

#413 Spatial Organ Atlas: A compendium of whole transcriptomes for functional subunits of organs

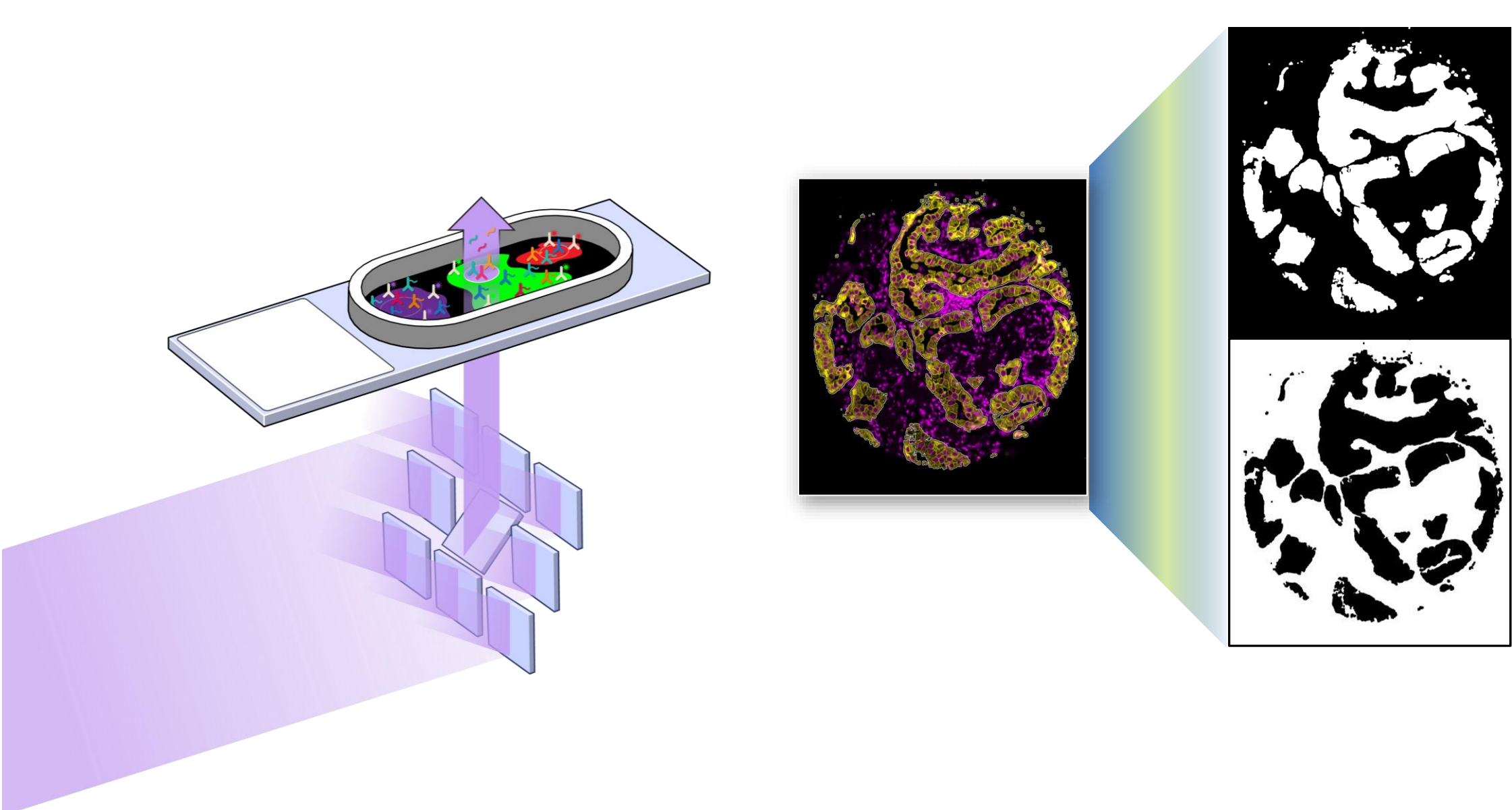
Michael Rhodes, Patrick Danaher, Jason Reeves, Tyler Hether, Megan Grout, Alison VanSchoiack, Jingjing Gong, Liang Zhang, Wei Yang, Charlie Glaser, Kathy Ton, David Kroeppler, Stefan Phelan, Kit Furhman, Nicholas Confuorto, Yan Liang, Sarah Warren
NanoString® Technologies, Seattle, WA

Abstract

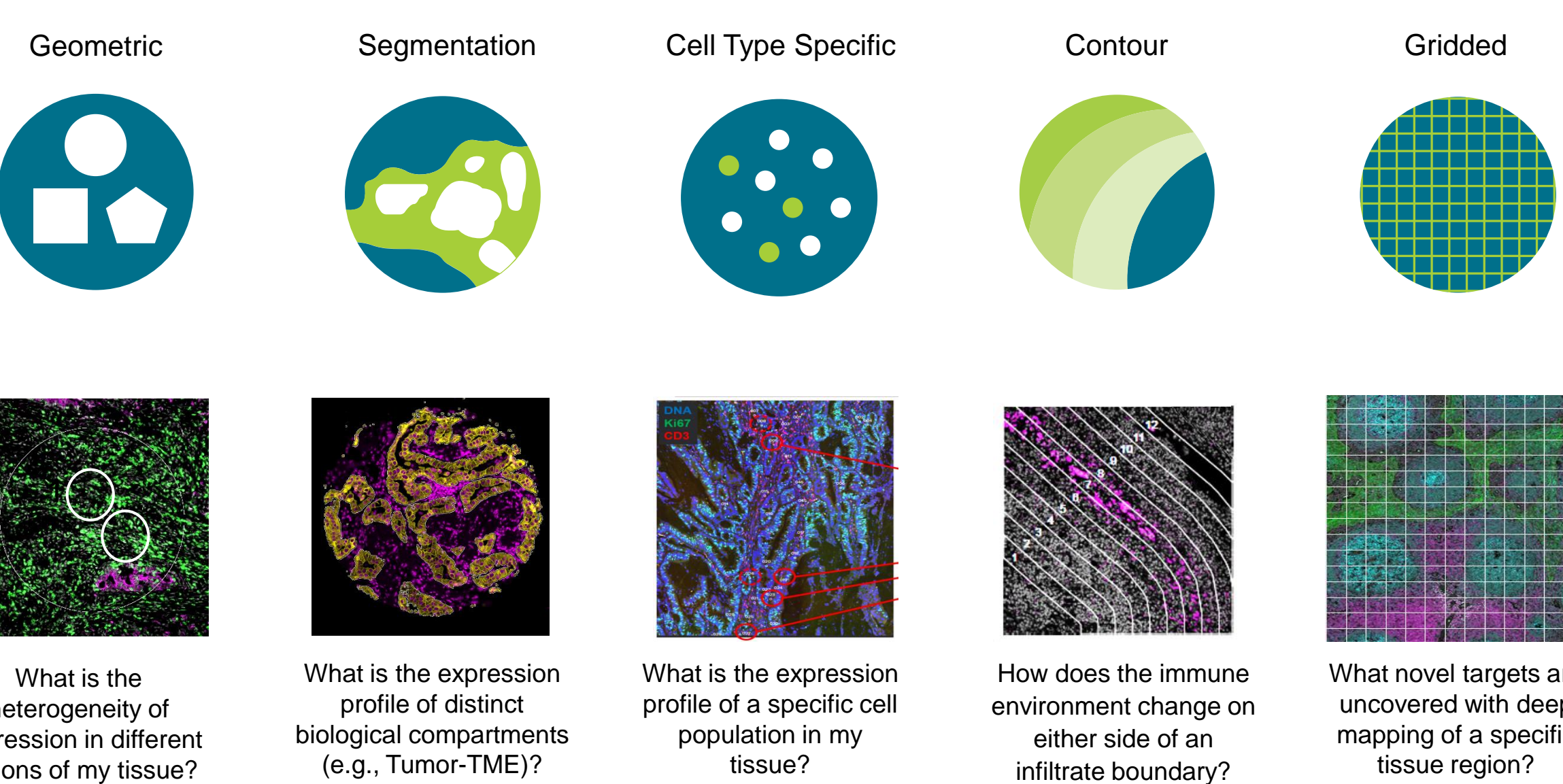
The Spatial Organ Atlas (SOA) is the first repository of in-situ whole transcriptome data generated from FFPE, non-diseased organs. The spatial whole transcriptomes were generated by Digital Spatial Profiling, allowing transcriptomes that match the exact shape of the functional histological organ features. In this first release of the SOA, data has been collected across six organs: human kidney, brain, lymph node, pancreas, colon, and mouse brain. A further set of data on mouse development at E9, E11, E13, E15 was just released. Regions of organs with complex geometries can be profiled with the whole transcriptome in a manner that exactly matches defined histological structures. This can be accomplished even when a structure is composed of a complete interweaving of varied cell types (e.g., the alpha and beta cells of the Islets-of-Langerhans), allowing capture of pure in-situ transcriptomes of the overlapping cell types. Over 2000 whole transcriptomes were measured in the SOA. Biological interpretation is facilitated using the interactive data viewer Minerva and supplied analysis vignettes. To further enable exploration of the data, the raw and processed data (high-resolution images in OME-Tiff format, the FASTQ files, and transcript counts) are available for download. Seurat data objects and GeoMx tools data objects are also available to support analyses using Bioconductor R based tools.

GeoMx® Digital Spatial Profiler the only system to segment regions with light

Both RNA probes and protein probes have UV cleavable linkers. The barcodes are released by DMD directed UV light. This means we can paint with light. In the example below a simple two stage segmentation is carried out. First the areas marked by the selected morphology markers are collected (white regions) then we simply reverse the selection and collected the inverse regions. This enables highly specific selection, for example pools of single cells. The region illuminated from which the barcodes are collected is called an Area Of Illumination (AOI)



In the diagram below the variety of ways in which AOI can be collected is highlighted



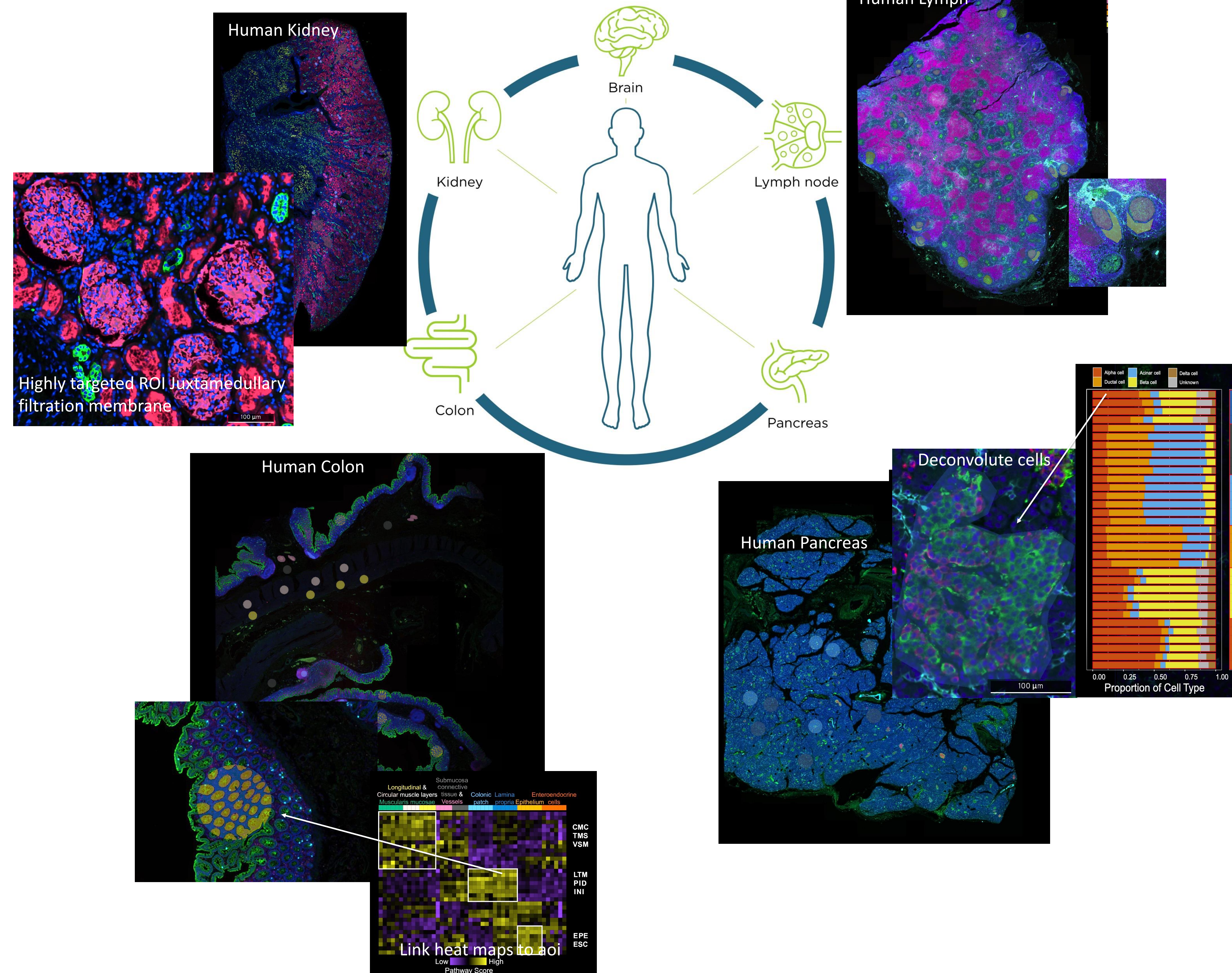
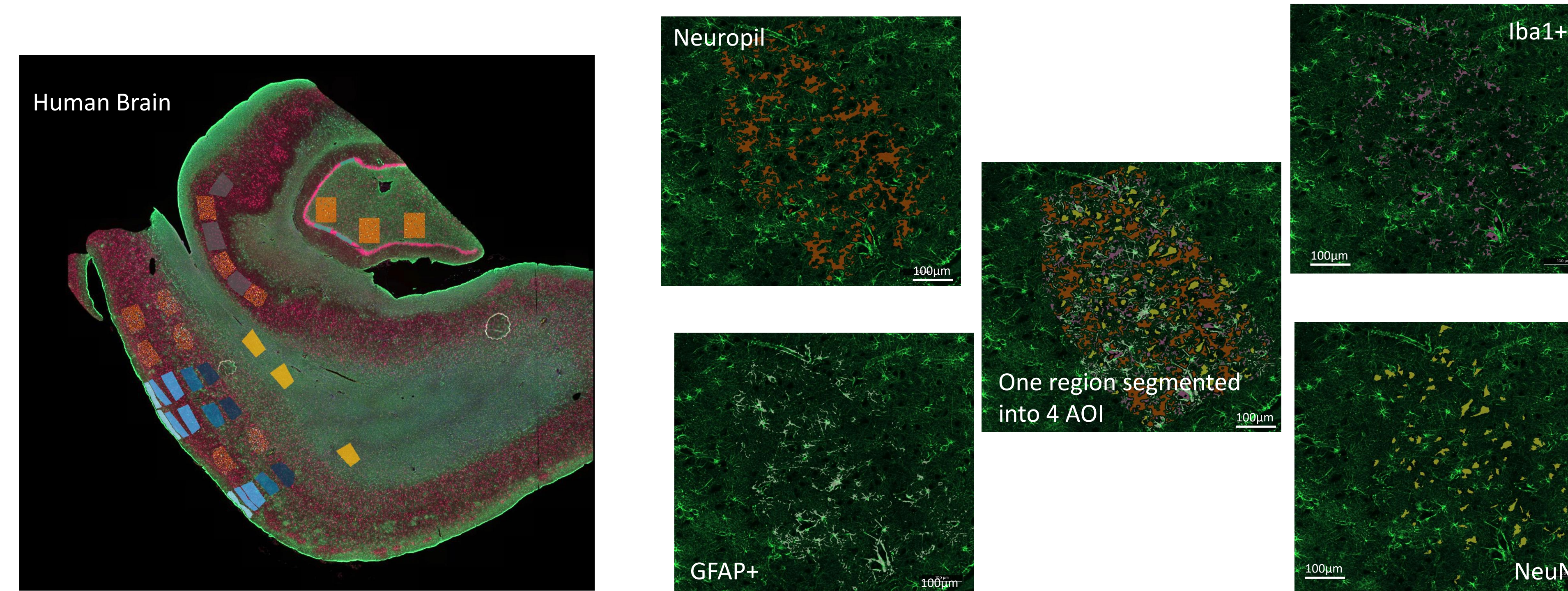
SOA contents

For each Tissue in the SOA there are 3-6 separate samples. There are 3 principal components for each tissue in the SOA

- Individual Web Page with metadata and links for Minerva story and data downloads
- Data Downloads for the complete workflow are available, users can download the images, sequencing reads, intermediate analysis and final analysis
- Minerva Story: a visual story showing images and results in a guided manner for more explanations of Minerva implementation for SOA see:

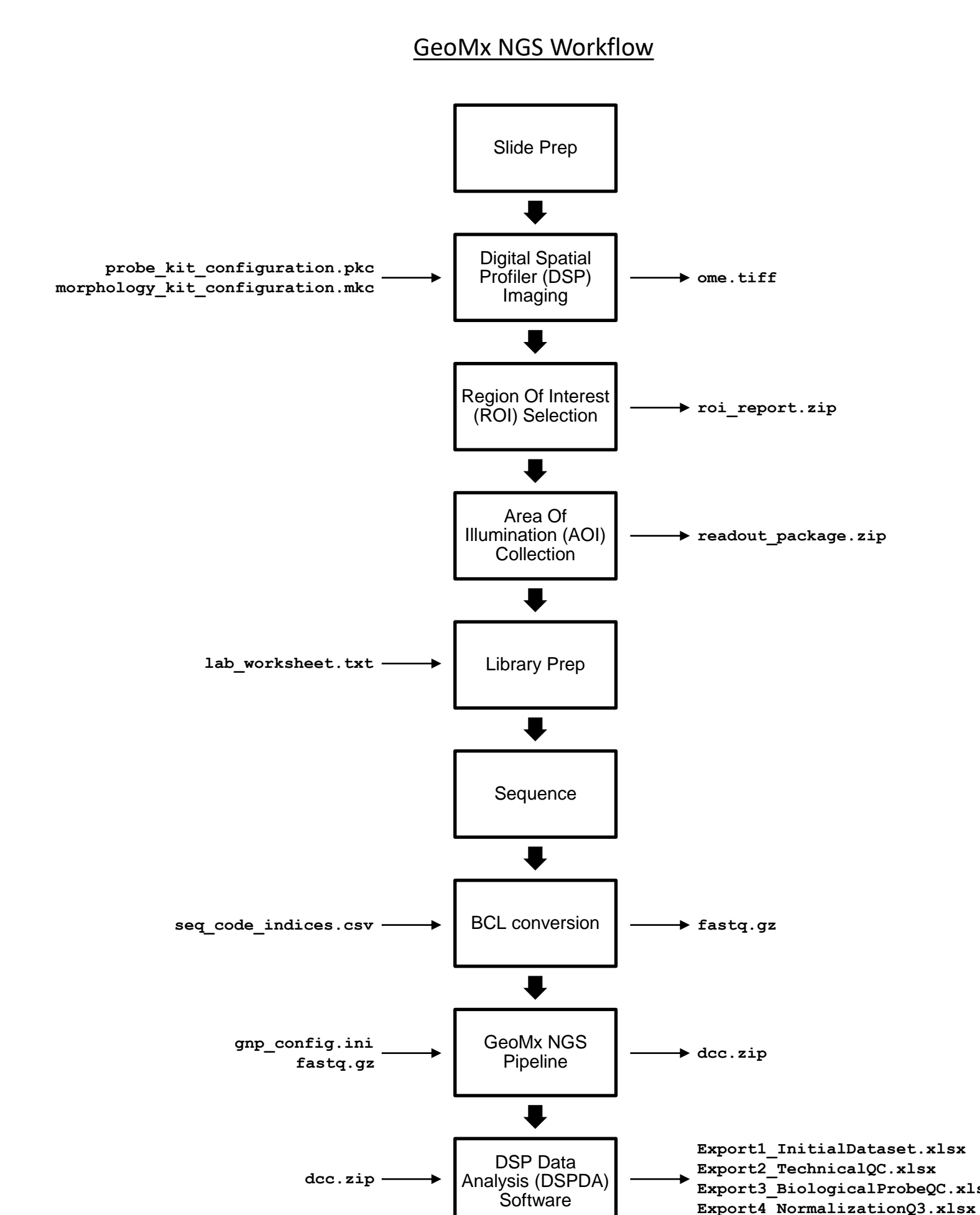
Poster # 516 Dynamically visualizing the link between histological structures and whole transcriptome expression data to explore the Spatial Organ Atlas

Tissue	Number of AOI	Number of Scans
Human Colon	173	4
Human Kidney	234	4
Human Lymph node	193	5
Human Pancreas	144	4
Human Brain	252	5
Mouse Brain	360	4
Mouse Development	747	13
Total regionally collected whole transcriptomes	2103	



All Data is Available for Download

The complete dataset from the GeoMx DSP runs are available for public download. Downloadable files include, tissue images (OME-TIFF), sequencing files (FASTQ), and raw and normalized probe counts (xlsx). Thus, any part of the workflow can be recreated, including tertiary analysis using GeoMx Data Analysis Software or GeomxTools on Bioconductor.



Bioconductor Ecosystem for Analysis

In order to facilitate analysis of data for those who do not have a GeoMx-DSP or wish to use data to create their own analysis pipelines we have created a suite of software modules

- GeoMxTools: Data processing and management
- SpatialDecon: Cell deconvolution
- GeoMxWorkflows: End to end Tutorials
- GeoDiff: Advanced modelling of GeoMx data

These are all available from Bioconductor and new modules are added with each new Bioconductor release.

DOI: 10.18129/B9.bioc.GeoMxWorkflows

One very important aspect of GeoMxTools is that it stores and links all of the expression, annotation, and probe information together in a single data object, the GeoMxSet object. This object is based on the ExpressionSet objects, so will be familiar in many interactions to experienced users of Bioconductor

Conclusions

The spatial organ atlas offers users;

- Exemplary stories showing analysis that can be undertaken using the unique features of the GeoMx DSP
- Access to complete data sets with 2103 spatially organized whole transcriptomes available, allowing users to
 - Compare to other samples to understand spatial variances
 - Mine for information and use in publications
 - Develop Analysis tools

Scan here to learn more about NanoString's Spatial Organ Atlas.



Scan here to learn more about NanoString at AGBT 2022.

