Dynamically visualizing the link between histological structures and whole transcriptome expression data to explore the Spatial Organ Atlas

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Introduction

GeoMx® Digital Spatial Profiling (DSP) datasets are rich in both imaging and genomics data and require extensive knowledge of tissue type, experimental design, and genomics analyses to fully comprehend. Here we adapted the Minerva Software Suite for interactive storytelling of GeoMx data from the Spatial Organ Atlas (SOA). Changes in Minerva software facilitate communicating SOA images, data, and experimental design in an accessible, interactive, and powerful way.

## Minerva Software Enables Guided & Interactive Tissue Narratives

Purpose
- Minerva suite is open-source mature software from Harvard Medical School's Laboratory of Systems Pharmacology.
- It is designed for digital pathology.
- Minerva Stories are guided, interactive narratives of tissue images and analyses.
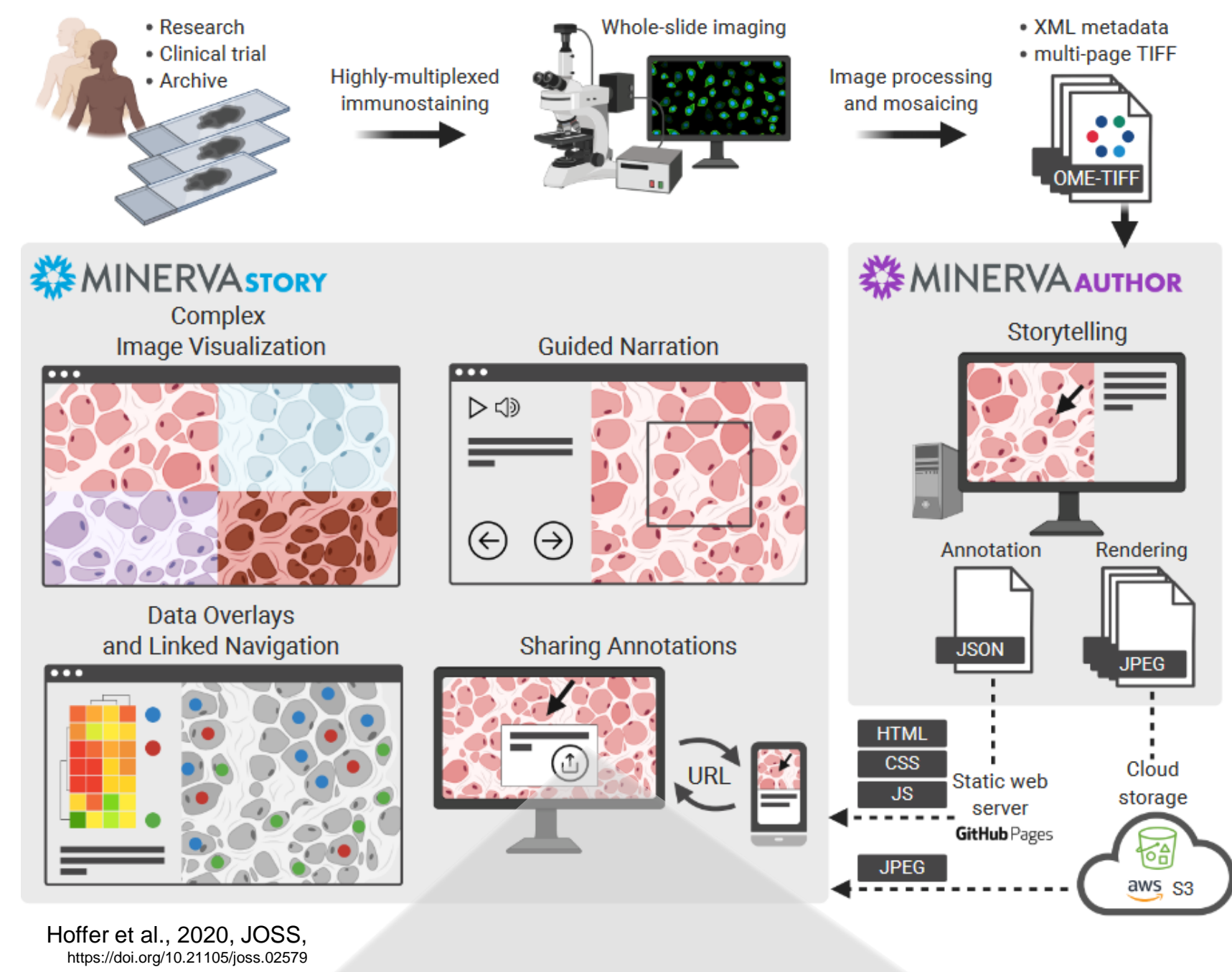
Minerva Suite Workflow
The author crafts a Story to guide user experience.
- Slide image(s)
- Image display settings
- Descriptive text
- Interactive plots

Hoffer et al., 2020, JOSS, https://doi.org/10.21105/joss.02579
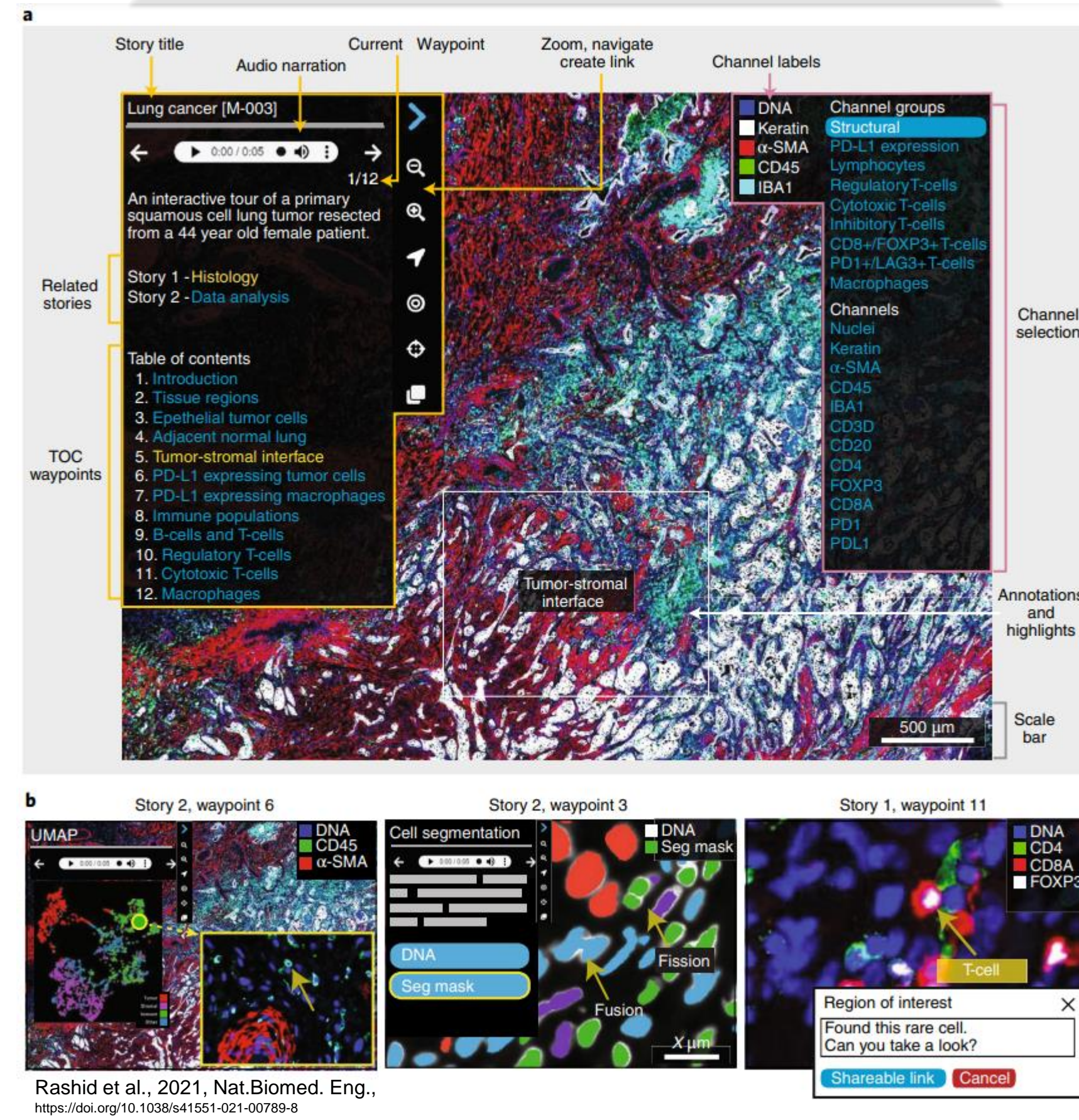
Minerva Story Features
Minerva Stories have many features designed to orient the user to the tissue and guide them through exploration.

Rashid et al., 2021, Nat.Biomed.Eng., https://doi.org/10.1038/s41551-021-00789-8
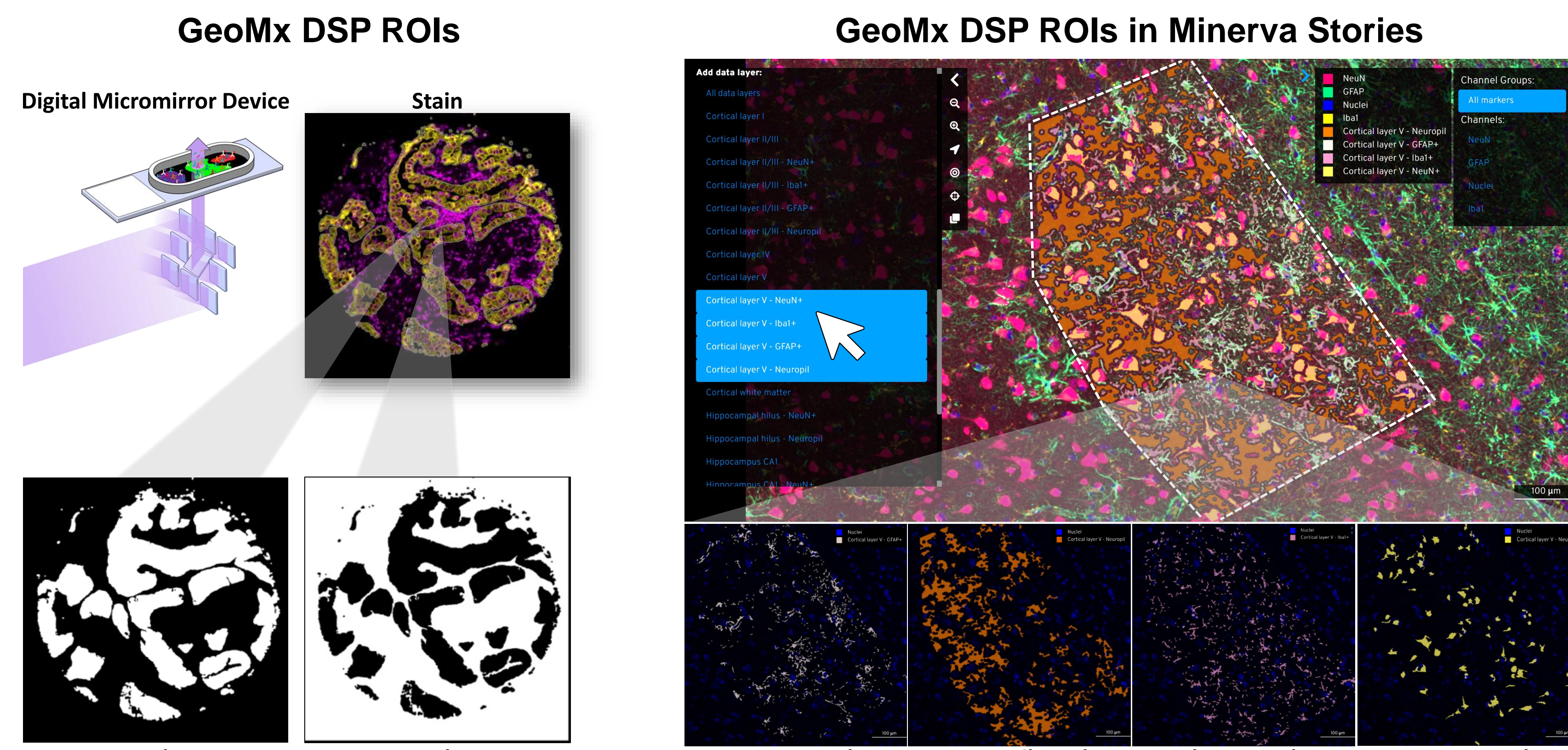
Minerva Story User Interface
Using an internet browser, the user can access, view, and interact with a Minerva Story.

GeoMx DSP Spatially Resolves Transcriptome in Section ROIs
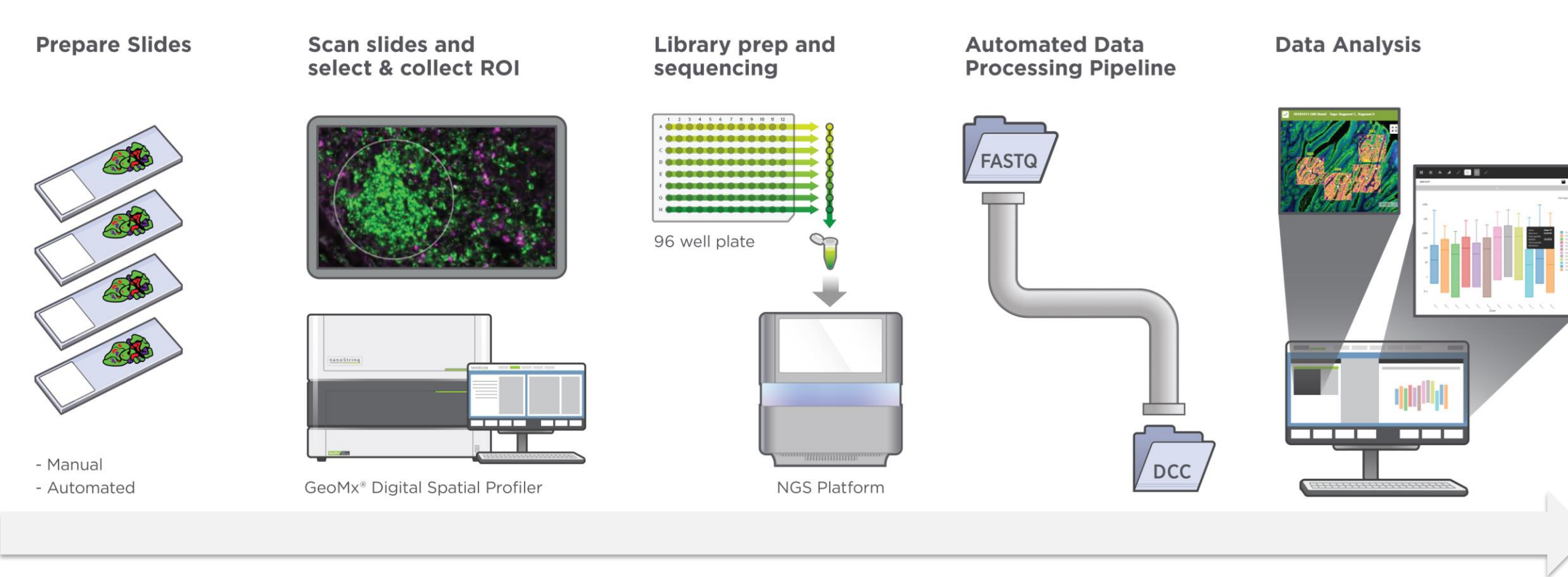
The GeoMx Digital Spatial Profiler (DSP) is a spatial biology technology that enables researchers to spatially analyze RNA and protein content in sample tissue by user-selected regions of interest (ROIs). The Whole Transcriptome Atlas (WTA) panels target 18-20 thousand RNA targets in human or in mouse. The DSP can deliver both high-quality (IHC) images as well as genomic analyses and plots through on- and off-instrument tools.

Minerva Stories Illustrate GeoMx's Capability of Cell Type-Specific Selection in situ

GeoMx DSP ROIs

Digital Micromirror Device

Stain

Mask 1   Mask 2

GeoMx DSP ROIs in Minerva Stories

GFAP+ Mask   Neuropil Mask   Iba1+ Mask   NeuN+ Mask

GeoMx DSP utilizes user- and staining-defined regions of interest (ROIs) to UV-cleave probes that annealed to RNA or protein targets. These regions are represented as translucent masks in SOA Minerva Stories. Toggle on and off segmentations in the human brain to demonstrate complex spatial biology. Here, interspersed Cortical layer V biological components are distinguished by Neuropil and NeuN+, Iba1+, and NeuN+ collections.

## Development of Minerva Stories Features for GeoMx Data Exploration
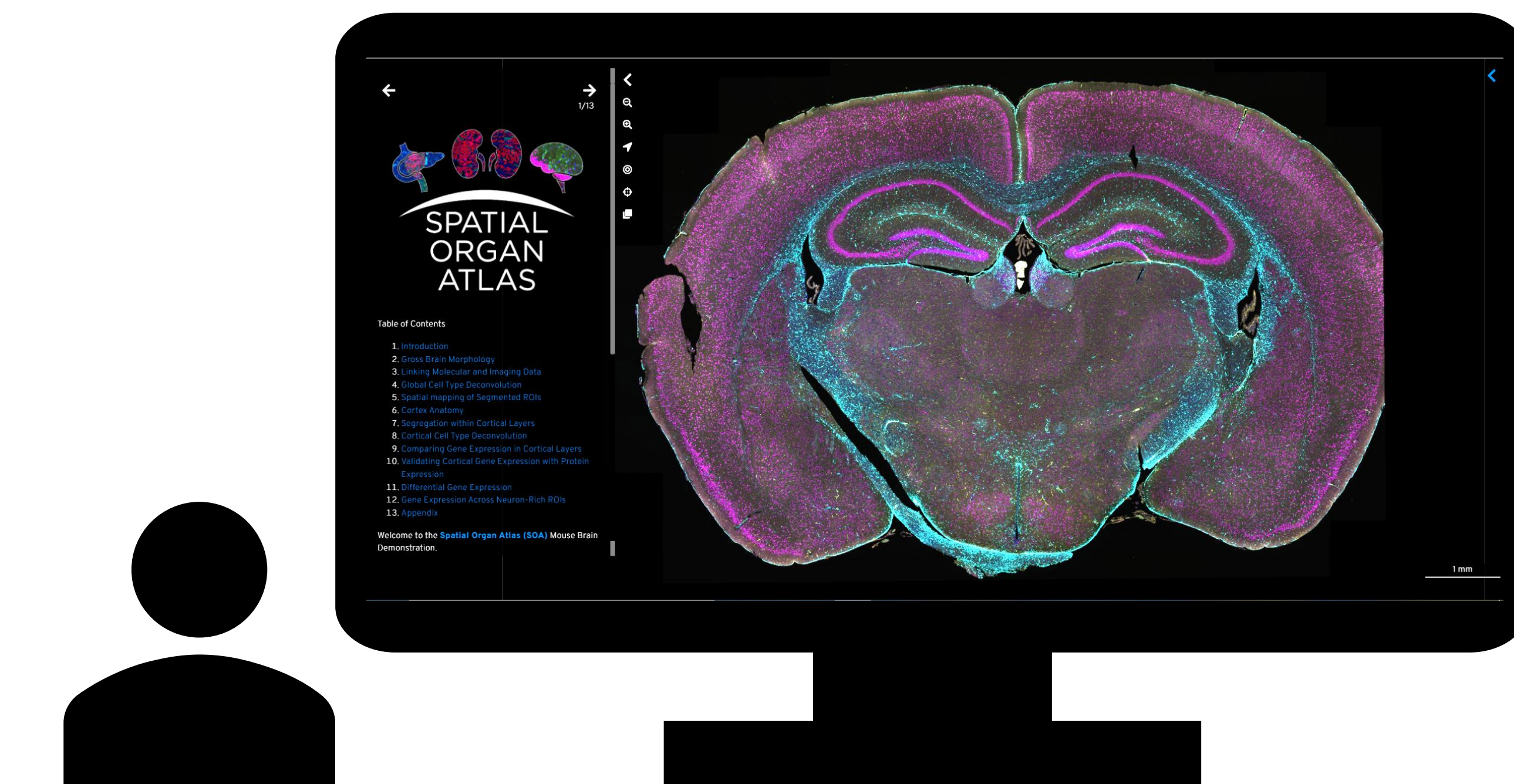
View NanoString's Minerva Stories on the web. Click through waypoints. Read text description and interact with clickable diagrams, plots, and hyperlinks—or explore freely using pan, zoom, and image view settings.

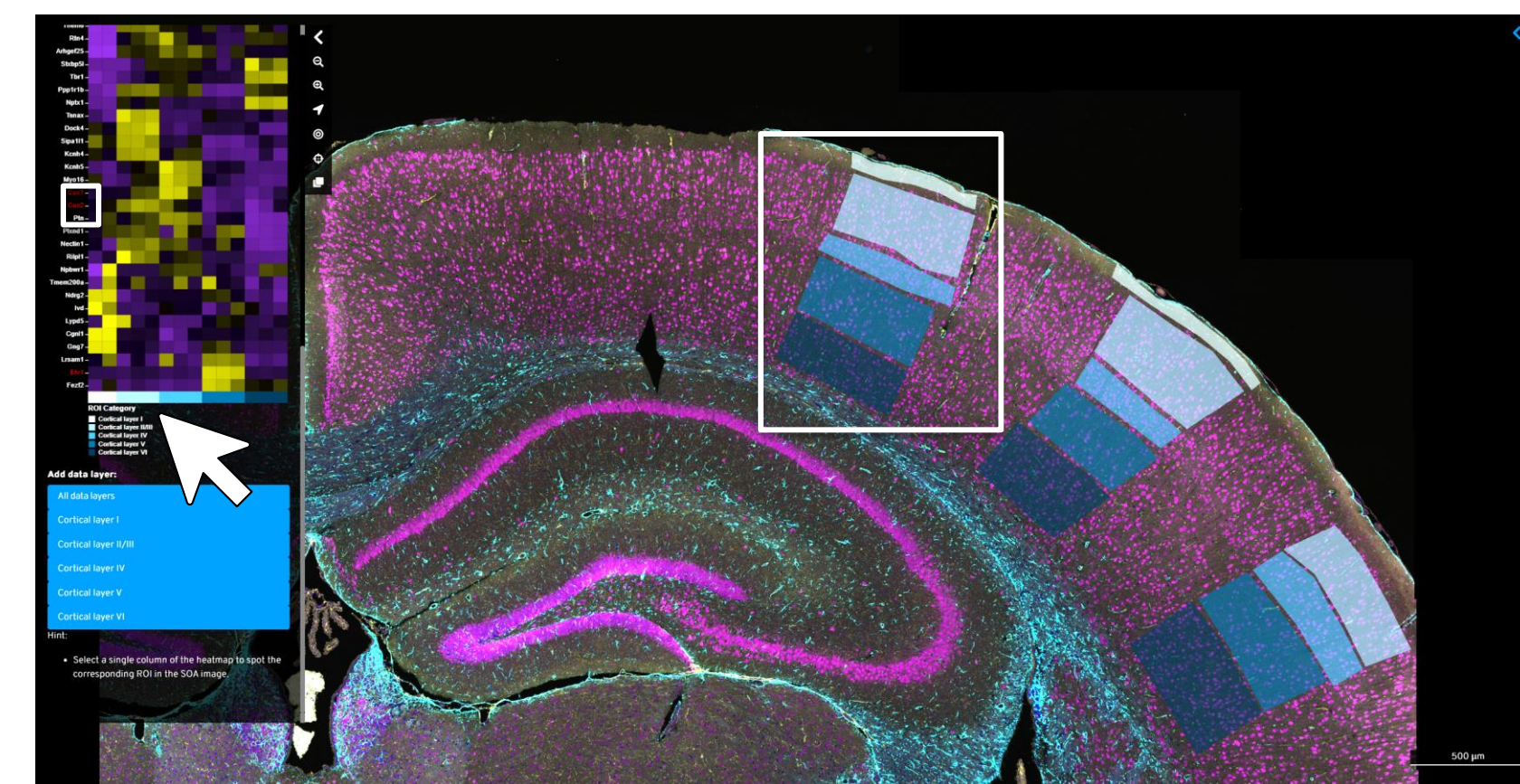Read narrative text to understand analyses. Orient to size with scale bar.
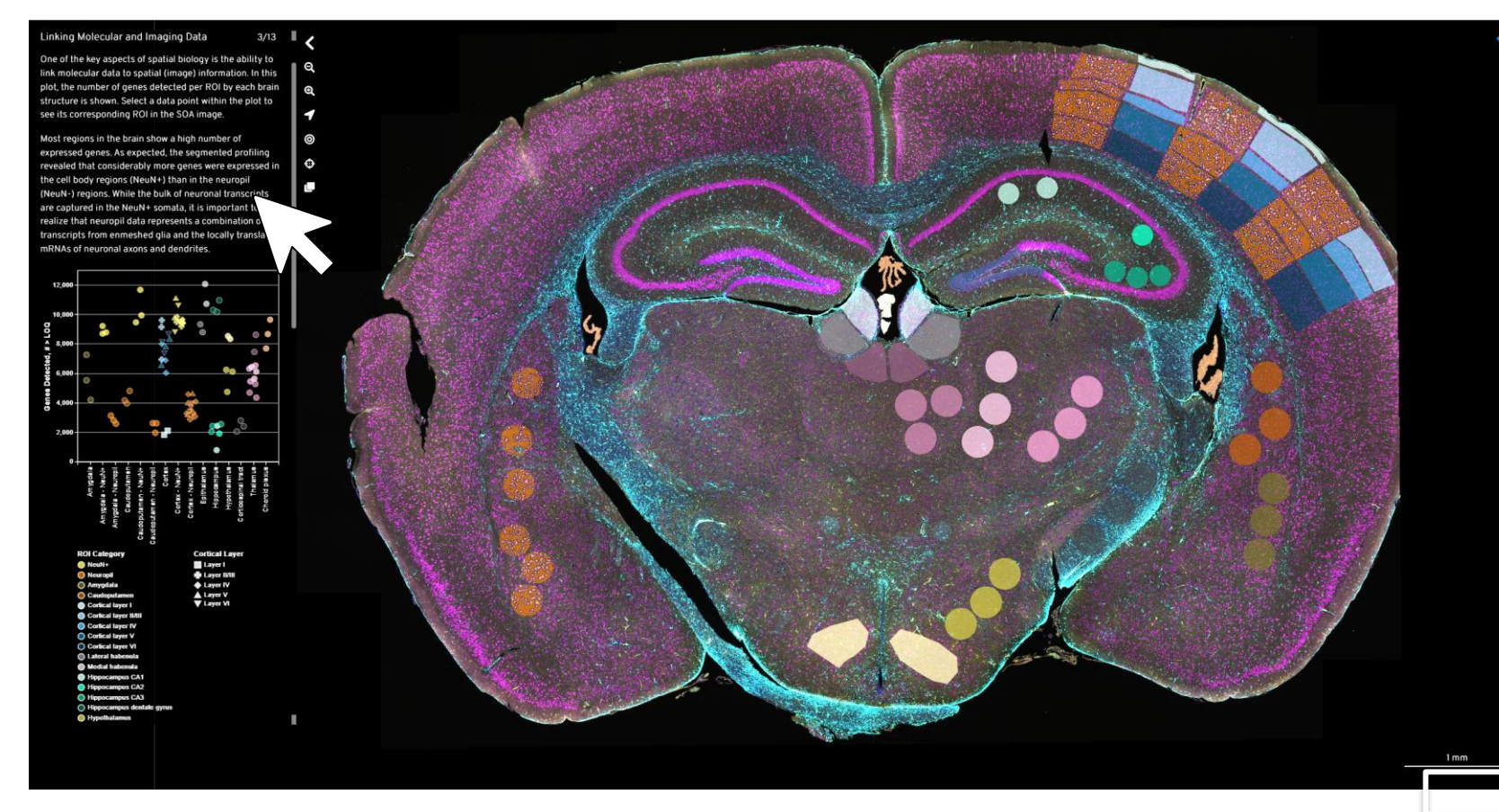
Select a plot point to pan to underlying ROI. View morphology through translucent masks.
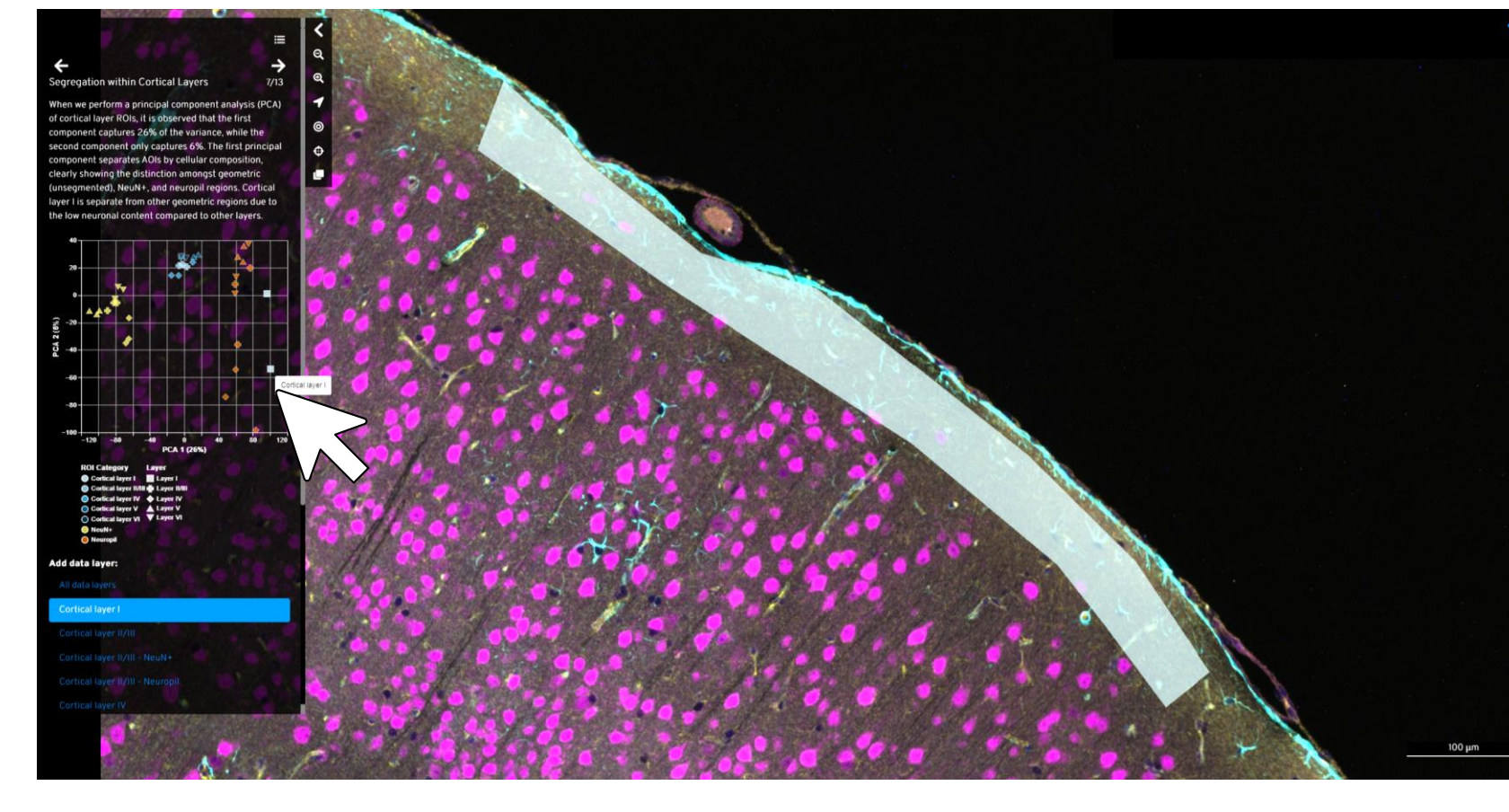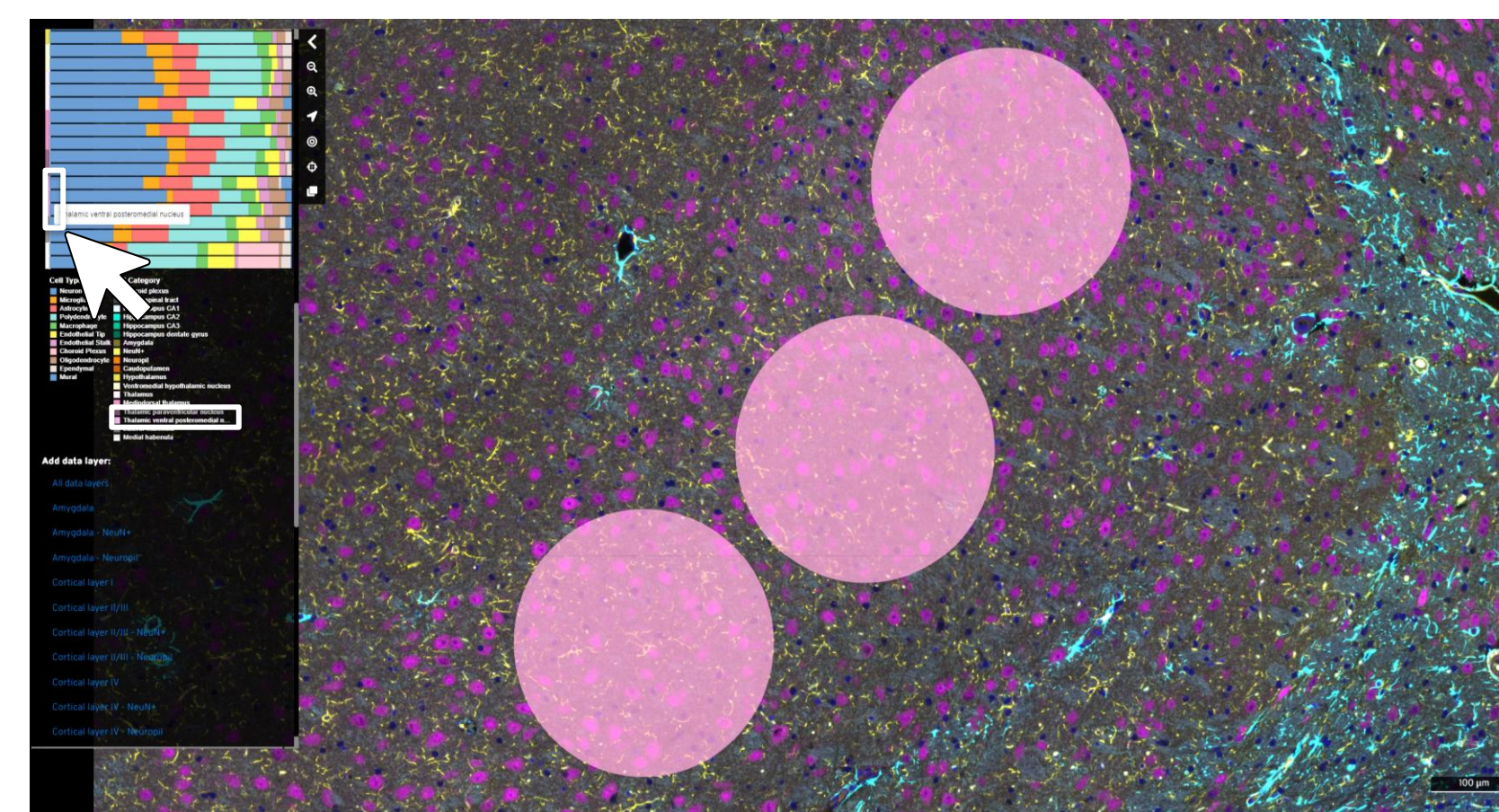
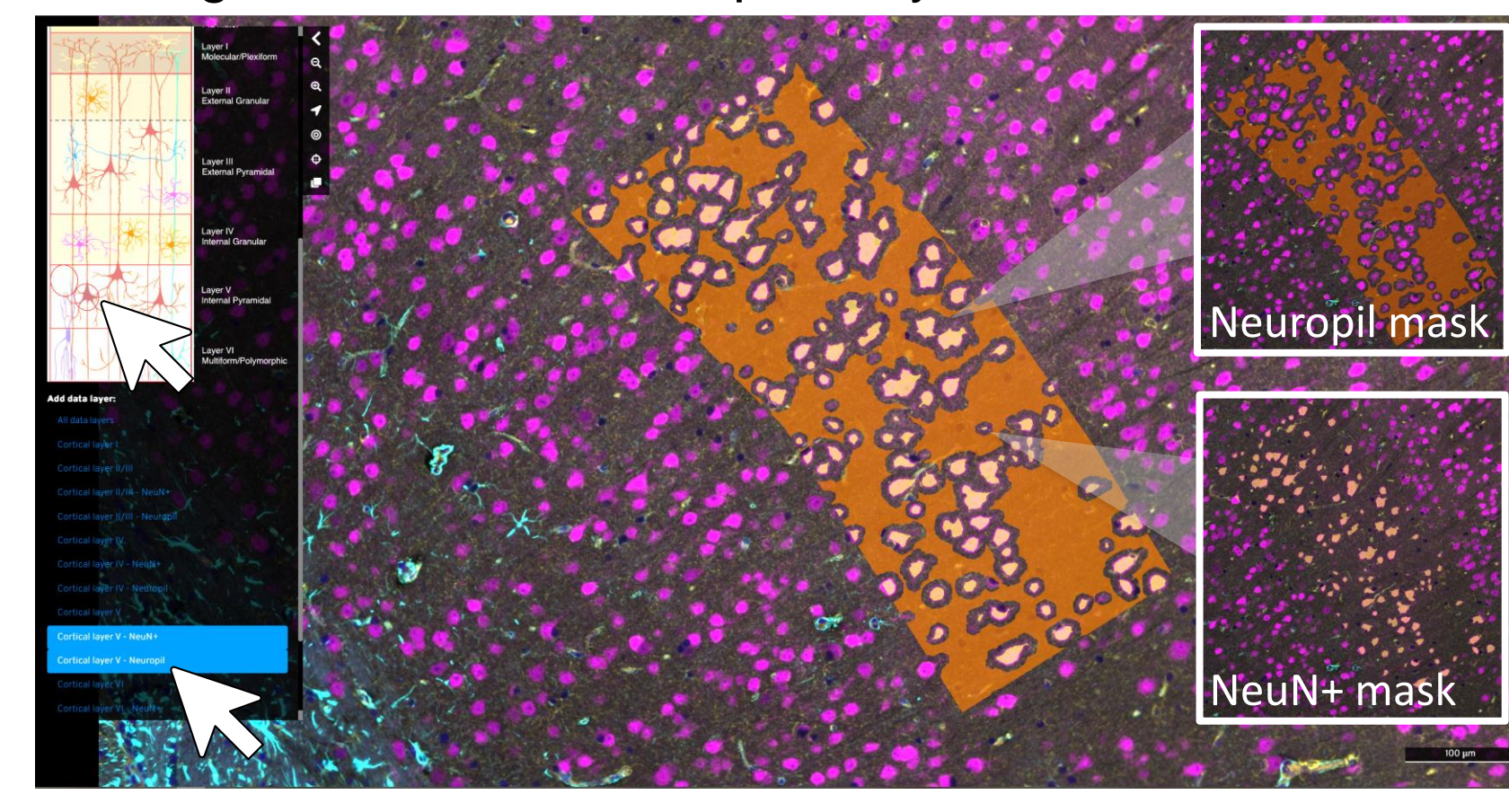Click on cartoon to indicate tissue components on section.

Heatmap annotations provide ROI context and can be clicked to toggle displayed layers.

Consistent terms and colors indicate histological structure through entire Story.

Click on cartoon to pan to ROIs. Toggle to display interdigitated collections separately.

Neuropil mask

NeuN+ mask

Explore Spatial Organ Profiles in NanoString's Spatial Organ Atlas

Each organ profiled in NanoString's Spatial Organ Atlas (SOA) consists of freely available downloadable data files on 4-13 sections. Each dataset is complemented with 1+ sections profiled in a Minerva Story. Interact with each Minerva Story directly in your web browser on the NanoString website, no download required. Learn more about the SOA in poster #413.

Interactive Exploration of Image with Data in the Spatial Organ Atlas

How does the heart develop during embryogenesis?

ROI mask coloring

Staining only   Histological structure   Gene expression

Embryonic stage   E11   E15
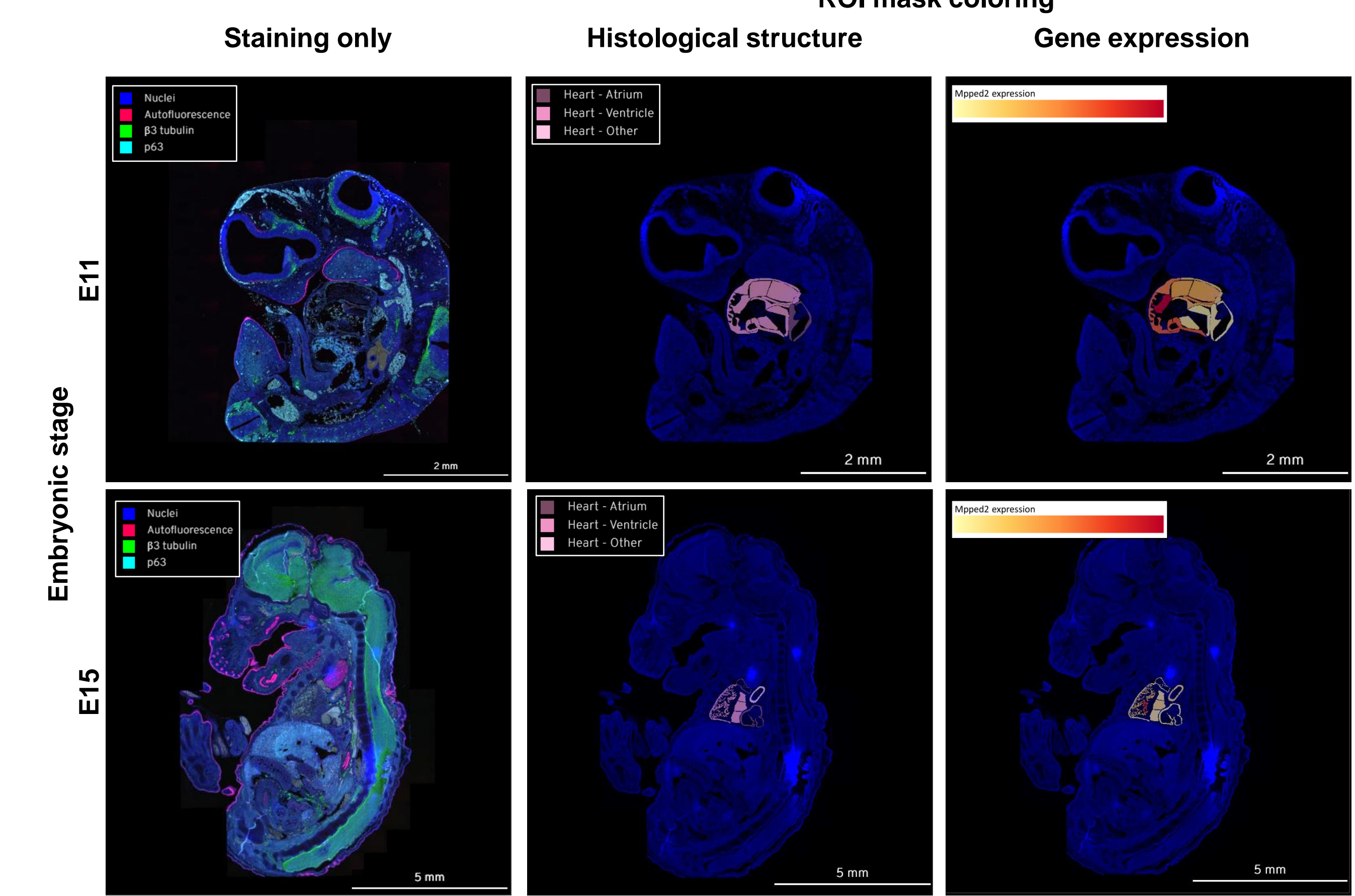
Explore four sections (E9, E11, E13, E15) in one Minerva Story. ROI layers indicate histological structure as well as gene expression. Observe patterns in gene expression across the heart in the IHC image below (E11, E15 shown).

How do heterogeneous glomeruli function as filtering units?
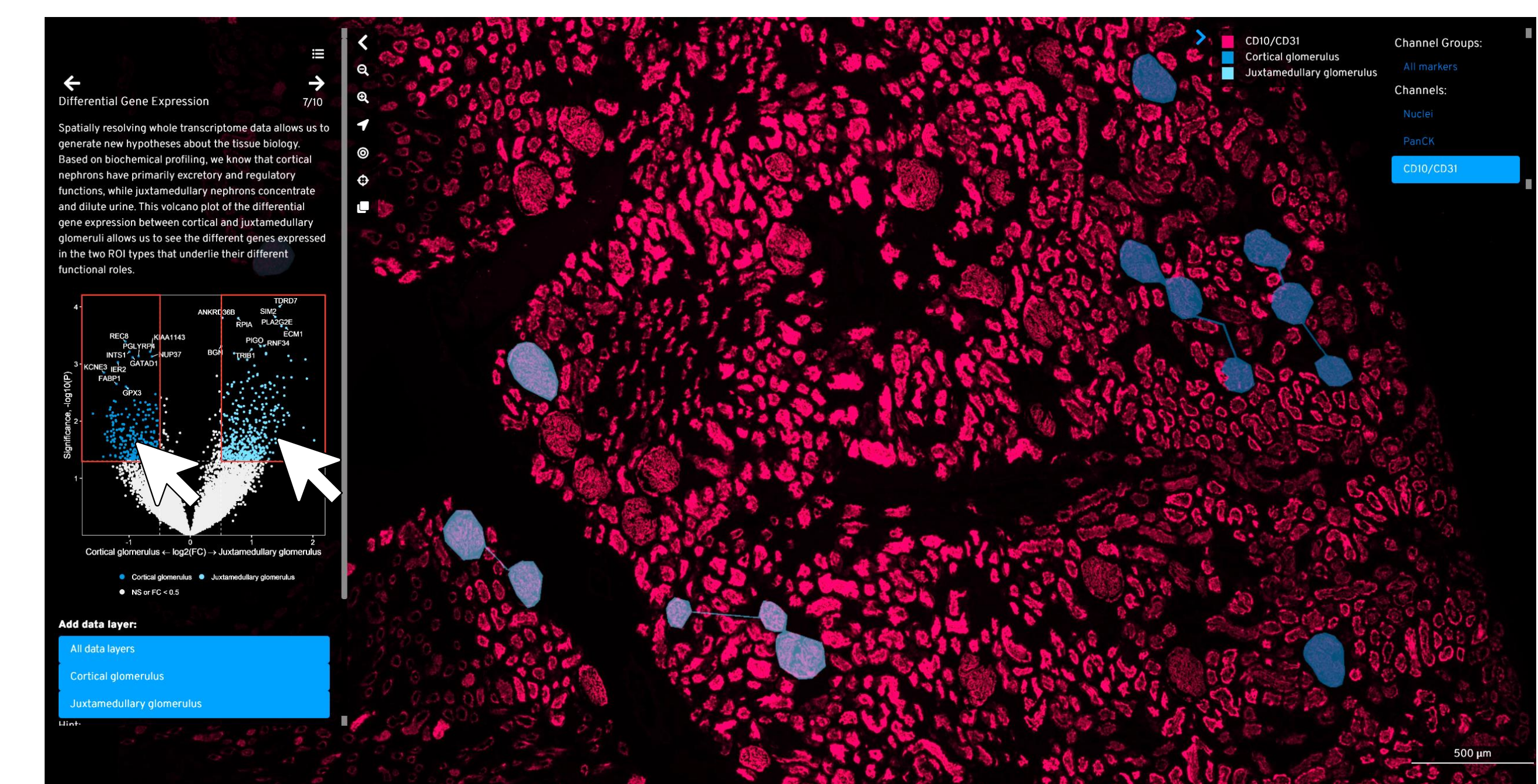
Explore differential gene expression across a tissue. Here, cortical and juxtamedullary glomeruli demonstrate distinct transcriptome signatures. Click on the outlined boxes to toggle ROI layers illustrating the underlying collected regions and learn how spatial positioning underlies expression patterns.

How are germinal centers spatially organized to fight infection?
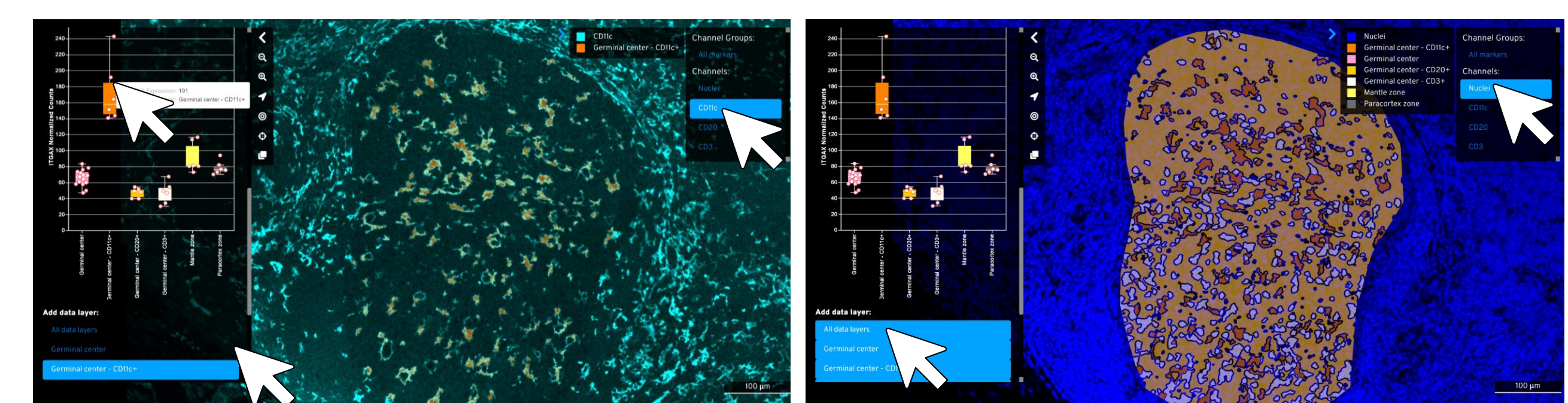
Here, ITGAX expression is greater in CD11c+ mask ROIs than in whole germinal center ROIs. Toggle data layers and channel settings to observe morphological differences between different structures within the same germinal center.

Conclusions

- The Minerva software suite exists as a fully operational, open-source tool to communicate complicated images and associated data analysis.
- Using existing and new features, we demonstrate a use case of Minerva Stories for spatial biology.
- The Spatial Organ Atlas's Minerva Stories provide guided interpretation of complex imaging and genomics data that maintains the relationship between underlying tissue morphology and resultant gene expression.

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NanoString at AGBT 2022

NanoString's Spatial Organ Atlas

SPATIAL ORGAN ATLAS