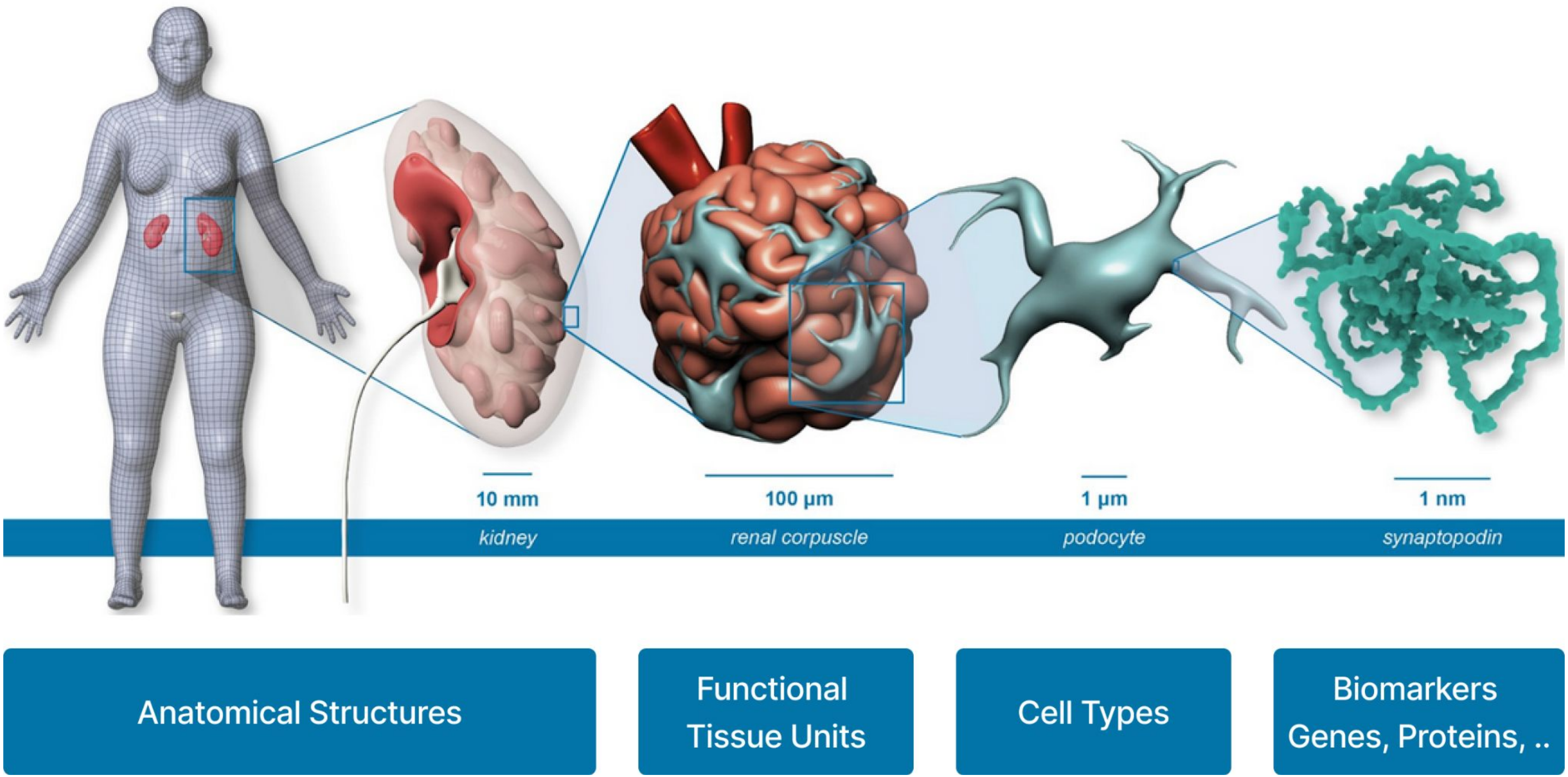
- HuBMAP started in 2018 with the goal of mapping the human body down to the cellular level
- The IU team started off with creating a common coordinate framework, that eventually evolved into the HRA
- In 2023, we published HRA v2.0
- We are now in the production phase of HuBMAP

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




10 mm
kidney
100 µm
renal corpuscle
1 µm
podocyte
1 nm
synaptopodin
Anatomical Structures
Functional Tissue Units
Cell Types
Biomarkers Genes, Proteins, ..

Anatomical Structures

Functional Tissue Units

Cell Types

Biomarkers Genes, Proteins, ..

Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

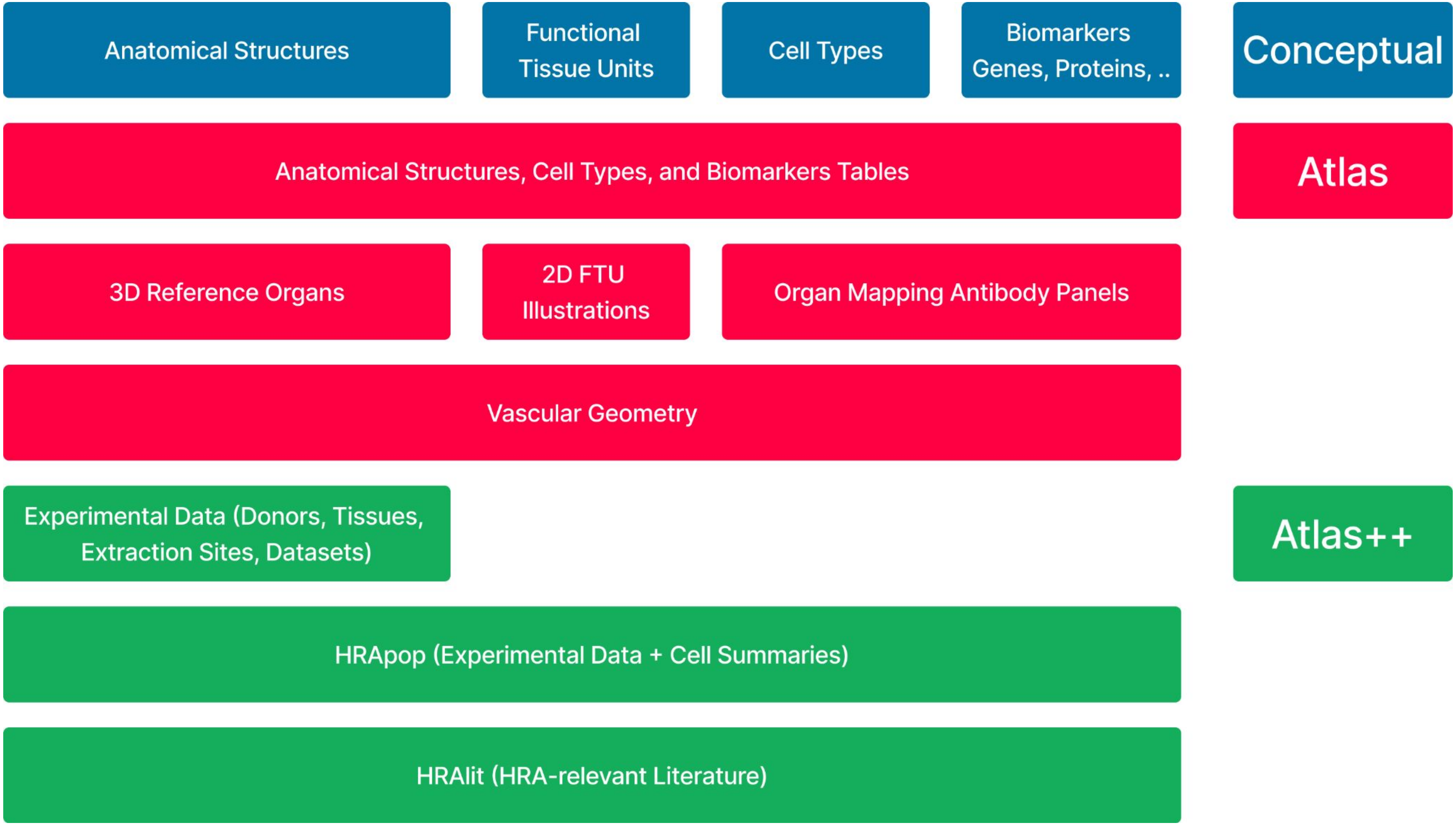
Atlas

3D Reference Organs

2D FTU Illustrations

Organ Mapping Antibody Panels

Vascular Geometry


Anatomical Structures
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Biomarkers Genes, Proteins, ..
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3D Reference Organs
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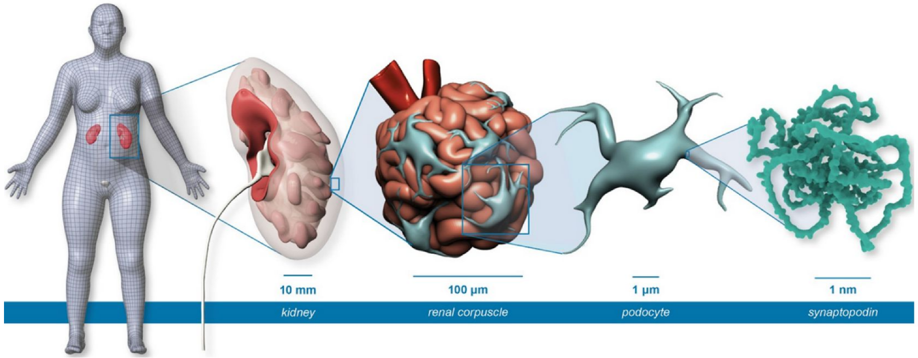
Vascular Geometry
Experimental Data (Donors, Tissues, Extraction Sites, Datasets)
Atlas++
HRApop (Experimental Data + Cell Summaries)
HRAlit (HRA-relevant Literature)



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)

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

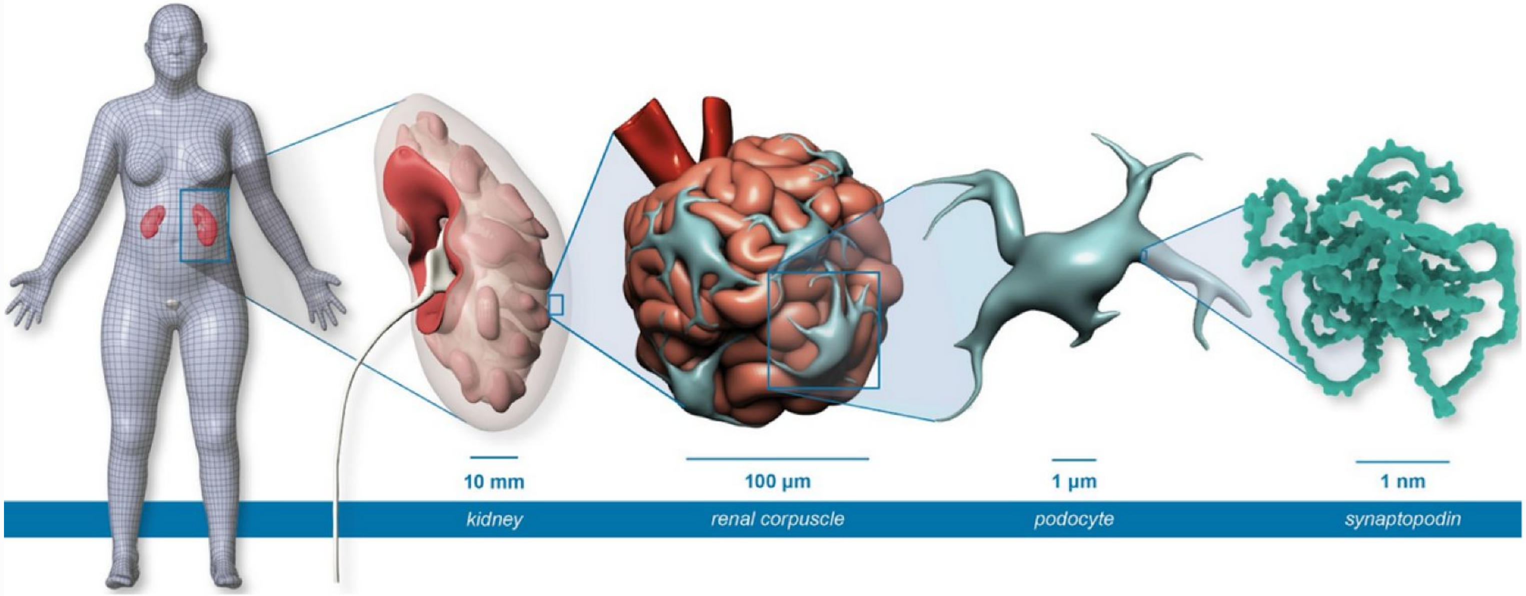
Human Reference Atlas

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

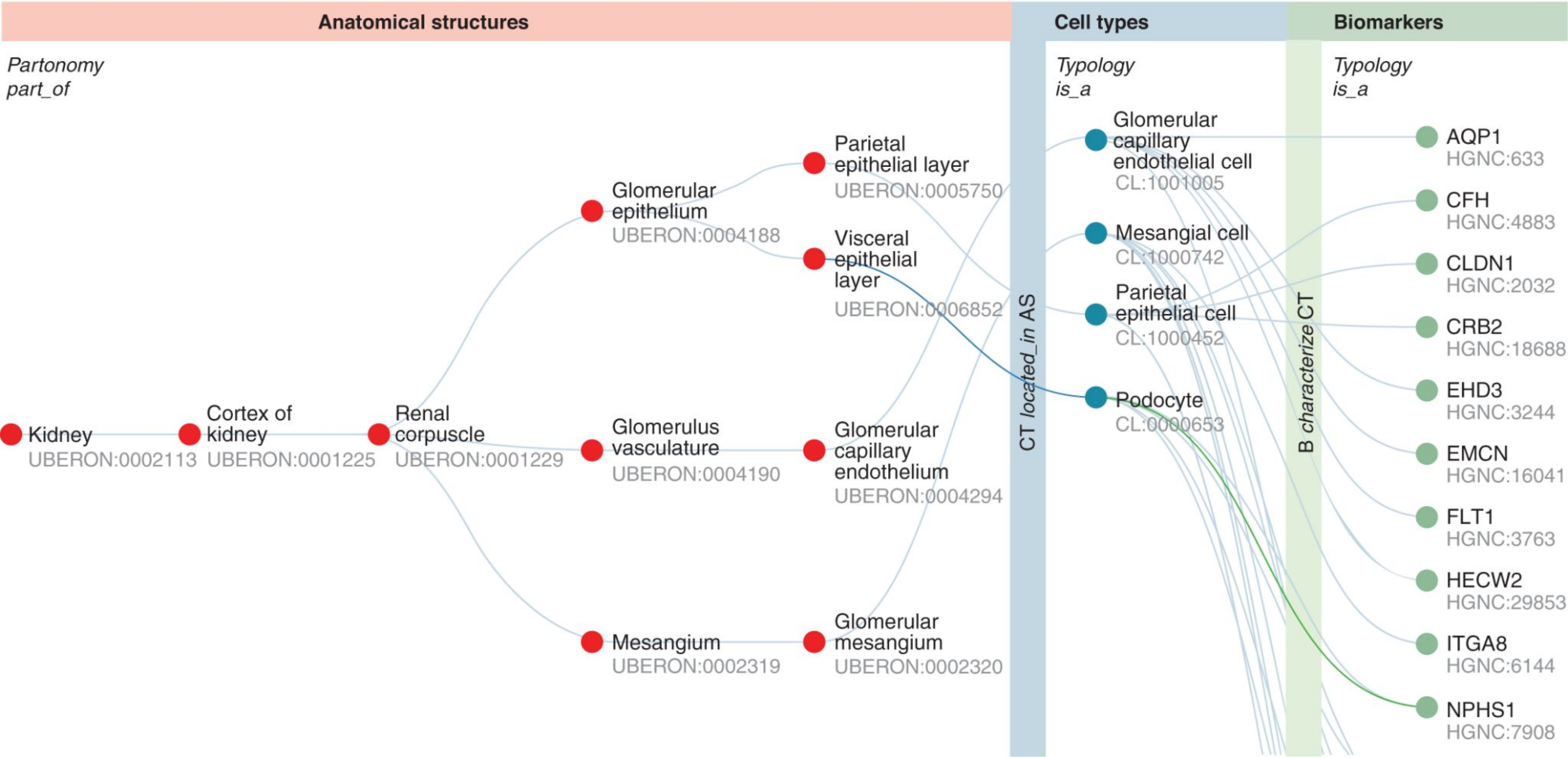


Anatomical Structures | Functional Tissue Units | Cell Types | Biomarkers Genes, Proteins, .. | **Conceptual**

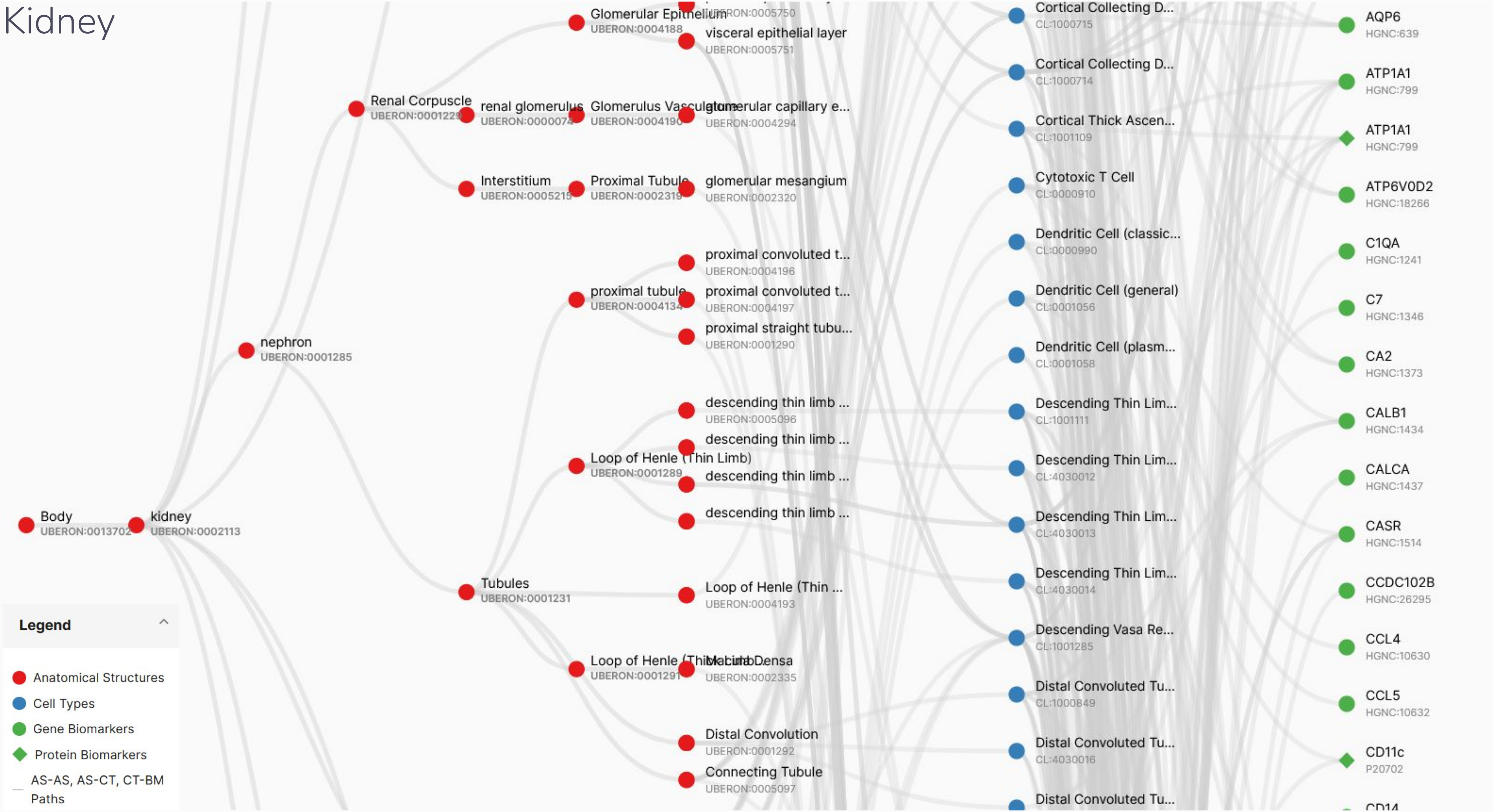
Anatomical Structures, Cell Types, and Biomarkers Tables | **Atlas**

3D Reference Organs | 2D FTU Illustrations | Organ Mapping Antibody Panels

ASCT+B Table Framework



Kidney


Glomerular Epithelium
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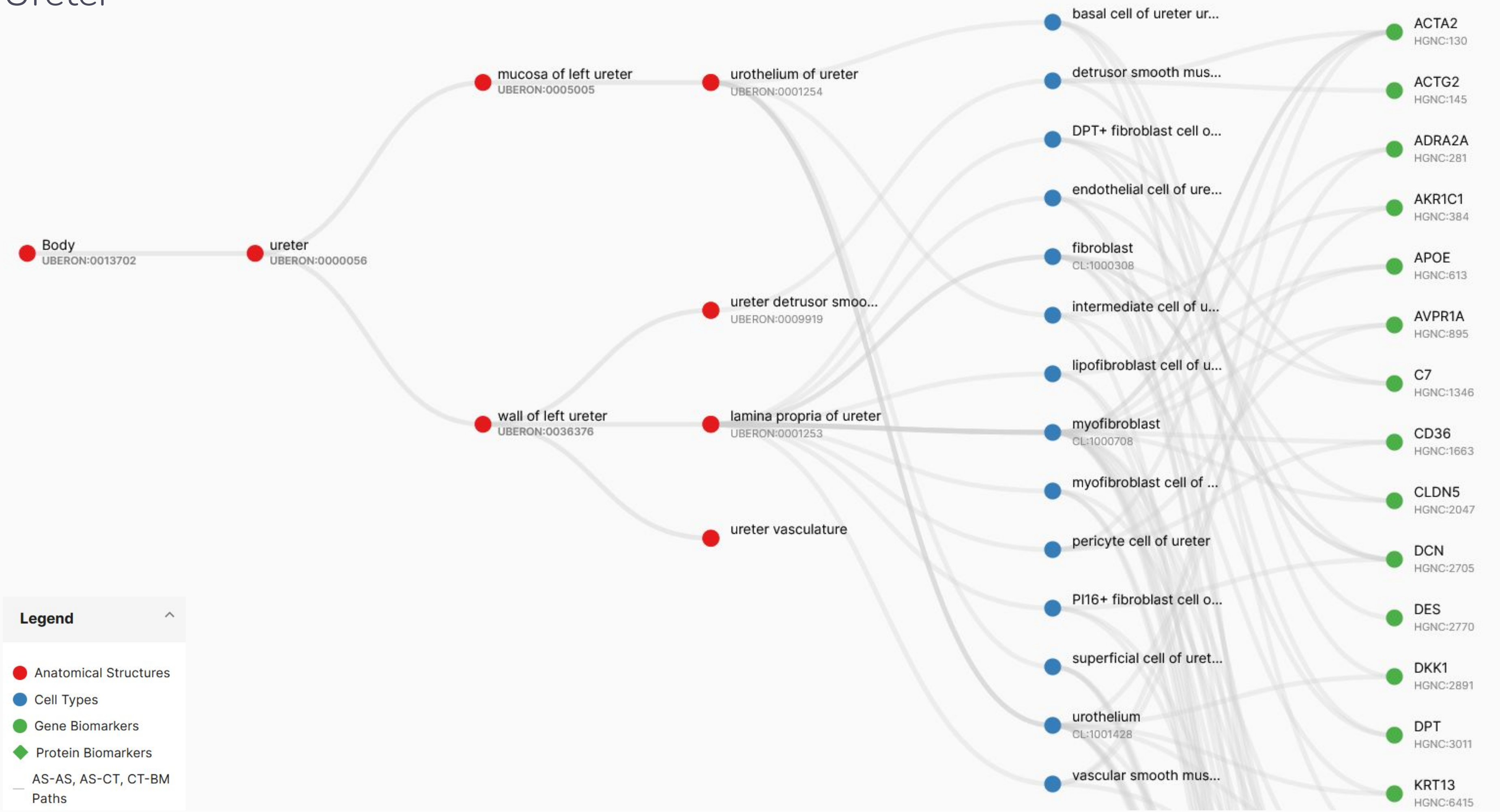
UBERON:0005750
visceral epithelial layer
UBERON:0005751
Renal Corpuscle
UBERON:0001229
renal glomerulus
UBERON:0000074
Glomerulus Vasculature
UBERON:0004190
glomerular capillary e...
UBERON:0004294
Interstitium
UBERON:0005215
Proximal Tubule
UBERON:0002319
glomerular mesangium
UBERON:0002320
proximal convoluted t...
UBERON:0004196
proximal tubule
UBERON:0004134
proximal convoluted t...
UBERON:0004197
proximal straight tubu...
UBERON:0001290
nephron
UBERON:0001285
descending thin limb ...
UBERON:0005096
descending thin limb ...
Loop of Henle (Thin Limb)
UBERON:0001289
descending thin limb ...
descending thin limb ...
Body
UBERON:0013702
kidney
UBERON:0002113
Tubules
UBERON:0001231
Loop of Henle (Thin ...
UBERON:0004193
Loop of Henle (Thi
UBERON:0001291
Macula Densa
UBERON:0002335
Distal Convolution
UBERON:0001292
Connecting Tubule
UBERON:0005097
Cortical Collecting D...
CL:1000715
Cortical Collecting D...
CL:1000714
Cortical Thick Ascen...
CL:1001109
Cytotoxic T Cell
CL:0000910
Dendritic Cell (classic...
CL:0000990
Dendritic Cell (general)
CL:0001056
Dendritic Cell (plasm...
CL:0001058
Descending Thin Lim...
CL:1001111
Descending Thin Lim...
CL:4030012
Descending Thin Lim...
CL:4030013
Descending Thin Lim...
CL:4030014
Descending Vasa Re...
CL:1001285
Distal Convoluted Tu...
CL:1000849
Distal Convoluted Tu...
CL:4030016
Distal Convoluted Tu...
AQP6
HGNC:639
ATP1A1
HGNC:799
ATP1A1
HGNC:799
ATP6V0D2
HGNC:18266
C1QA
HGNC:1241
C7
HGNC:1346
CA2
HGNC:1373
CALB1
HGNC:1434
CALCA
HGNC:1437
CASR
HGNC:1514
CCDC102B
HGNC:26295
CCL4
HGNC:10630
CCL5
HGNC:10632
CD11c
P20702
Legend
Anatomical Structures
Cell Types
Gene Biomarkers
Protein Biomarkers
AS-AS, AS-CT, CT-BM Paths

Ureter


Body
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ureter
UBERON:0000056
mucosa of left ureter
UBERON:0005005
wall of left ureter
UBERON:0036376
urothelium of ureter
UBERON:0001254
ureter detrusor smoo...
UBERON:0009919
lamina propria of ureter
UBERON:0001253
ureter vasculature
basal cell of ureter ur...
detrusor smooth mus...
DPT+ fibroblast cell o...
endothelial cell of ure...
fibroblast
CL:1000308
intermediate cell of u...
lipofibroblast cell of u...
myofibroblast
CL:1000708
myofibroblast cell of ...
pericyte cell of ureter
PI16+ fibroblast cell o...
superficial cell of uret...
urothelium
CL:1001428
vascular smooth mus...
ACTA2
HGNC:130
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
HGNC:6415
Legend
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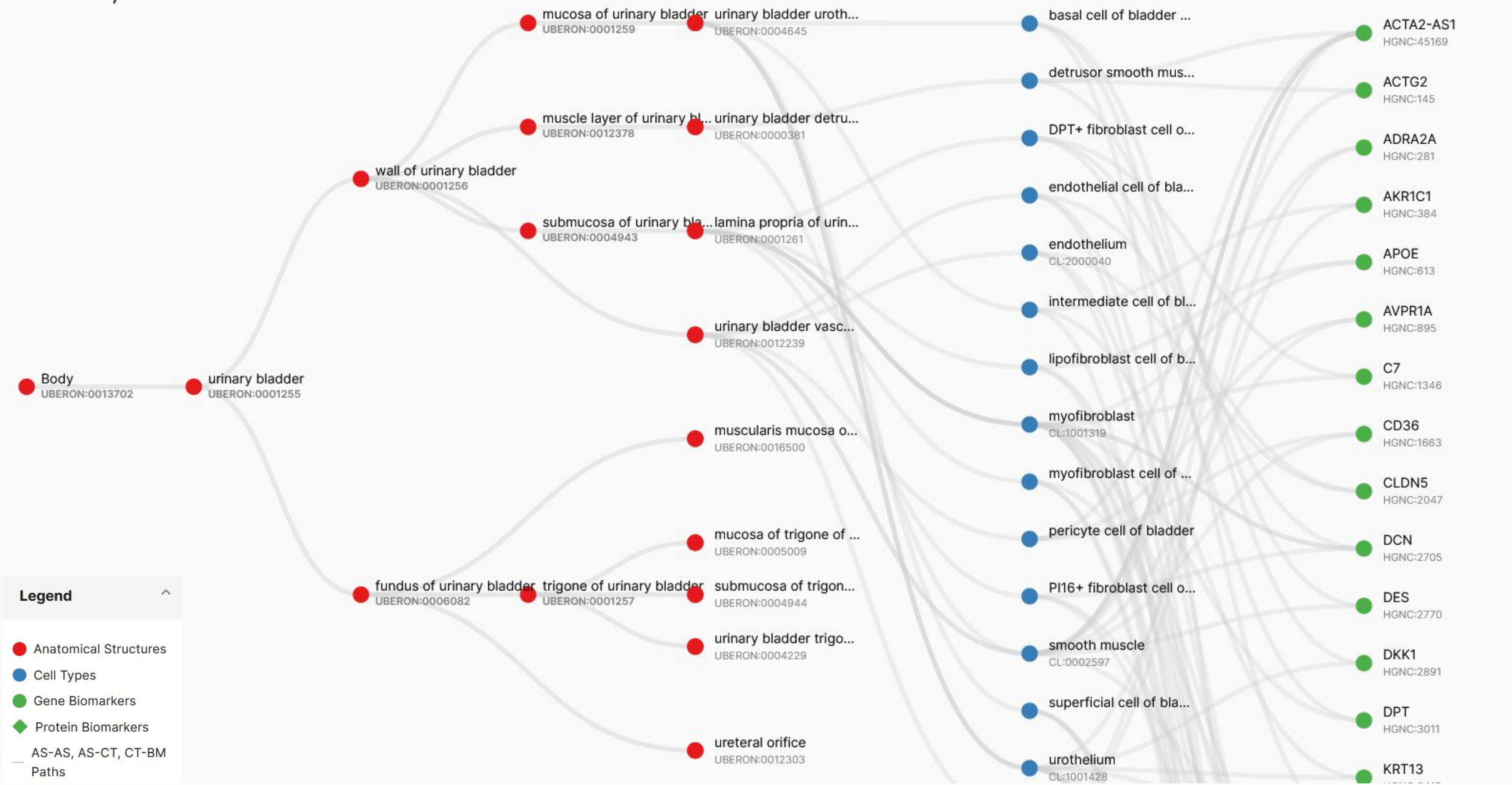
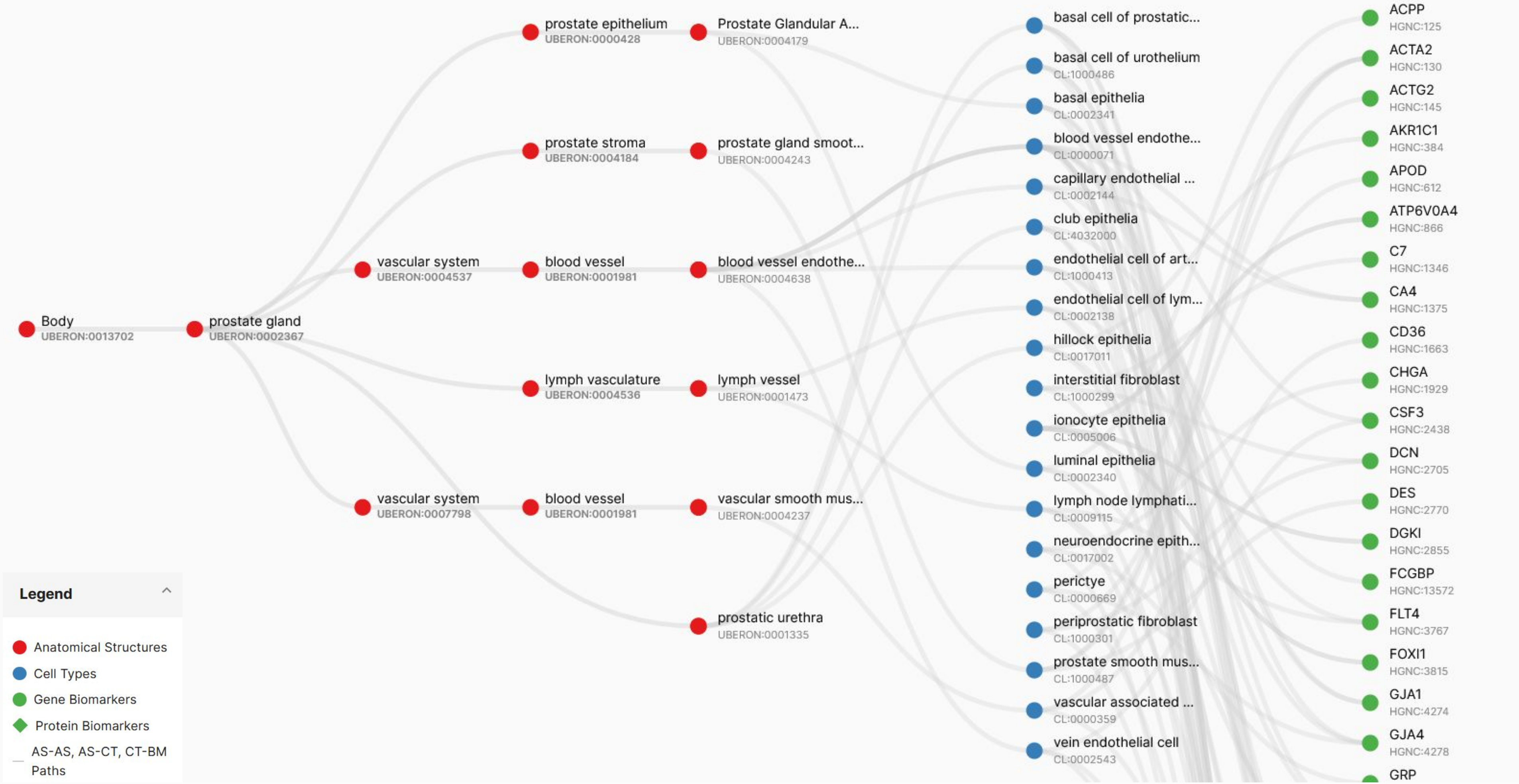
Urinary Bladder



Prostate



Body
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prostate gland
UBERON:0002367
vascular system
UBERON:0004537
vascular system
UBERON:0007798
prostate epithelium
UBERON:0000428
prostate stroma
UBERON:0004184
blood vessel
UBERON:0001981
lymph vasculature
UBERON:0004536
blood vessel
UBERON:0001981
Prostate Glandular A...
UBERON:0004179
prostate gland smoot...
UBERON:0004243
blood vessel endothe...
UBERON:0004638
lymph vessel
UBERON:0001473
vascular smooth mus...
UBERON:0004237
prostatic urethra
UBERON:0001335
basal cell of prostatic...
basal cell of urothelium
CL:1000486
basal epithelia
CL:0002341
blood vessel endothe...
CL:0000071
capillary endothelial ...
CL:0002144
club epithelia
CL:4032000
endothelial cell of art...
CL:1000413
endothelial cell of lym...
CL:0002138
hillock epithelia
CL:0017011
interstitial fibroblast
CL:1000299
ionocyte epithelia
CL:0005006
luminal epithelia
CL:0002340
lymph node lymphati...
CL:0009115
neuroendocrine epith...
CL:0017002
perictye
CL:0000669
periprostatic fibroblast
CL:1000301
prostate smooth mus...
CL:1000487
vascular associated ...
CL:0000359
vein endothelial cell
CL:0002543
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HGNC:125
ACTA2
HGNC:130
ACTG2
HGNC:145
AKR1C1
HGNC:384
APOD
HGNC:612
ATP6V0A4
HGNC:866
C7
HGNC:1346
CA4
HGNC:1375
CD36
HGNC:1663
CHGA
HGNC:1929
CSF3
HGNC:2438
DCN
HGNC:2705
DES
HGNC:2770
DGKI
HGNC:2855
FCGBP
HGNC:13572
FLT4
HGNC:3767
FOXI1
HGNC:3815
GJA1
HGNC:4274
GJA4
HGNC:4278
GRP
Legend
Anatomical Structures
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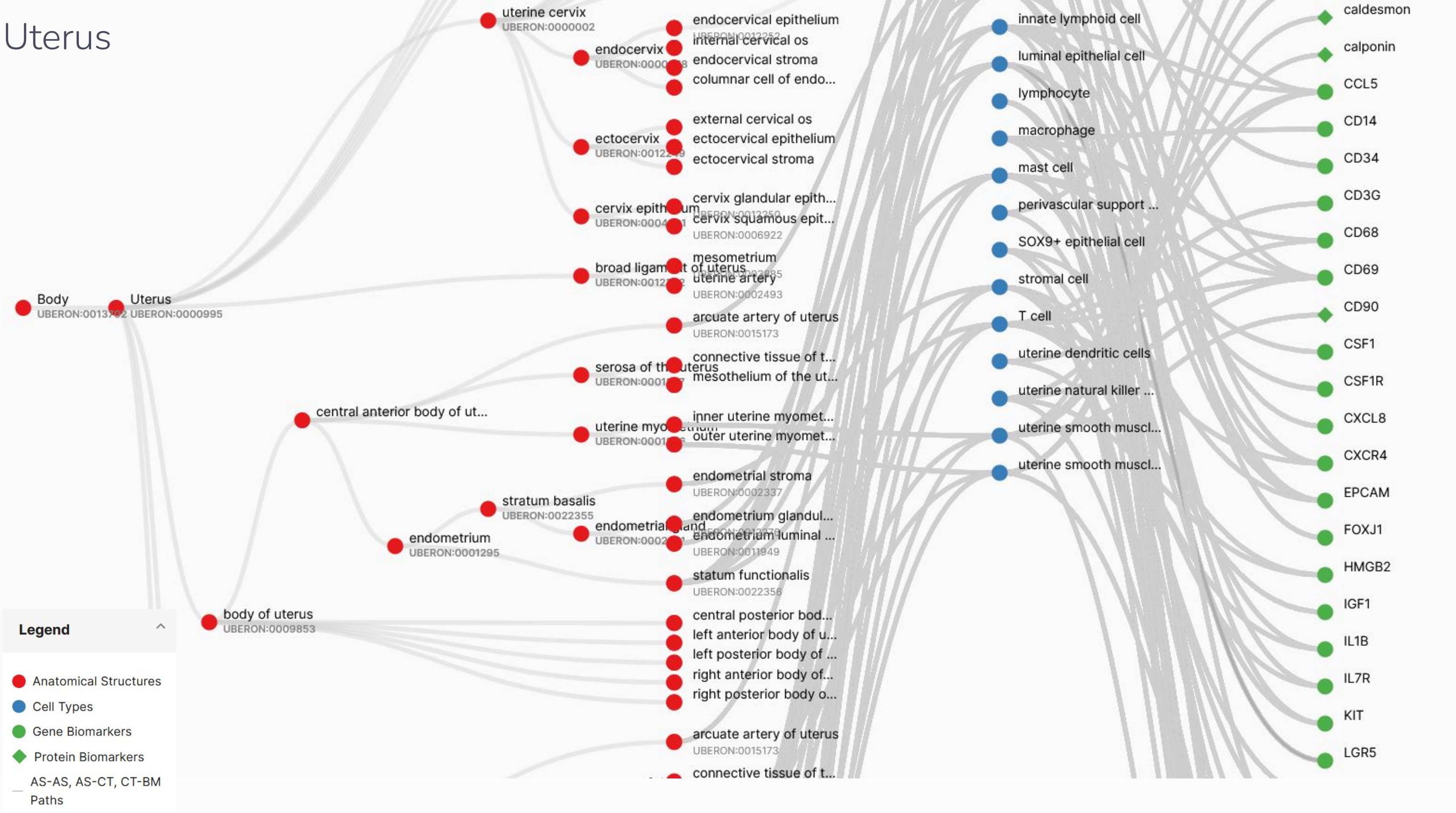
Uterus


Body
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Uterus
UBERON:0000995
uterine cervix
UBERON:0000002
endocervix
ectocervix
cervix epithelium
broad ligament of uterus
serosa of the uterus
uterine myometrium
central anterior body of ut...
stratum basalis
UBERON:0022355
endometrial gland
endometrium
UBERON:0001295
body of uterus
UBERON:0009853
endocervical epithelium
internal cervical os
endocervical stroma
columnar cell of endo...
external cervical os
ectocervical epithelium
ectocervical stroma
cervix glandular epith...
cervix squamous epit...
UBERON:0006922
mesometrium
uterine artery
UBERON:0002493
arcuate artery of uterus
UBERON:0015173
connective tissue of t...
mesothelium of the ut...
inner uterine myomet...
outer uterine myomet...
endometrial stroma
UBERON:0002337
endometrium glandul...
endometrium luminal ...
UBERON:0011949
statum functionalis
UBERON:0022356
central posterior bod...
left anterior body of u...
left posterior body of ...
right anterior body of...
right posterior body o...
arcuate artery of uterus
UBERON:0015173
connective tissue of t...
innate lymphoid cell
luminal epithelial cell
lymphocyte
macrophage
mast cell
perivascular support ...
SOX9+ epithelial cell
stromal cell
T cell
uterine dendritic cells
uterine natural killer ...
uterine smooth muscl...
uterine smooth muscl...
caldesmon
calponin
CCL5
CD14
CD34
CD3G
CD68
CD69
CD90
CSF1
CSF1R
CXCL8
CXCR4
EPCAM
FOXJ1
HMGB2
IGF1
IL1B
IL7R
KIT
LGR5
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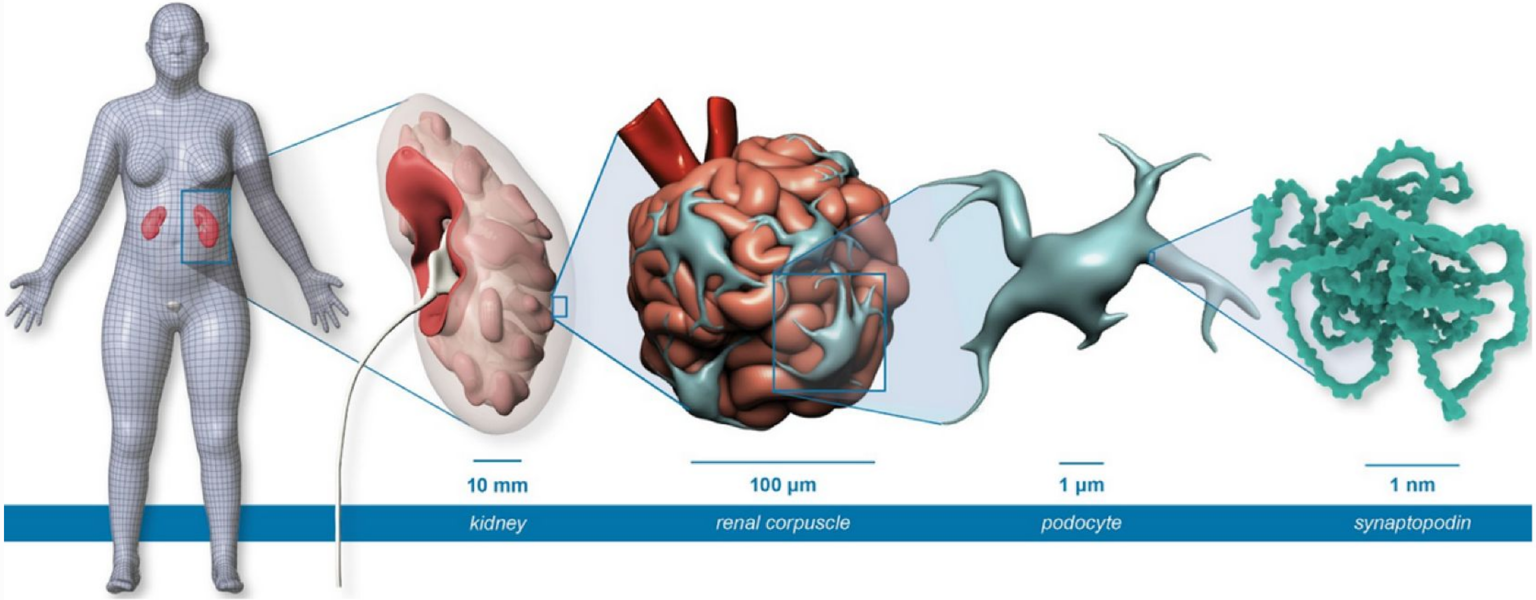

Anatomical Structures

Functional Tissue Units

Cell Types

Biomarkers Genes, Proteins, ..

Conceptual

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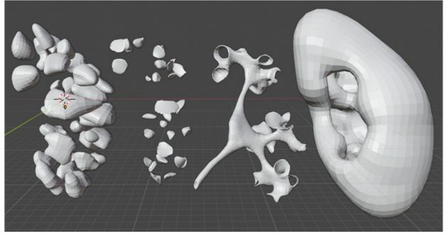
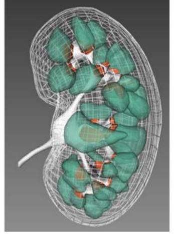
3D Reference Organs

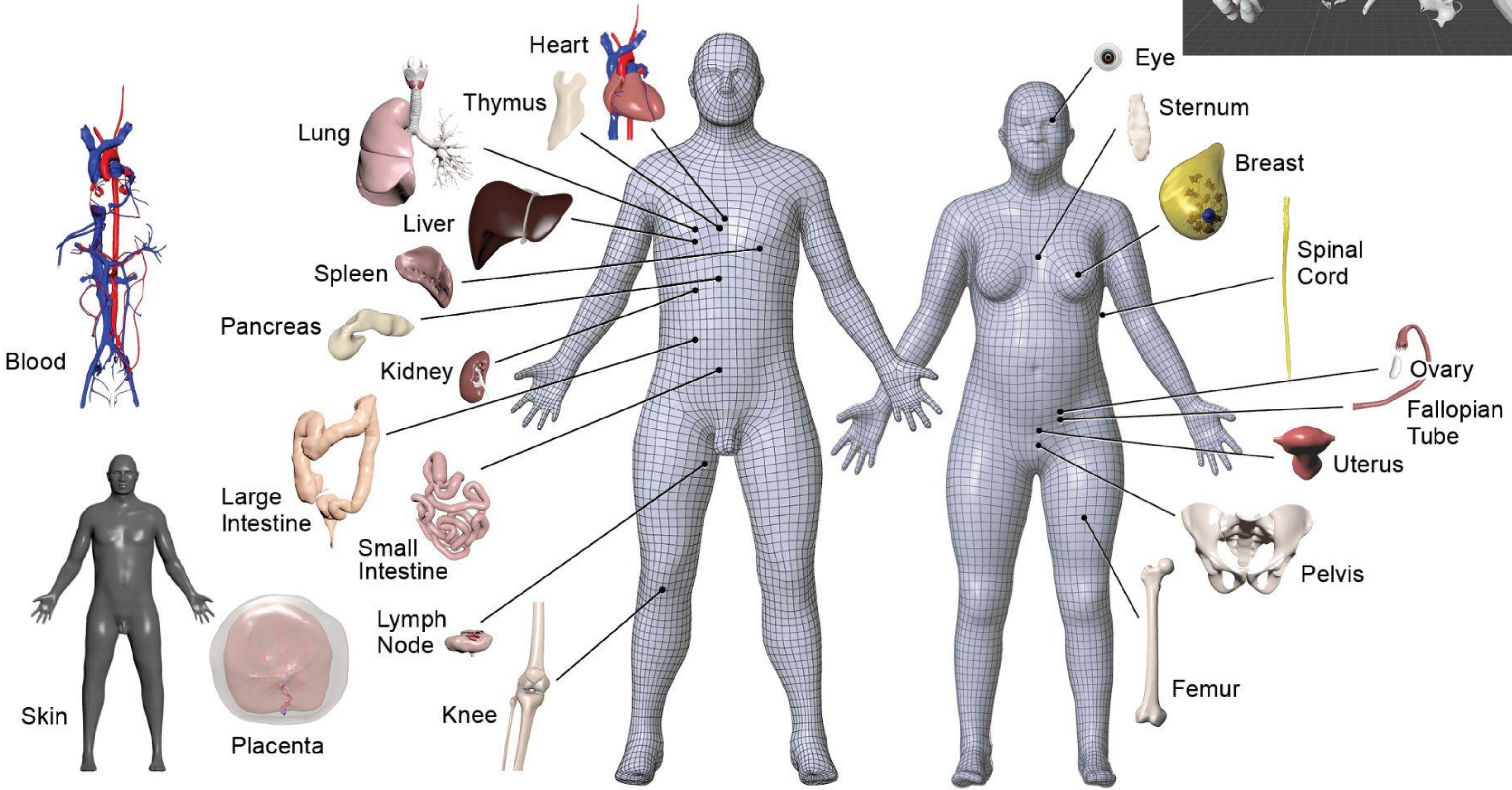
2D FTU Illustrations

Organ Mapping Antibody Panels

HRA 3D Reference Organs

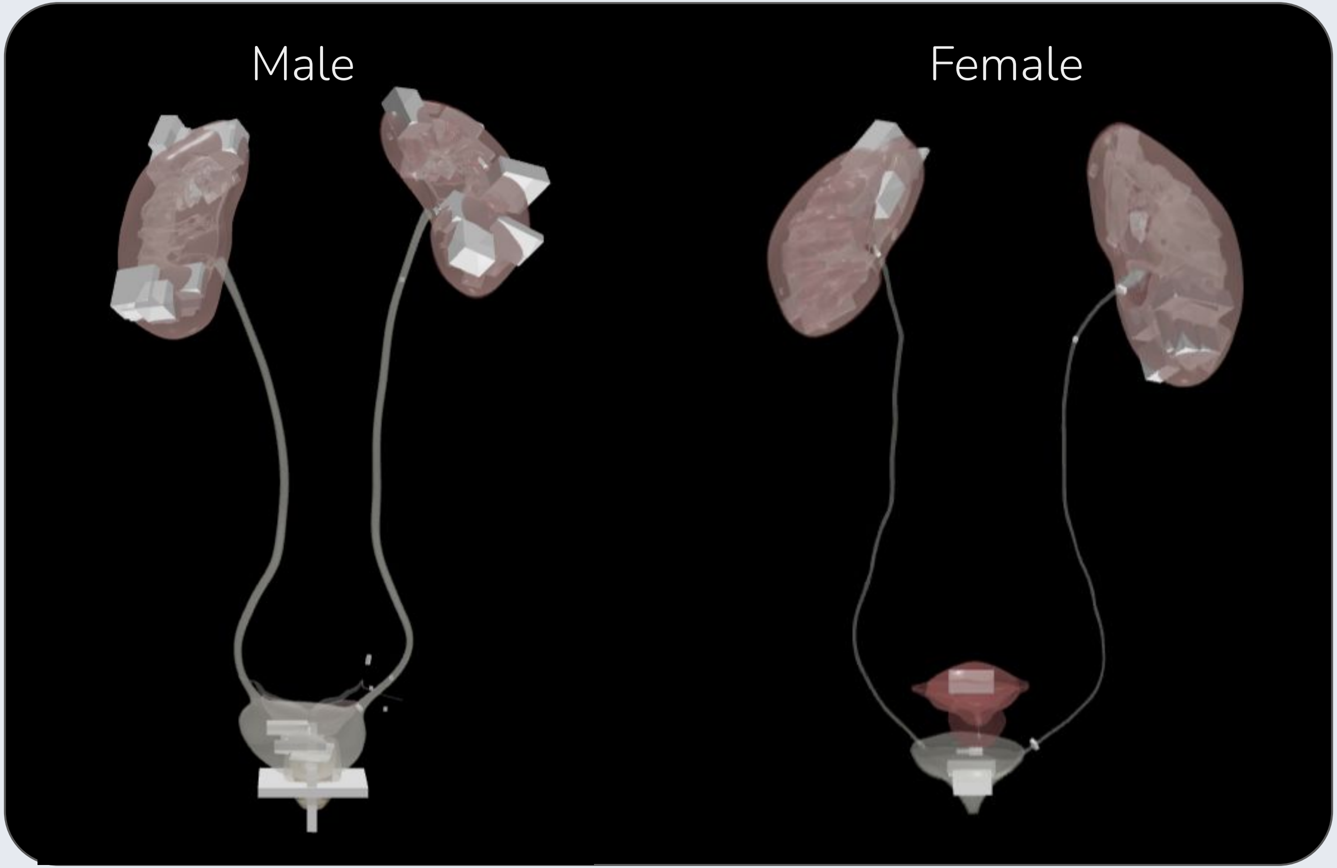


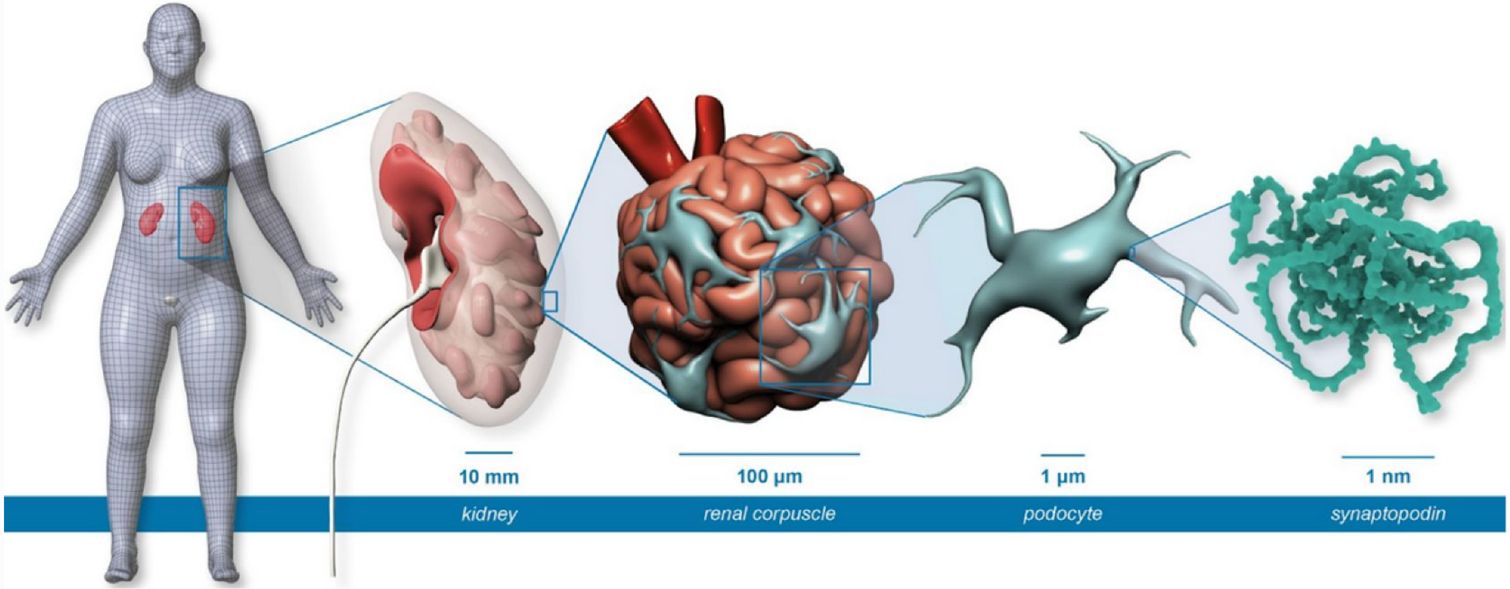




https://www.nature.com/articles/s42003-022-03644-x | Data: https://humanatlas.io/3d-reference-library

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





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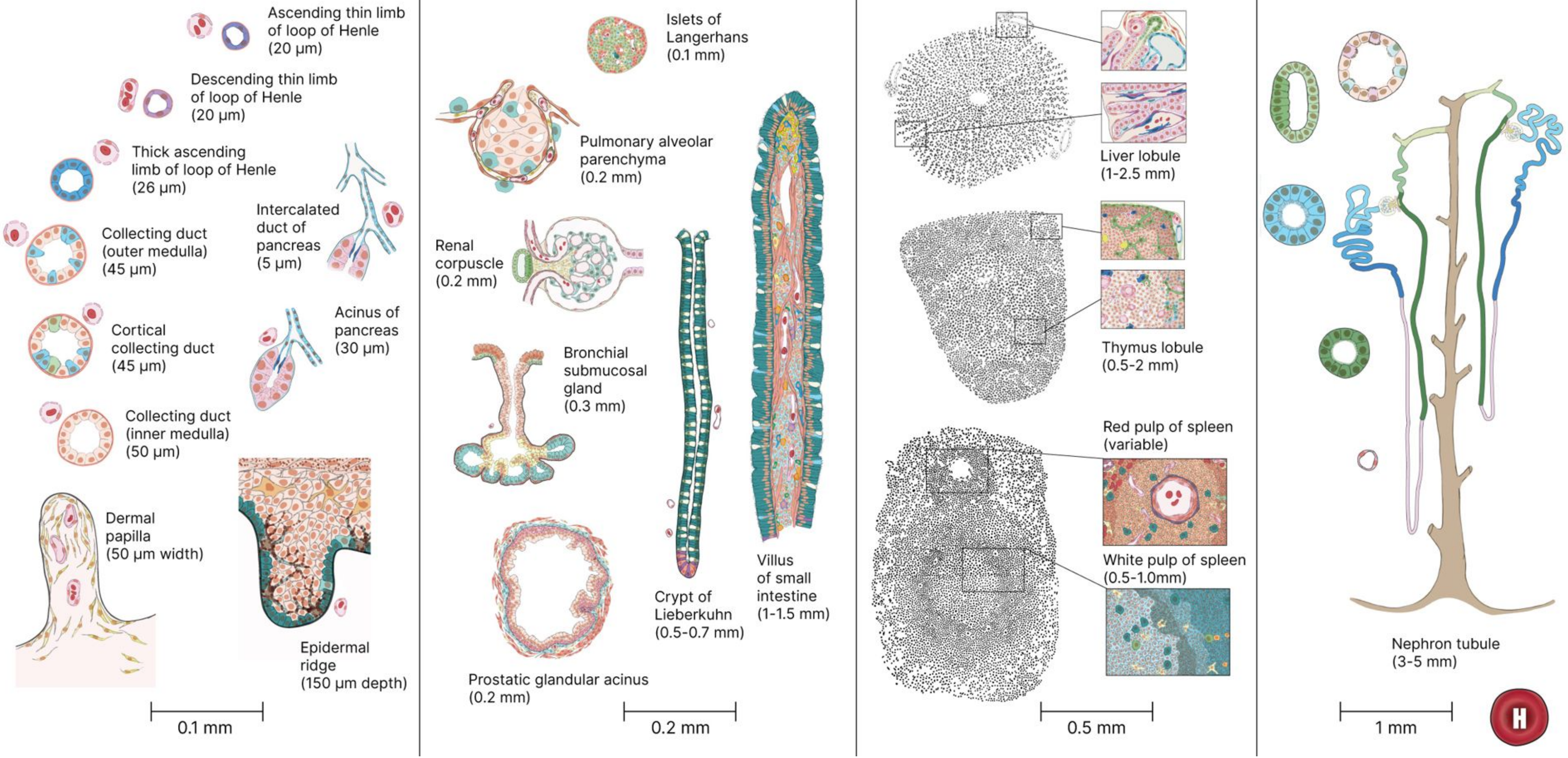
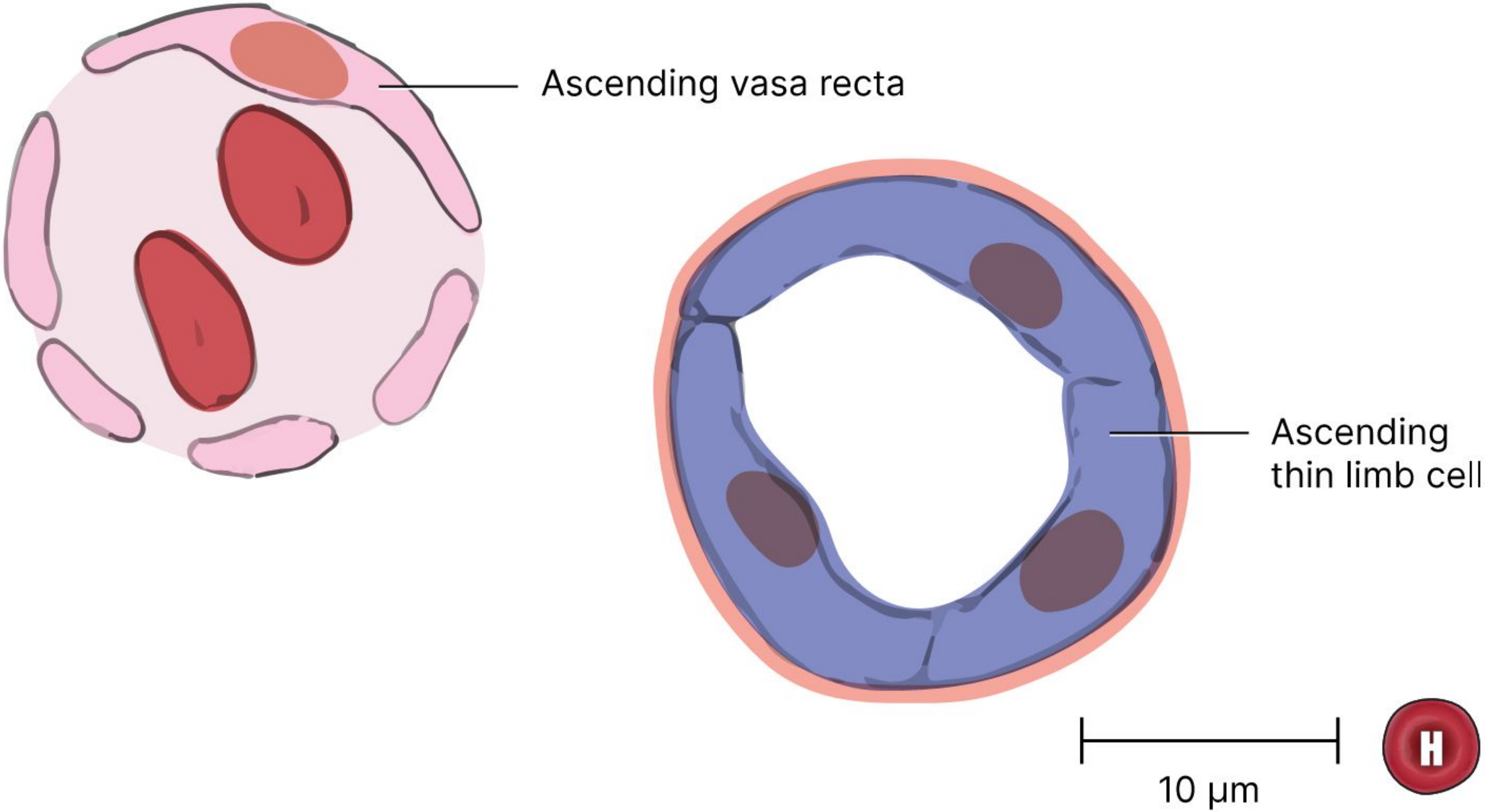
HRA Functional Tissue Units (FTUs)

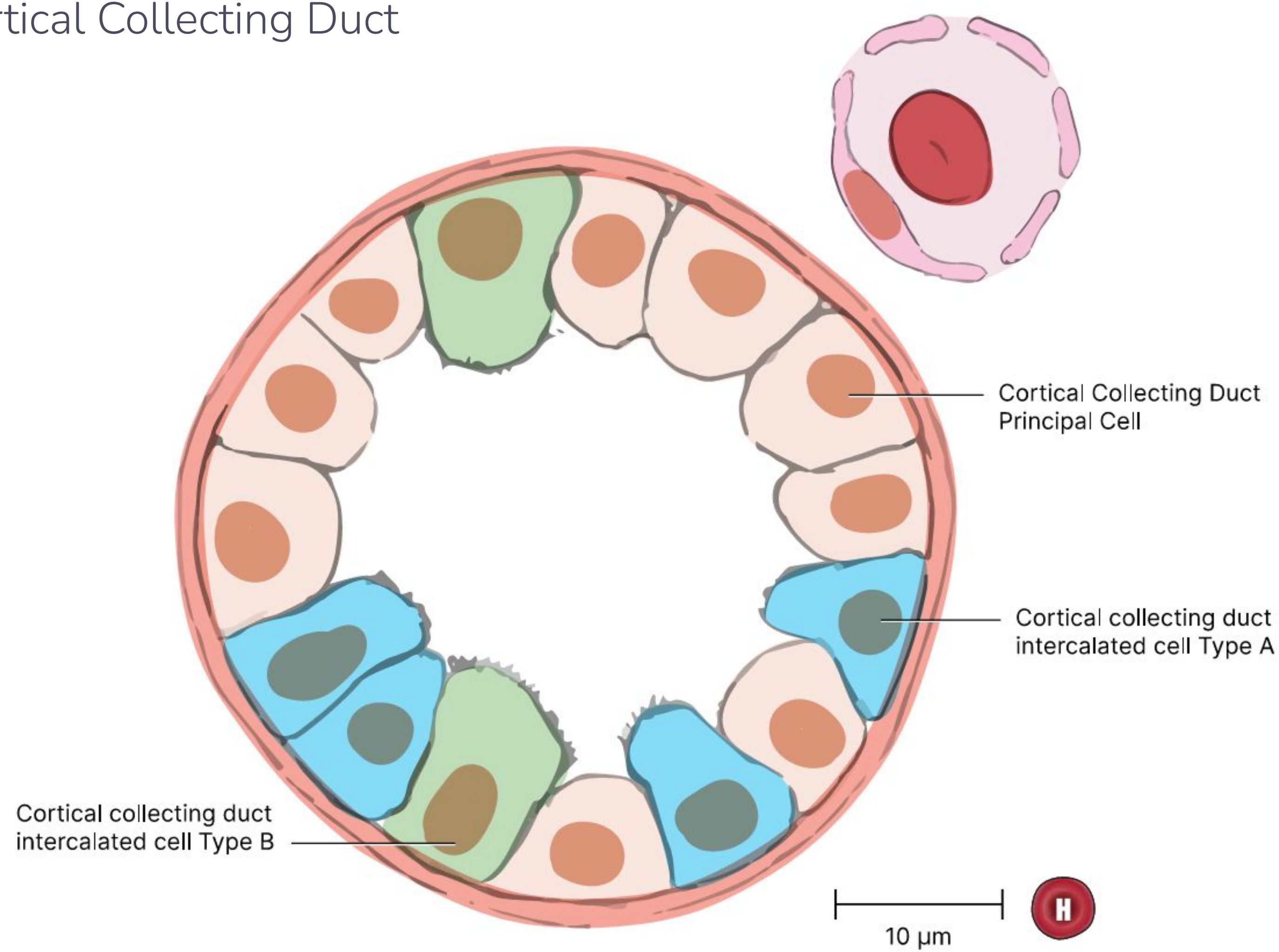


https://www.biorxiv.org/content/10.1101/2023.10.16.562593v3 | Data: https://humanatlas.io/2d-ftu-illustrations

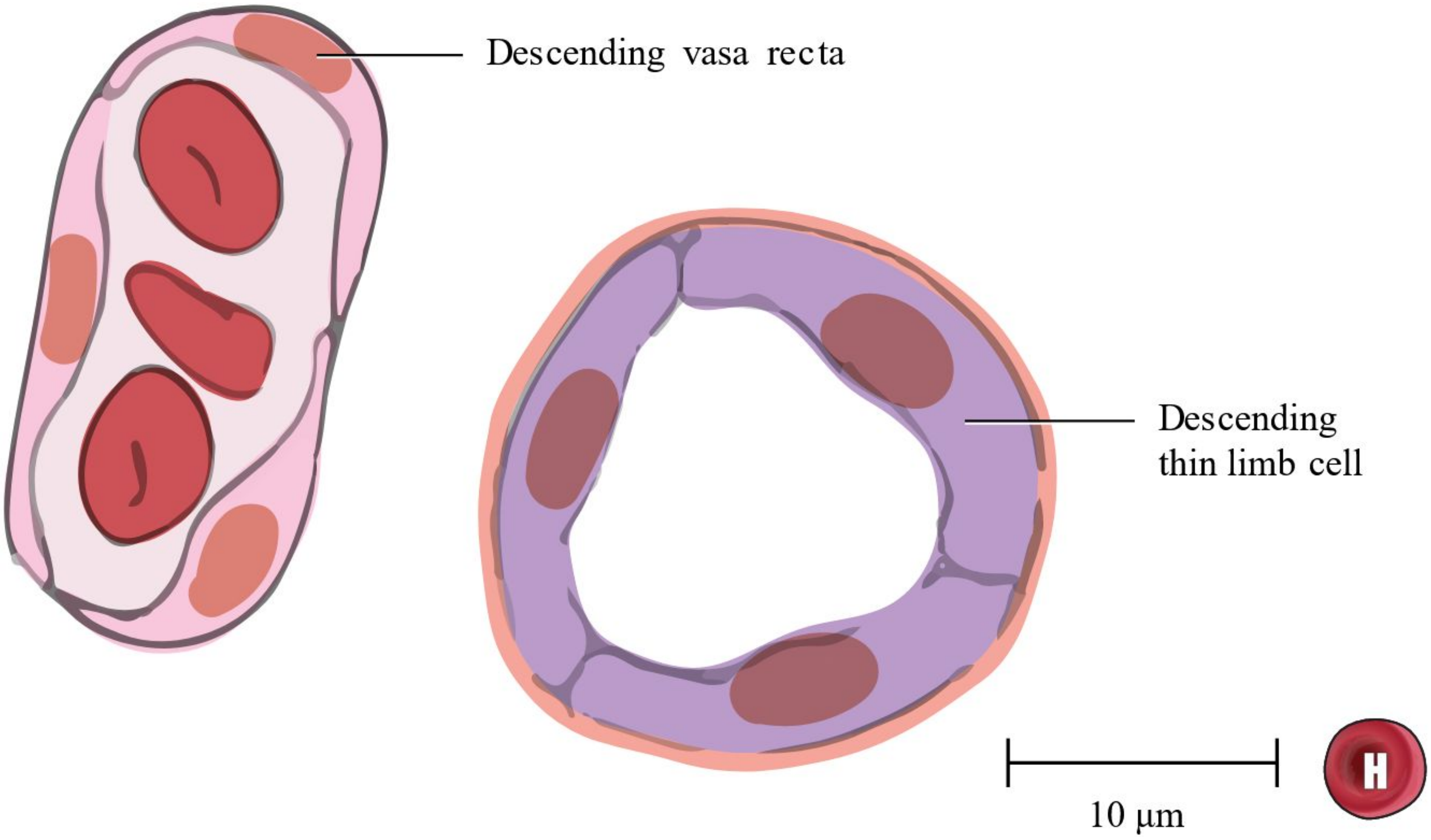
Kidney - Ascending Thin Loop Of Henle



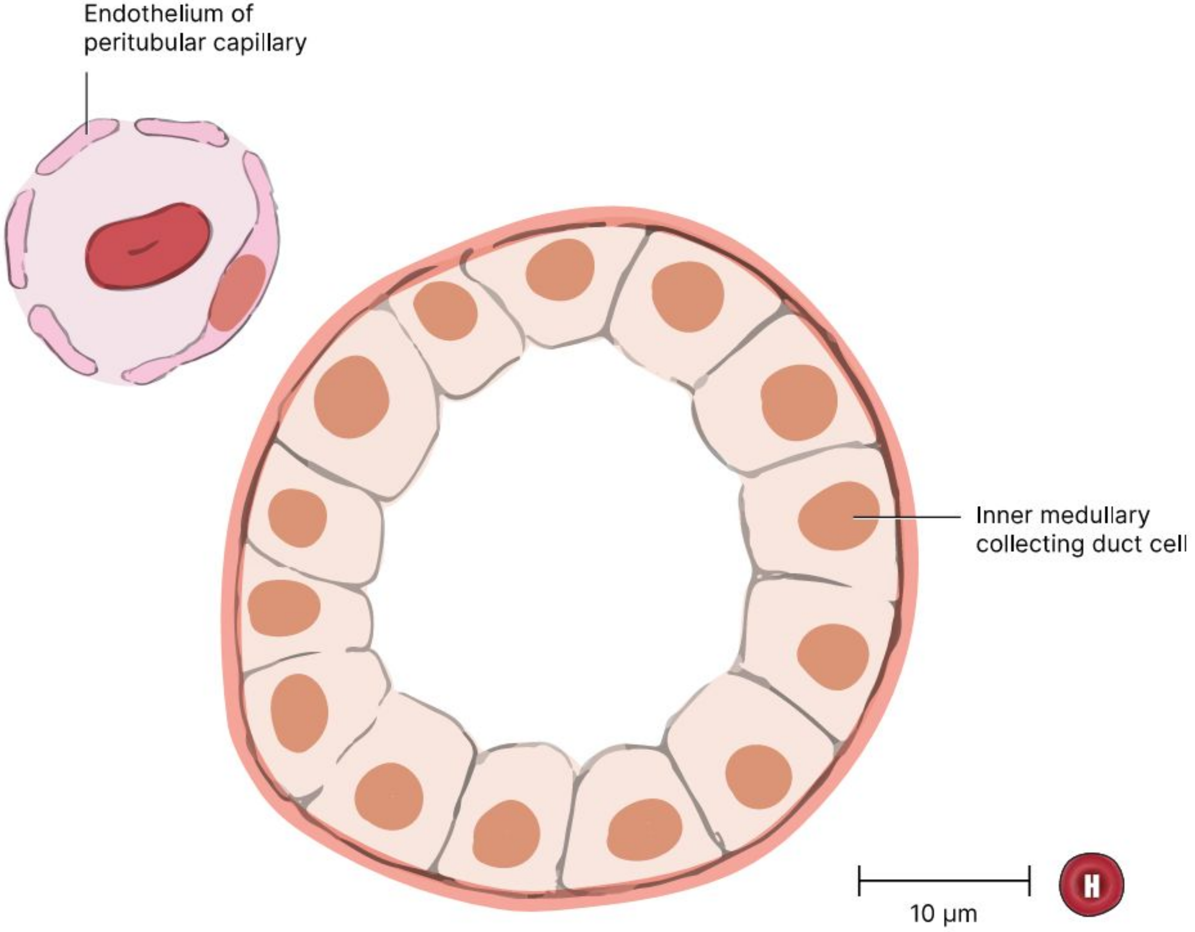
Kidney - Cortical Collecting Duct



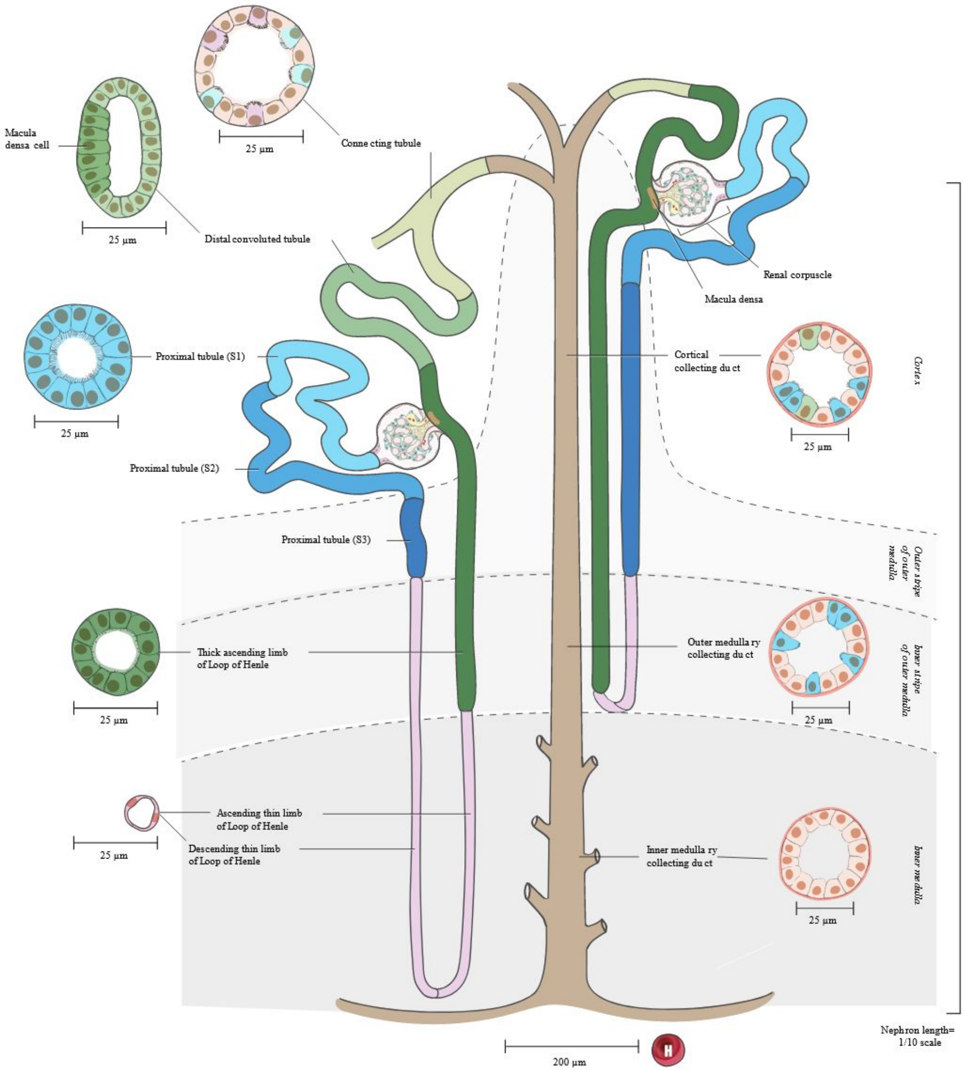
Kidney - Descending Thin Loop Of Henle



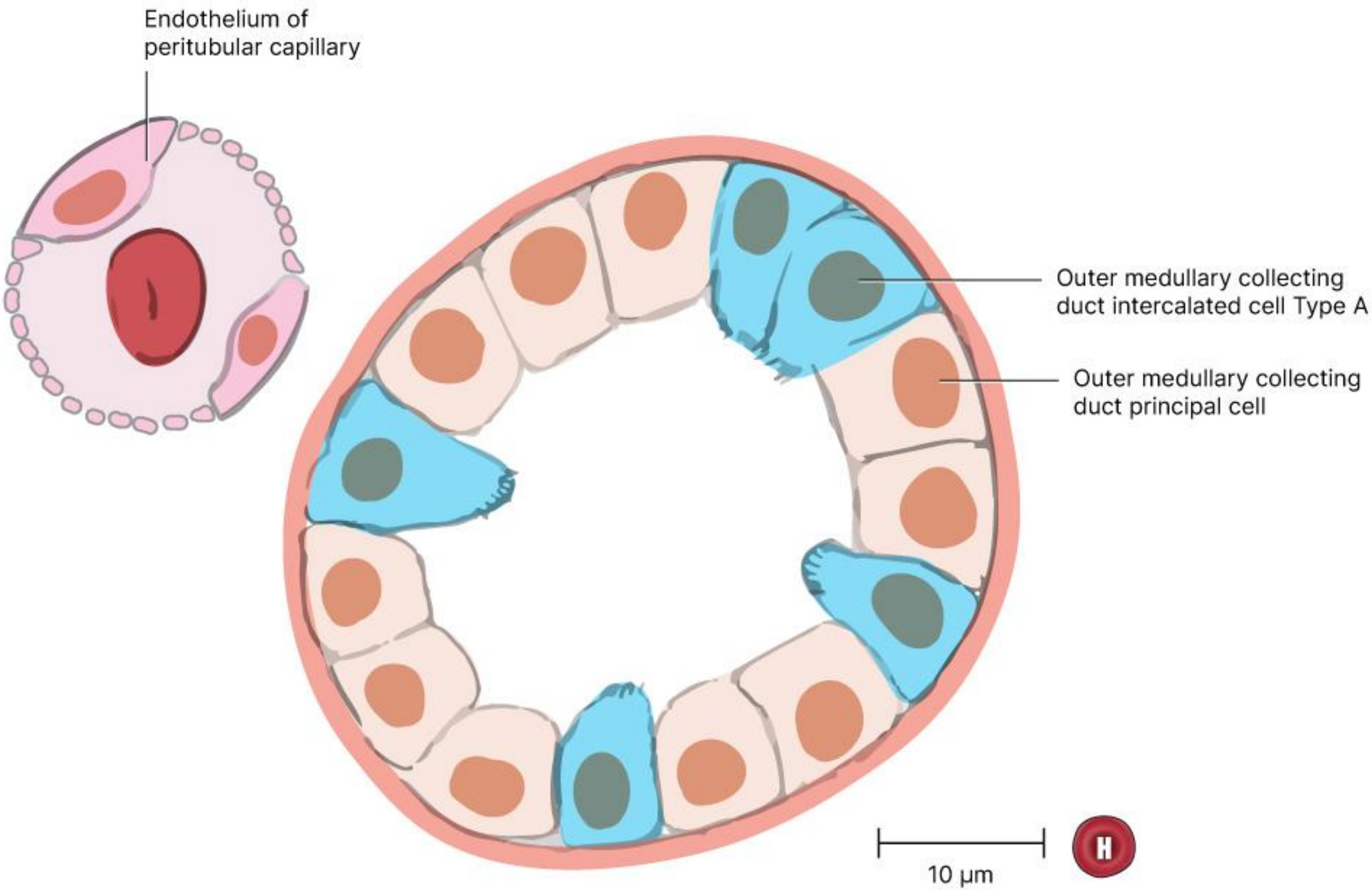
Kidney - Inner Medullary Collecting Duct



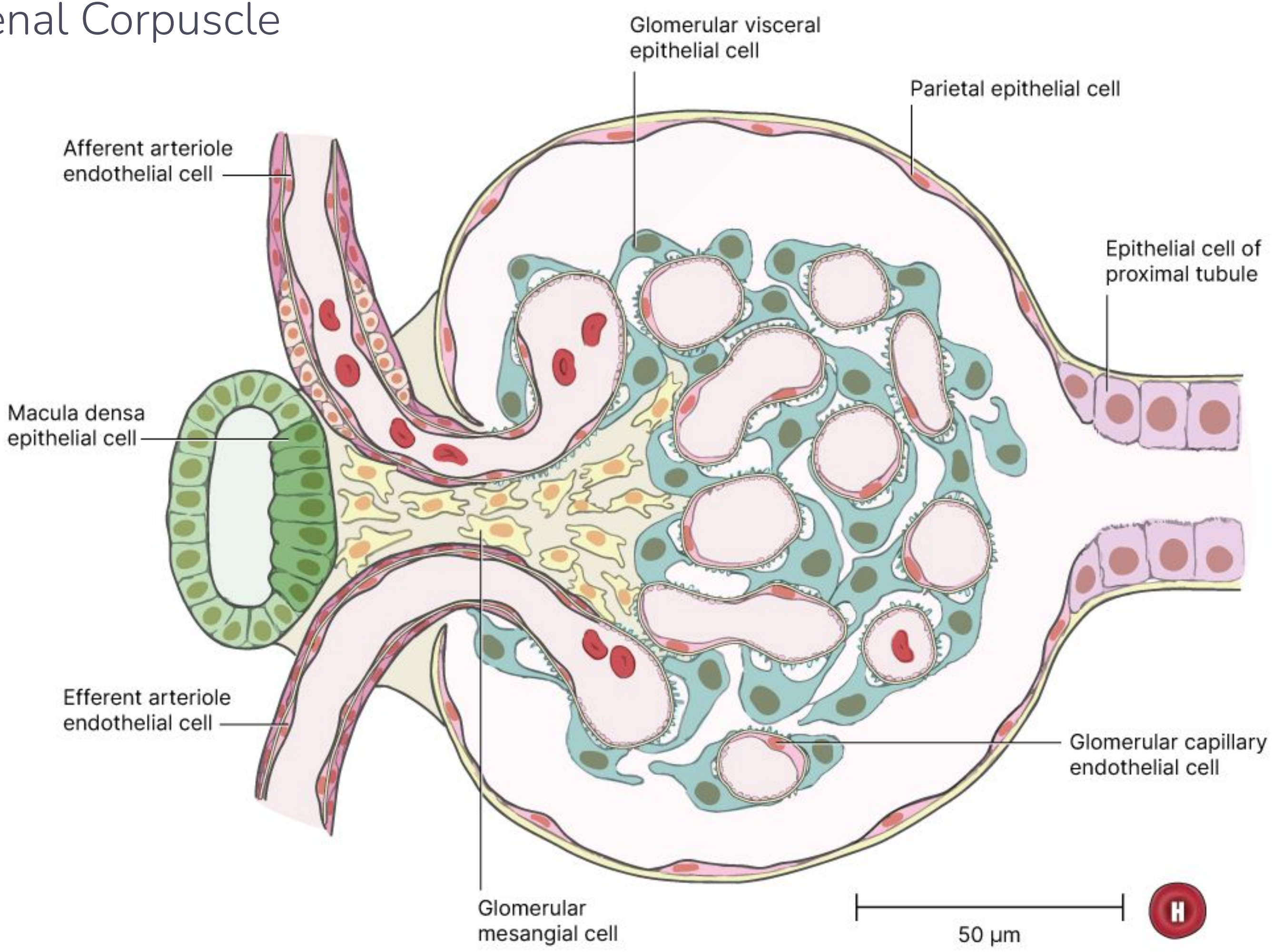
Kidney - Nephron



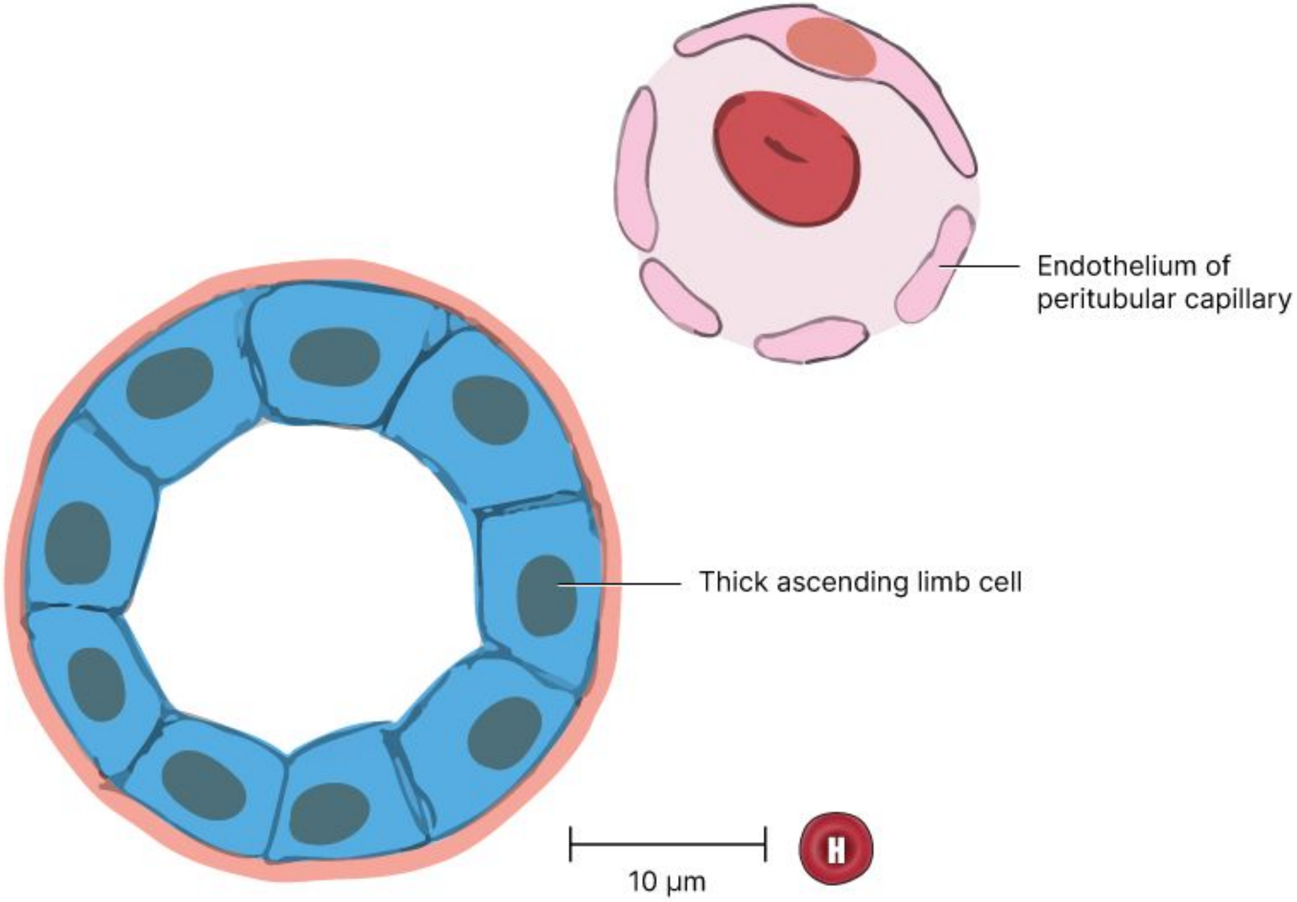
Kidney - Outer Medullary Collecting Duct



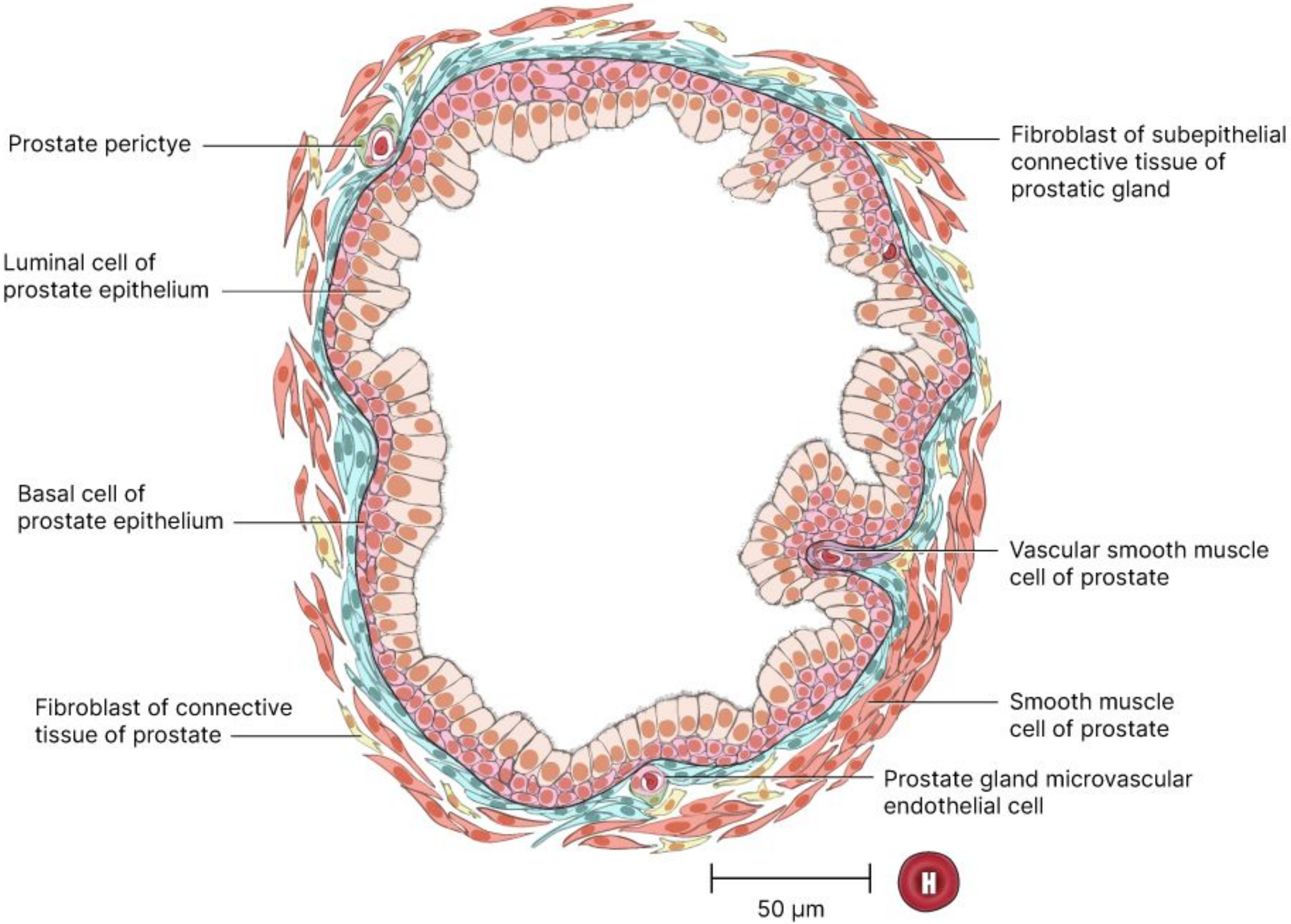
Kidney - Renal Corpuscle

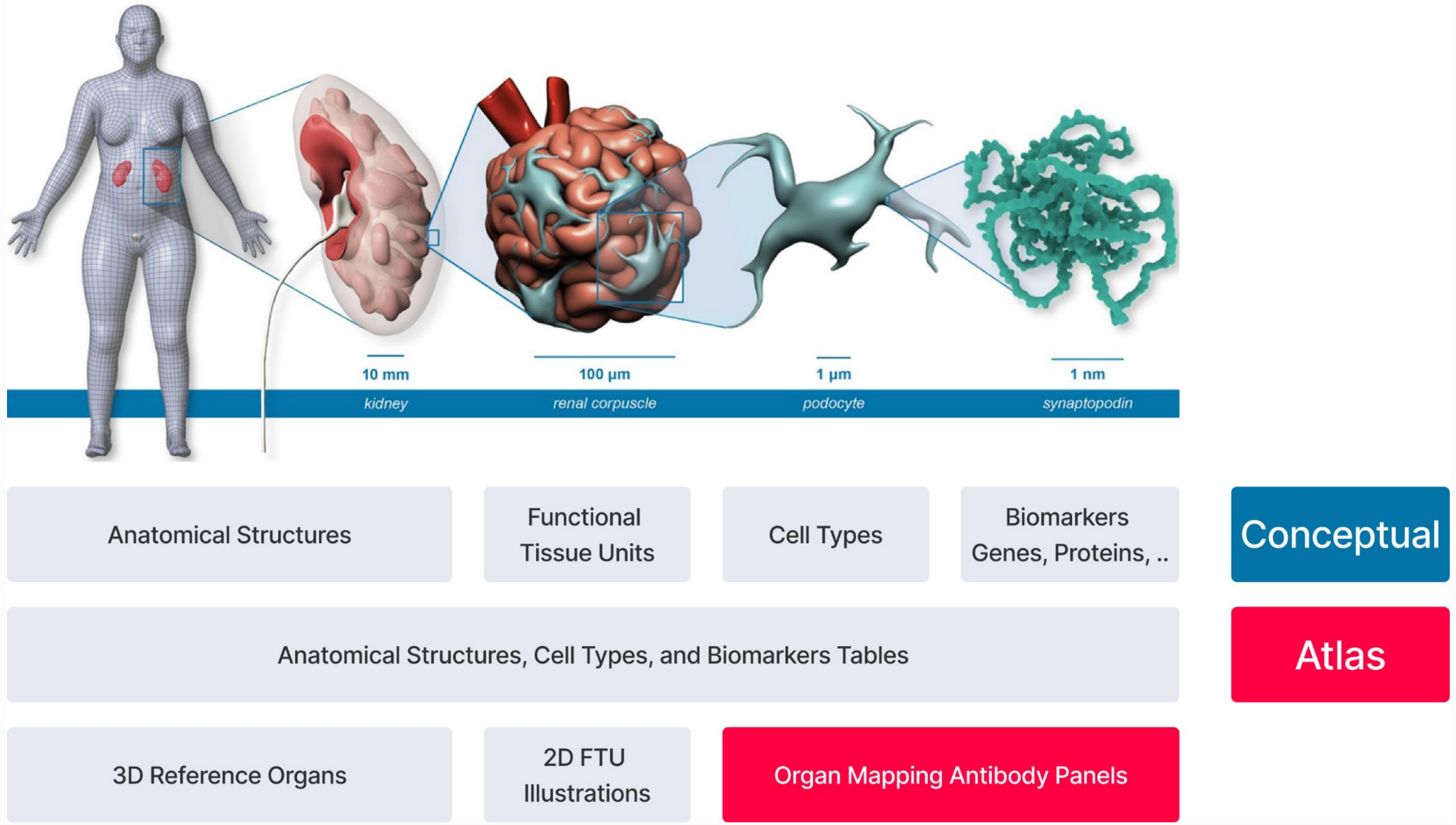


Kidney - Thick Ascending Loop Of Henle



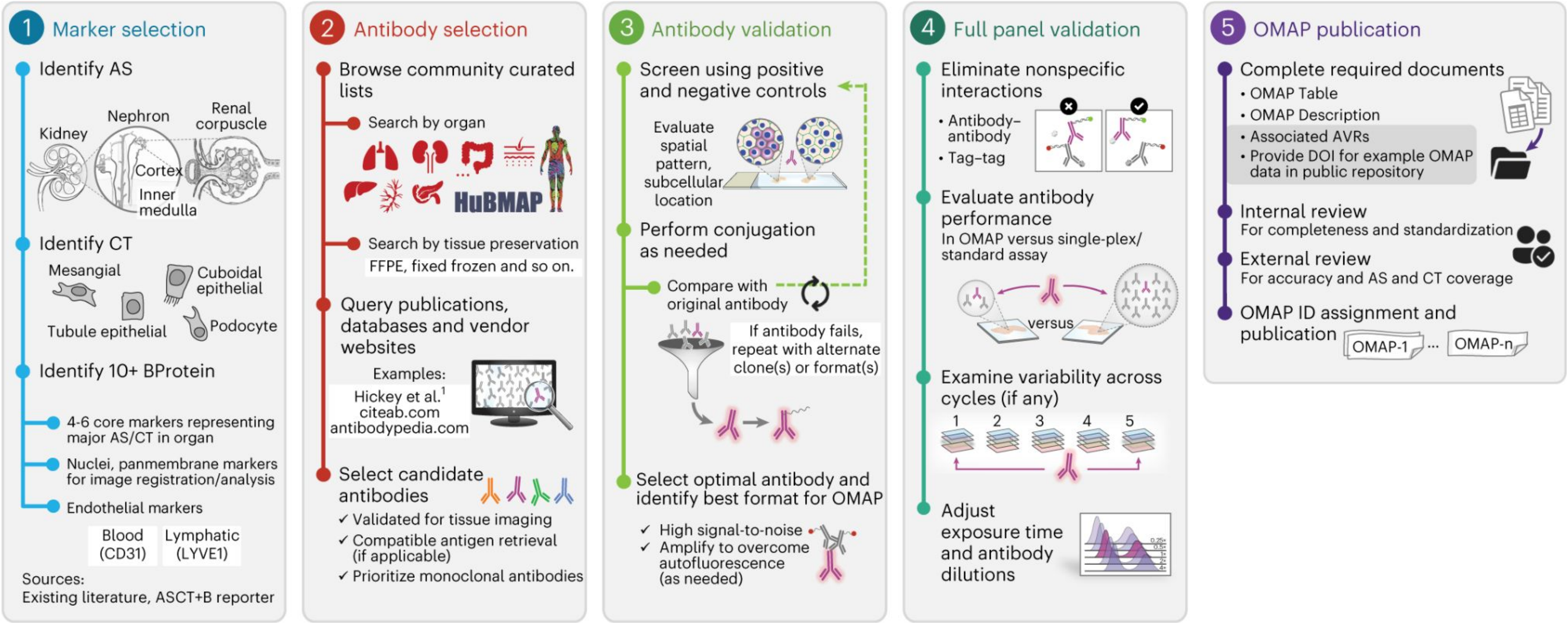
Prostate - Glandular Acinus



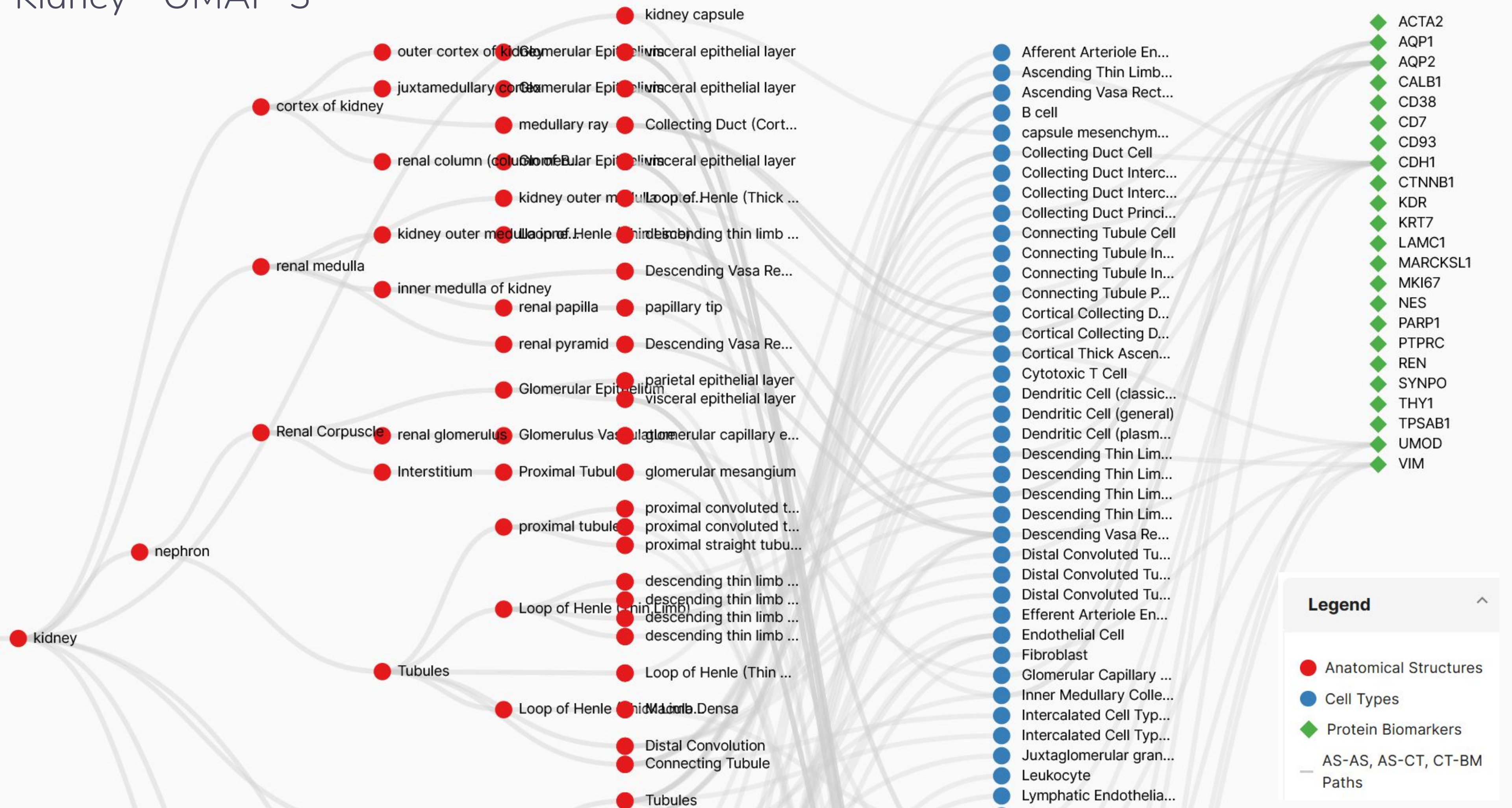

10 mm
kidney
100 µm
renal corpuscle
1 µm
podocyte
1 nm
synaptopodin
Anatomical Structures
Functional Tissue Units
Cell Types
Biomarkers Genes, Proteins, ..
Conceptual
Anatomical Structures, Cell Types, and Biomarkers Tables
Atlas
3D Reference Organs
2D FTU Illustrations
Organ Mapping Antibody Panels

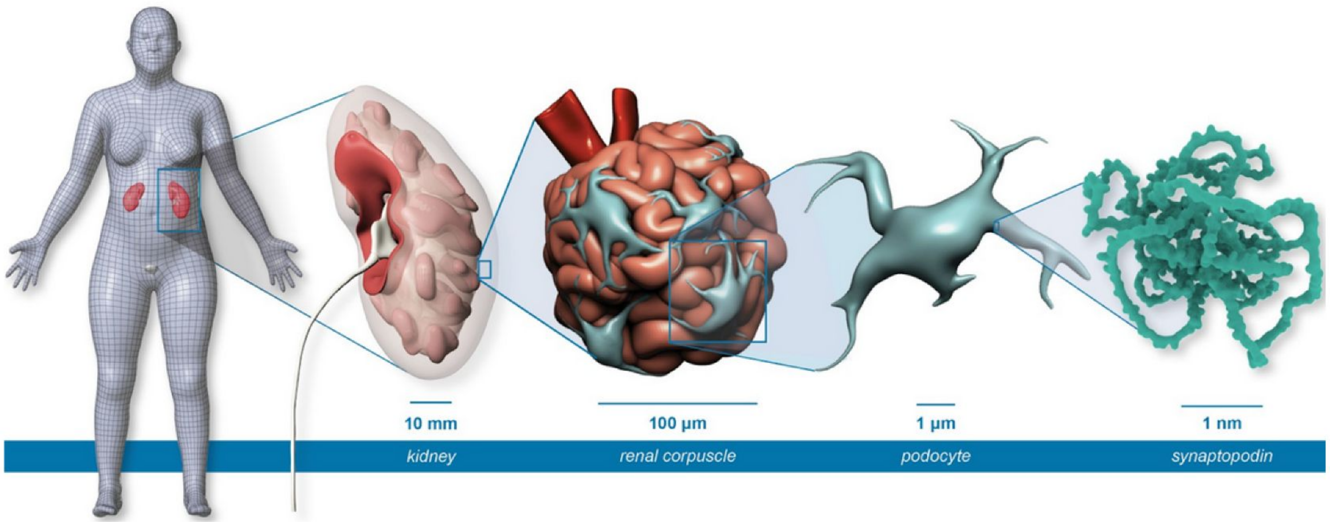
OMAP Framework

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





Anatomical Structures | Functional Tissue Units | Cell Types | Biomarkers Genes, Proteins, ..

Conceptual

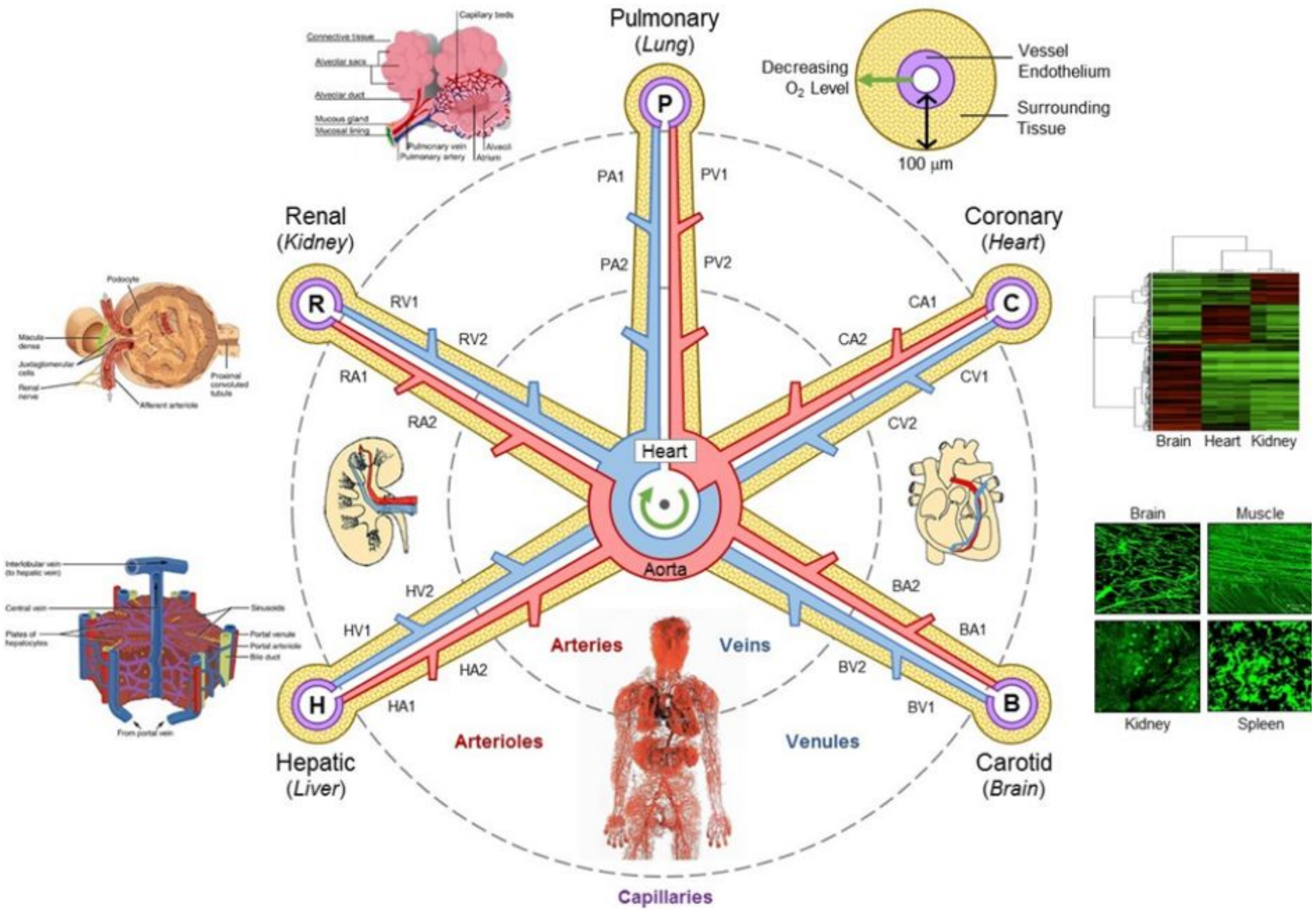
Anatomical Structures, Cell Types, and Biomarkers Tables

Atlas

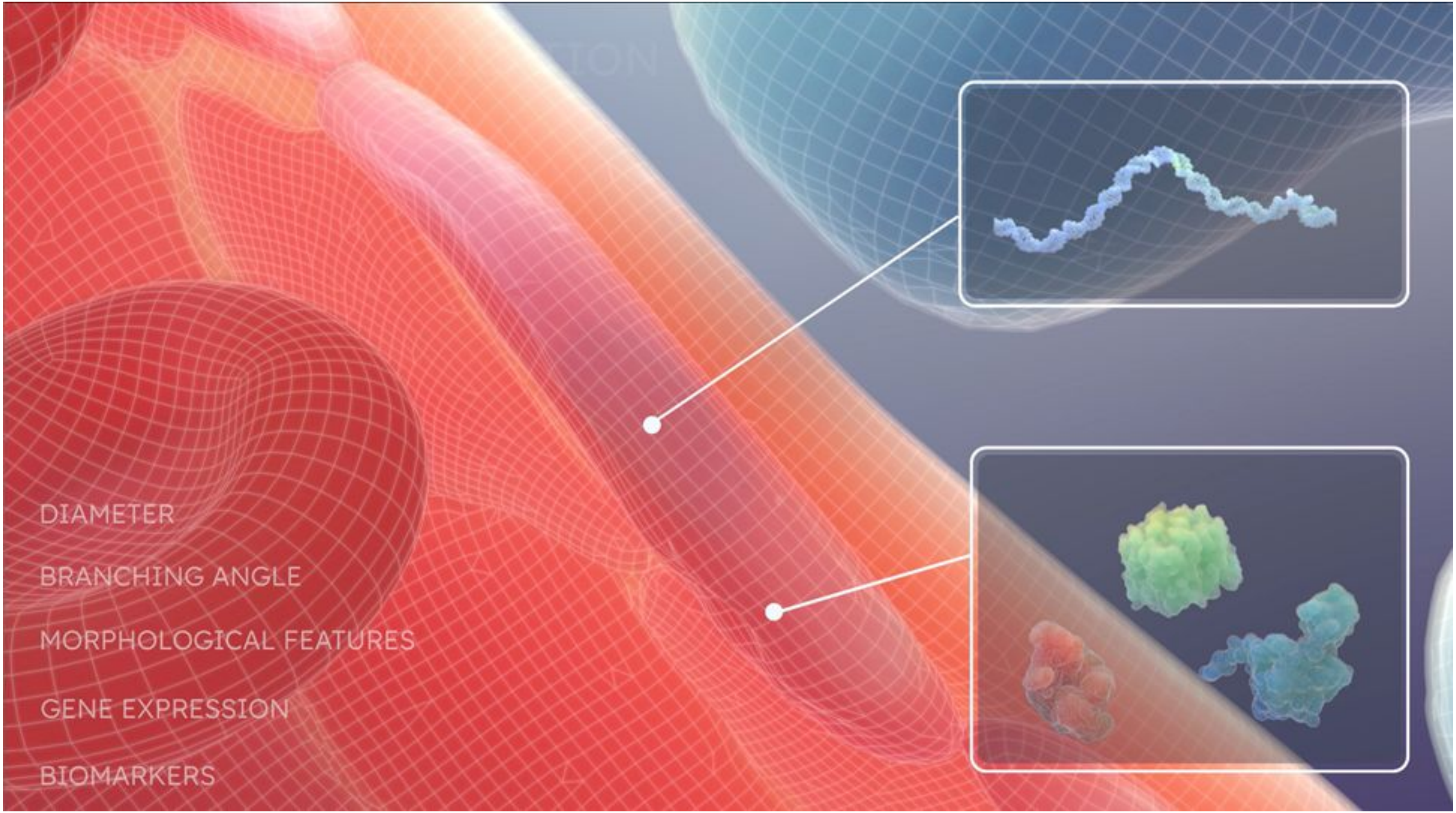
3D Reference Organs | 2D FTU Illustrations | Organ Mapping Antibody Panels

Vascular Geometry

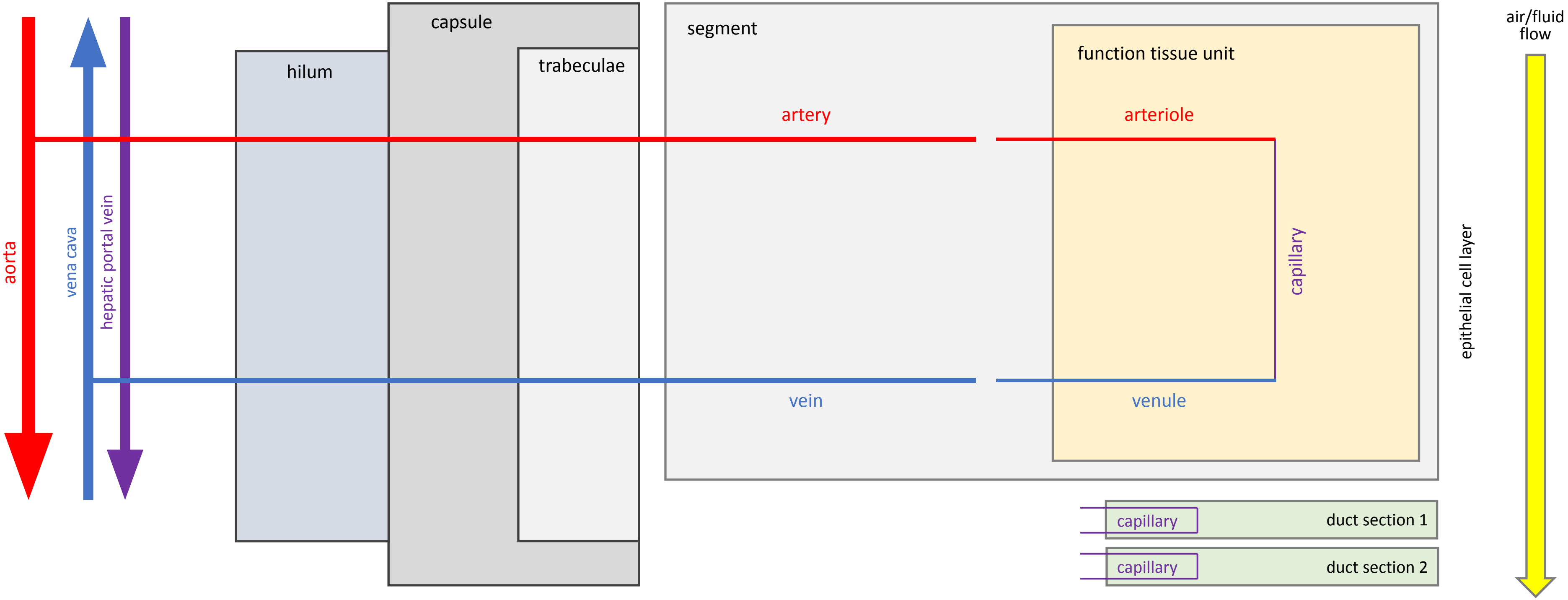
Vasculature Common Coordinate Framework



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

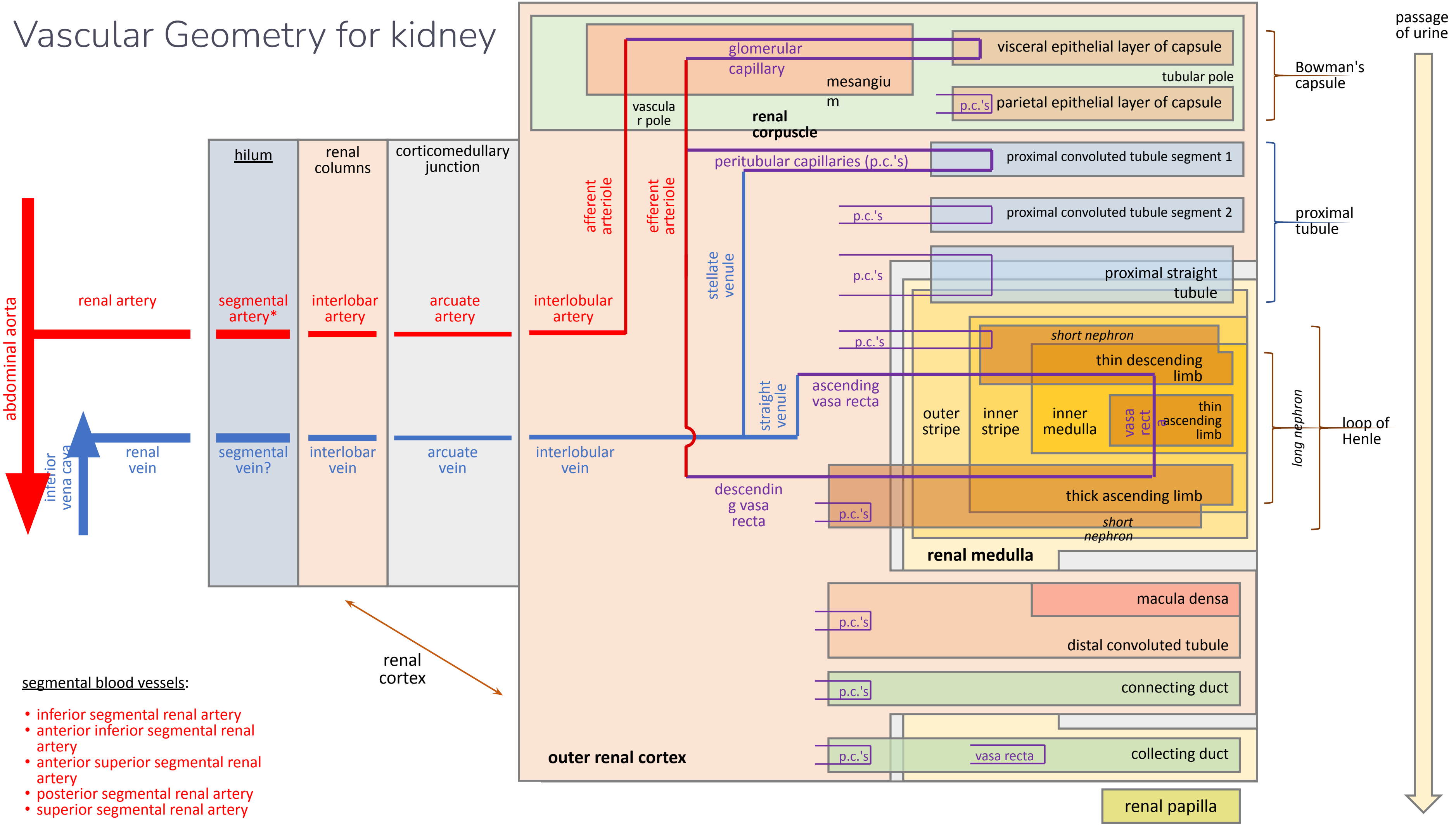


Template



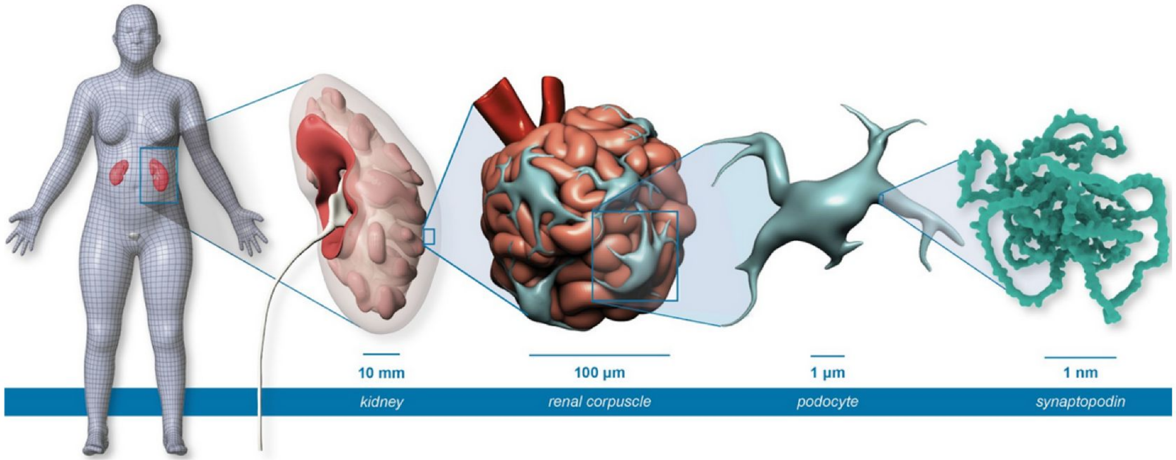
aorta
vena cava
hepatic portal vein
hilum
capsule
trabeculae
segment
function tissue unit
artery
arteriole
capillary
vein
venule
epithelial cell layer
air/fluid flow
capillary
duct section 1
capillary
duct section 2

Vascular Geometry for kidney



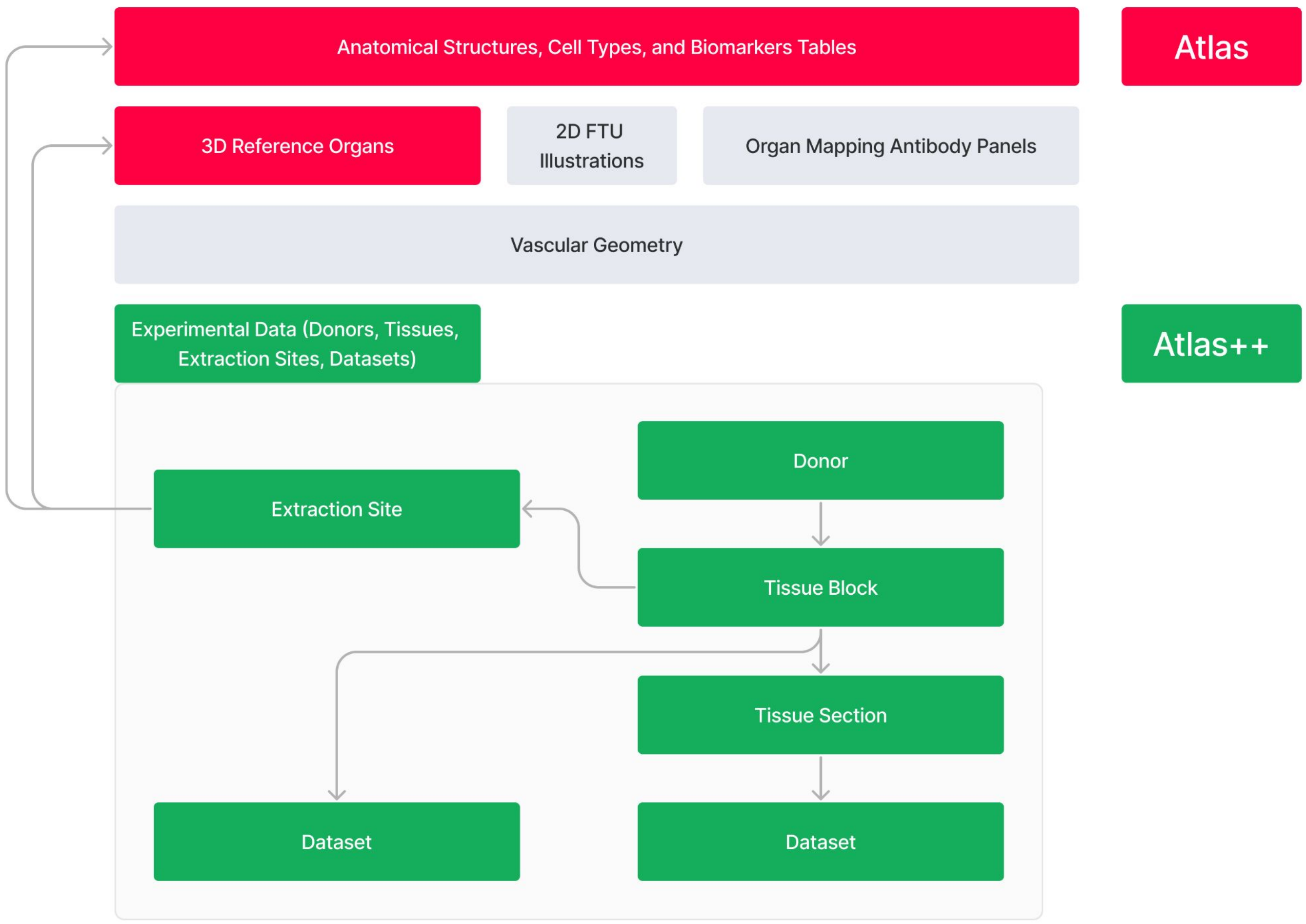
segmental blood vessels:

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



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++

Experimental Dataset Framework

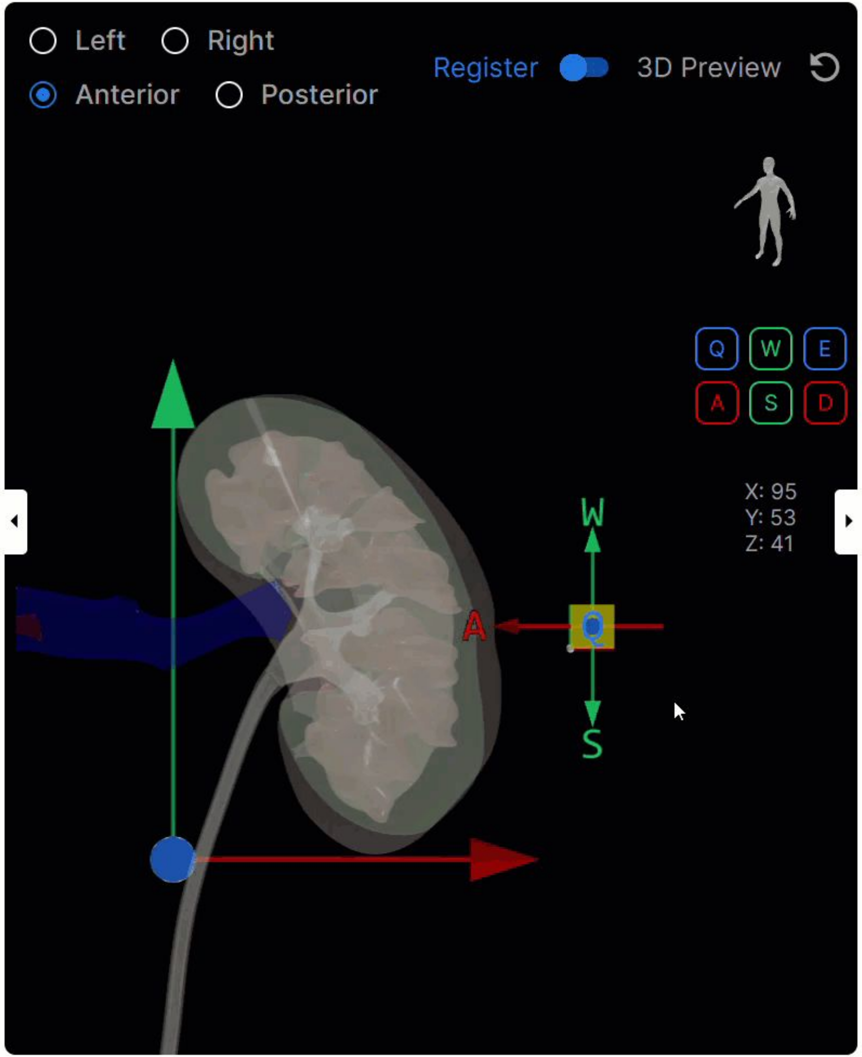


Anatomical Structures

- 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 calyxes
- minor calyxes



Tissue Block Controls

Tissue Block Dimensions (mm)

Width (X)	Height (Y)	Depth (Z)
10	10	10

Tissue Sections

Thickness

Sections

Tissue Block Rotation

X 0

Y 0

Z 0

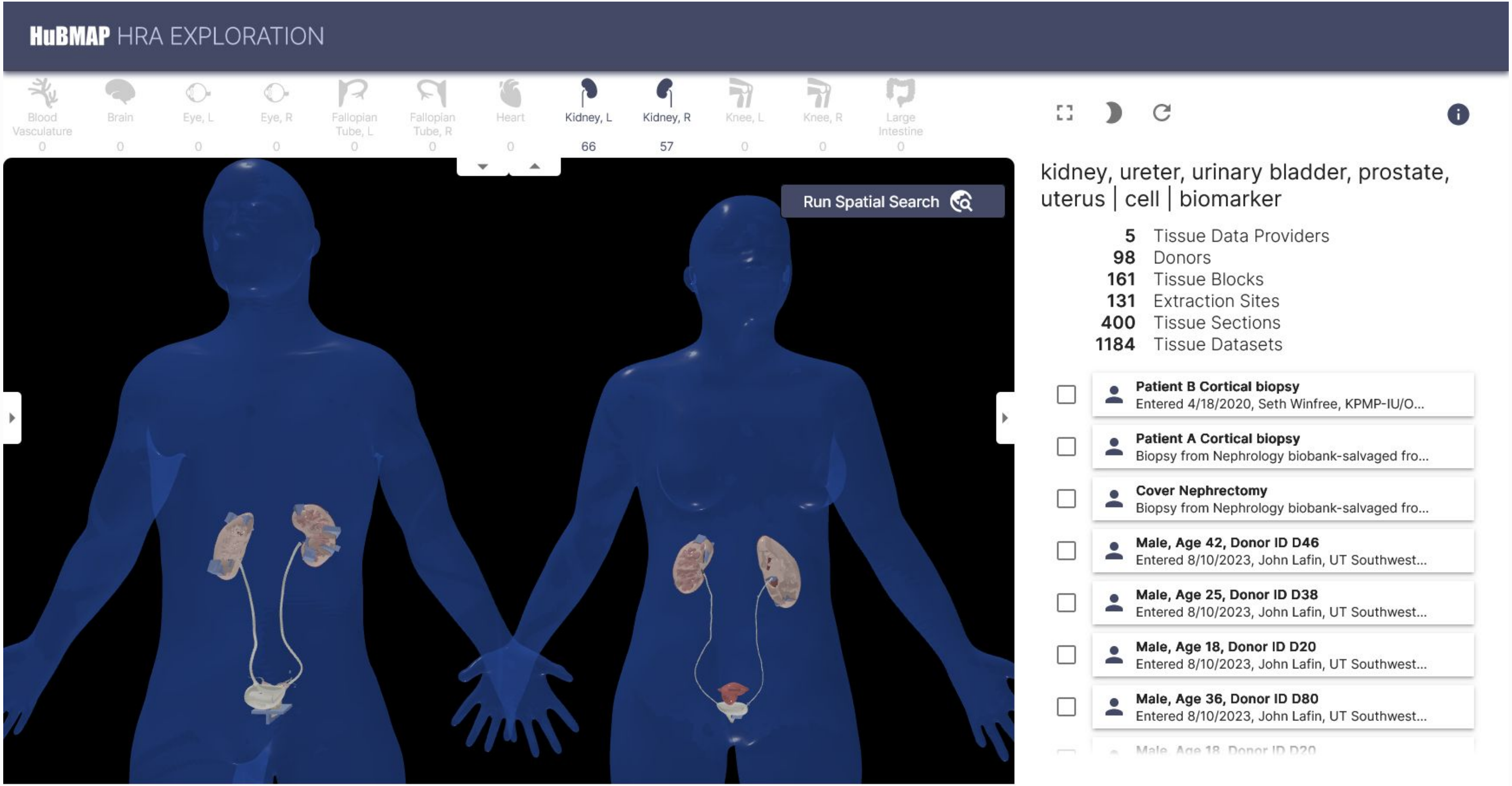
Anatomical Structure Tags

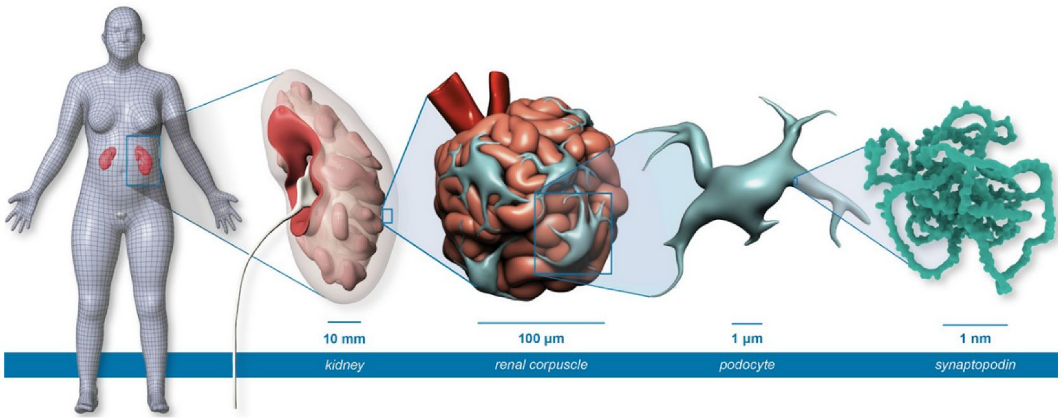
Add Anatomical Structures ... +

Assigned Added

Review and Download

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





Anatomical Structures

Functional Tissue Units

Cell Types

Biomarkers Genes, Proteins, ..

Conceptual

Anatomical Structures, Cell Types, and Biomarkers Tables

Atlas

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2D FTU Illustrations

Organ Mapping Antibody Panels

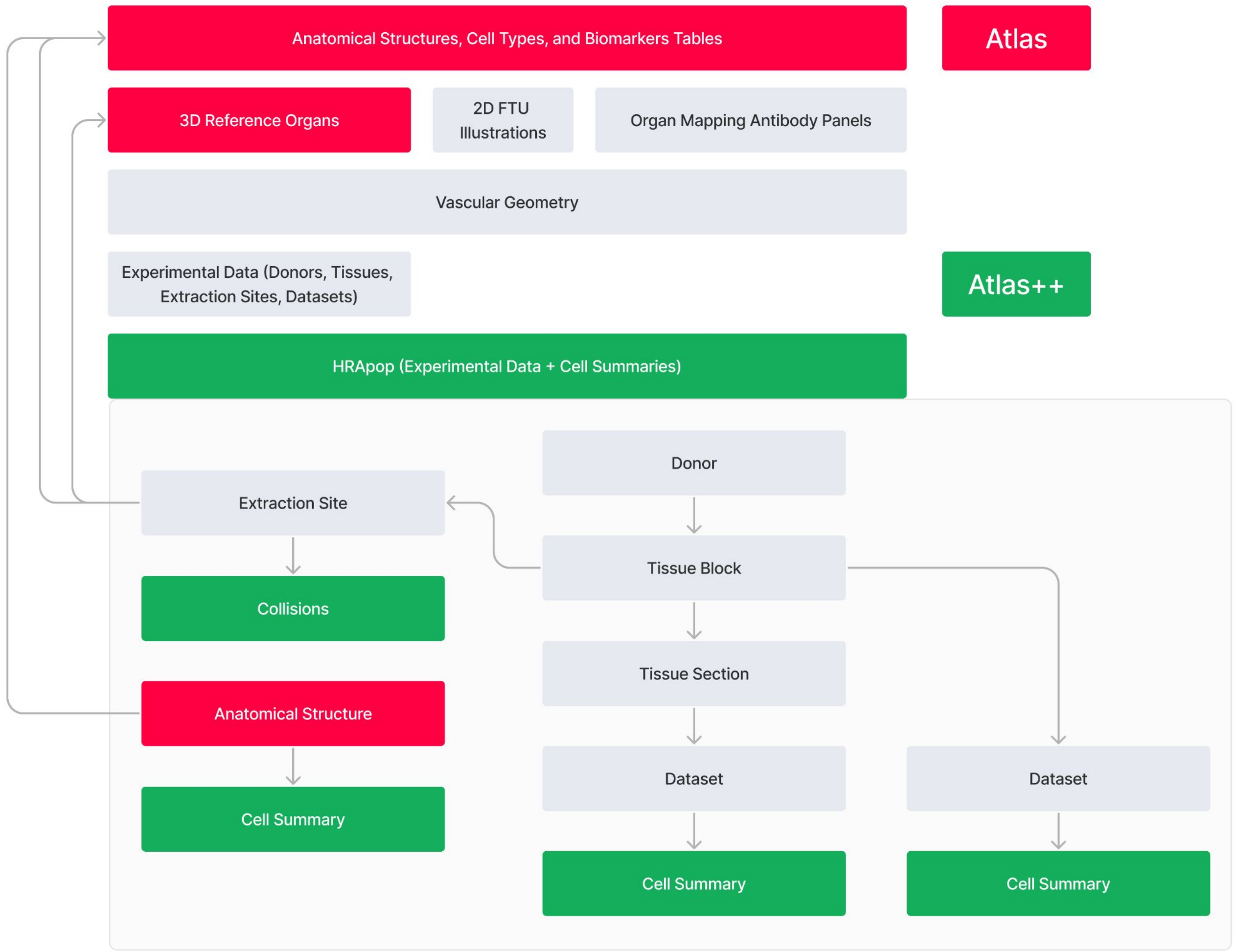
Vascular Geometry

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

Atlas++

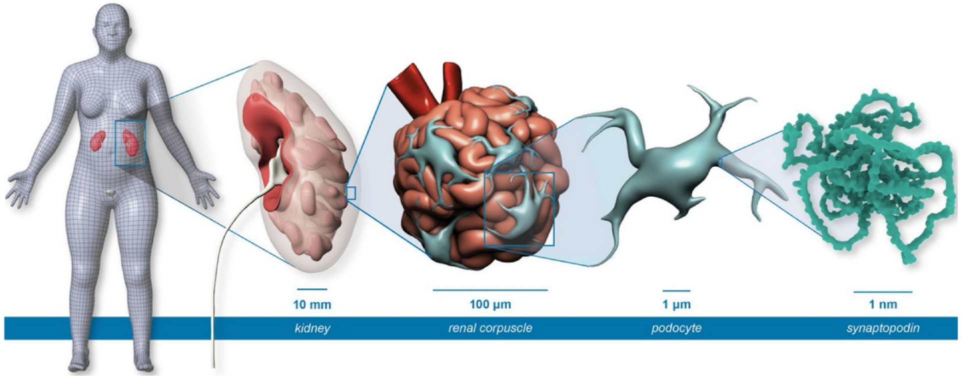
HRApop (Experimental Data + Cell Summaries)

HRApop Framework



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

		ASCT+B and 3D Reference Organs			Cell Type Annotation Tools		
Organ	**Datasets with H5AD file**	**#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, ..

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Vascular Geometry

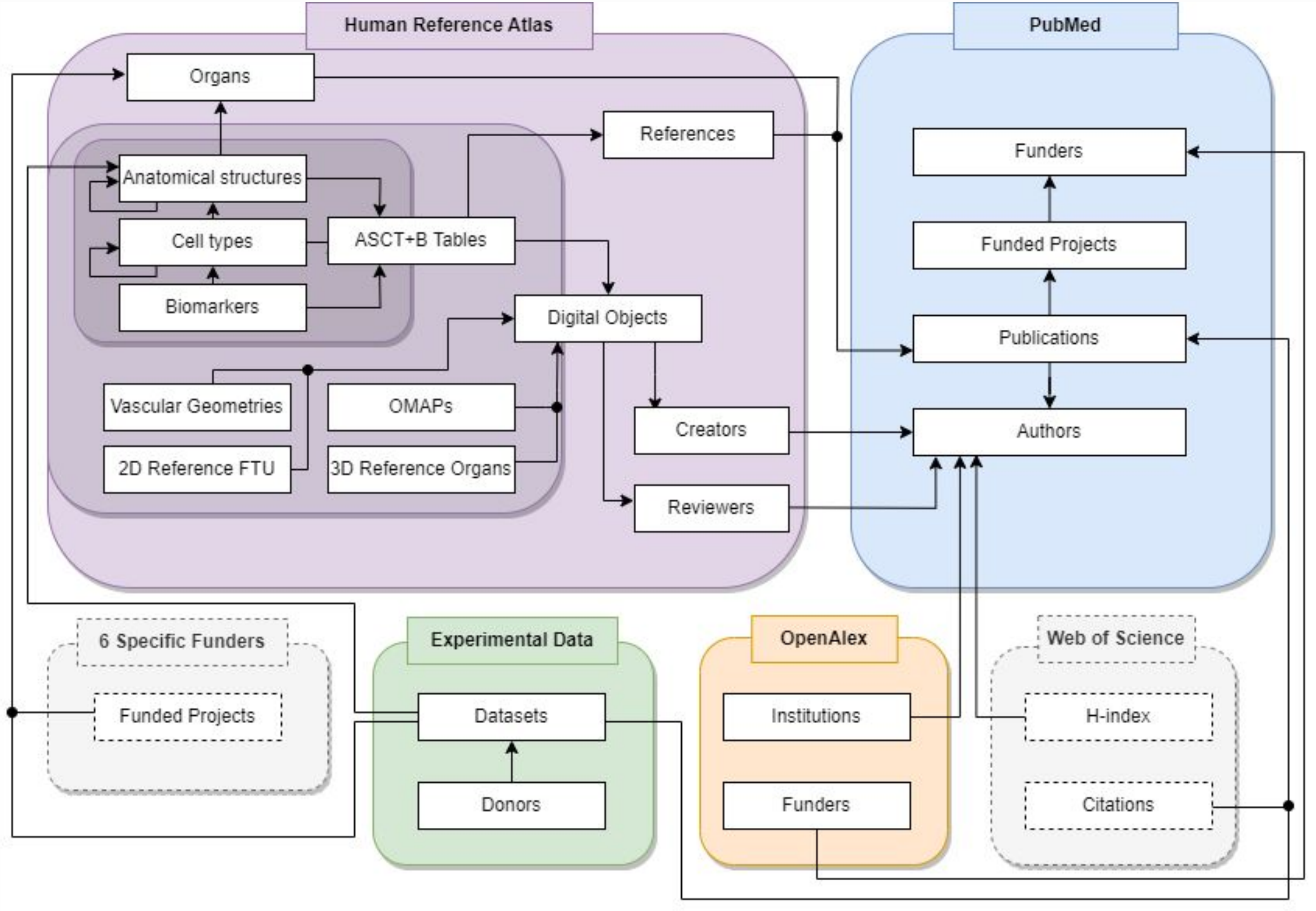
Experimental Data (Donors, Tissues, Extraction Sites, Datasets)

Atlas++

HRApop (Experimental Data + Cell Summaries)

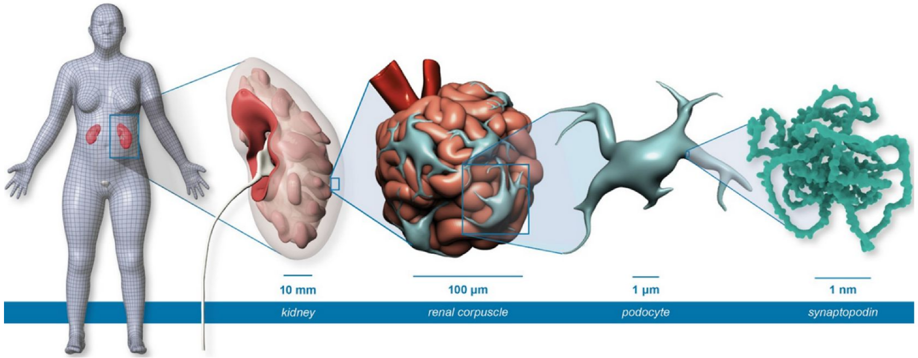
HRAlit (HRA-relevant Literature)

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**



Anatomical Structures | Functional Tissue Units | Cell Types | Biomarkers Genes, Proteins, .. | **Conceptual**

Anatomical Structures, Cell Types, and Biomarkers Tables | **Atlas**

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Vascular Geometry

Experimental Data (Donors, Tissues, Extraction Sites, Datasets) | **Atlas++**

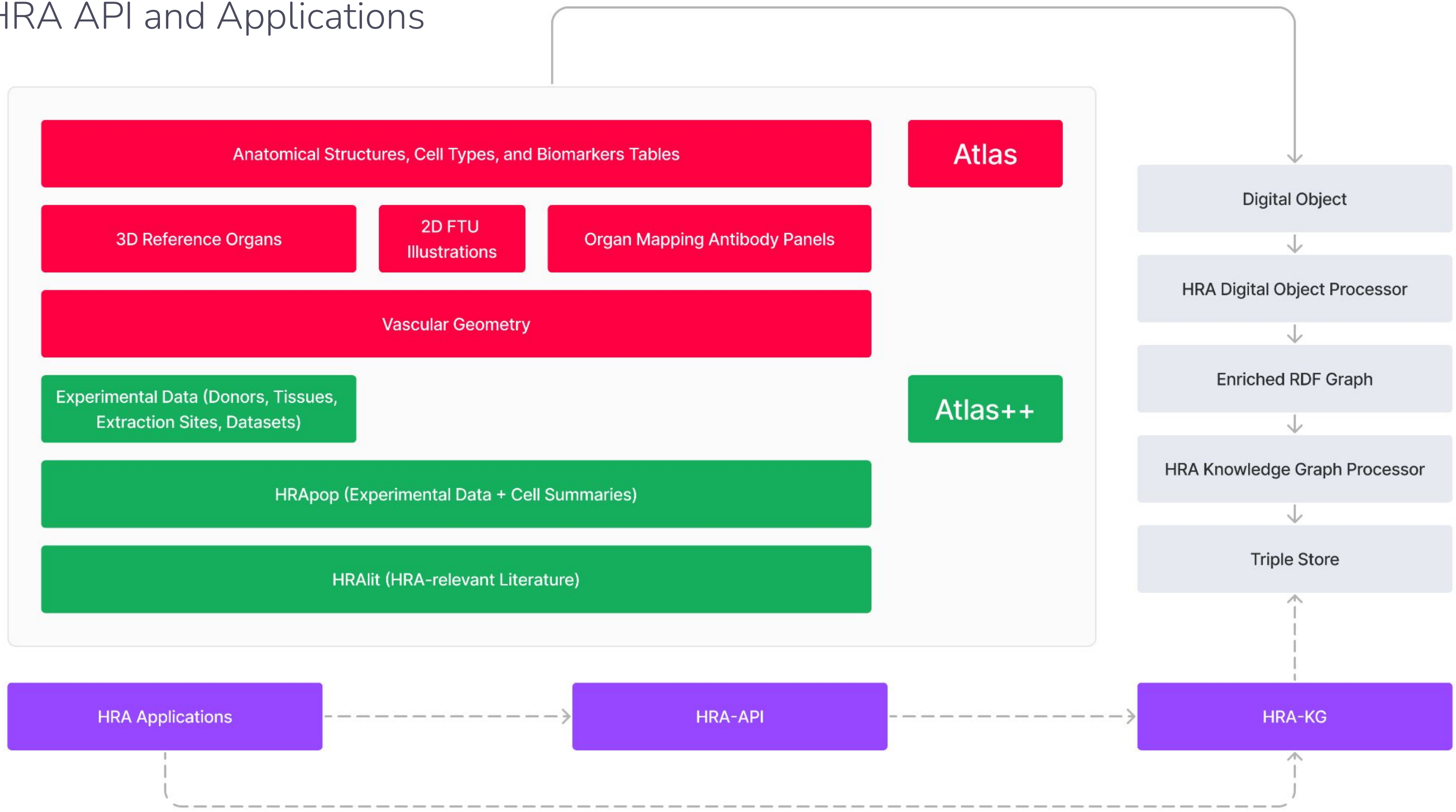
HRApop (Experimental Data + Cell Summaries)

HRAlit (HRA-relevant Literature)

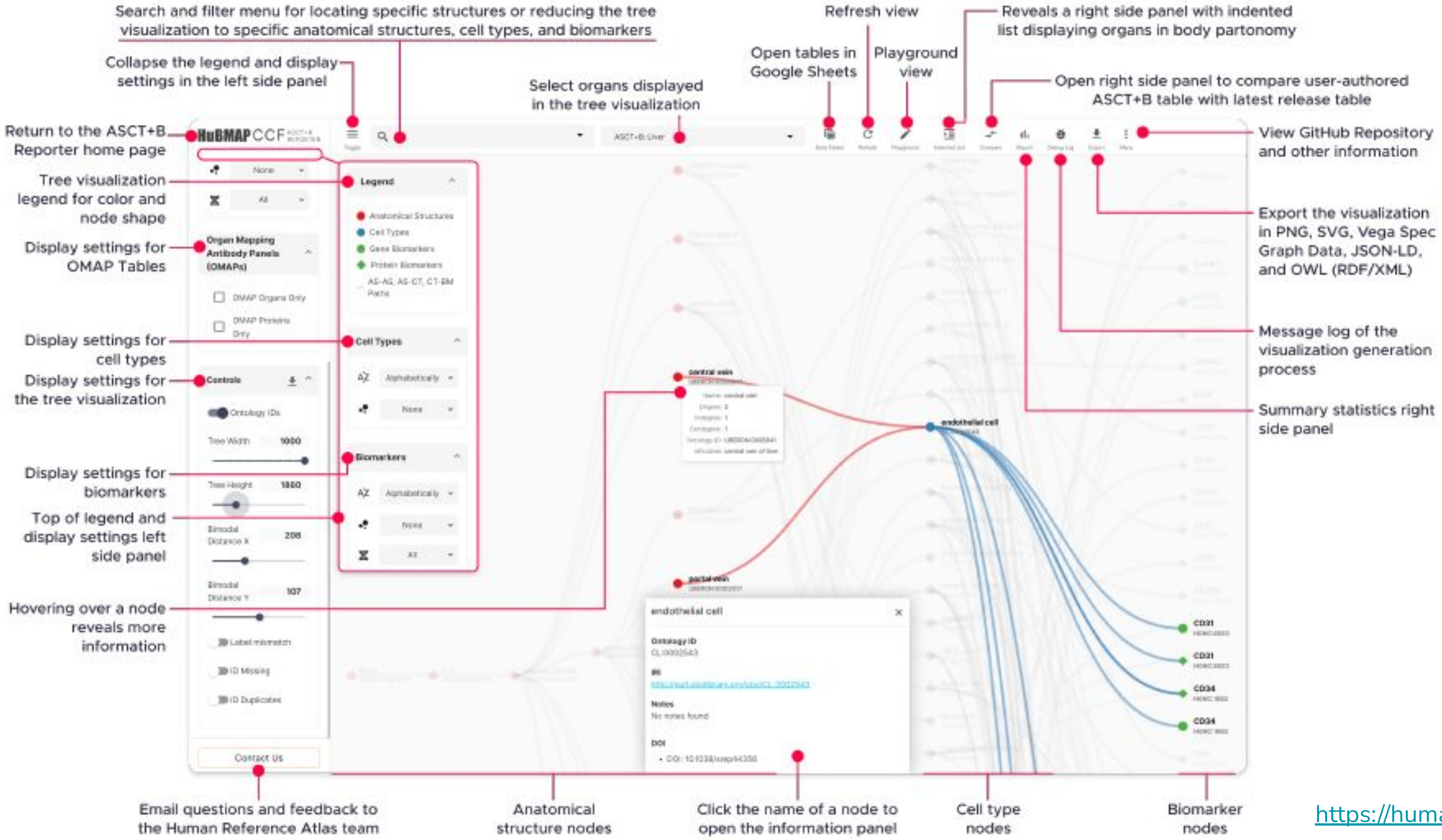
Using the HRA

HRA Knowledge Graph Framework

HRA API and Applications

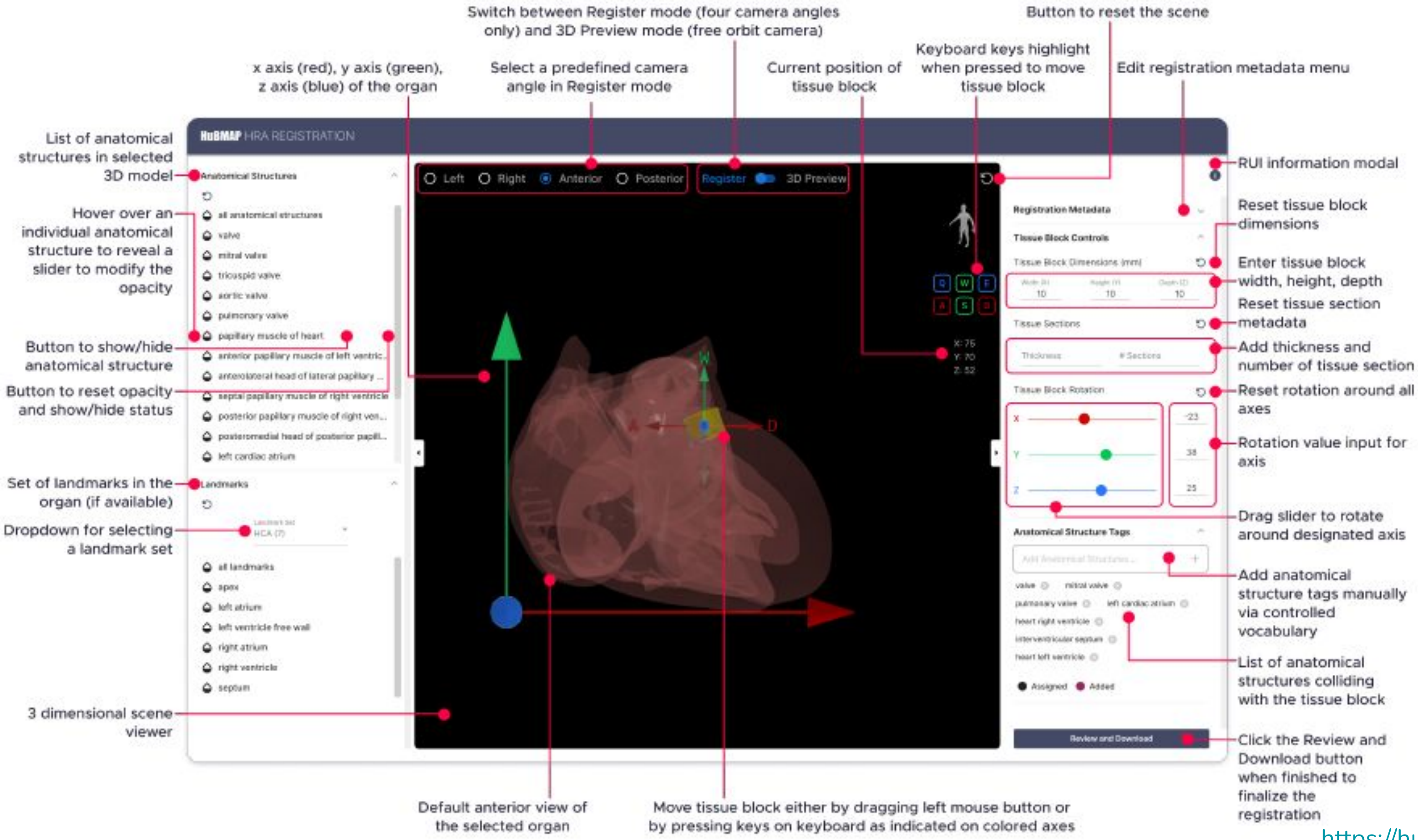


ASCT+B Reporter User Interface



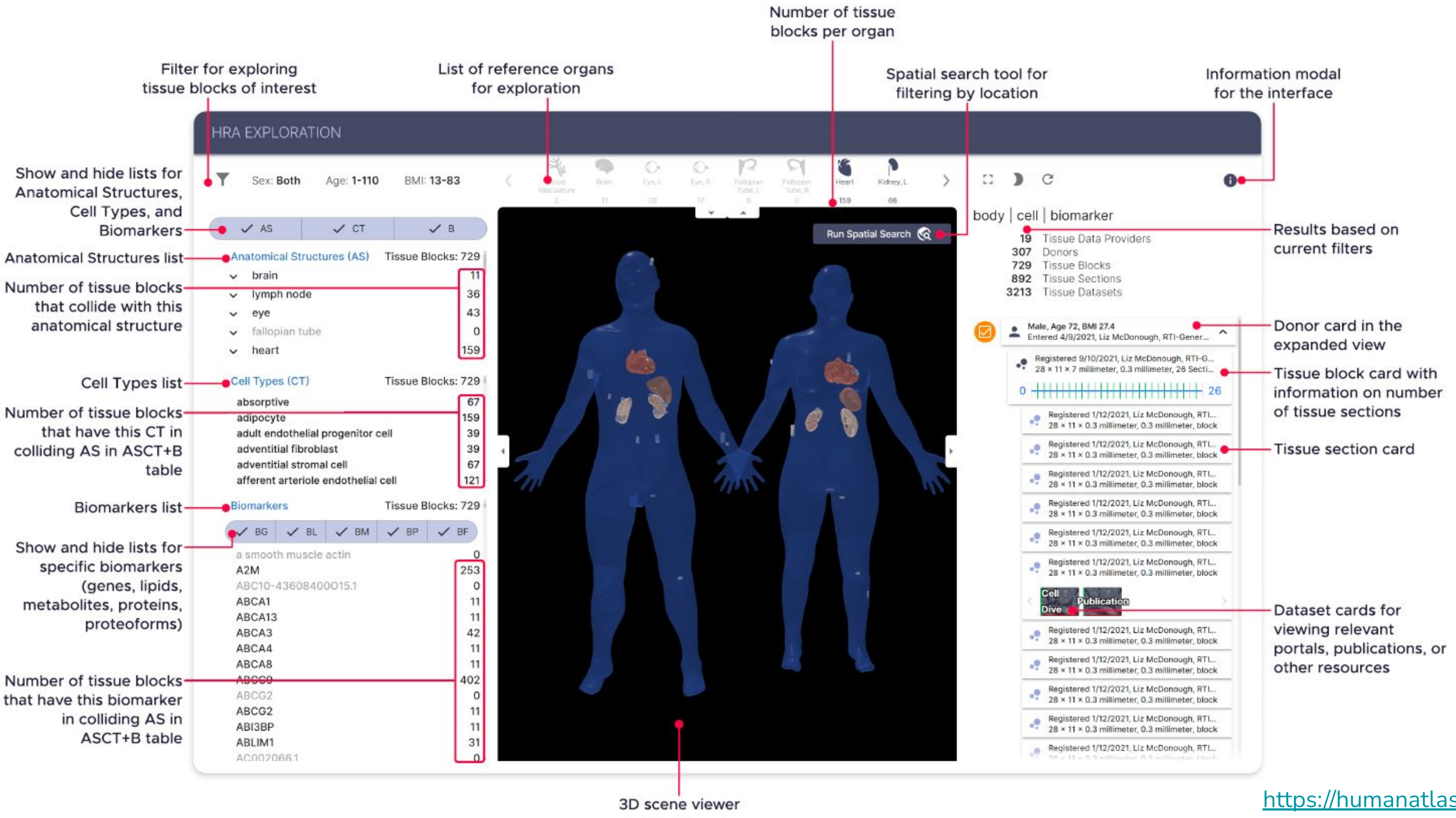
https://humanatlas.io/overview-tools

Registration User Interface (RUI)



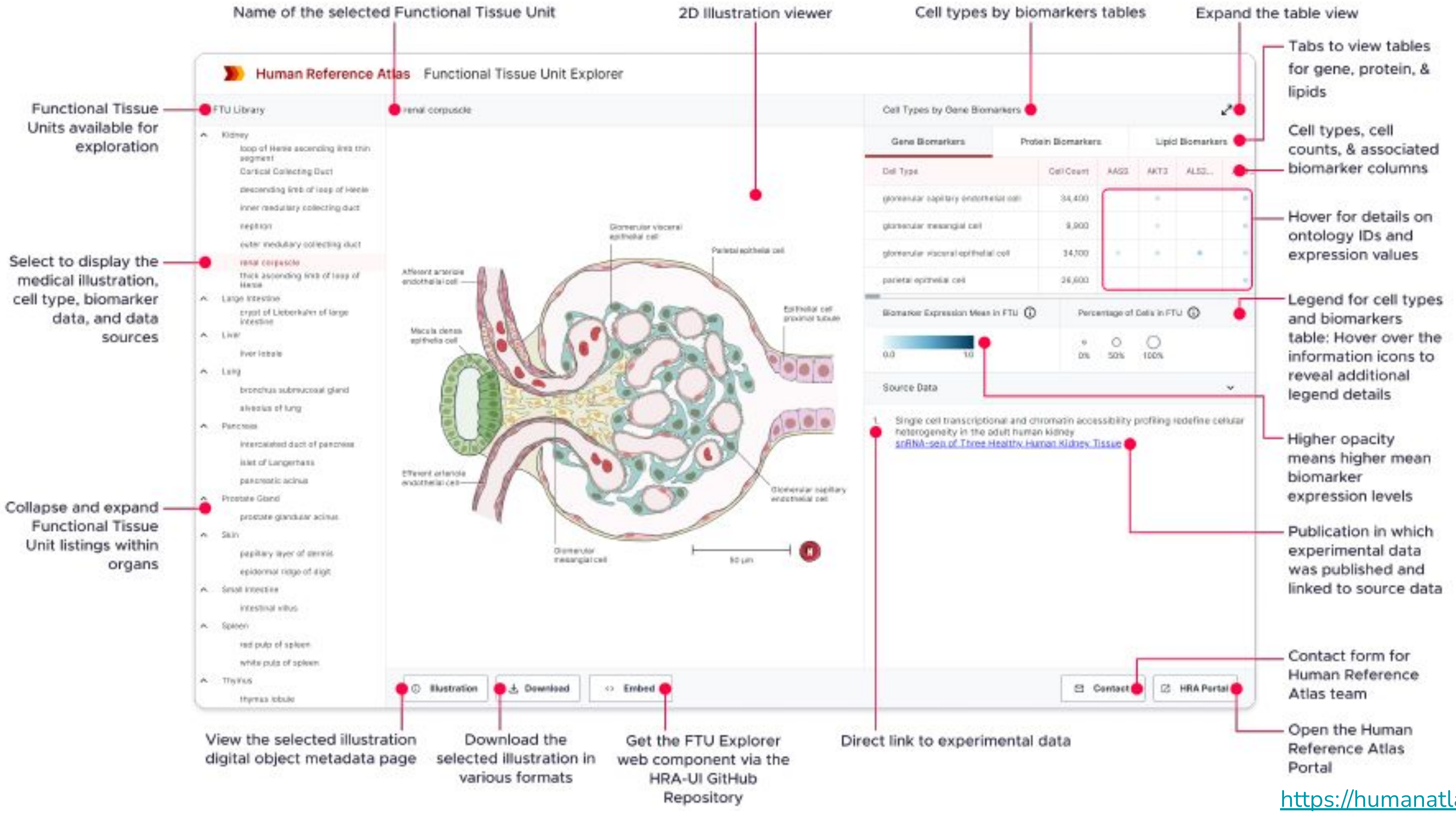
https://humanatlas.io/overview-tools

Exploration User Interface (EUI)



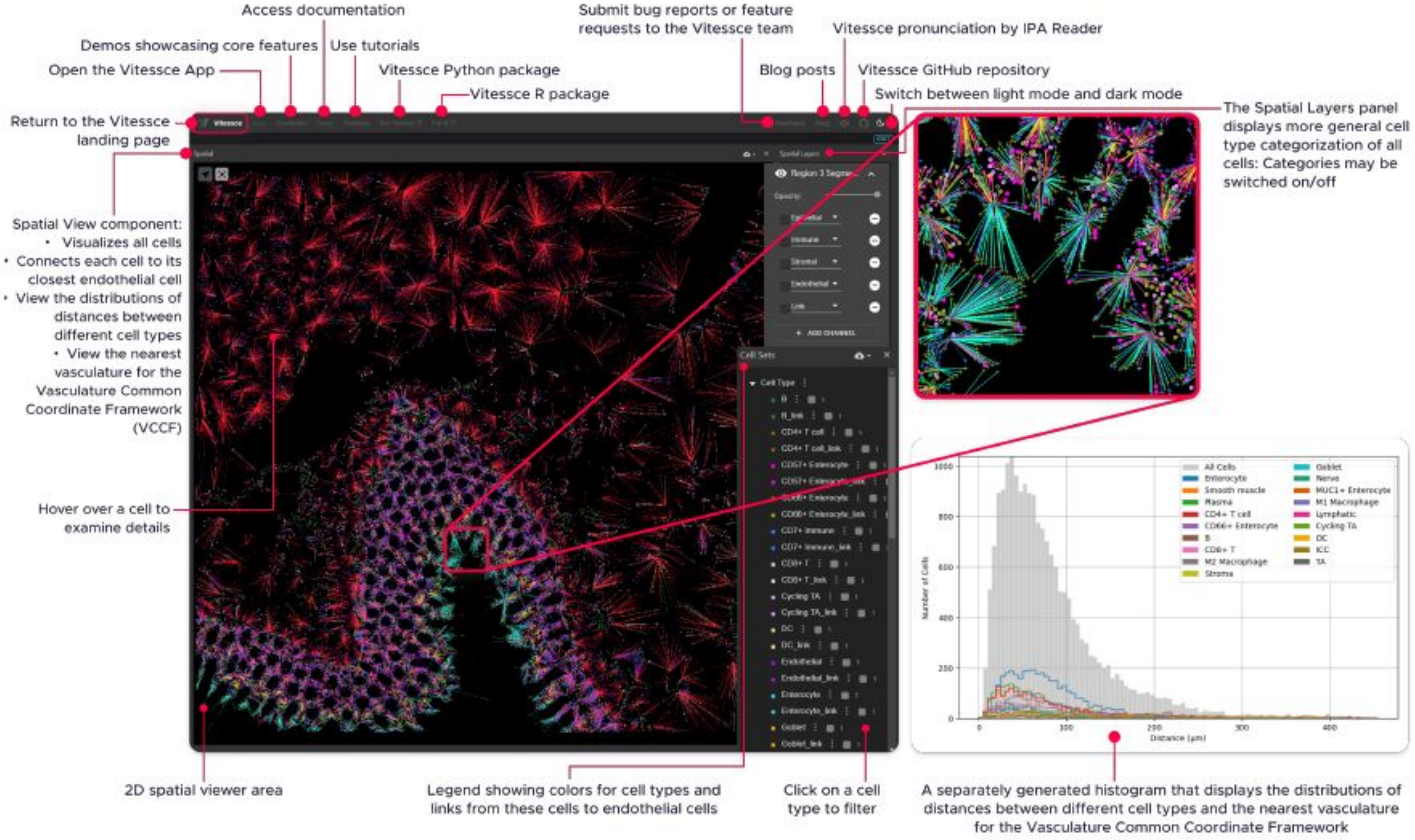
https://humanatlas.io/overview-tools

Interactive FTU Explorer



https://humanatlas.io/overview-tools

Cell Distance Visualizations



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

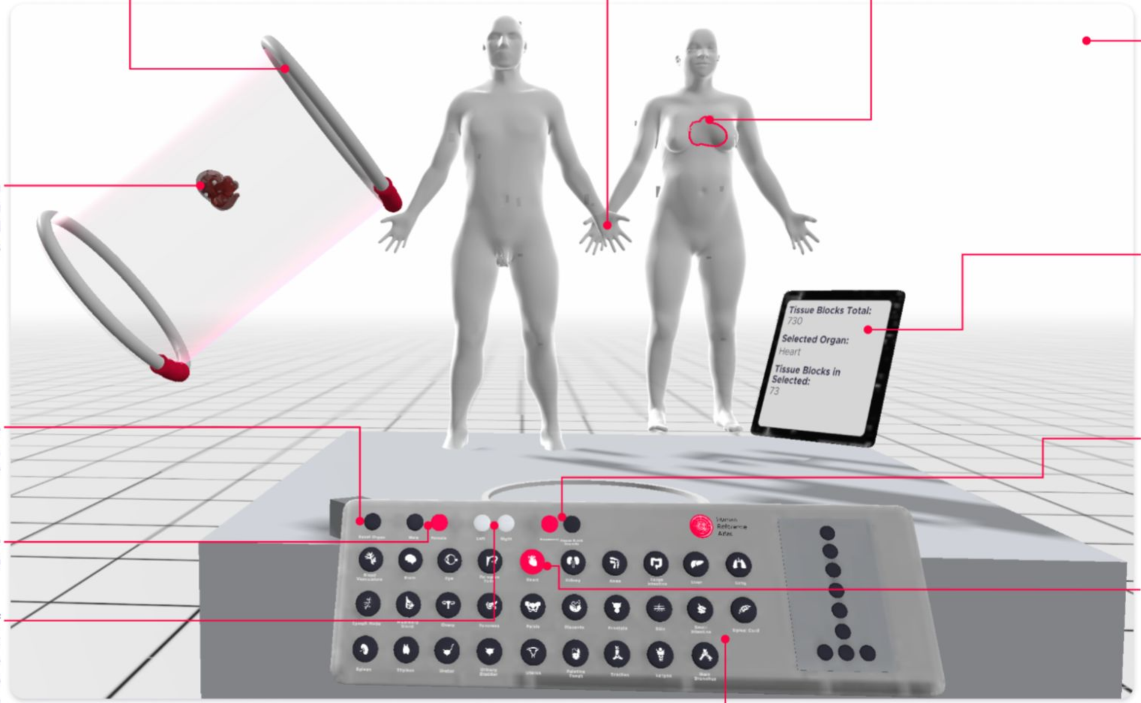
Application is used while sitting and user can exit application by pressing menu button on controller

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



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

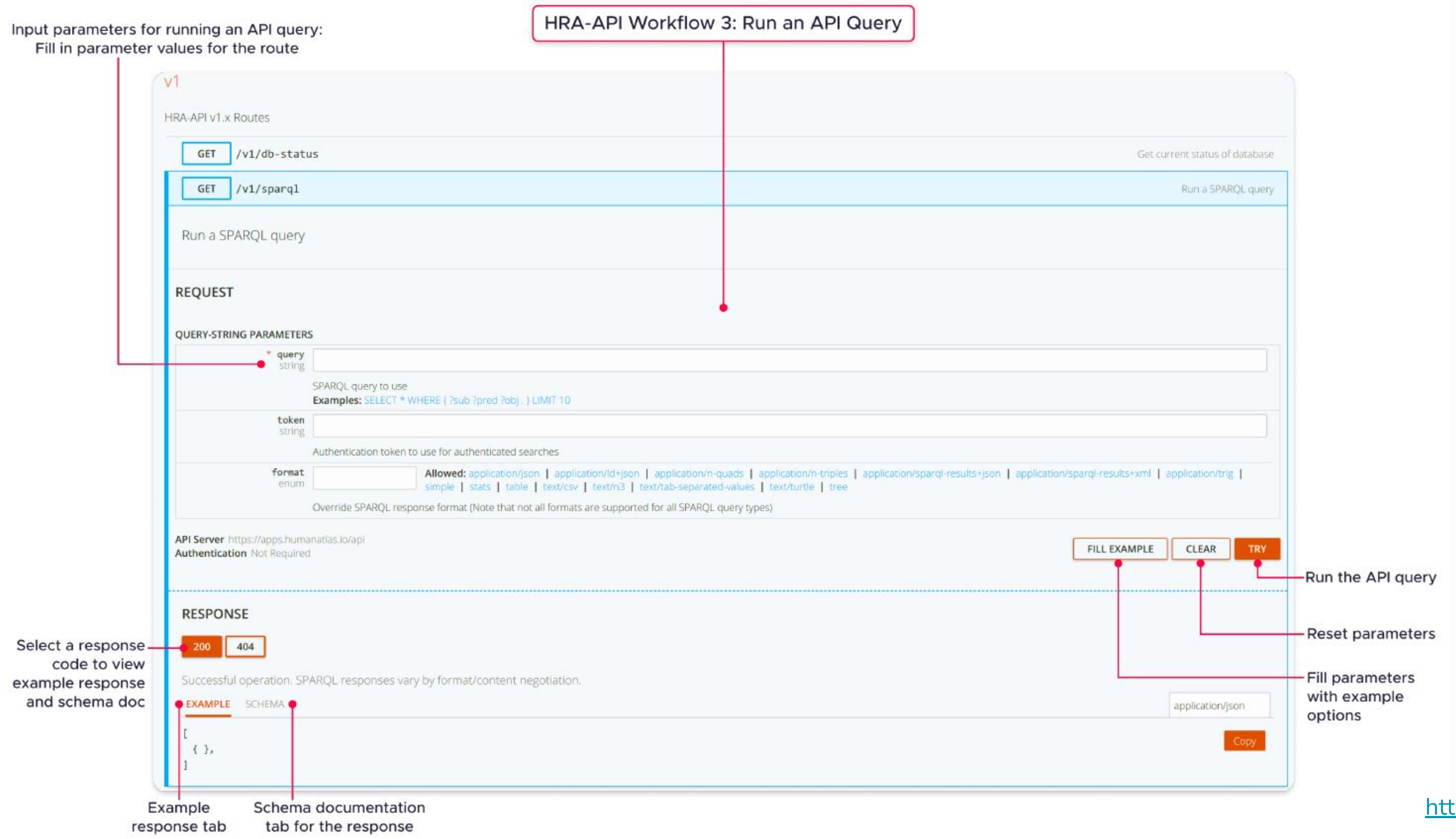
Switch to change between using controllers for movement and manipulating tissue blocks

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

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

https://www.meta.com/experiences/5696814507101529

HRA API: Run an API Query



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.

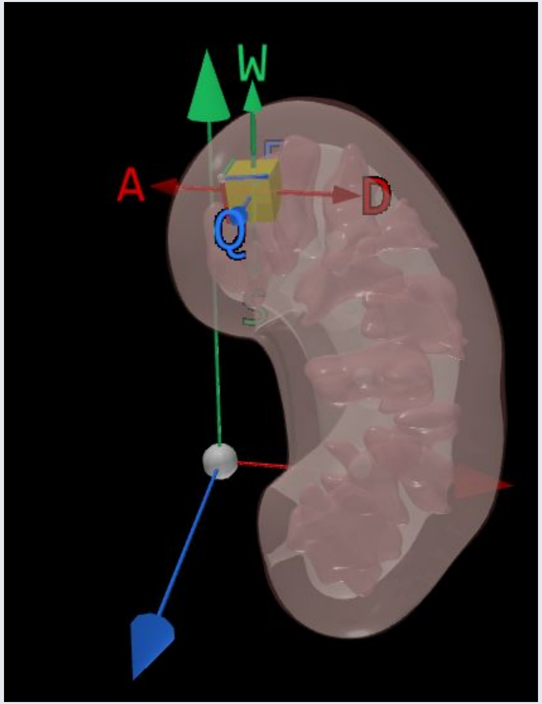
In addition, six programmers from different human atlas projects were surveyed.

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
*Facilitate atlas **construction** by aligning new tissue blocks with existing data*			
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.
***Use** the atlas to gain insights into changes that occur at all levels in the body with aging or disease*			
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.
*Ensure atlas **sustainability** with processes that encourage collaboration and guide future development*			
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
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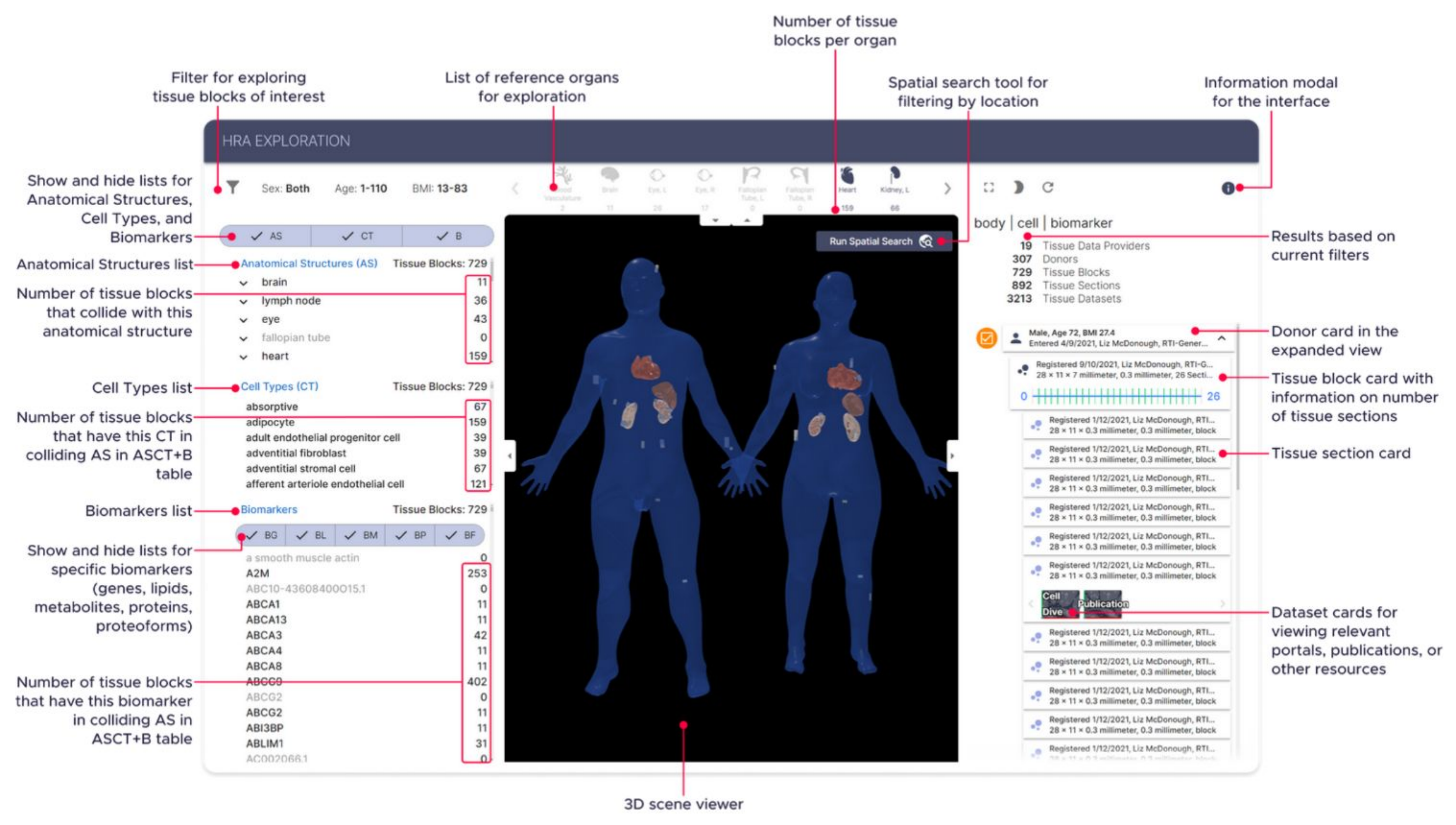
2.9%	95,842	Fibroblast
2.7%	87,883	Cortical Collecting Duct Principal
2.1%	66,948	Macula Densa
1.8%	59,228	Medullary Fibroblast

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

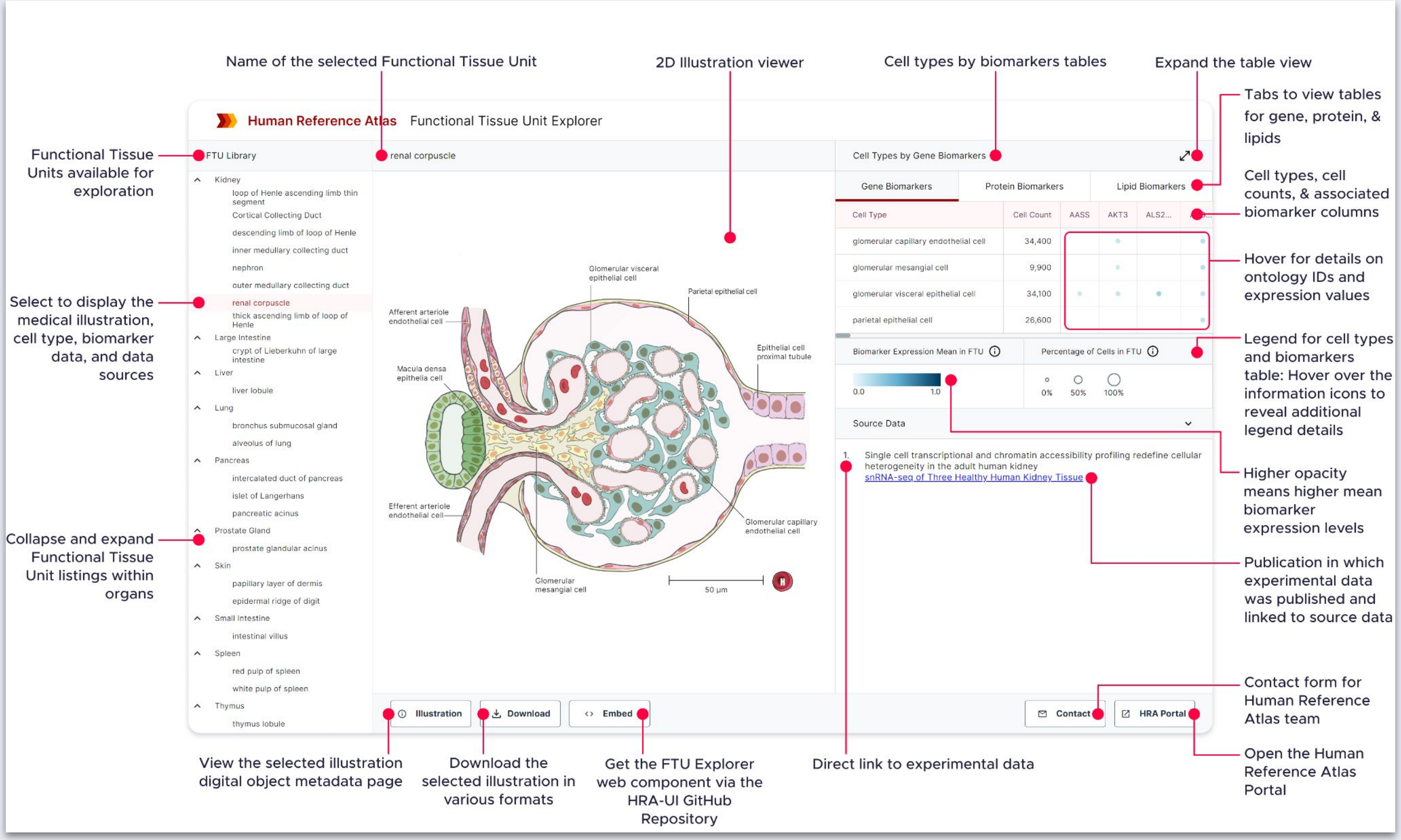
https://apps.humanatlas.io/us2/

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



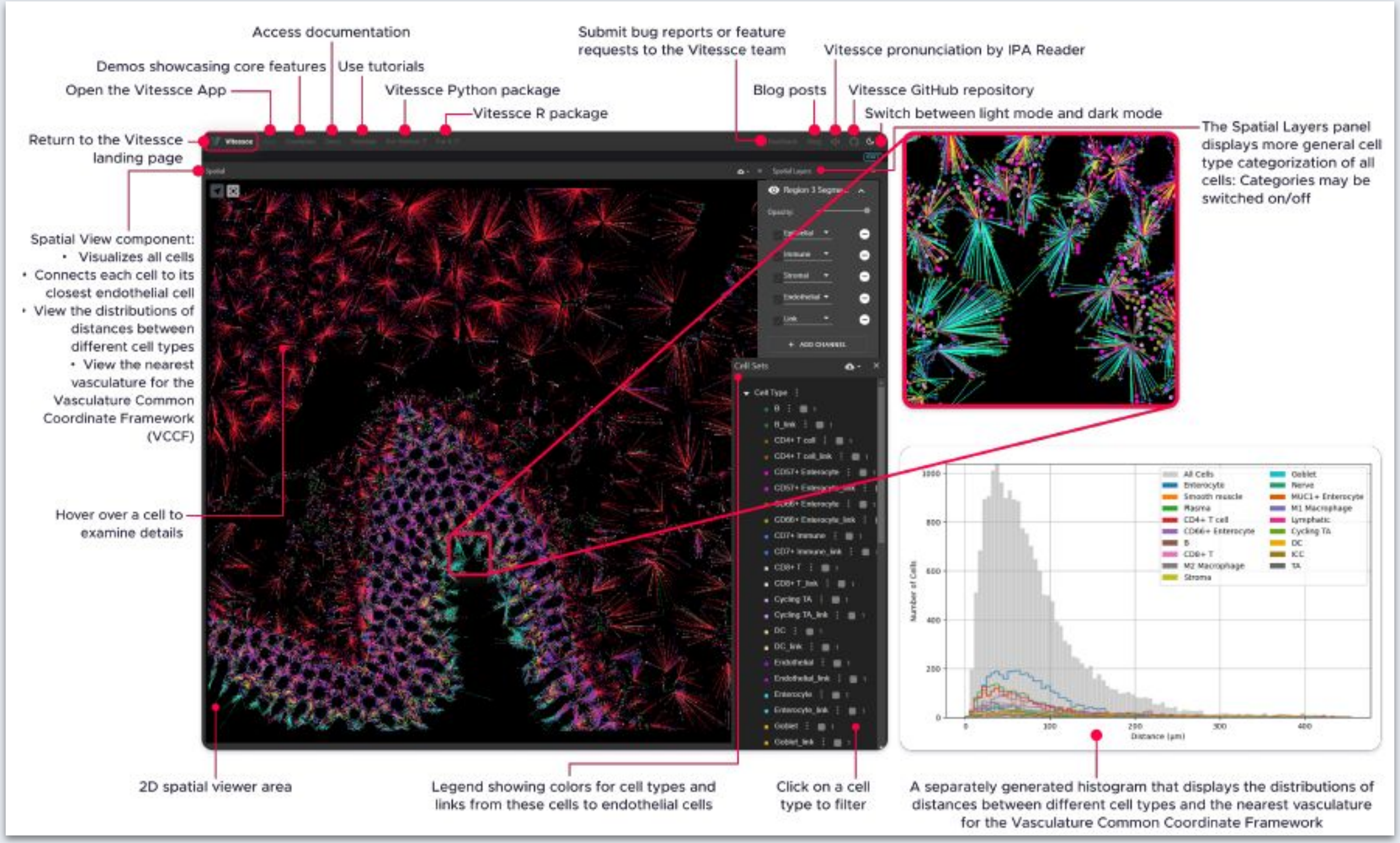
https://apps.humanatlas.io/eui/

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



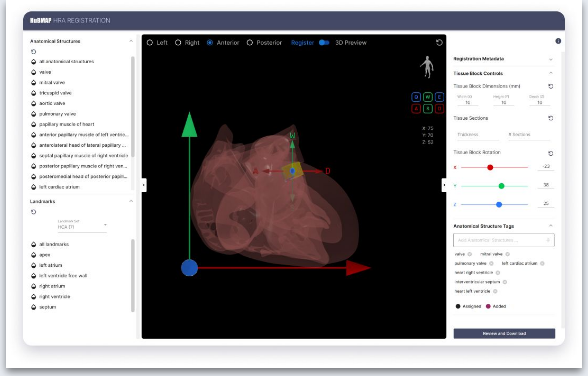
https://apps.humanatlas.io/ftu-explorer/

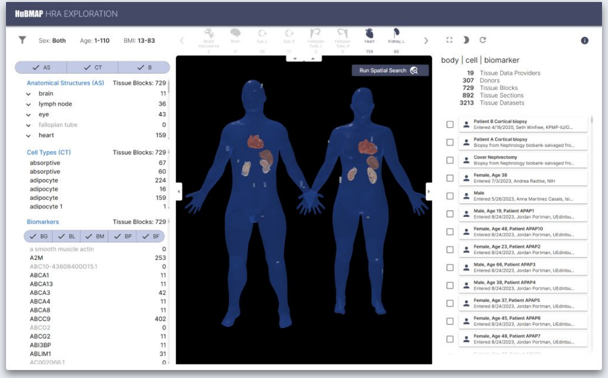
US#5. Provide cell distance distribution visualizations

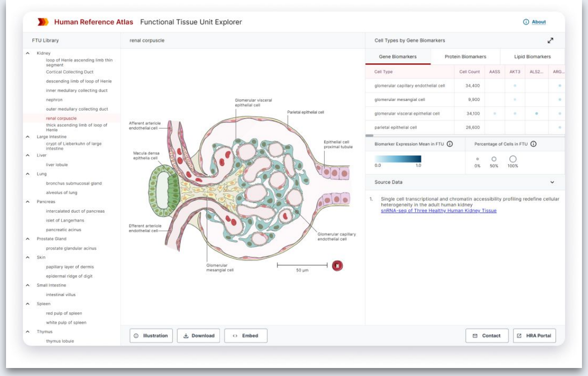


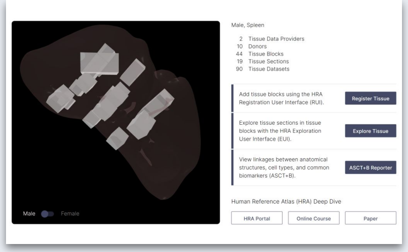
Coming June 14th on humanatlas.io

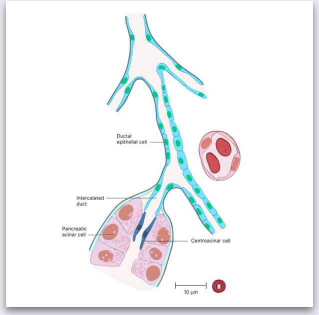
US#6. Develop lightweight atlas components

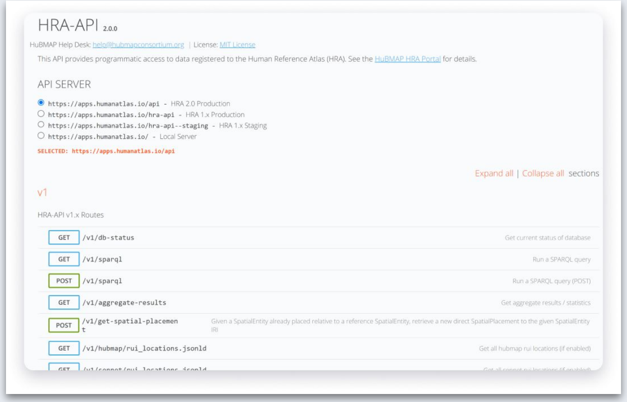


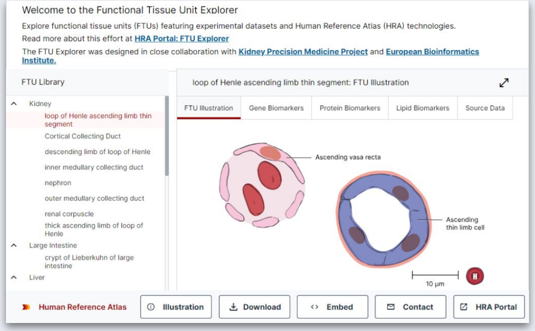






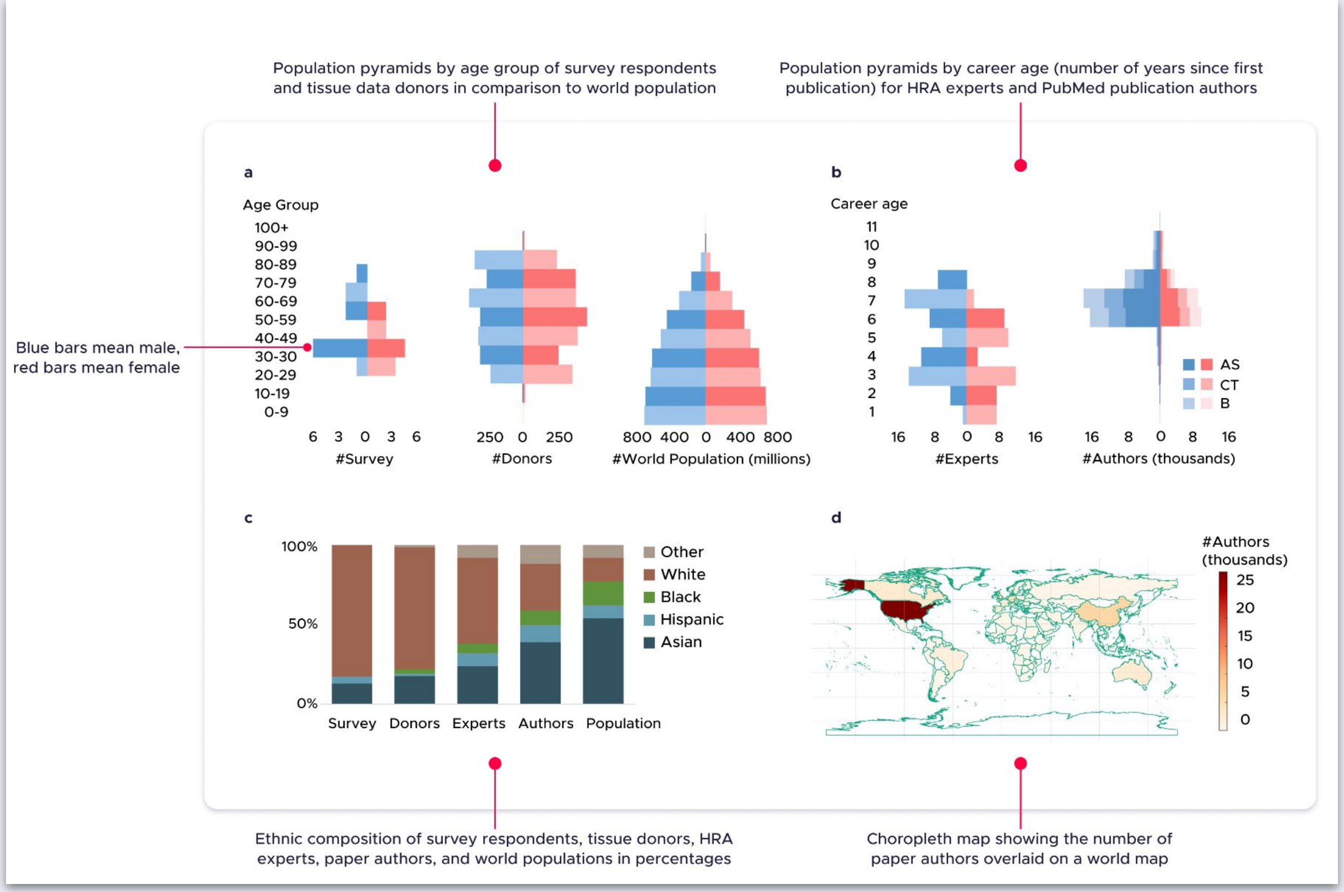






Coming June 14th on humanatlas.io

US#7. Implement dashboard for HRA

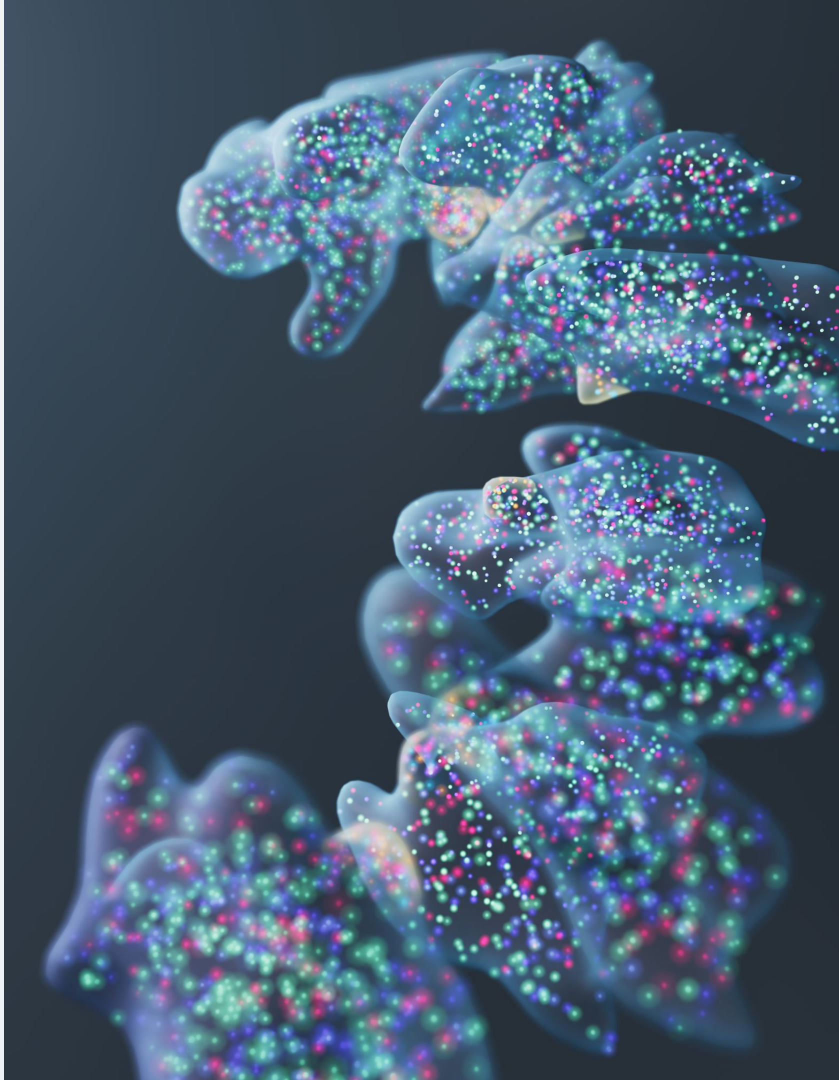


Coming June 14th on humanatlas.io

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

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

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CNS Director

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Ontologist

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Griffin Weber
Associate Professor of Medicine

NIH
National Institutes of Health

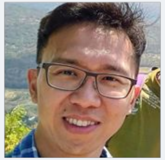
NSF

CIFAR

Full Time Staff

Daniel Bolin
Software Developer

Andreas Bueckle
Research Lead



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Software Developer

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CNS Technical Director

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Edward Lu
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Libby Maier
User Experience Designer

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CNS Associate Director

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Supriya Bidanta
Research Assistant

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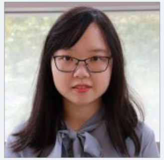

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Thank you!

Resources at:
https://humanatlas.io/events/AUA2024

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