

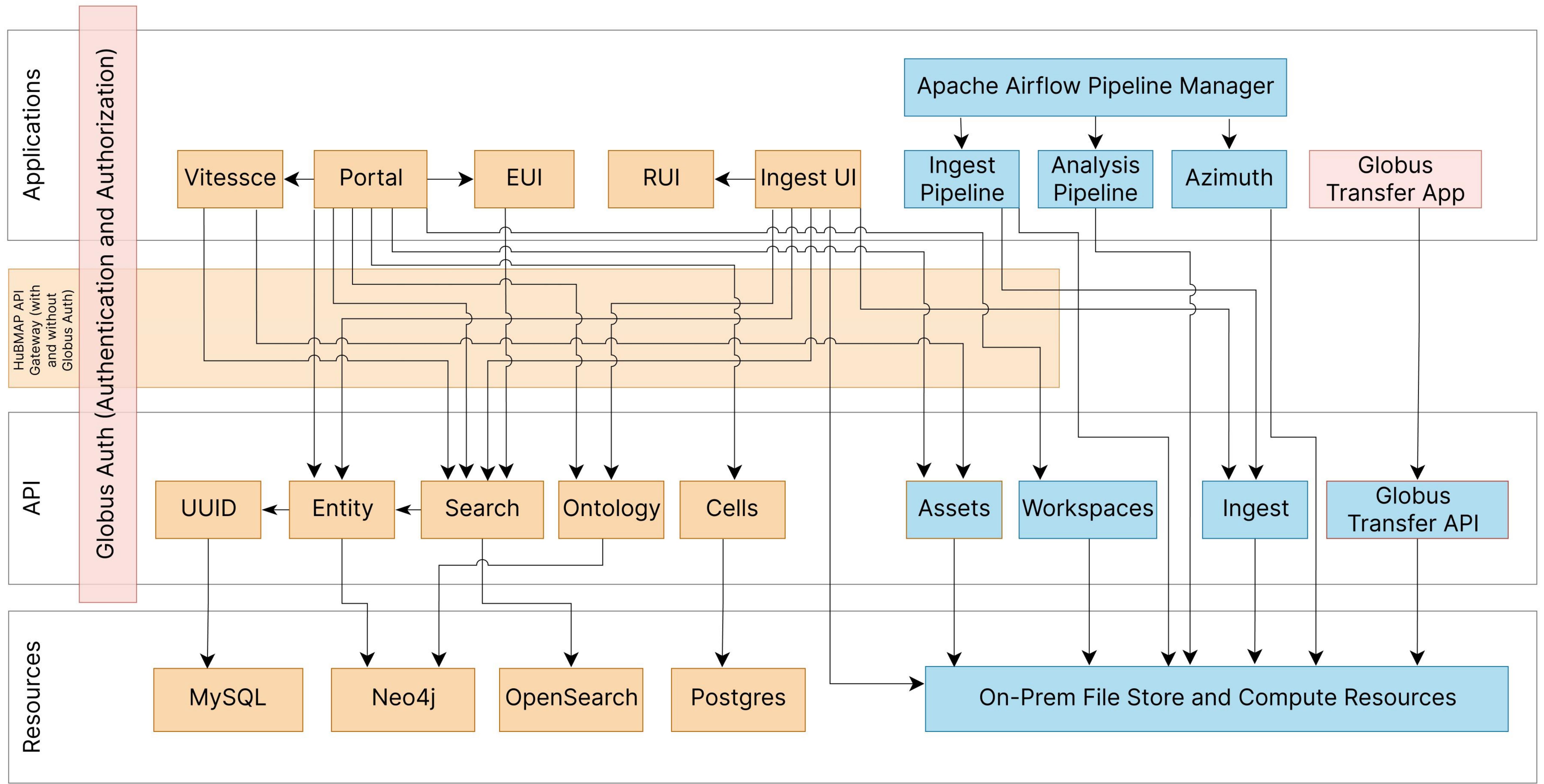


Supplementary information

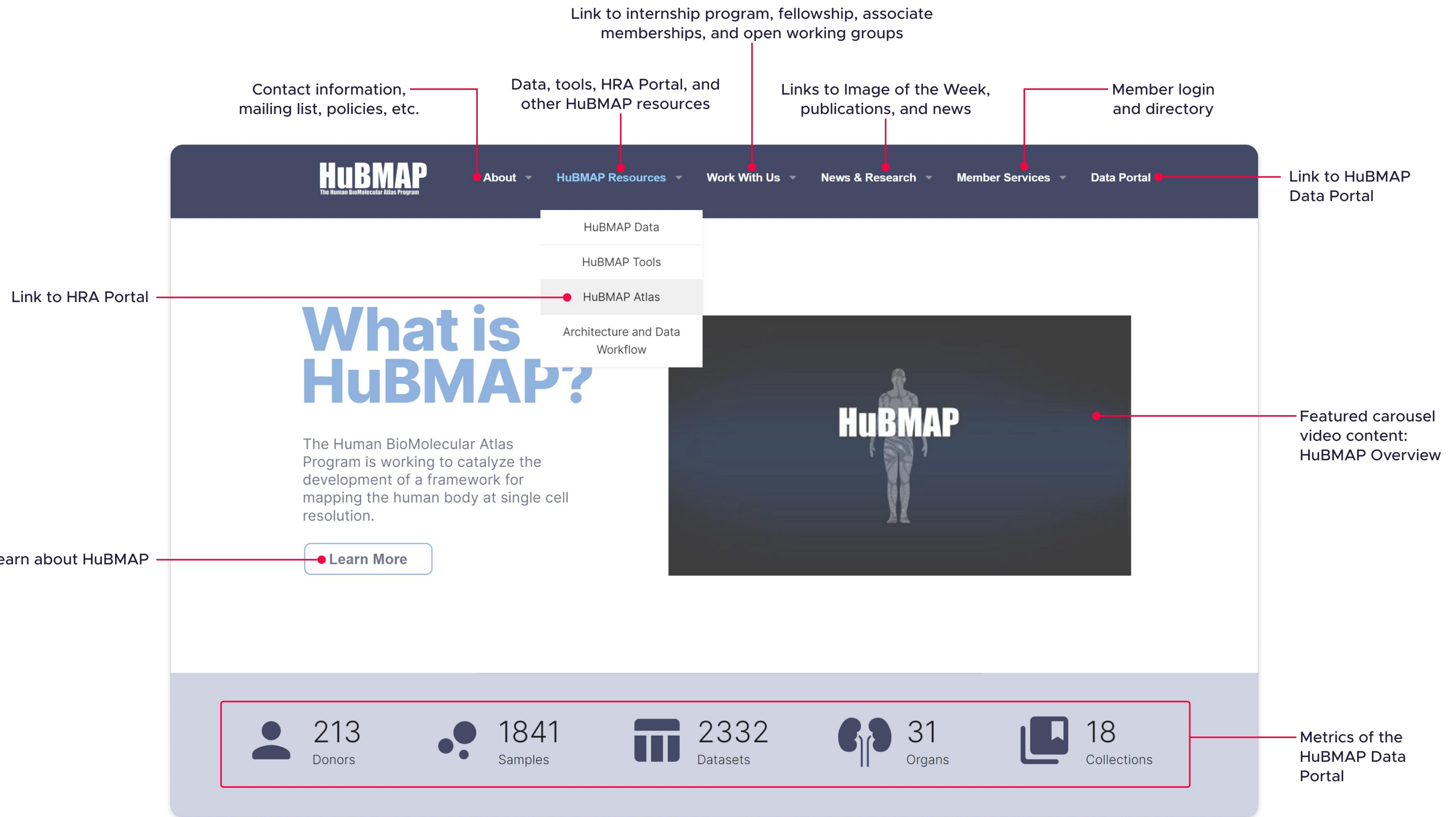
<https://doi.org/10.1038/s41592-024-02563-5>

Human BioMolecular Atlas Program (HuBMAP): 3D Human Reference Atlas construction and usage

In the format provided by the
authors and unedited



Supplemental Figure 1. Hybrid Cloud Microservices System Architecture



Supplemental Figure 2. HuBMAP Consortium Website

Explore HRA data: ASCT+B Tables, VCCF Files, 2D FTU Illustrations, 3D Reference Objects, OMAPs, and route to the HuBMAP Data Portal

Explore HRA applications

Explore HRA user interfaces

Explore HRA learning modules, standard operating procedures, events and more

HuBMAP Human Reference Atlas

Human Reference Atlas
3D Multiscale Biomolecular Human Reference Atlas

The 6th Release of the Human Reference Atlas (v2.0) is now available! See what's new in [HRA v2.0 in our Release Notes](#).

A Human Reference Atlas (HRA) is a comprehensive, high-resolution, three-dimensional atlas of all the cells in the healthy human body. The Human Reference Atlas provides standard terminologies and data structures for describing specimens, biological structures, and spatial positions linked to existing ontologies.

Map the human body at single-cell resolution

Learn more about the thousands of experts building the Human Reference Atlas.

Read the flagship paper of the Human Reference Atlas (HRA) published in *Nature Cell Biology*

Click the carousel buttons to view more slides about the HRA

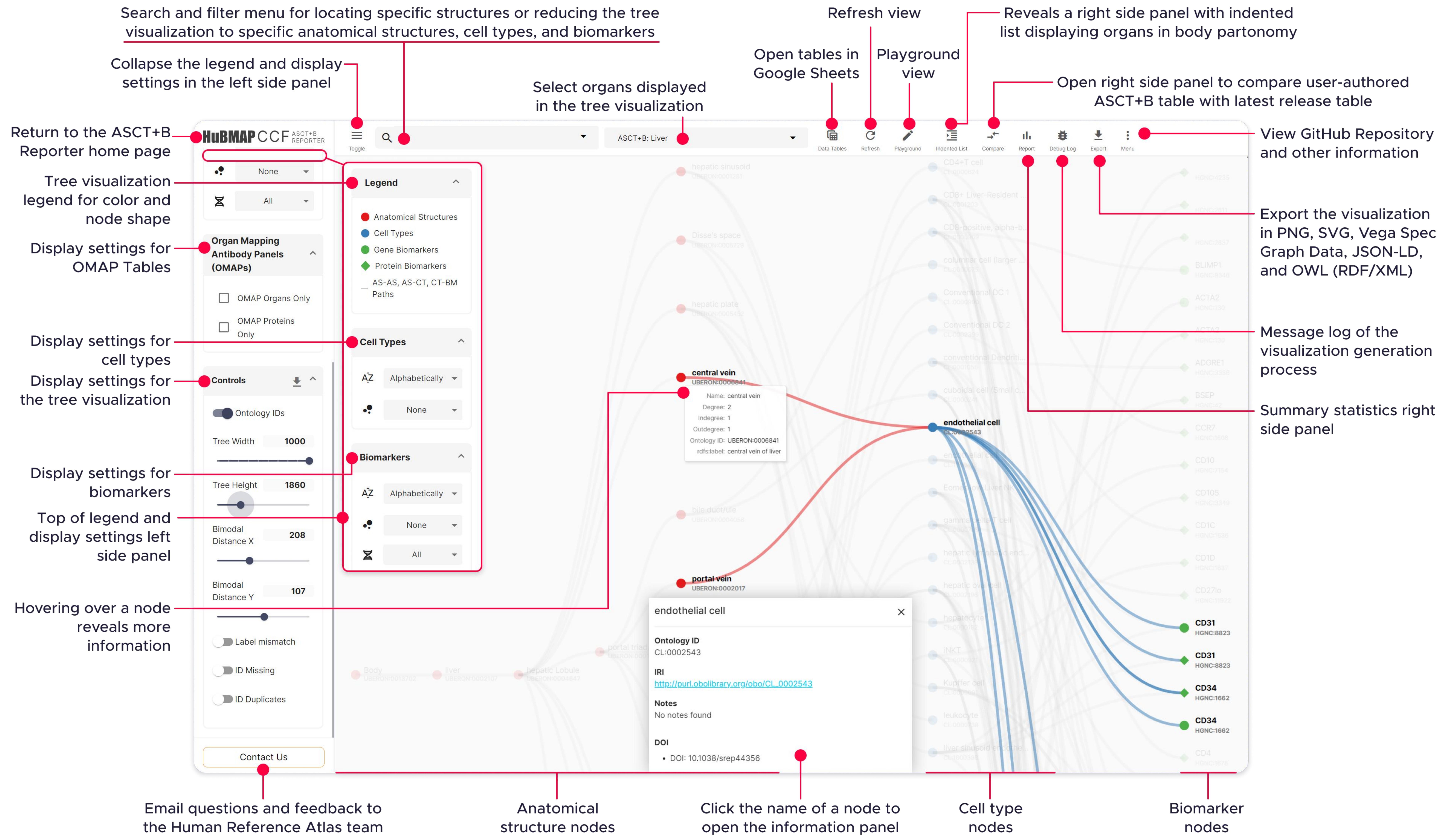
Metrics of the evolving Human Reference Atlas

Learn about the HRA team and editorial board

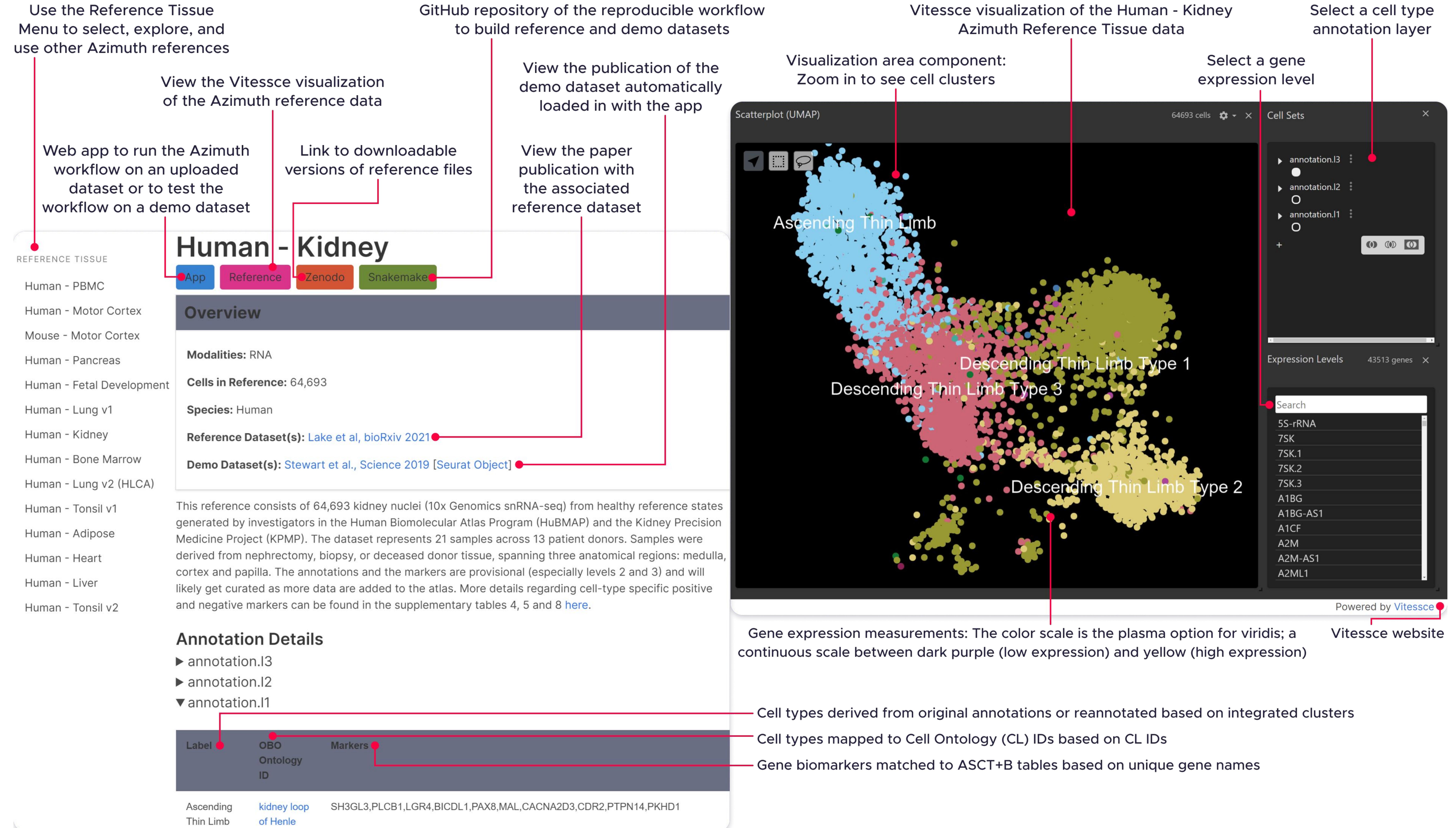
Access detailed release notes

A figure from the HRA flagship paper


Supplemental Figure 3. Human Reference Atlas Portal



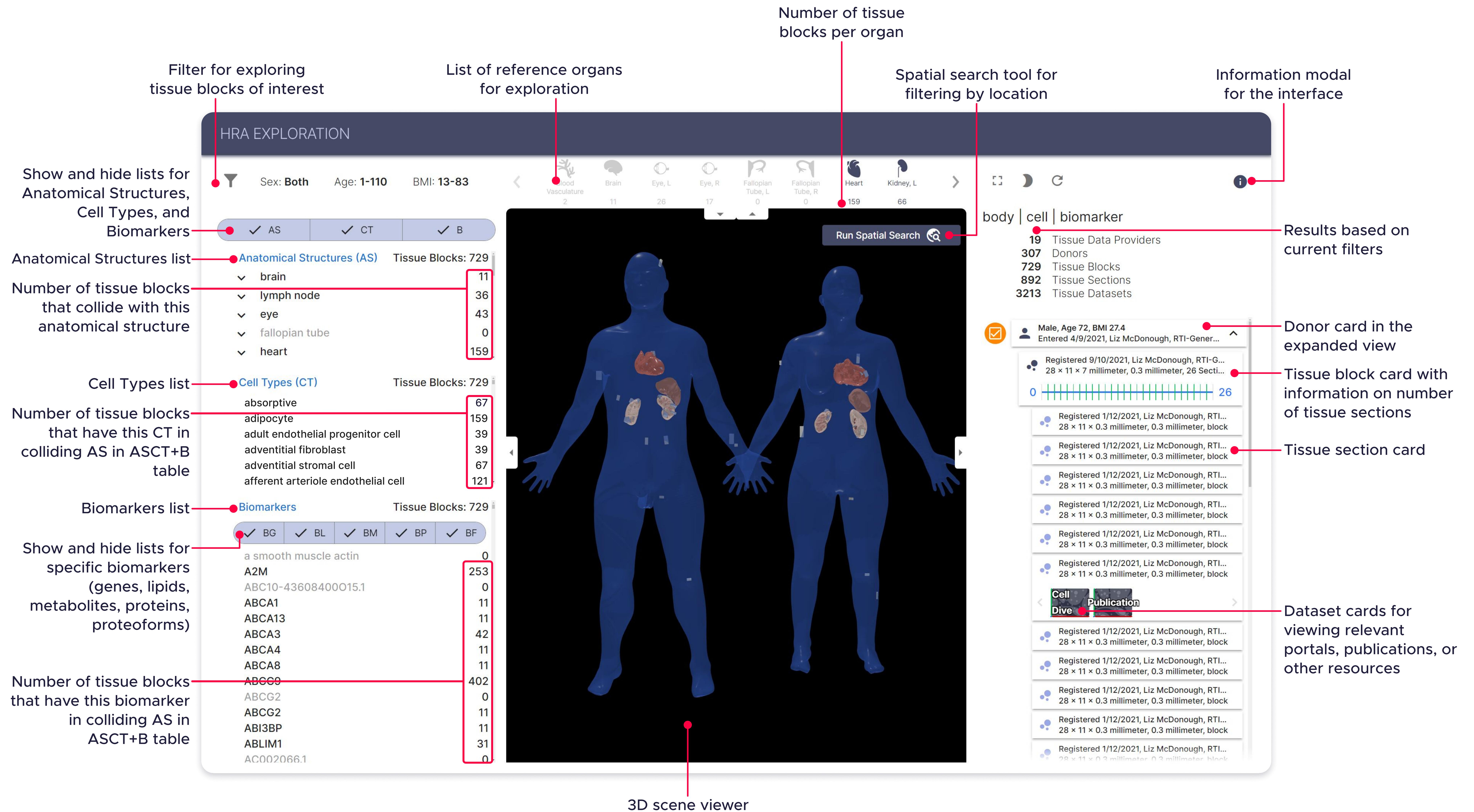
Supplemental Figure 4: ASCT+B Reporter User Interface



Supplemental Figure 5. Azimuth Portal and Reference Explorer User Interface



Supplemental Figure 6. Registration User Interface (RUI)



Supplemental Figure 7: Exploration User Interface (EUI)

HuBMAP HRA EXPLORATION

LOGIN

The figure displays the HuBMAP HRA Exploration interface. At the top, a navigation bar includes a filter icon, sex and age/bmi filters (Sex: Both, Age: 1-110, BMI: 13-83), and a search bar with icons for blood vessels, brain, eyes, heart, kidneys, and knee/large intestine. Below the filter bar is a table of tissue counts:

| Tissue Type | Count |
|-------------------|-------|
| Blood Vascular | 0 |
| Brain | 0 |
| Eye, L | 0 |
| Eye, R | 0 |
| Fallopian Tube, L | 0 |
| Fallopian Tube, R | 0 |
| Heart | 24 |
| Kidney, L | 64 |
| Kidney, R | 54 |
| Knee, L | 2 |
| Knee, R | 10 |
| Large Intestine | 51 |

Below the table are three tabs: Anatomical Structures (AS), Cell Types (CT), and Biomarkers. The AS tab shows a list of anatomical structures with their counts:

| Anatomical Structure | Count |
|----------------------|-------|
| brain | 0 |
| lymph node | 35 |
| eye | 0 |
| fallopian tube | 0 |
| heart | 24 |
| kidney | 118 |

The CT tab shows a list of cell types with their counts:

| Cell Type | Count |
|-------------|-------|
| absorptive | 65 |
| absorptive | 57 |
| adipocyte | 83 |
| adipocyte | 12 |
| adipocyte | 24 |
| adipocyte 1 | 0 |

The Biomarkers tab shows a list of biomarkers with their counts:

| Biomarker | Count |
|-----------------------|-------|
| a smooth muscle actin | 0 |
| A2M | 114 |
| ABC10-43608400015.1 | 0 |
| ABCA1 | 0 |
| ABCA13 | 0 |
| ABCA3 | 10 |
| ABCA4 | 0 |
| ABCA8 | 0 |
| ABCC9 | 211 |
| ABCG2 | 0 |
| ABCG2 | 0 |
| ABI3BP | 0 |
| ABLIM1 | 31 |
| AC002066.1 | 0 |

In the center, two blue human silhouettes are shown from the front, with various tissue blocks represented as colored shapes (red/orange, yellow, green) distributed across their bodies, indicating their spatial distribution.

On the right side, a sidebar lists "body | cell | biomarker" categories and their counts:

- 7 Tissue Data Providers
- 140 Donors
- 446 Tissue Blocks
- 856 Tissue Sections
- 2359 Tissue Datasets

Below this is a list of donor entries, each with a checkbox and details:

- Female, Age 67, BMI 30.2
Entered 12/27/2019, Yiling Lin, TMC-Stanford
- Female, Age 67, BMI 30.2
Entered 12/27/2019, Yiling Lin, TMC-Stanford
- Female, Age 14, BMI 19.7
Entered 2/16/2020, Marda Jorgensen, TMC-F...
- Female, Age 54
Entered 11/30/2021, Amanda Knoten, TMC-U...
- Female, Age 21, BMI 37.1
Entered 10/19/2020, Marda Jorgensen, TMC-...
- Male, Age 18, BMI 27.1
Entered 2/17/2020, Marda Jorgensen, TMC-F...
- Male, Age 47
Entered 8/3/2022, Marda Jorgensen, TMC-FI...
- Male, Age 18, BMI 27.1
Entered 2/17/2020, Marda Jorgensen, TMC-F...
- Male, Age 18, BMI 25.5
Entered 2/16/2020, Marda Jorgensen, TMC-F...
- Male, Age 20
Entered 6/6/2022, Marda Jorgensen, TMC-FI...
- Male, Age 45, BMI 33.1
Entered 12/11/2020, Yiling Lin, TMC-CalTech
- Male, Age 56, BMI 32.5
Entered 12/26/2019, Jamie Allen, TMC-Vande...
- Male, Age 43, BMI 41.3
Entered 2/10/2021, Yiling Lin, TMC-CalTech
- Male, Age 38, BMI 29.0
Entered 9/7/2021, Daniel Cotter, TMC-Stanford
- Male, Age 78, BMI 35.1
Entered 2/19/2020, Yiling Lin, TMC-Stanford
- Male, Age 78, BMI 35.1
Entered 2/19/2020, Yiling Lin, TMC-Stanford
- Male, Age 56
Entered 8/24/2022, Melissa Olmer, TMC-UCo...

SenNet

Sex: Both

Age: 1-110

BMI: 13-83

| | | |
|--|-------------------|---|
| | Blood Vasculation | 0 |
| | Brain | 0 |
| | Eye, L | 0 |
| | Eye, R | 0 |
| | Fallopian Tube, L | 0 |
| | Fallopian Tube, R | 0 |
| | Heart | 0 |
| | Kidney, L | 0 |

AS CT B

Anatomical Structures (AS)

- brain
- lymph node
- eye
- fallopian tube
- heart

Tissue Blocks: 2

Run Spatial Search

Cell Types (CT)

- absorptive
- absorptive
- adipocyte
- adipocyte
- adipocyte

Tissue Blocks: 2

Biomarkers

BG BL BM BP BF

a smooth muscle actin

A2M

ABC10-43608400015.1

ABCA1

ABCA13

ABCA3

ABCA4

ABCA8

ABCC9

ABCG2

ABCG2

ADAM22

body | cell | biomarker

1 Tissue Data Providers

2 Donors

2 Tissue Blocks

2 Tissue Sections

4 Tissue Datasets

Male, Age 37

Entered 11/4/2022, Matthew Wyczalkowski, W...

Registered 5/11/2023, Matthew Wyczalkowski...

20 x 15 x 10 millimeter, 10 millimeter, 1 Sections

Registered 4/27/2023, Matthew Wyczalko...

20 x 15 x 10 millimeter, 10 millimeter, Block

Female, Age 69

Entered 4/20/2023, Matthew Wyczalkowski, ...

Registered 5/11/2023, Matthew Wyczalkowski...

20 x 15 x 10 millimeter, 10 millimeter, 1 Sections

Registered 4/20/2023, Matthew Wyczalko...

20 x 15 x 10 millimeter, 10 millimeter, Block

GTEx Portal

Home Downloads Expression Single Cell QTL IGV Browser Tissues & Histology Documentation

Search Gene or SNP ID...

GTEx tissue sites mapped to the HuBMAP Human Reference Atlas

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

Anatomical Structures (AS) Tissue Blocks: 475

- ✓ brain
- ✓ lymph node
- ✓ eye
- ✓ fallopian tube

Cell Types (CT)

- absorptive
- absorptive
- adipocyte
- adipocyte
- adipocyte

Biomarkers Tissue Blocks: 475

- ✓ BG ✓ BL ✓ BM ✓ BP ✓ BF
- a smooth muscle actin
- A2M
- ABC10-43608400015.1
- ABCA1
- ABCA13
- ABCA3
- ABCA4
- ABCA8
- ABCC9
- ABCG2
- ARCG2

Blood Vasculation 2

Brain 0

Eye, L 0

Eye, R 0

Fallopian Tube, L 0

Fallopian Tube, R 0

Heart 28

Kidney, L 66

Run Spatial Search

body | cell | biomarker

8 Tissue Data Providers

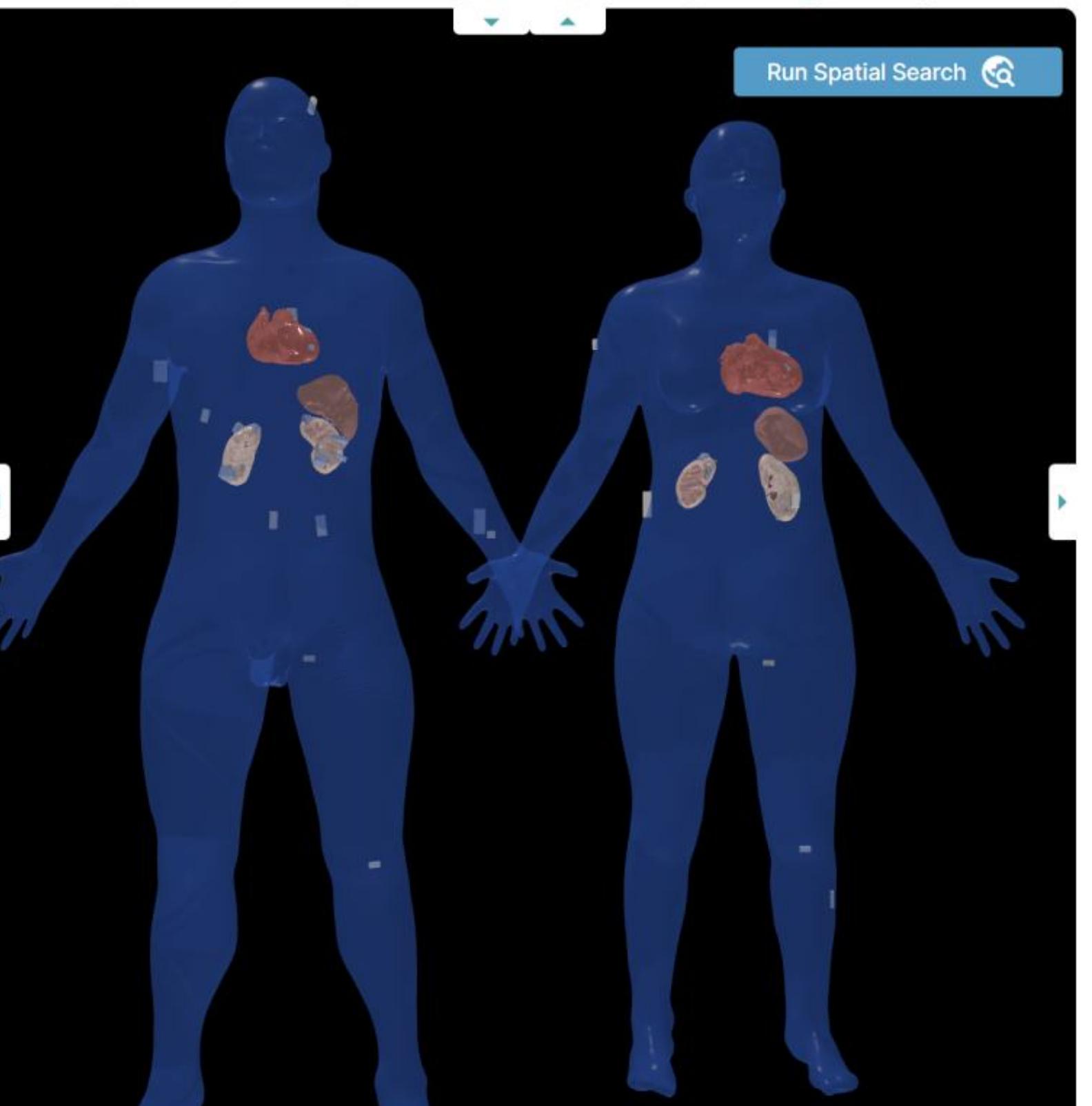
169 Donors

475 Tissue Blocks

856 Tissue Sections

2394 Tissue Datasets

- Females (n=94), Mean Age 53.5 (range 21-70)
Entered 1/26/2022, Kristin Ardlie, GTEx Project
- Males (n=146) Mean Age 54.3 (range 20 - 70)
Entered 1/26/2023, Kristin Ardlie, GTEx Project
- Females (n=297), Mean Age ? (range 20-79)
Entered 9/17/2021, Kristin Ardlie, GTEx Project
- Females (n=133) Mean Age 51.7 (range 21 - 7...
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Males (n=240) Mean Age 52.3 (range 20 - 70)
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Males (n=259) Mean Age 50.3 (range 21 - 70)
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Females (n=136) Mean Age 55 (range 21 - 70)
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Males (n=293) Mean Age 56.4 (range 20 - 70)
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Females (n=138) Mean Age 53.2 (range 21 - ...
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Males (n=294) Mean Age 54.9 (range 20 - 70)
Entered 5/18/2021, Kristin Ardlie, GTEx Project
- Females (n=19) Mean Age 56.4 (range 30 - 69)
Entered 9/17/2021, Kristin Ardlie, GTEx Project



The interface displays two 3D human silhouettes side-by-side, each showing various internal organs represented as colored 3D models. The organs include the heart, lungs, liver, kidneys, and intestines. The count of tissue blocks for each organ is listed above the corresponding silhouette.

Select Registration UI for new HRA 3D Coordinate 

X Close 

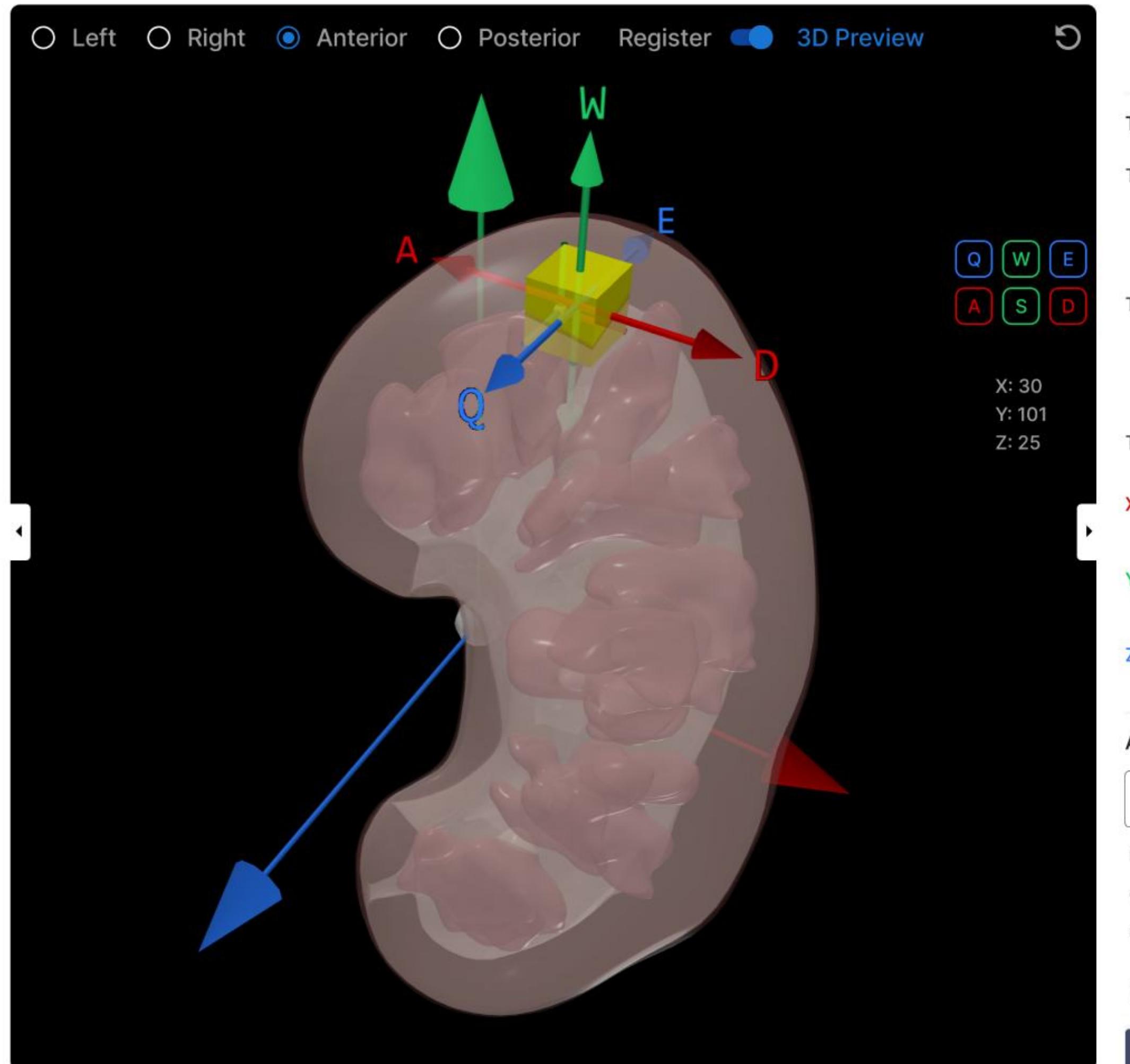
Anatomical Structures

Left Right Anterior Posterior Register  3D Preview 

 all anatomical structures
 kidney capsule
 hilum of kidney
 cortex of kidney
 renal column
 outer cortex of kidney
 renal medulla
 renal papilla
 renal pyramid

Landmarks

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



The central image shows a 3D rendering of a kidney with various anatomical features highlighted in different colors: green (kidney capsule, hilum, cortex), yellow (renal column), pink (outer cortex, renal medulla, renal papilla, renal pyramid), and red (bisection line, left renal artery, left renal pelvis, left renal vein, left ureter). A blue arrow points from the bottom left towards the renal papilla. A yellow cube labeled 'Q' is positioned near the renal papilla. A red arrow labeled 'D' points towards the renal pyramid. A green arrow labeled 'W' points upwards. A red arrow labeled 'A' points towards the renal capsule. A blue arrow labeled 'E' points towards the renal cortex. The background is black.

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

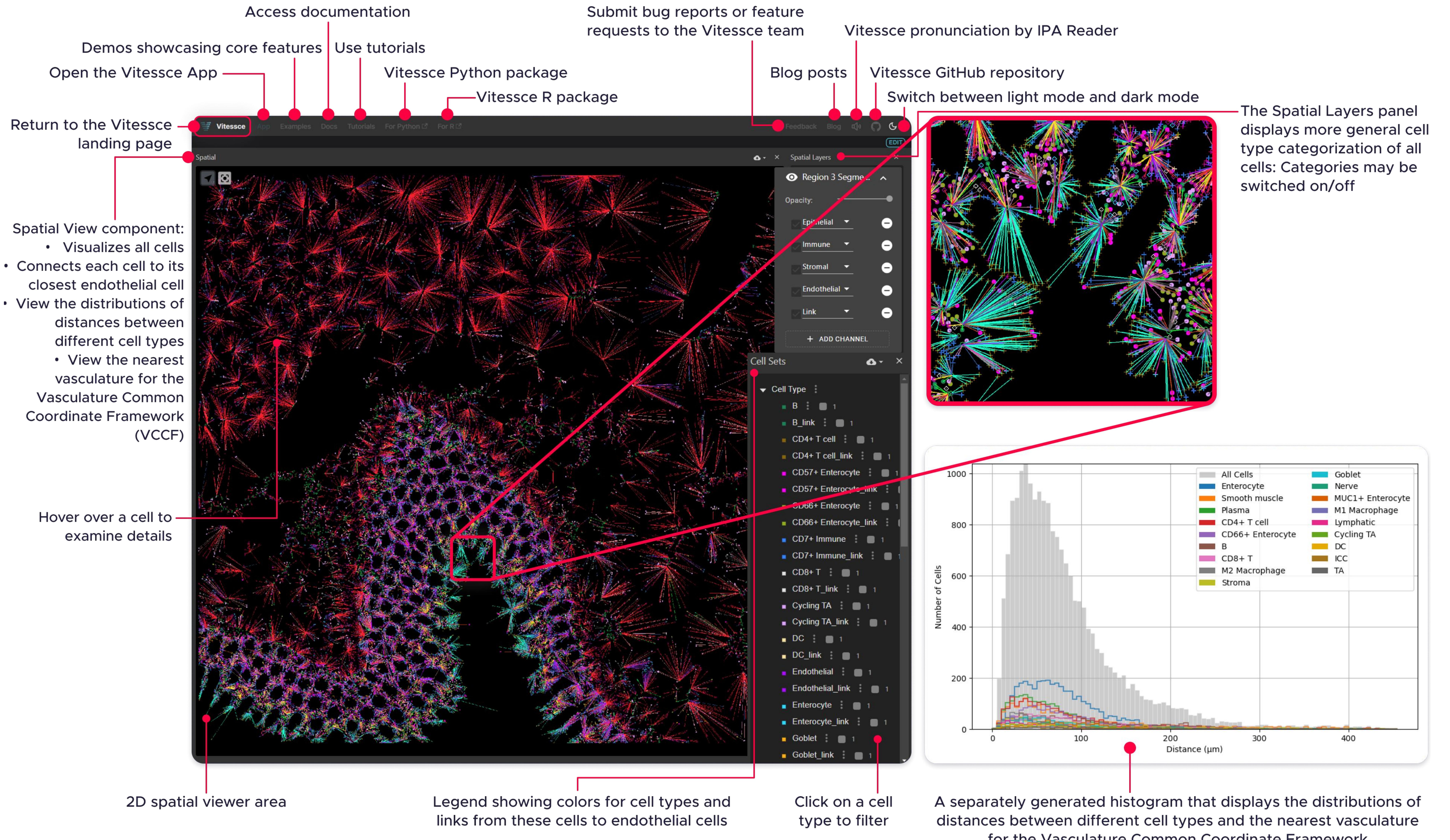
Add Anatomical Structures ... 

kidney capsule  cortex of kidney 
outer cortex of kidney  renal medulla 
renal pyramid 

 Assigned  Added

Review and Register

Supplemental Figure 8: Customized, Branded Deployment of EUI in HuBMAP, SenNet, GTEx, and RUI in GUDMAP



Supplemental Figure 9: Vasculature Common Coordinate Framework Distance Visualizations

Functional Tissue Units available for exploration

Name of the selected Functional Tissue Unit

2D Illustration viewer

Cell types by biomarkers table

Tabs to view tables for gene, protein, and lipids

Expand the table view

Cell types, cell counts, and associated biomarker columns

Hover for details on ontology IDs and expression values: Higher opacity means higher mean biomarker expression levels

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

Collapse and expand Functional Tissue Unit listings within organs

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

View the selected illustration digital object metadata page

Show/hide specific source datasets in the cell types by biomarkers tables

Download the selected illustration in various formats

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

Download Illustration

Illustration Metadata

FTU Library

renal corpuscle

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

thick ascending limb of loop of Henle

Large Intestine

crypt of Lieberkühn 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

Glomerular visceral epithelial cell

Parietal epithelial cell

Epithelial cell proximal tubule

Macula densa epithelia cell

Afferent arteriole endothelial cell

Efferent arteriole endothelial cell

Glomerular capillary endothelial cell

Glomerular mesangial cell

50 µm

Human Reference Atlas

Functional Tissue Unit Explorer

Cell Types by Gene Biomarkers

| Cell Type | Cell Count | A2M [ENSG000... | AASS [ENSG00... | AKAP9 [ENSG0... | AKT3 [ENSG00... | AKT3 [ENSG00... | ALDHIA2 [ENS... | ALS2CL [ENSG... | ANKRD36 [LENS... | ANKRD36 [LENS... | ANKRD36C [EN... |
|--------------------------------------|------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|-----------------|
| glomerular capillary endothelial ... | 344 | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● |
| glomerular mesangial cell | 99 | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● |
| glomerular visceral epithelial cell | 341 | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● |
| parietal epithelial cell | 266 | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● |

Cell Types by Protein Biomarkers

Cell Types by Lipid Biomarkers

FTU Explorer

Functional Tissue Unit Name: renal corpuscle

Uberon ID: <https://purl.humanatlas.io/2d-ftu/kidney-renal-corpuscle>

#Datasets: 1

Cell Type Name: parietal epithelial cell

CL ID: http://purl.obolibrary.org/obo/CL_1000452

Number of Cells: 266

Gene Name: ANKRD36 [ENSG00000291582]

HGNC ID: HGNC:1982

Mean Expression Value: 0.294899

Source Data

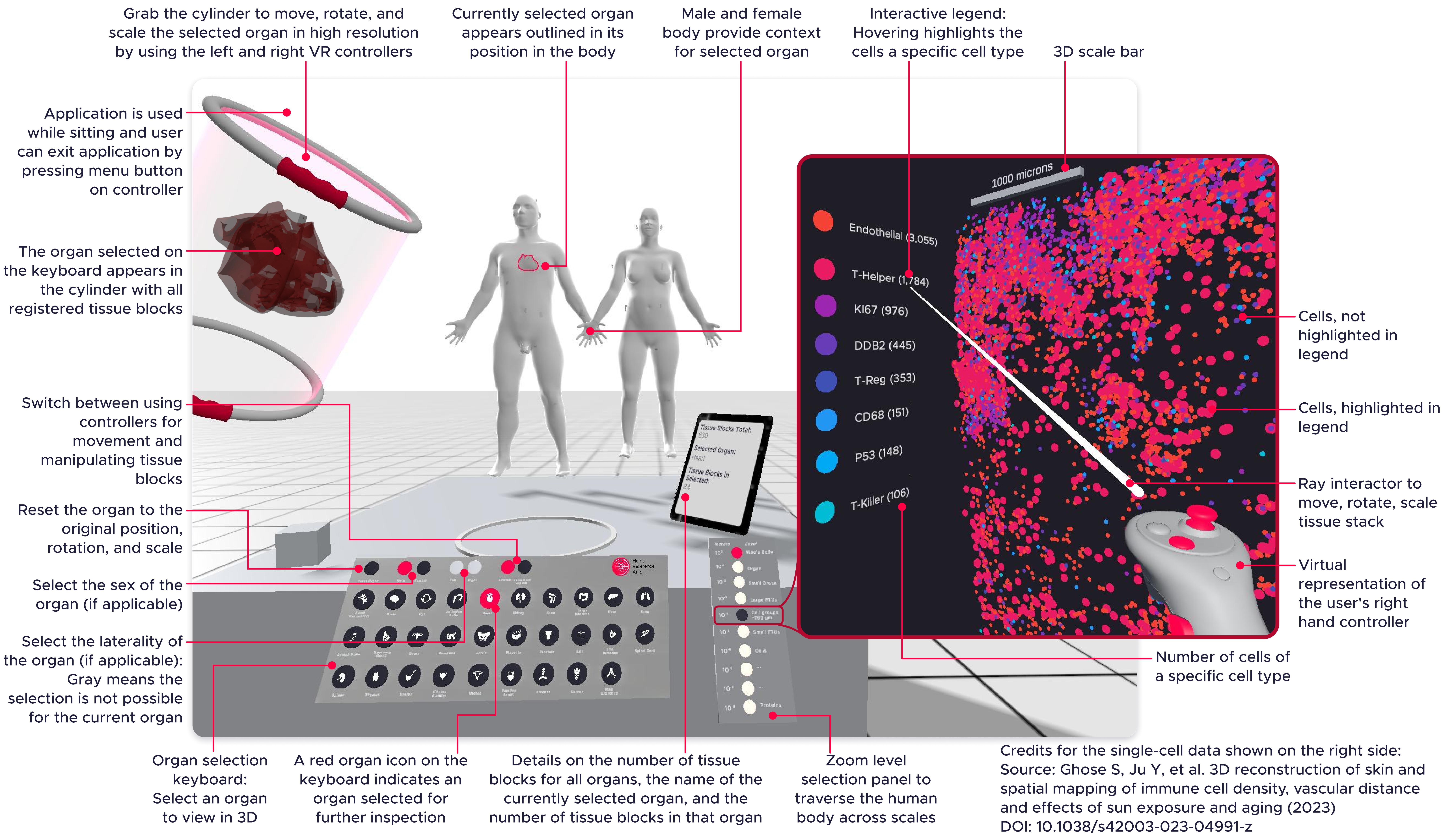
| <input checked="" type="checkbox"/> Authors | Year | Paper Title | Paper DOI |
|---|------|---------------------------------|---|
| Yoshiharu Muto, Parker C. ... | 2021 | Single cell transcriptional ... | https://doi.org/10.103... |

Sort source data by authors, year, paper title, and paper DOI

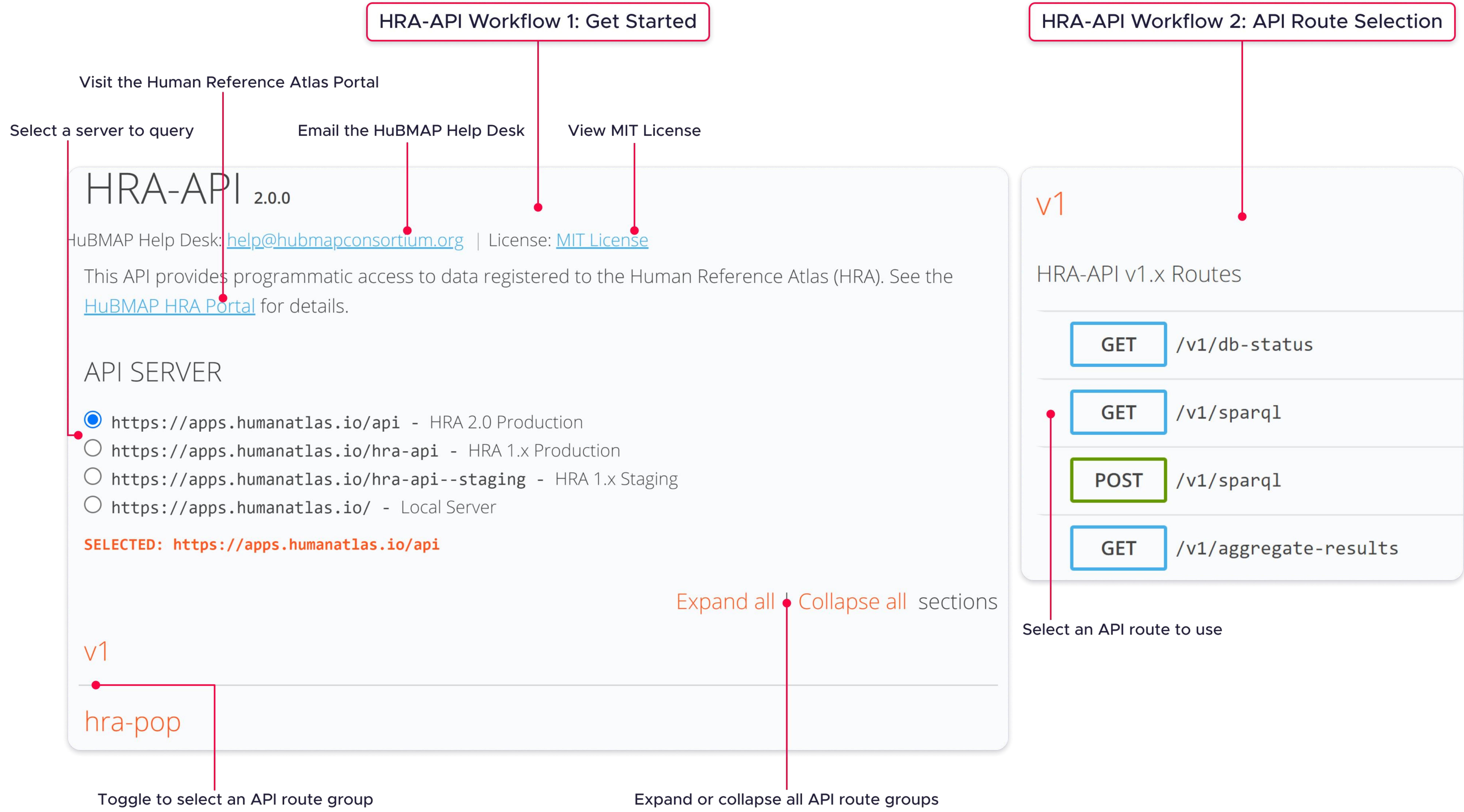
Publication title in which experimental data was published

Publication Digital Object Identifier URL linking directly to the experimental data

Supplemental Figure 10: Interactive FTU Explorer



Supplemental Figure 11: HRA Organ Gallery



Supplemental Figure 12: Human Reference Atlas Application Programming Interface: Get Started and API Route Selection

Input parameters for running an API query:

Fill in parameter values for the route

HRA-API Workflow 3: Run an API Query

v1

HRA-API v1.x Routes

GET /v1/db-status Get current status of database

GET /v1/sparql Run a SPARQL query

Run a SPARQL query

REQUEST

QUERY-STRING PARAMETERS

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

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

RESPONSE

200 404

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

EXAMPLE SCHEMA

[
]
]

application/json

Copy

FILL EXAMPLE

CLEAR

TRY

Select a response code to view example response and schema doc

Example response tab

Schema documentation tab for the response

Run the API query

Reset parameters

Fill parameters with example options

Supplemental Figure 13: Human Reference Atlas Application Programming Interface: Run an API Query

HRA-API Workflow 4: View Query Response

GET /v1/sparql
Run a SPARQL query

Run a SPARQL query

REQUEST

QUERY-STRING PARAMETERS

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

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

FILL EXAMPLE
CLEAR
TRY

View CURL command to reproduce query

View response headers

View real response from a query

RESPONSE

Response Status: 200
 Took 173 milliseconds

RESPONSE HEADERS

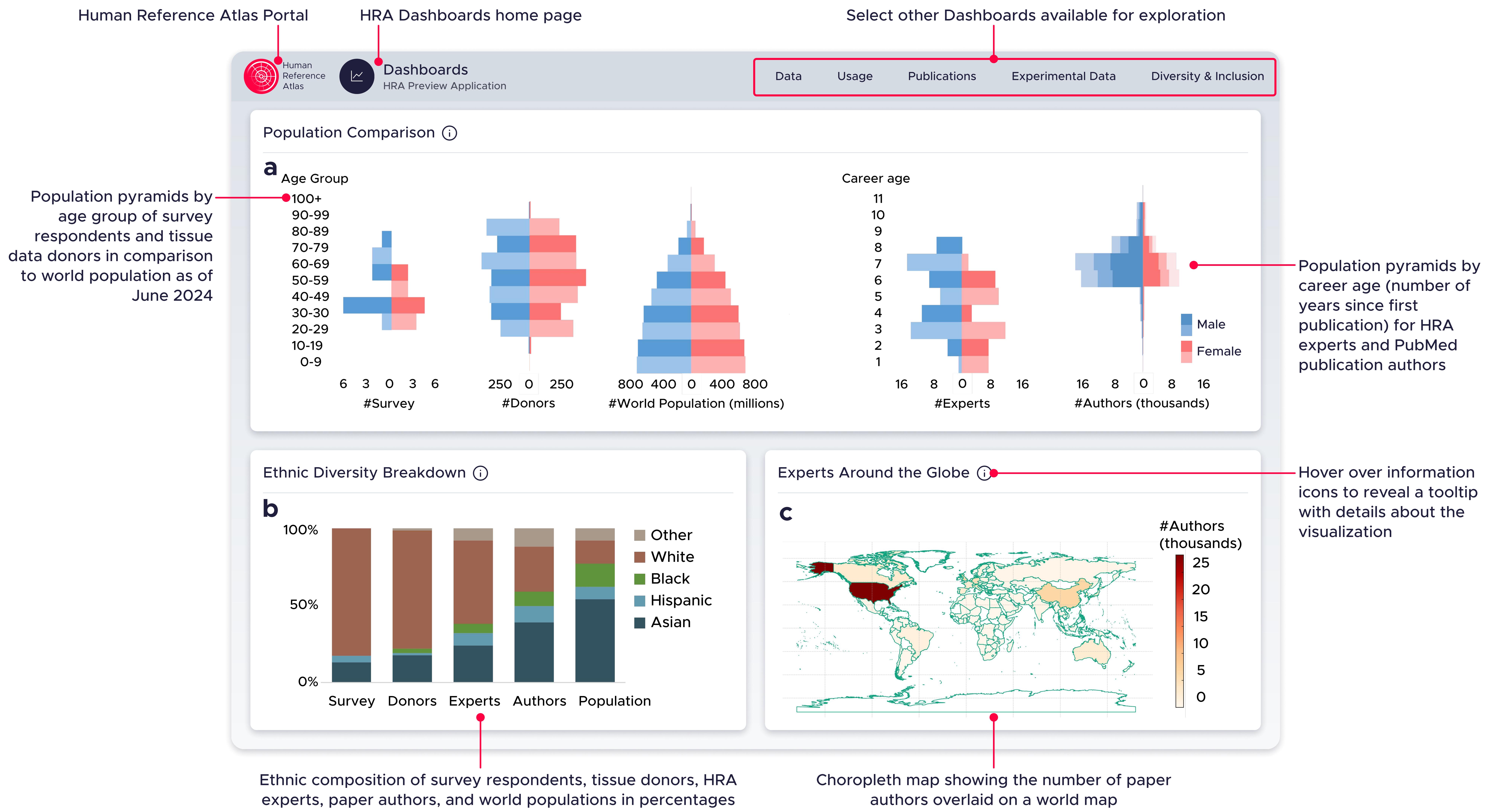
CURL

```
sub,pred,obj
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/1999/02/22-rdf-syntax-ns#type,http://www.w3.org/2002/07/owl#NamedIndi
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/1999/02/22-rdf-syntax-ns#type,http://www.w3.org/2004/02/skos/core#Cor
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/2000/01/rdf-schema#label,Laser ablation
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/2004/02/skos/core#broader,https://purl.humanatlas.io/vocab/hrav
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/2004/02/skos/core#definition,"Removal, separation, detachment, extirp
http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C111241,http://www.w3.org/2004/02/skos/core#inScheme,https://purl.humanatlas.io/vocab/hrav
```

CLEAR RESPONSE • Reset the response

Copy • Copy the response

Supplemental Figure 14: Human Reference Atlas Application Programming Interface: View Query Response



Supplemental Figure 15. HRA Equity Dashboard

Course navigation menu

Collapse the course navigation menu

Account menu

Canvas Dashboard:

- View all courses
- View to do list

View recent feedback

View course grades

View upcoming assignments

List of courses

View calendars for all Canvas courses

Message inbox

Recent user history log menu

Use the Kaltura API to link Kaltura media to Canvas

Opens the external TimelyCare app for 24/7 virtual care

Help menu to use Canvas Guides, asking your instructor a question, submitting feature ideas and feedback

Minimizes global navigation menu

Title of the current course being viewed

HuBMAP-VHMOOC

No Expiration

Download course in alternative formats, such as ePub and electronic braille

HuBMAP Visible Human MOOC

Goals

The Visible Human Massive Open Online Course (VHMOOC) aims to:

- Communicate tissue data acquisition and analysis,
- Demonstrate single-cell analysis and CCF mapping techniques, and
- Introduce major features of the HuBMAP portal.

1st HuBMAP Portal Release (Oct. 2020)

HuBMAP Overview

- Project Goals, Setup, and Ambitions

Tissue Data Acquisition and Analysis

- Behind the Scenes at Vanderbilt University

Biomolecular Data Harmonization

- An Introduction to Seurat

Recent activity of messages from discussions, grading updates, private messages between you and other users, and more

VHMOOC course calendar

View Course Stream

View Course Calendar

View Course Notifications

To Do

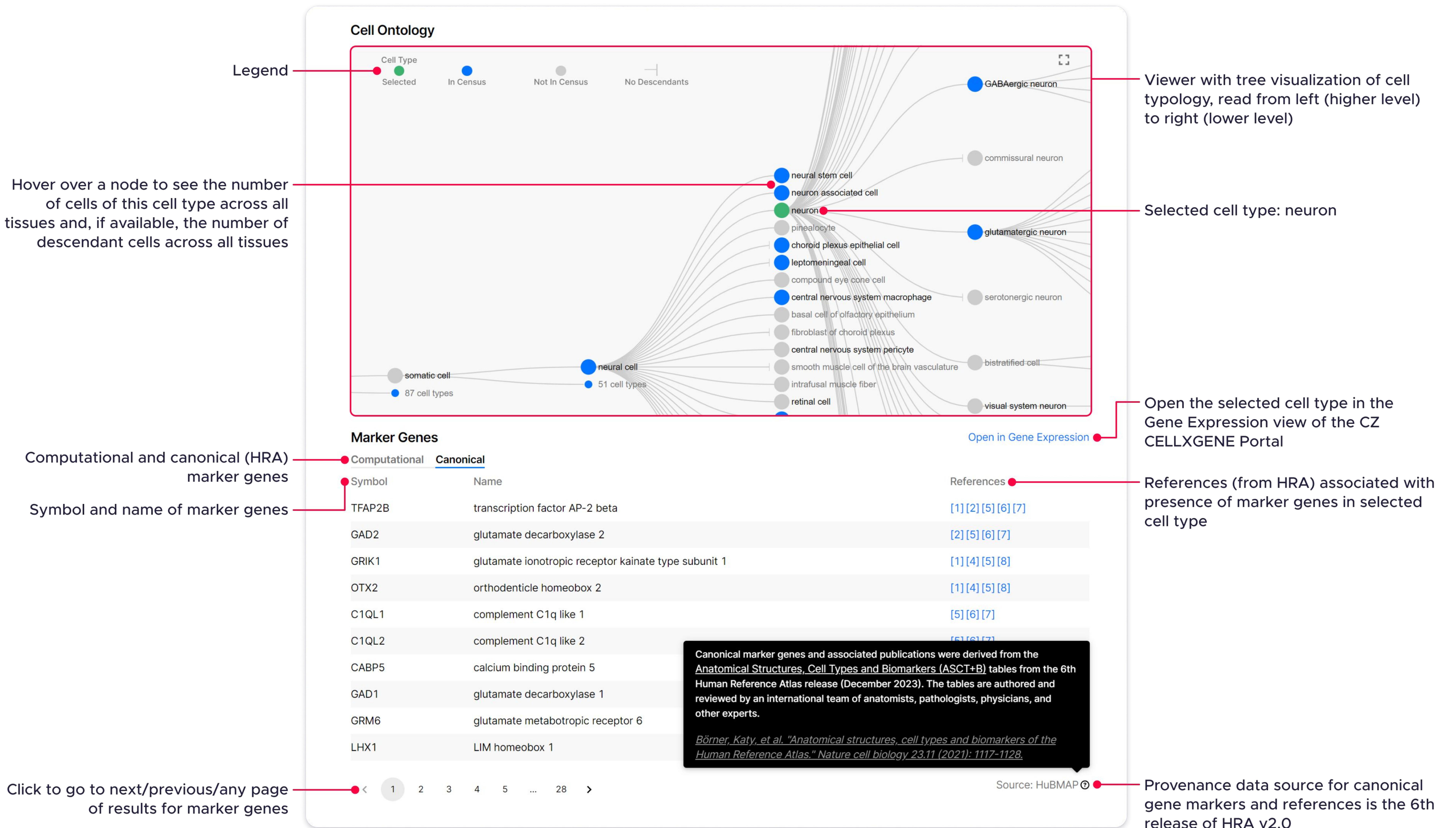
Nothing for now

Recent Feedback

Nothing for now

View and edit notification settings for this course

Supplemental Figure 16: Visible Human Massive Open Online Course (MOOC)



Supplemental Figure 17: CZ CellGuide Visualization With ‘Canonical’ Marker Genes And ‘References’ From The HRA