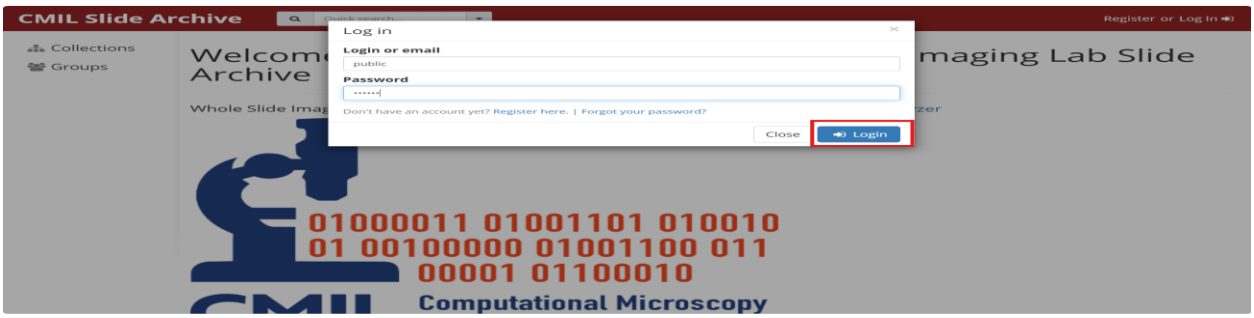
A User can access the Digital Slide Archive (DSA; https://athena.rc.ufl.edu/) by logging in as a public user with the following credentials: Login or email: public; password: public (see Supp. Fig. 1a-b).

Supp. Fig. 1a. Homepage of DSA, showing the Log In button located in the top-right corner.

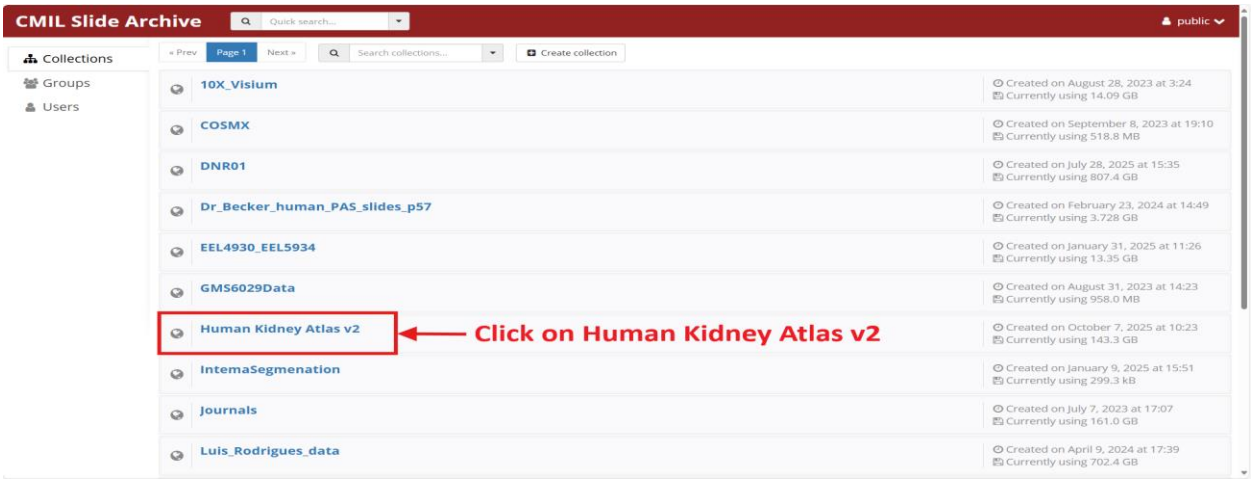


Supp. Fig. 1b. Login window of the DSA where users can enter the public credentials (*Login or email:* public; *Password:* public) to access the resources.

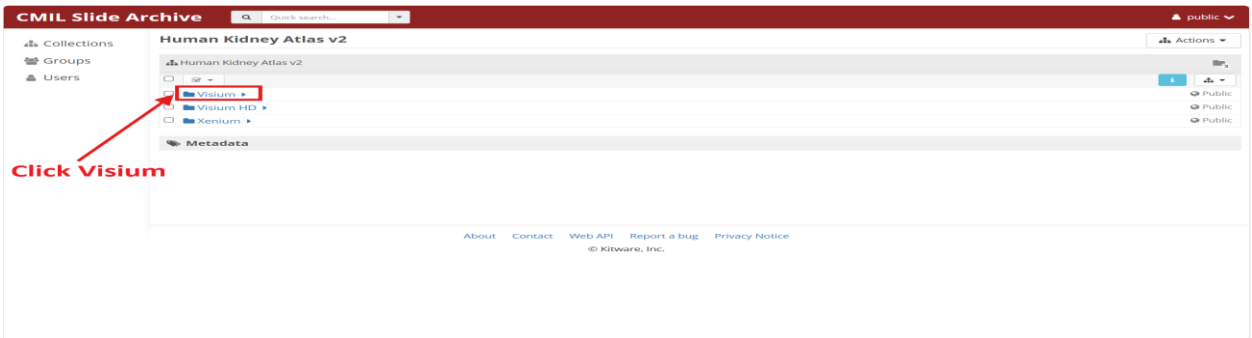
The Whole Slide Images (WSIs) can be accessed under the path: *Collections → Human Kidney Atlas v2 → Visium → Visium Frozen* (see Supp. Fig. 2a–e). To navigate, first click on Collections from the left-hand panel (see Supp. Fig. 2a). Then, select Human Kidney Atlas v2 from the list of available collections (see Supp. Fig. 2b). Within this collection, click on the Visium folder (see Supp. Fig. 2c), and then open the Visium Frozen directory (Supp. Fig. 2d) to view the list of available WSIs (see Supp. Fig. 2e).

Users can navigate through the list or use the Filter field to locate specific slides by entering a Patient ID in the filter box to filter and view slides belonging to that patient (see Supp. Fig. 2f).

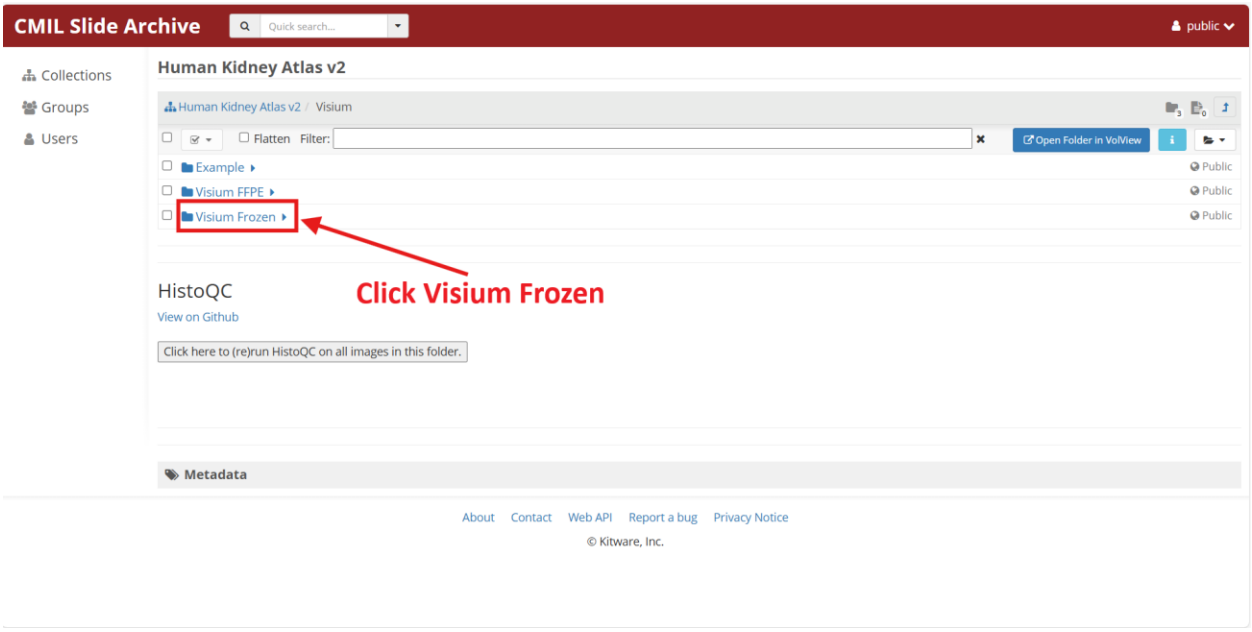
Supp. Fig. 2a. DSA homepage showing the Collections option in the left-hand panel, where users can begin navigation to access available datasets.



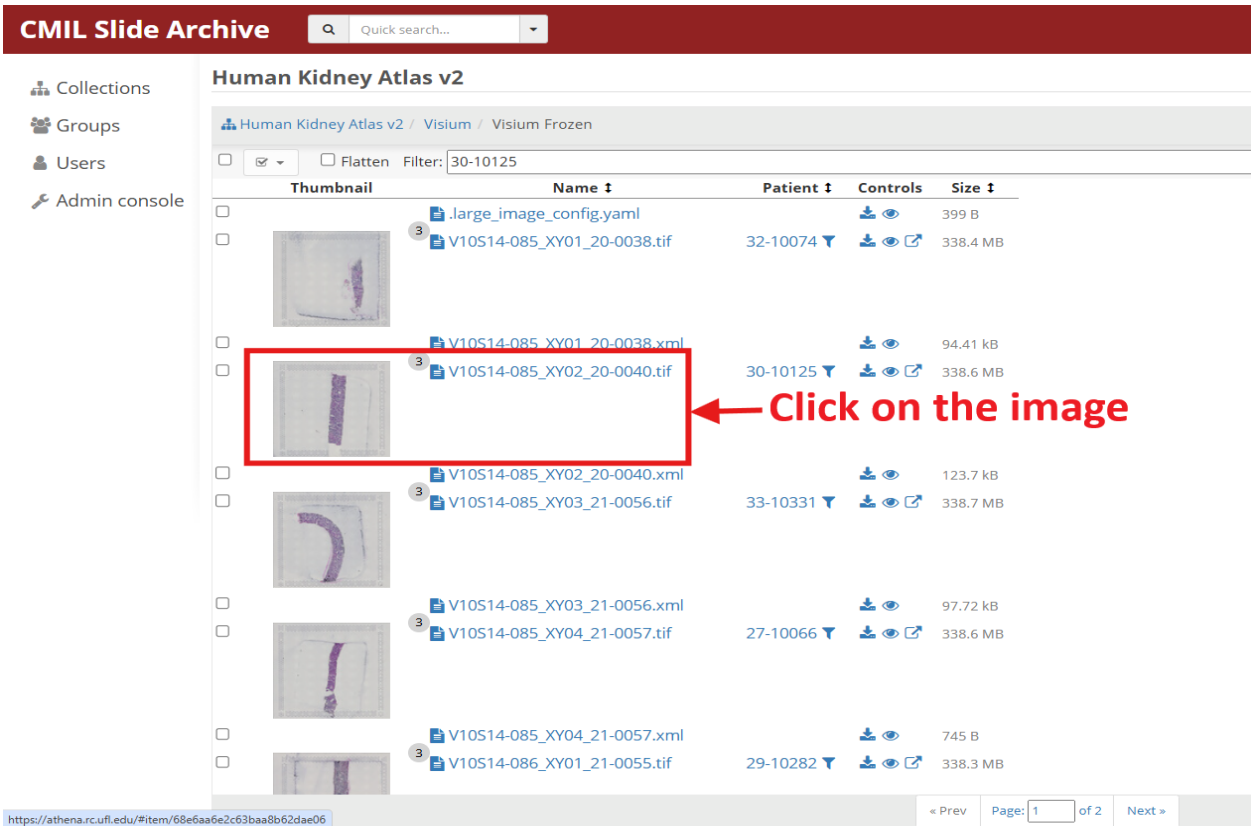
Supp. Fig. 2b. List of available collections in the DSA interface. The Human Kidney Atlas v2 collection is highlighted, containing multiple spatial transcriptomics datasets.



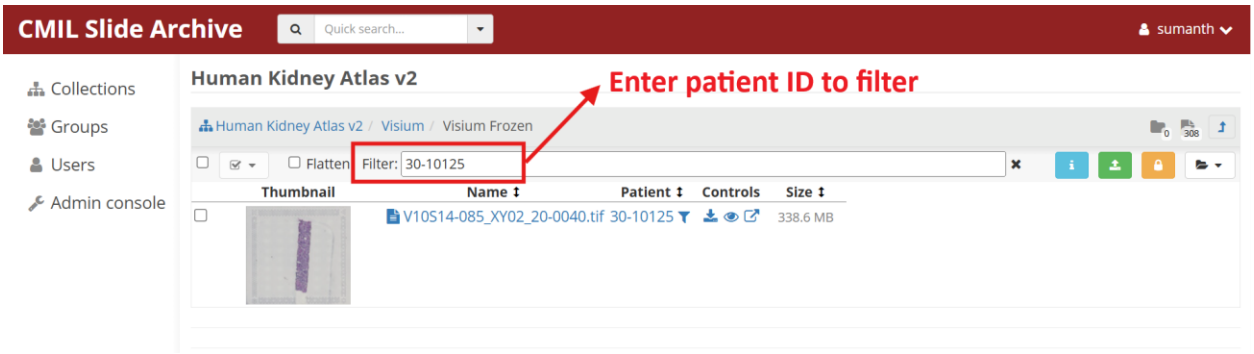
Supp. Fig. 2c. Directory view within the Human Kidney Atlas v2 collection showing subfolders for *Visium*, *Visium HD*, and *Xenium*. Click on the *Visium* folder to access the WSIs.



Supp. Fig. 2d. Within the *Visium* folder, click on the *Visium Frozen* directory to access the list of available WSIs and associated files.



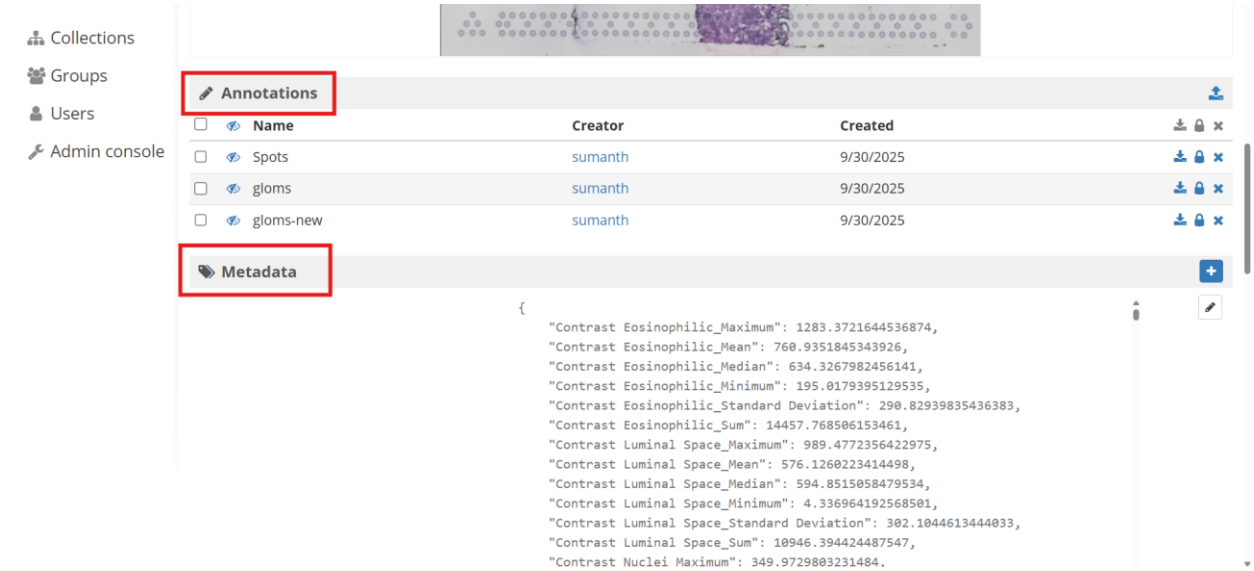
Supp. Fig. 2e. The *Visium Frozen* directory lists all available Whole Slide Images (WSIs) and associated files. Click on any image filename to view the corresponding WSI in the viewer interface.



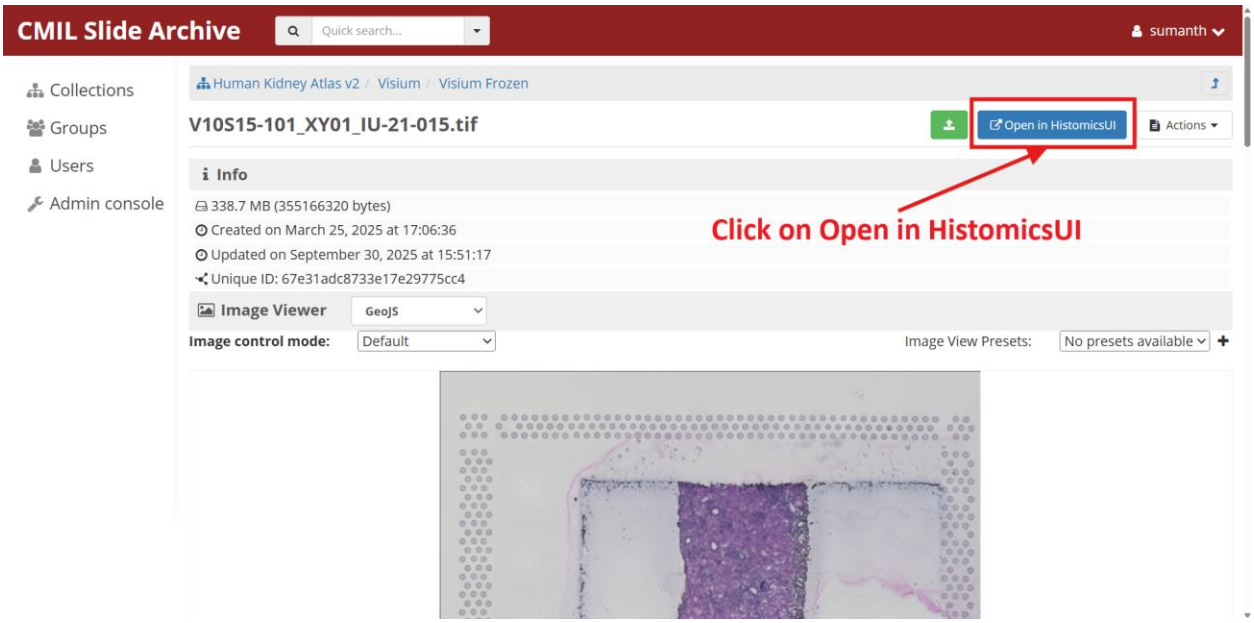
Supp. Fig. 2f. Users can filter slides by entering a specific Patient ID in the filter box, enabling quick access to WSIs corresponding to individual patients.

In addition to *Visium Frozen*, the Human Kidney Atlas v2 collection also includes other spatial transcriptomics datasets such as *Visium FFPE*, *Visium HD*, and *Xenium*, providing multiple modalities for integrated tissue analysis.

Selecting a WSI and clicking on its file name opens a dedicated page where the image is displayed along with its associated computational annotations (in JSON format) and image metadata, available under the Annotations and Metadata sections, respectively (see Supp. Fig. 3a). To interactively view the WSI, click the "Open in HistomicsUI" button located at the top right of the page (see Supp. Fig. 3b). In the HistomicsUI viewer, users can zoom in and out, navigate across the slide, and hover over different regions to examine various structures in fine detail.



Supp. Fig. 3a. Upon opening a WSI in a separate page, the associated computational segmentation data (downloadable in JSON format) and corresponding non-clinical metadata are accessible from the same interface.



Supp. Fig. 3b. The WSI can be viewed in HistomicsUI (a plugin for visualizing large-scale image data in the cloud via DSA) by clicking the "Open in HistomicsUI" button.

To visualize the computational annotations, the user can click the "Other" button under the *Annotations* tab, which expands to display three annotation files in JSON format (see Supp. Fig. 4a). Each annotation is listed with an eye icon next to its name; clicking this icon overlays the corresponding annotation boundaries on the WSI. For instance, when the *Spots* annotation is activated, the spatial spots become visible on the WSI (see Supp. Fig. 4b), and users can zoom in to explore each structure in greater detail. It is important to note that, since these annotations are rendered in the cloud for scalable visualization, loading may take a few seconds depending on the server's response time.

There are three available annotations: Spots, Gloms, and Gloms-new.

- The Spots annotation represents spatial transcriptomics spots, each containing cell-type composition information derived from transcriptomic data.
- The Gloms annotation corresponds to the segmented glomerular regions identified directly on the tissue.
- The Gloms-new annotation includes the same glomerular boundaries as Gloms, but with additional cell-type composition information that has been spatially aggregated from the surrounding *Spots* annotations. This integration was performed using the *Spatial Aggregation* plugin, enabling visualization of cell-type distributions within individual glomeruli.

For detailed information on the available cell types, subtypes, and their molecular markers, please refer to this sheet, which lists hierarchical subclass levels, cellular states, structures, and key distinguishing gene markers.

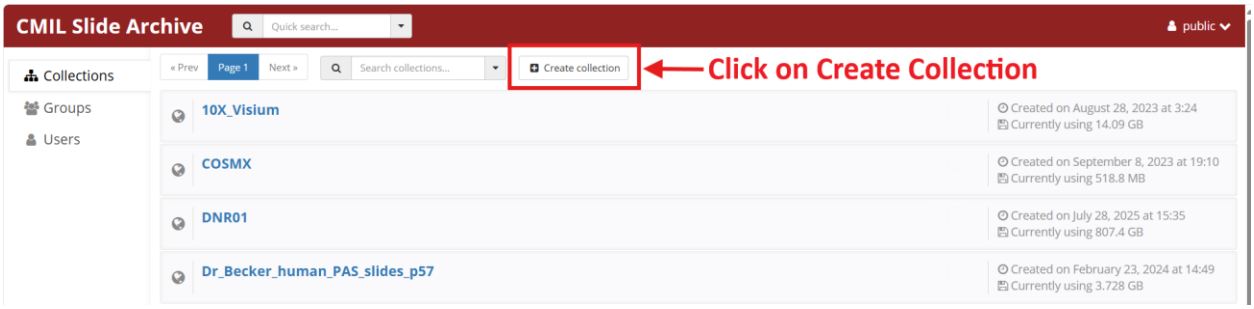
In addition to cell-type composition information, a set of 72 quantitative morphometric and intensity-based features is extracted for each annotated structure using the *Expanded Granular Feature Extraction* plugin. These features capture detailed histomorphometric properties such as object size, shape, color intensity, texture, and spatial organization of tissue components including nuclei, eosinophilic regions, and luminal spaces. These measurements provide a comprehensive representation of both molecular and morphological characteristics of each glomerulus or spot.

Supp. Fig. 4a. Annotations tab in HistomicsUI showing "Other" button expanded to reveal three available annotation files in JSON format.

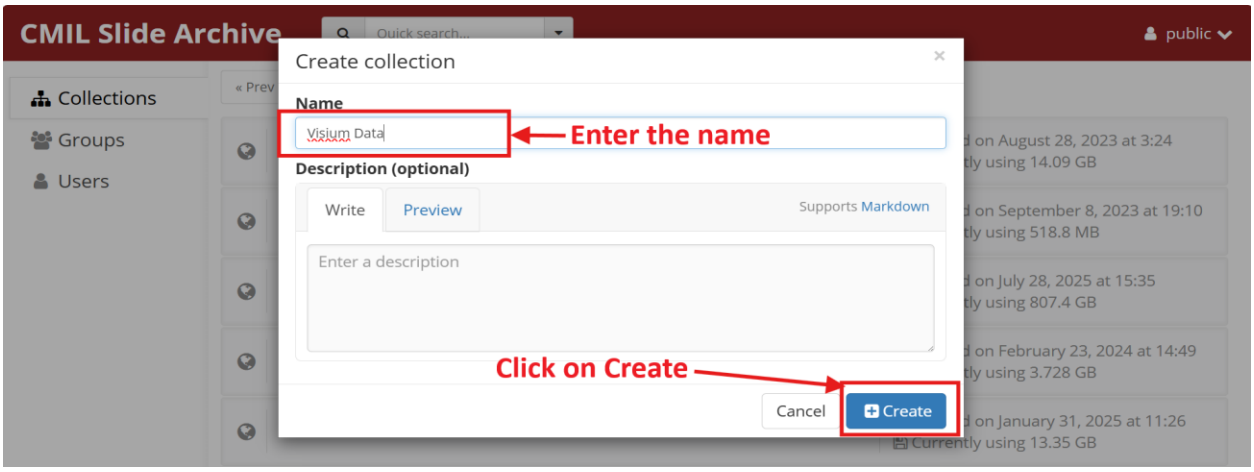
Supp. Fig. 4b. Visualization of spatial spot annotations overlaid on the WSI after activating the Spots layer; users can zoom in to examine individual structures in detail.

Users who wish to analyze the pre-uploaded Visium Frozen KPMP datasets described in the previous section (*Human Kidney Atlas v2* → *Visium* → *Visium Frozen*) may skip ahead to page 12, where the workflow for running analyses using the *Renal Path* and *Metadata Plot* plugins is detailed.

If the user wishes to upload their own data, they can create a new collection by selecting "Collections" from the menu on the left in DSA interface, clicking the "Create Collection" button (see Supp. Fig. 5a), and entering the desired name for the collection (see Supp. Fig. 5b). Once created, Whole Slide Images (WSIs) can be uploaded to the collection in either .svs or .tif format.

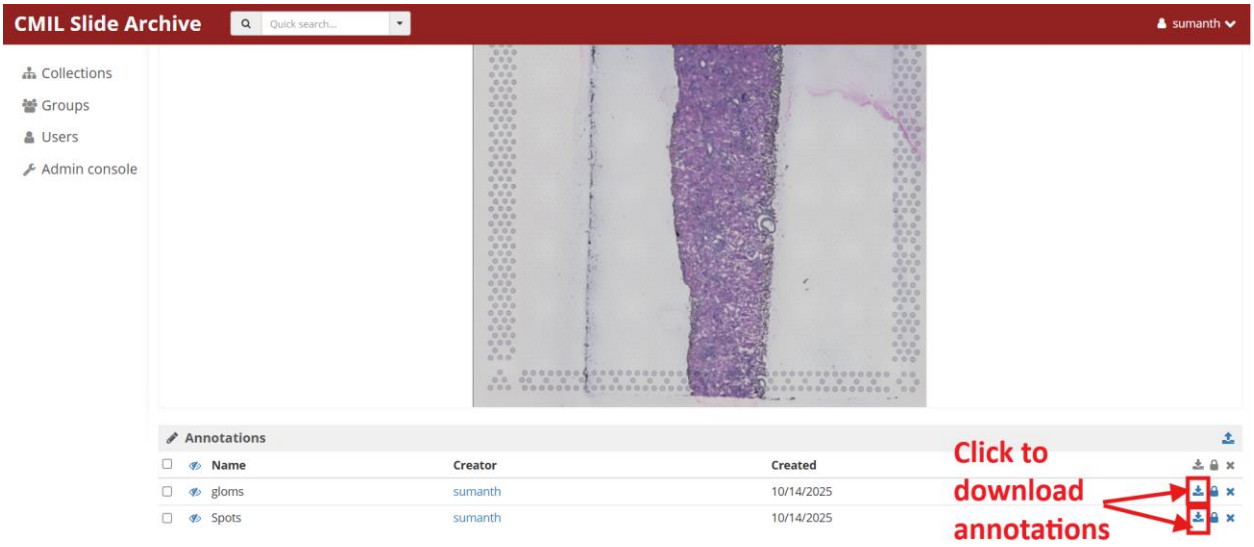


Supp. Fig. 5a. Create a new collection in the Digital Slide Archive (DSA) by selecting "Collections" from the left menu and clicking the "Create Collection" button.



Supp. Fig. 5b. Interface specifying the name and details of the newly created collection in the DSA before WSIs.

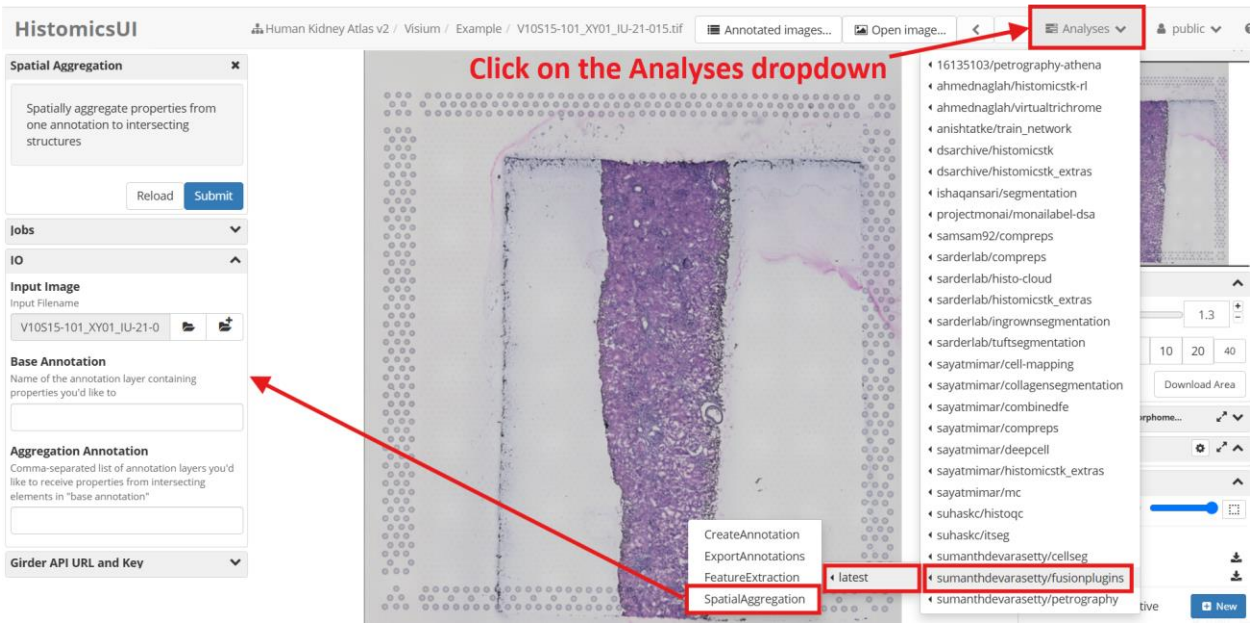
Each uploaded WSI should be associated with spot and glom annotations, which should follow a specific JSON structure to ensure compatibility with the visualization tools. To review the required format, users can visit this image and download the sample annotations by clicking on the download icon under the Annotations section (see Supp. Fig. 6). Each spot in the annotation should include cell-type information and related metadata consistent with the structure illustrated in the sample annotation.



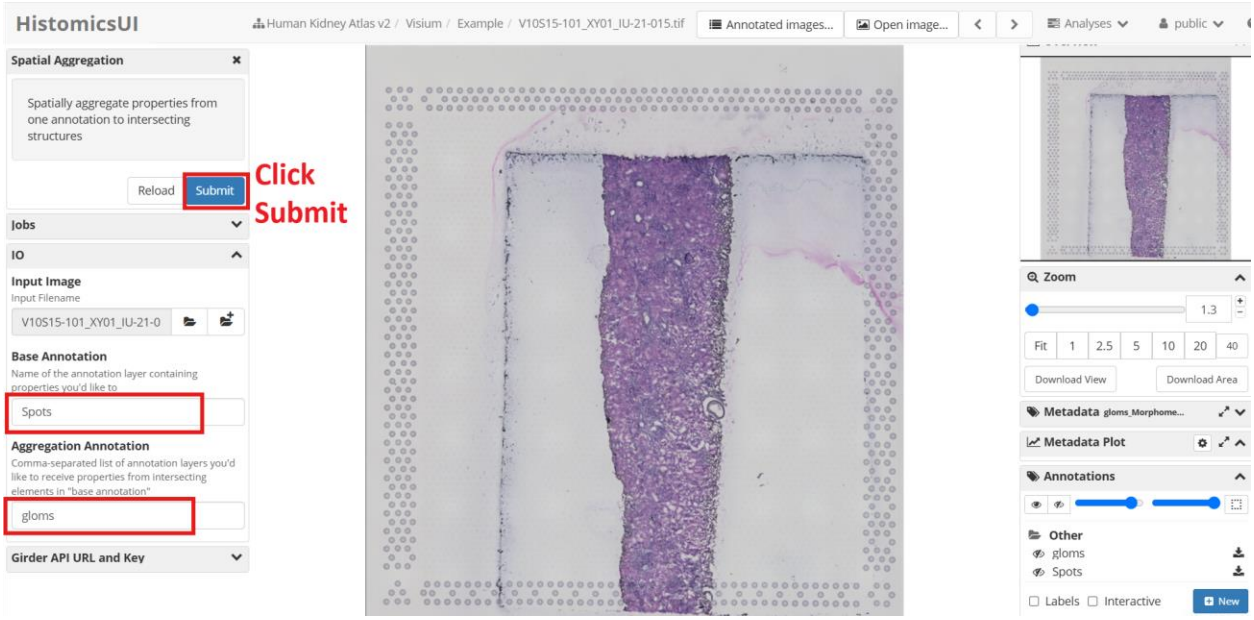
Supp. Fig. 6. Example of WSI in the DSA interface showing downloadable sample annotation files under the *Annotations* section, which illustrates the required JSON structure for spot and glom annotations.

Once the user has both spot annotations (with cell-type information) and glomerular annotations (gloms) in the required JSON format, they can perform spatial aggregation to integrate cell-type data with the glomerular regions.

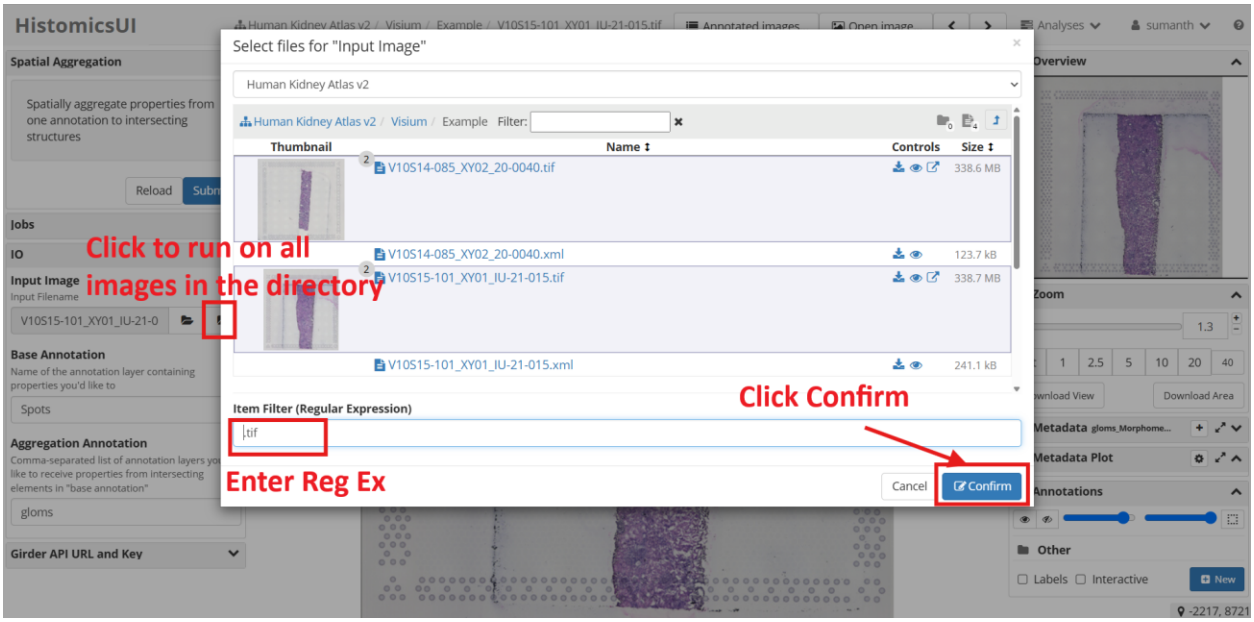
To do this, open the image in *HistomicsUI*, navigate to the Analyses drop-down menu, and select the Spatial Aggregation plugin located under *sumanthdevarasetty/fusionplugins:latest* (see Supp. Fig. 7a). The input image field will automatically populate with the currently opened WSI. Specify Spots as the *Base Annotation* and gloms as the *Aggregation Annotation*, then click Submit to execute the job (see Supp. Fig. 7b). Alternatively, users can run the Spatial Aggregation plugin on all WSIs within a directory by clicking the folder icon beside the input field, entering a regular expression (e.g., ".tif") to select all relevant images, and confirming the selection (see Supp. Fig. 7c).



Supp. Fig. 7a. Selection of the *Spatial Aggregation* plugin from the **Analyses** dropdown under *sumanthdevarasetty/fusionplugins:latest* in *HistomicsUI*.



Supp. Fig. 7b. Configuration panel of the *Spatial Aggregation* plugin showing the automatically populated *Input Image*, and manual entry of *Spots* as the Base Annotation and *gloms* as the Aggregation Annotation before clicking Submit to run the analysis on the currently opened WSI.

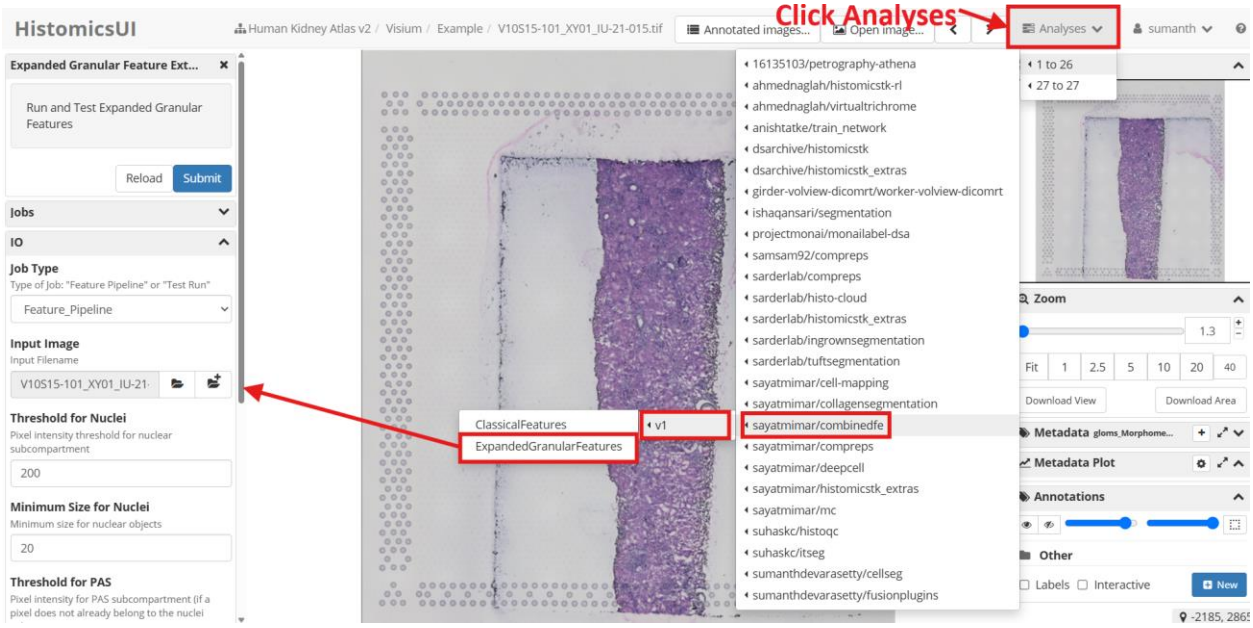


Supp. Fig. 7c. Option to run the *Spatial Aggregation* plugin on all WSIs within a directory by selecting the folder icon, entering a regular expression (e.g., ".tif"), and confirm to run the batch processing.

After the spatial aggregation process is completed, a new annotation layer named gloms-new is created, containing the glomerulus with aggregated cell-type composition information.

To extract the 72 morphometric and intensity-based features for each glomerulus, the user must run the Expanded Granular Feature Extraction plugin available under *sayatmimar/combinedfe:v1*.

From the Analyses menu, select this plugin (see Supp. Fig. 8a). In the input configuration panel, choose the desired input image or directory to process. To run the plugin on multiple WSIs, click the folder icon with a plus sign and follow the same steps illustrated earlier for running analyses on multiple images (see Supp. Fig. 7c). Next, expand the Girder API URL and Key section and enable the Annotations with Feature Data option on the left-hand side (see Supp. Fig. 8b). Finally, click Submit to run the feature extraction and obtain updated glomerular annotations with morphometric information.



Supp. Fig. 8a. Selection of the *Expanded Granular Feature Extraction* plugin under *sayatmimar/combinedfe:v1* from the Analyses dropdown in *HistomicsUI*.

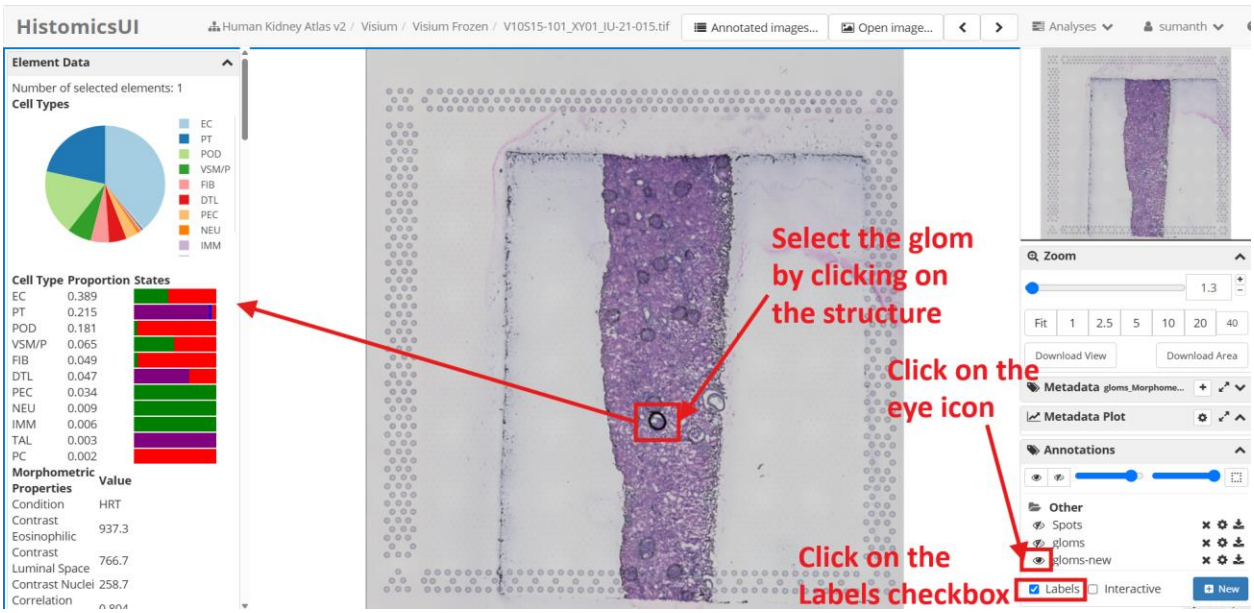
Supp. Fig. 8b. Configuration panel of the *Expanded Granular Feature Extraction* plugin showing the Girder API URL and Key dropdown with the Annotations with Feature Data option enabled prior to running the analysis.

Once the feature extraction process is completed, users can visualize both cell-type composition and morphometric feature values for any selected annotation directly within the HistomicsUI viewer.

By selecting an annotation (e.g., glomerulus) and enabling the Labels checkbox in the *Annotations* panel, a visualization panel appears on the left side of the screen (see Supp. Fig. 9).

This panel provides detailed quantitative summaries for the selected element (selected glomeruli in this case), including:

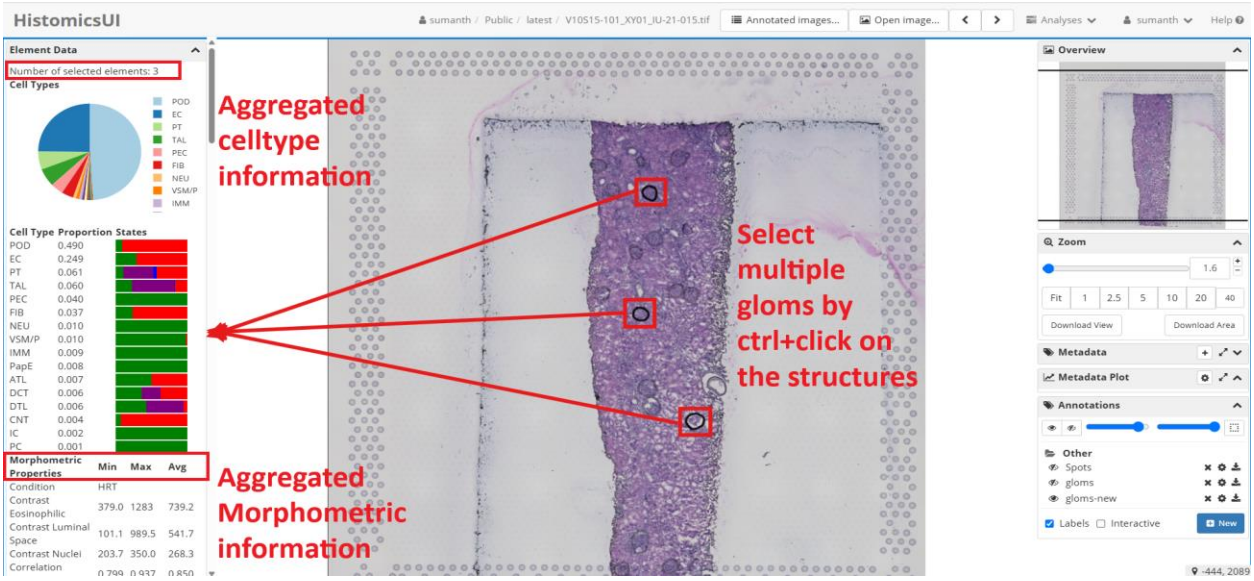
- A pie chart showing the relative proportions of major cell types (e.g., PT, TAL, POD, DCT).
- A color-coded bar chart representing cell-type proportion states.
- A table of morphometric properties, displaying 72 quantitative feature values related to *contrast*, *correlation*, *energy*, *area metrics, etc.*



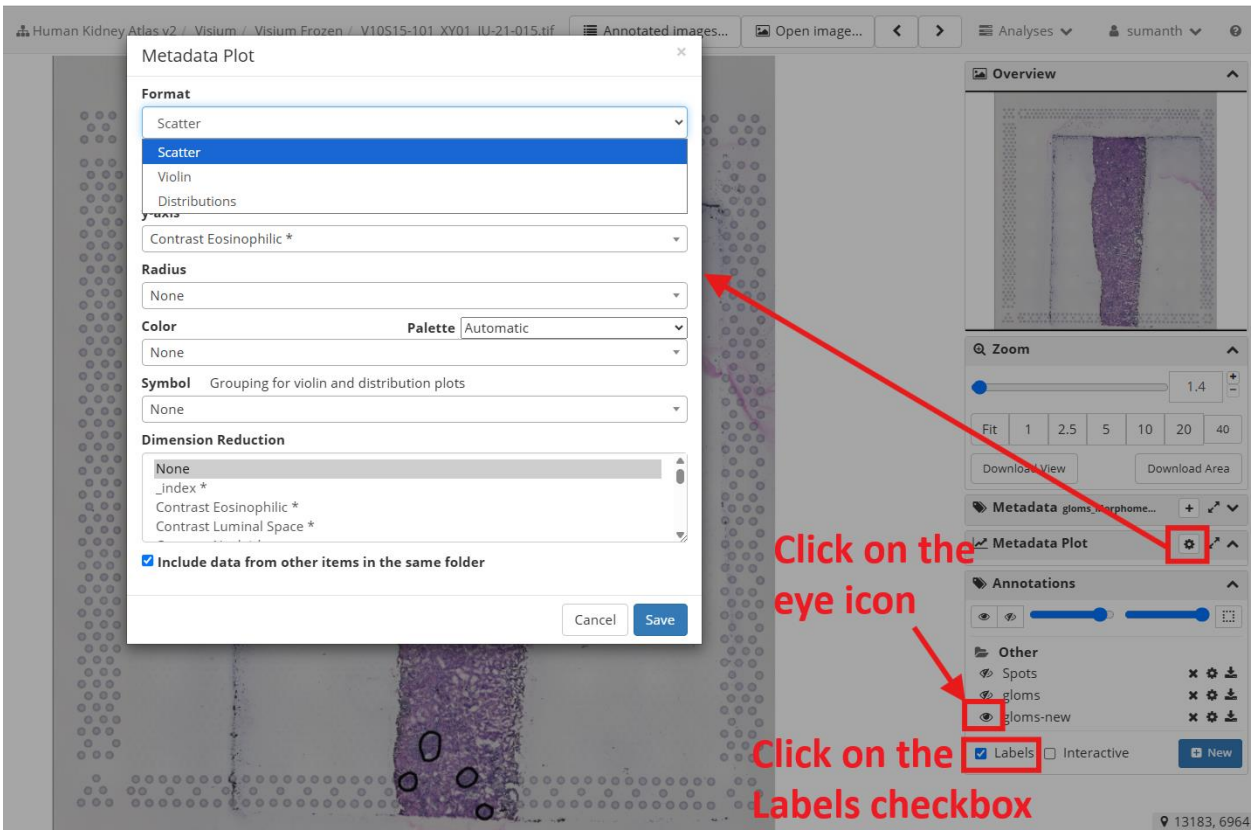
Supp. Fig. 9. Interactive view in HistomicsUI showing cell-type proportions and morphometric properties for a selected glomerulus after enabling *Labels* in the *Annotations* panel. The left panel displays pie and bar charts for cell-type composition along with quantitative feature values extracted from the image.

Users can also select multiple glomeruli simultaneously by holding the Ctrl key and clicking on individual glomeruli, allowing the system to automatically compute and display the aggregated statistics for the selected regions. When multiple annotations are highlighted, the cell-type composition (pie chart and bar chart) and morphometric feature values in the panel are dynamically updated to show the average values across all selected glomeruli (see Supp. Fig. 10).

To visualize relationships between morphometric features or compare morphometric and cell type properties across all the slides in the dataset, users can utilize the Metadata Plot feature available in the *HistomicsUI* interface. After selecting an annotation layer (e.g., *Gloms-new*) by clicking on the eye icon, click on the gear icon next to the *Metadata Plot* panel to configure a new visualization (see Supp. Fig. 11).



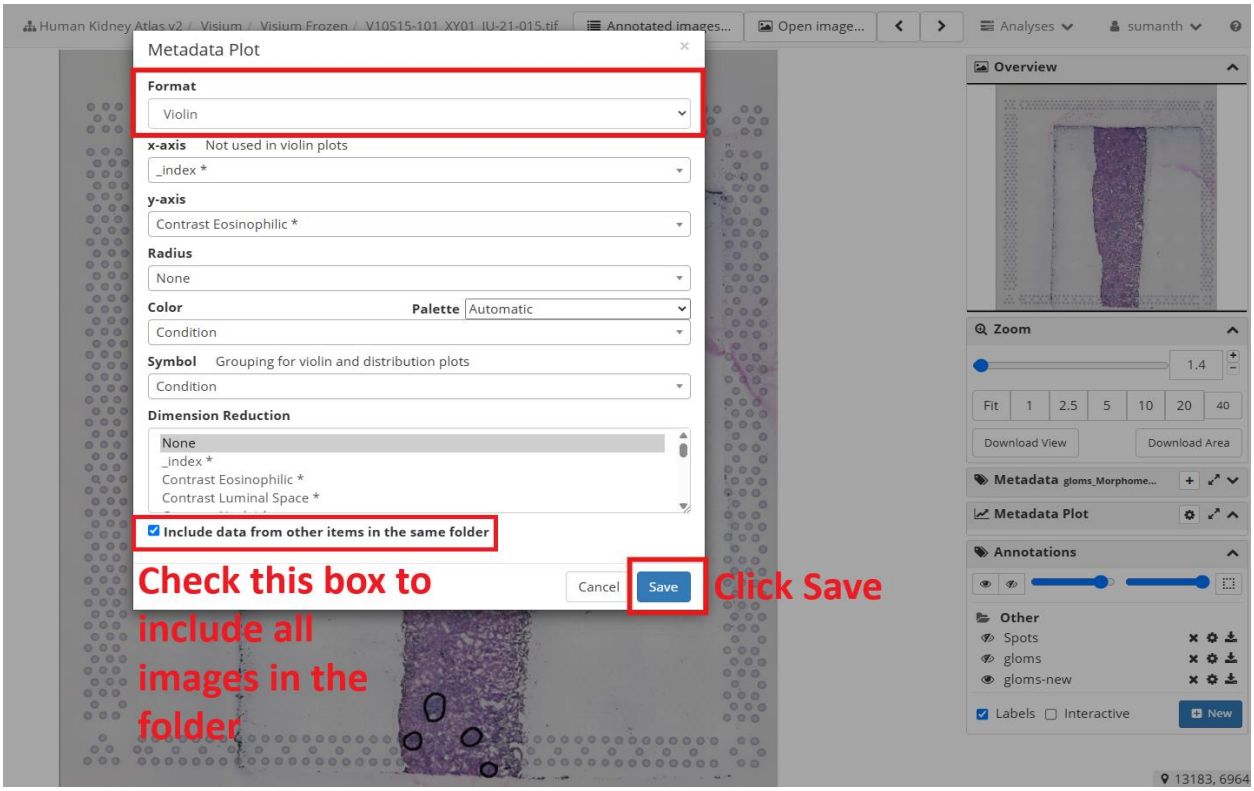
Supp. Fig. 10. Visualization of multiple selected glomeruli in HistomicsUI. When multiple annotations are selected, the cell-type proportions and morphometric feature values in the left panel are automatically averaged and displayed as aggregate summaries.



Supp. Fig. 11. Configuration interface of the *Metadata Plot* tool in HistomicsUI showing available plot formats (Scatter, Violin, Distribution) and customizable axes and grouping options.

The *Metadata Plot* tool supports three plot formats Scatter, Violin, and Distribution for different types of feature exploration. Users can assign variables to the x-axis and y-axis by selecting from the available metadata attributes (e.g., *Contrast Nuclei*, *Energy Eosinophilic*, *Correlation Luminal Space*, etc.). The Color and Symbol fields can be used to group or differentiate data points, for example, by Condition (AKI, HRT, CKD) or by Annotation ID. Once the desired parameters are configured, click the Save button to generate and display the plot (see Supp. Fig. 12a-c).

At the bottom of the configuration window, the checkbox “Include data from other items in the same folder” enables cross-image aggregation. When selected, the plot incorporates feature data from all WSIs within the same directory, allowing users to compare morphometric or cell-type properties across multiple samples simultaneously.



Supp. Fig. 12a. Configuration panel of the *Metadata Plot* tool showing parameter selection for generating a Violin plot. Users can assign metadata attributes to the x-axis and y-axis, choose color and symbol groupings, and enable the option “Include data from other items in the same folder” to aggregate data across multiple WSIs before clicking Save to render the plot.

Supp. Fig. 12b. Example of a violin plot generated using the Metadata Plot tool in *HistomicsUI*, showing the distribution of *Contrast Eosinophilic* values across different conditions (AKI, DKD, and HRT) in glomeruli. Each violin represents the spread and density of feature values within that condition. Click on the expand icon to view the plot in full screen.

Supp. Fig. 12c. Example Violin Plot visualization displaying the distribution of *Contrast Eosinophilic* values across tissue conditions (*AKI, CKD, DKD, HRT*). Each violin represents the feature distribution for one condition

When hovering over any point within the plot, a tooltip appears showing detailed metadata for the corresponding annotation (see Supp. Fig. 12c) This typically includes:

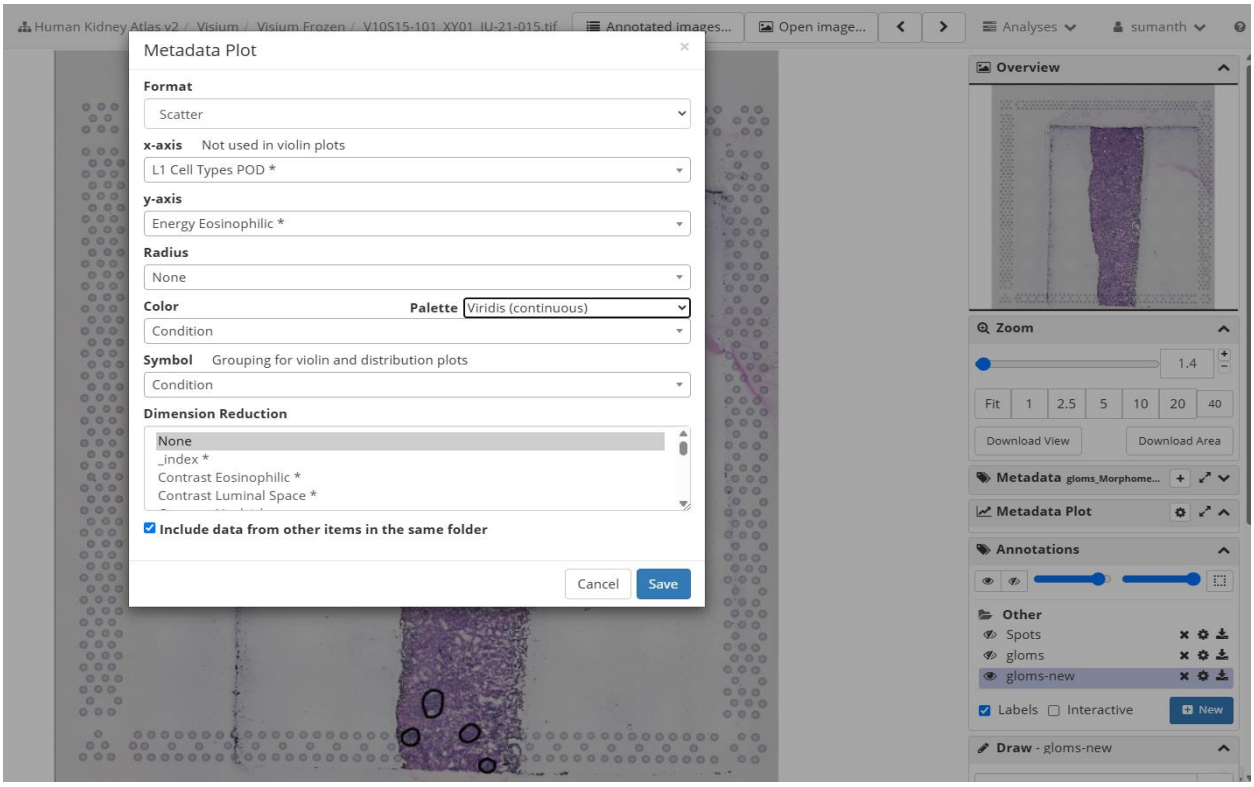
- Item Name: the filename of the WSI from which the data point originates (always displayed), and
- The feature values and grouping variables (e.g., attributes selected for *y-axis*, *Color*, or *Symbol*) such as *Contrast Eosinophilic*, *Condition*, or any other metadata chosen during plot configuration.

Additionally, the tooltip provides a thumbnail image of the corresponding annotation region, allowing users to visually associate numerical feature values with their spatial tissue context.

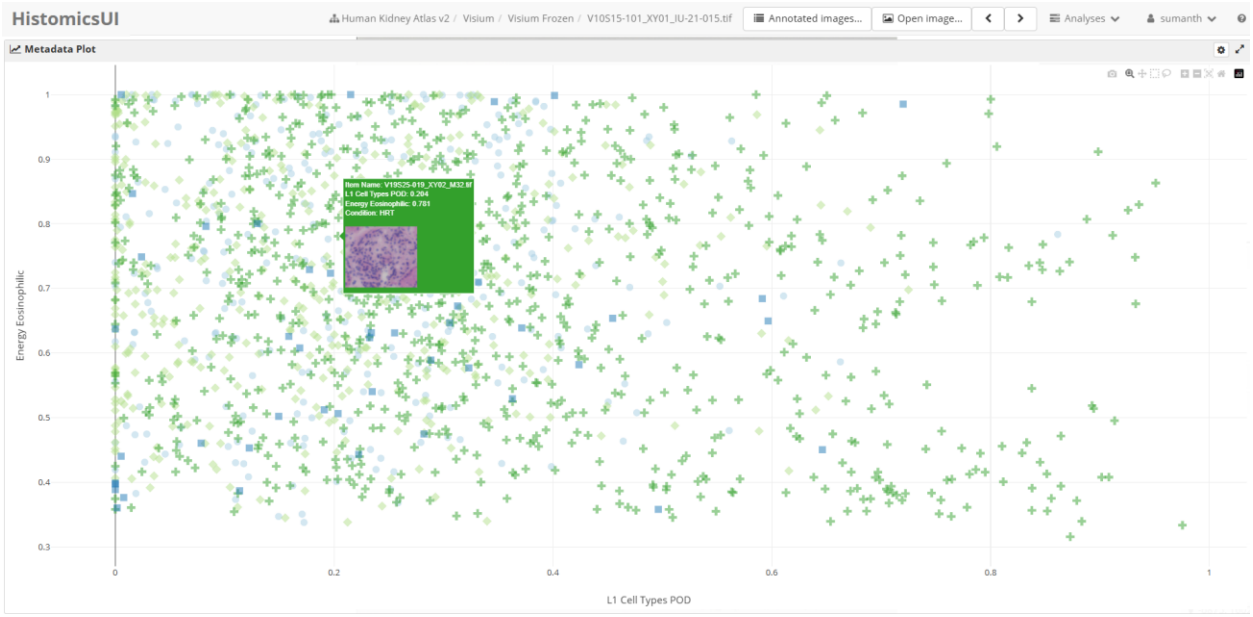
The Lasso Select feature in the *Metadata Plot* panel allows users to interactively select a subset of data points within any generated plot (e.g., violin, scatter, or distribution). By clicking on the lasso icon at the top-right corner of the plot interface (see Supp. Fig. 13a), users can draw a freeform boundary around data points of interest. Once selected, the corresponding annotations on the WSI are automatically highlighted (see Supp. Fig. 13b).

Supp. Fig. 13a. The Lasso Select tool in the *Metadata Plot* interface. Click on the lasso icon to interactively select data points within the plot for further inspection or spatial correlation in the corresponding WSI viewer.

Supp. Fig. 13b. Corresponding glomeruli (Gloms) highlighted on the WSI for the data points selected using the Lasso tool in the Metadata Plot. The *Element Data* panel displays detailed morphometric and cell-type composition metrics for the selected regions.



Supp. Fig. 14a. Configuration panel of the *Metadata Plot* tool for generating a Scatter plot, where the x-axis and y-axis represent selected quantitative metadata features.



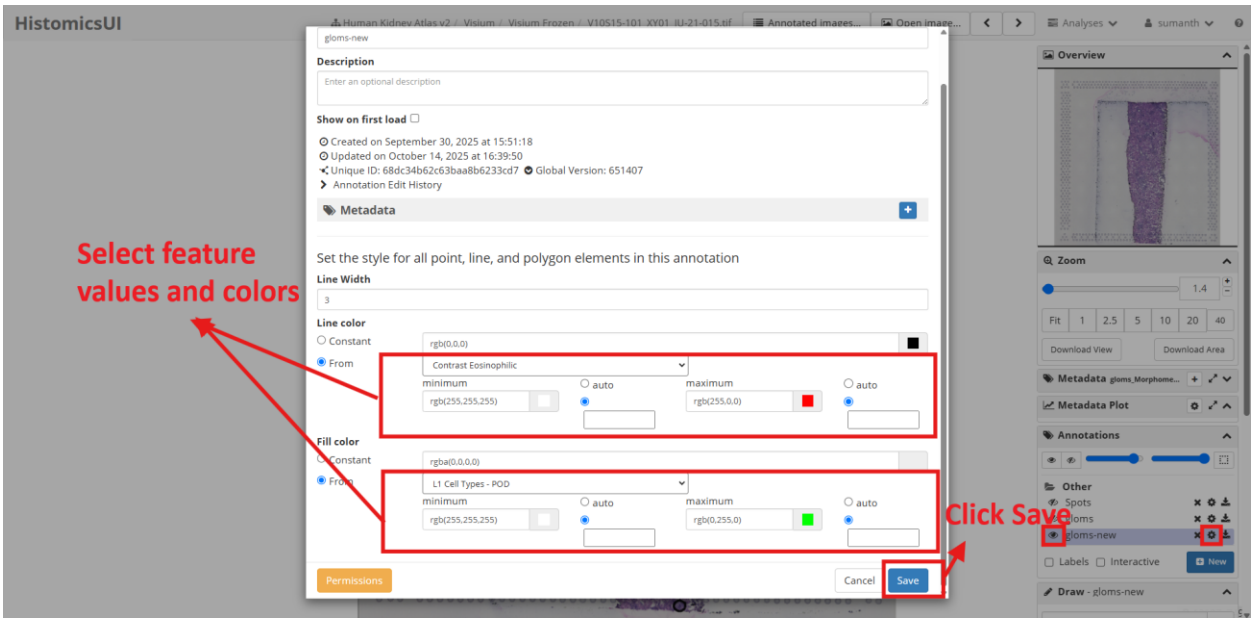
Supp. Fig. 14b. Example Scatter Plot visualization showing the relationship between *L1 Cell Types POD* and *Energy Eosinophilic* across glomeruli. Each point represents an individual annotation, colored by condition, with tooltips displaying feature values and thumbnail previews of the corresponding tissue region.

Users can also customize the **visual representation of annotations** within the HistomicsUI viewer to highlight specific biological or morphometric properties. By clicking on the **gear icon** beside an annotation layer (e.g., *gloms-new*), the **Edit Annotation** panel opens, allowing the user to modify parameters such as **line width**, **line color**, and **fill color** (see Supp. Fig. 16).

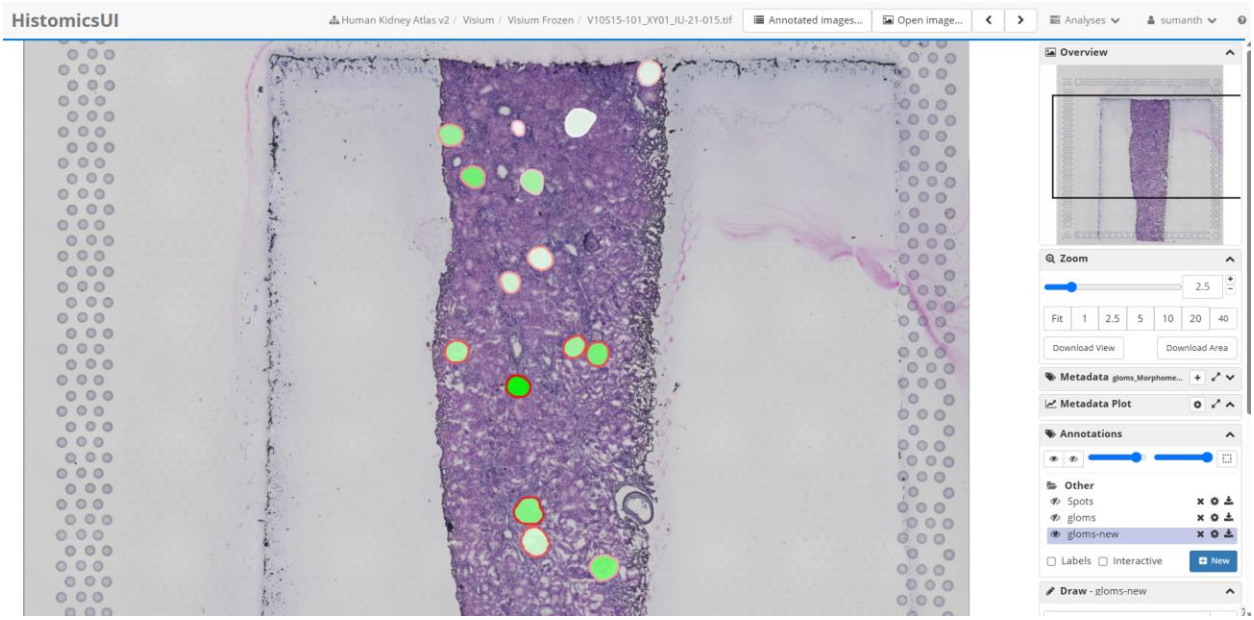
Within this panel, both **line color** and **fill color** can be dynamically mapped to feature values using color gradients. For instance, as shown in the example (see Supp. Fig. 17), the **line color** is set to vary from *light red to dark red* based on the *Correlation Eosinophilic*

value, while the **fill color** transitions from *light green to dark green* according to the *L1 Cell Types – POD (Podocytes)* feature.

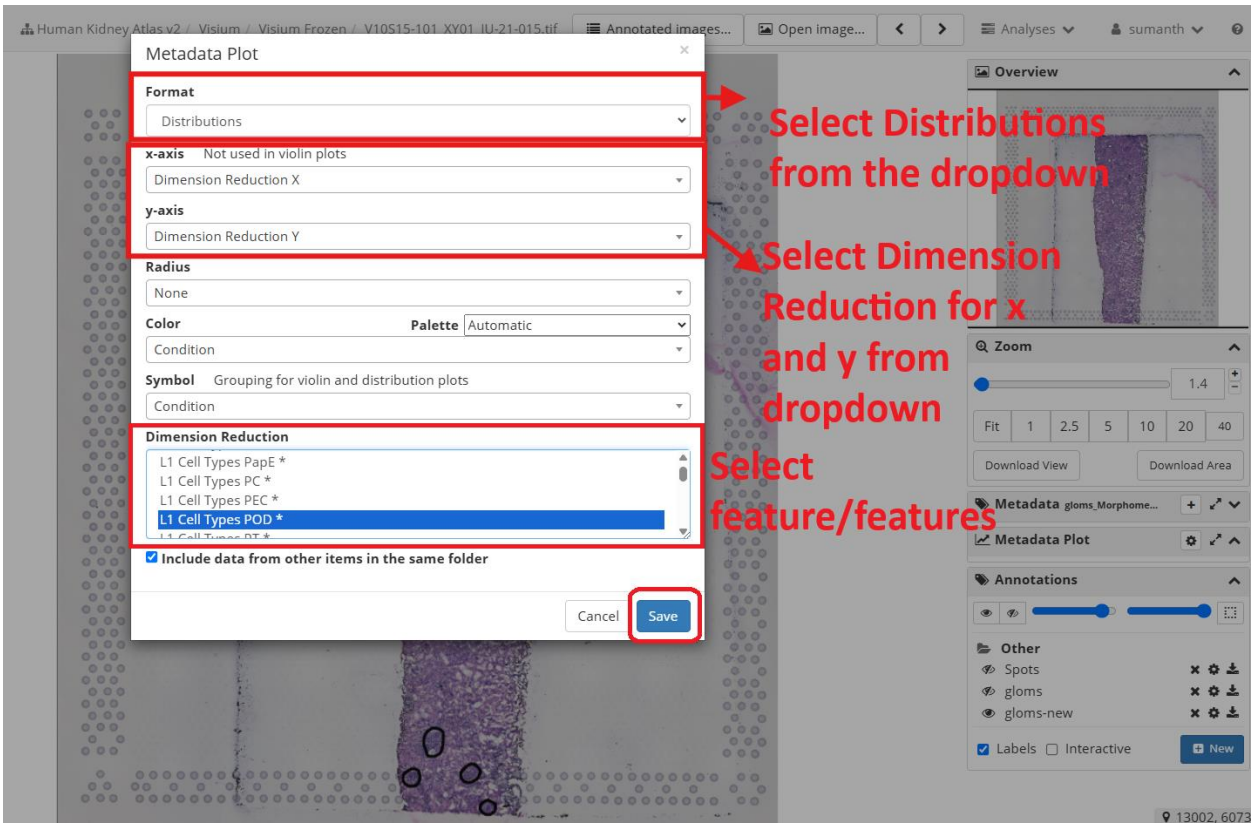
This functionality enables intuitive visual encoding of quantitative features, such as using one color gradient to represent a **functional tissue unit (FTU)** property (e.g., abundance of a specific cell type) and another to depict its **morphological state** (e.g., degree of degeneration or correlation intensity). Such multi-dimensional visualization helps users quickly interpret spatial and structural variations across tissue regions.



Supp. Fig. 16. Editing annotation visualization in HistomicsUI. Users can configure line and fill color gradients based on feature values (e.g., *Correlation Eosinophilic* and *L1 Cell Types – POD*)



Supp. Fig. 17. Visualization of glomerular annotations after applying feature-based line and fill color gradients in *HistomicsUI*. The red outline intensity corresponds to *Correlation Eosinophilic* values, while the green fill gradient represents the proportion of *L1 Cell Types – Podocytes (POD)* within each glomerulus


Metadata Plot
Format
Distributions
x-axis Not used in violin plots
Dimension Reduction X
y-axis
Dimension Reduction Y
Radius
None
Color
Palette Automatic
Condition
Symbol Grouping for violin and distribution plots
Condition
Dimension Reduction
L1 Cell Types PapE *
L1 Cell Types PC *
L1 Cell Types PEC *
L1 Cell Types POD *
Include data from other items in the same folder
Cancel
Save
Select Distributions from the dropdown
Select Dimension Reduction for x and y from dropdown
Select feature/features
Overview
Zoom
1.4
Fit 1 2.5 5 10 20 40
Download View
Download Area
Metadata gloms_Morphome...
Metadata Plot
Annotations
Other
Spots
gloms
gloms-new
Labels Interactive
New