Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care
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Multi-Omics-Driven Precision Nephrology: from Mapping the Immune Activation Trajectory to Targeted Nanotherapy

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Background. Glomerular diseases that share a histological label can follow very different cellular trajectories and clinical outcomes. Precision nephrology therefore requires reading molecular biology directly — at compartment-level resolution, in both tissue and circulation — rather than relying on morphology alone. KORNERSTONE is the prospective biopsy cohort and multi-omics platform we have been building at Korea to fill this gap, comprising over 2,100 biopsies across nine diagnostic categories, paired with more than 110,000 biospecimens. Methods and findings. This lecture presents six interlocking studies built on this platform. (i) A single-nucleus atlas of 125 biopsies and 889,646 nuclei decomposes biopsy biology into two orthogonal coordinates — tubular transport and tissue remodeling — and yields a compact 8-gene readout that carries disease-anchored prognostic signal across IgAN, FSGS, MCD, MN, and DKD. (ii) Co-registered Xenium spatial transcriptomics and PAS histology, across 2,770 fields, partition local biology into a morphology-predicted layer and a morphology-orthogonal residual; the residual carries the clinically meaningful disease signal and reveals a peritubular immune endotype of IgAN that histology underestimates. (iii) Projection onto the KPMP single-nucleus reference confirms a shared transport–injury core across cohorts and isolates compartment-specific divergent layers. (iv) On the OLINK Explore HT platform across nearly 400 participants, the JASN 2026 paper differentiates four primary glomerular subtypes from plasma alone (AUROCs 0.80–0.98). A follow-up, kidney-anchored, 8-protein panel charts a podocytopathy-to-remodeling axis between MCD and FSGS and reaches AUROC 0.94, outperforming clinical features layered with raw plasma. (v) Sorted-cell 5′-seq with paired V(D)J in collaboration with Columbia shows that the IgAN-defining galactose-deficient IgA1 axis tracks directly with the per-sample fraction of

expanded activated-B-cell clones. (vi) Multi-omics-nominated targets are delivered through biomimetic RBC- and macrophage-hybrid nanoparticles; in vivo dCas9-ANG1 therapy restores glomerular architecture and podocin in advanced diabetic kidney disease. Conclusion. KORNERSTONE moves precision nephrology from cell-state biology, to non-invasive biomarkers, to targeted nano-therapy — closing the loop from a single biopsy to a treatable mechanism.

Keywords: KORNERSTONE, glomerular disease, multiomics, proteome, nanoparticle