

Prognostic Glomerular Morphometric Phenotype Discovery via Clustering Across Large Datasets

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Background

Microscopic glomerular assessment is diagnostic and prognostic for a diverse array of renal parenchymal disorders. Digital renal pathology enables complex morphometric studies that may identify prognostic information imperceptible to the human eye. We use clustering and feature enrichment to discover morphometric phenotypes that may relate to patient prognosis.

Methods

A convolutional network extracted glomeruli from 29 Periodic acid-Schiff stained transplant biopsies. 315 features were calculated on each glomerulus and clustered with a modularity-based community detection algorithm available in Seurat. Clusters were compared with patient outcome (eGFR decline at 1 year). A Wilcoxon rank sum test identified features enriching each cluster. Uniform manifold approximation and projection (UMAP) was used to visualize the clusters in low dimension.

Results

Clustering revealed 5 glomerular populations (Fig. 1A), and glomeruli of different patients were well admixed across clusters (Simpson's Diversity Index: 0.78 - 0=no diversity, 1=infinite).

Patients were separated in two classes ($\text{eGFR} \geq 5$ or < 5 mL/min/year), and these labels were projected into the cluster space (Fig. 1B). We observed the clusters show different frequencies of glomeruli from patients with higher eGFR decline. Two of the clusters (2 and 4) had $>90\%$ of their morphometrically similar glomeruli solely from slower eGFR decline patients. The distribution of two example features (glomerular area and total nuclei) per cluster are shown in Figs. 1C & D, though the full analysis revealed hundreds of significant features enriching each cluster.

Conclusion

The adoption of an -omics style analysis for renal histology may be feasible to mine prognostically significant morphometric information.

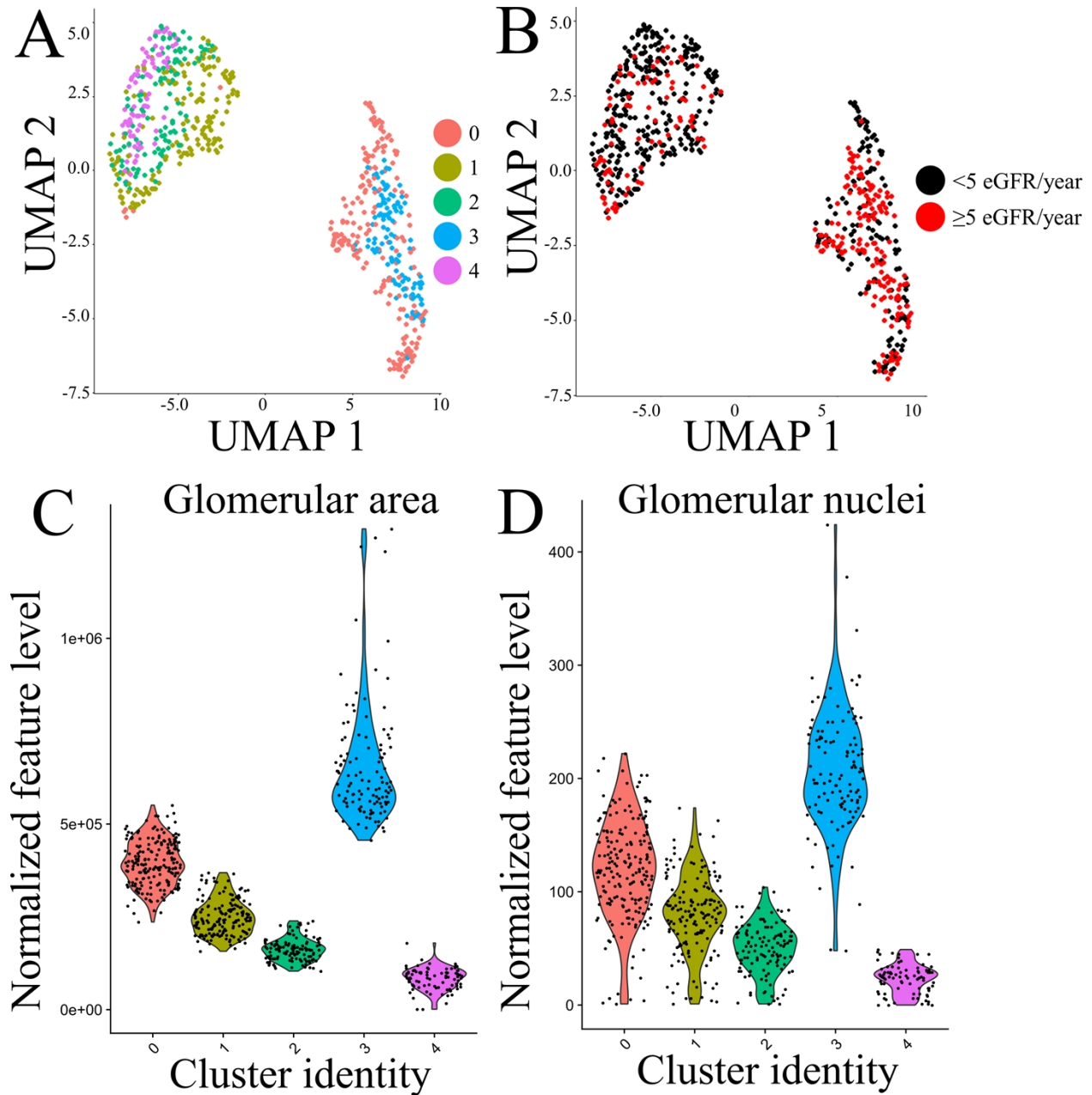


Figure 1. Glomerular morphometric analysis. A) UMAP dimension reduction of the 5 discovered glomerular populations. B) Same glomeruli from A with progression status overlaid as color. C) Normalized glomerular area difference between the clusters. D) Normalized glomerular nuclei between the clusters.

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