Computational Segmentation of Glomeruli to Align Histomorphology With Spatial Transcriptomic Signature

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Group or Team Name

- Kidney Precision Medicine Project

Background

Glomerular histomorphology establishes kidney disease diagnosis and prognosis. Spatial transcriptomics facilitates spatial resolution of molecular signatures superimposed upon histology. We trained a machine learning (ML) method to automatically segment glomeruli and quantify pixel level image features to align with spatial transcriptomics (ST) performed on the same section.

Methods

Brightfield histology images of 17 kidney disease biopsies and 3 reference kidney sections were used for training a deep learning model for glomerular segmentation. We used 3 additional reference images for testing. Unsupervised clustering of ML features was performed across all glomeruli using Seurat. Transcriptomic signatures of 10X Visium ST spots were deconvoluted with Seurat 3.2.3 transfer scores using the kidney precision medicine project (KPMP) snRNA-seq atlas as reference. Association between cell type composition and ML classification was assessed.

Results

The ML glomerular segmentation achieved sensitivity/specificity/precision 0.88/1.0/0.97. The glomeruli were classified into 3 clusters; with cluster one statistically associated with increases in degenerative podocyte; and a second cluster with a glomerular capillary signature ($p < 0.033$).

Conclusion

Our pipeline will serve as a framework to map molecular to histomorphologic data over large areas captured from large sample libraries, and will aide in the development of kidney precision medicine.
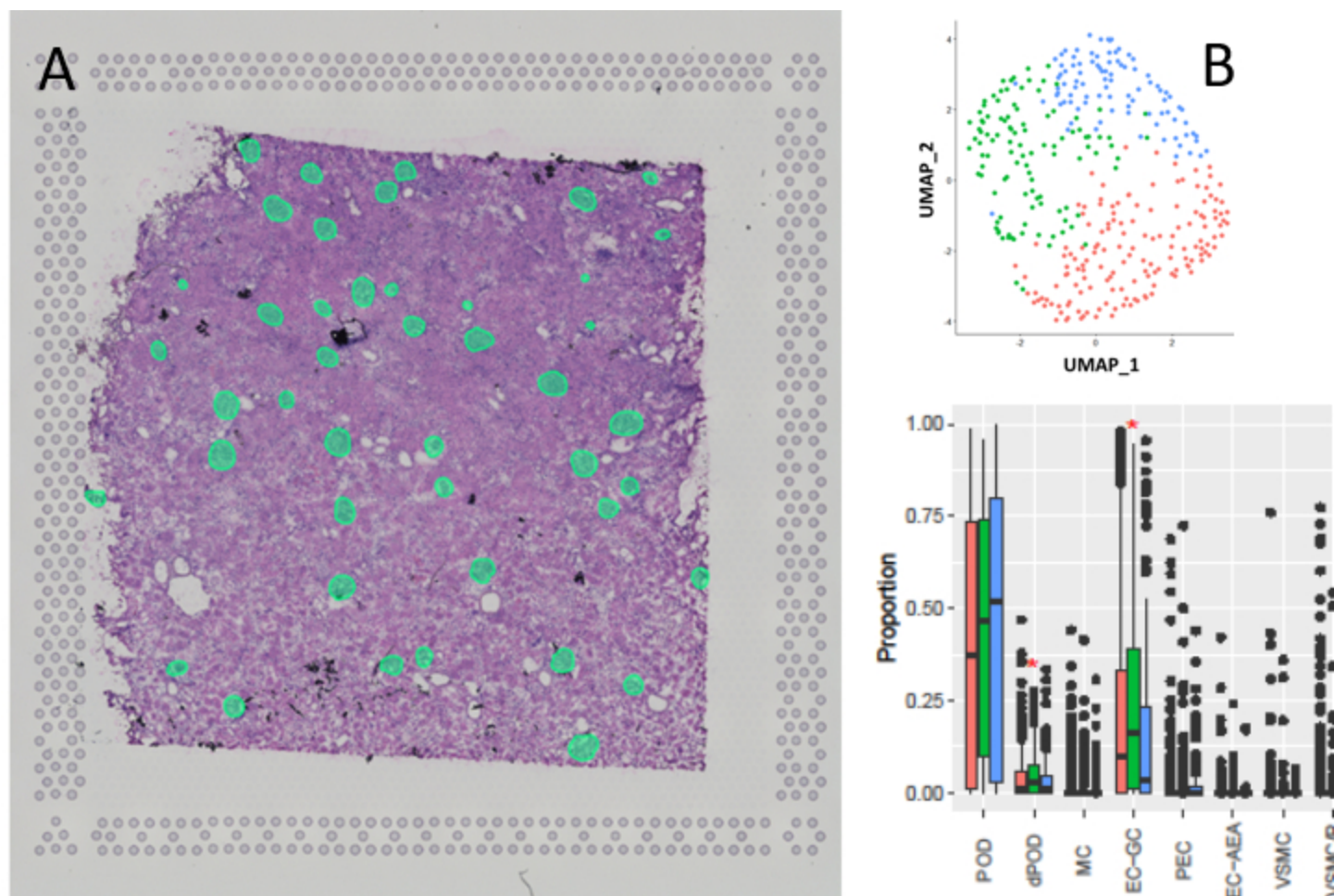
Fig. 1. [A] Computationally segmented glomerular boundaries overlaid on frozen section via 10X slide. [B] Uniform Manifold Approximation and Projection of glomeruli from features defining glomerular sub-cellular morphometry. Each dot is a glomerulus. [C] for spatial transcriptomics spots associated with glomeruli in each glomerular cluster asterisk indicates significance ($p < 0.033$).

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