

An Unbiased and Automated Approach: AI-based Pipeline for Glomerulosclerosis Scoring in Rodent Models of Chronic Kidney Disease (CKD)

1 AI-based detection of kidney whole-section and glomeruli

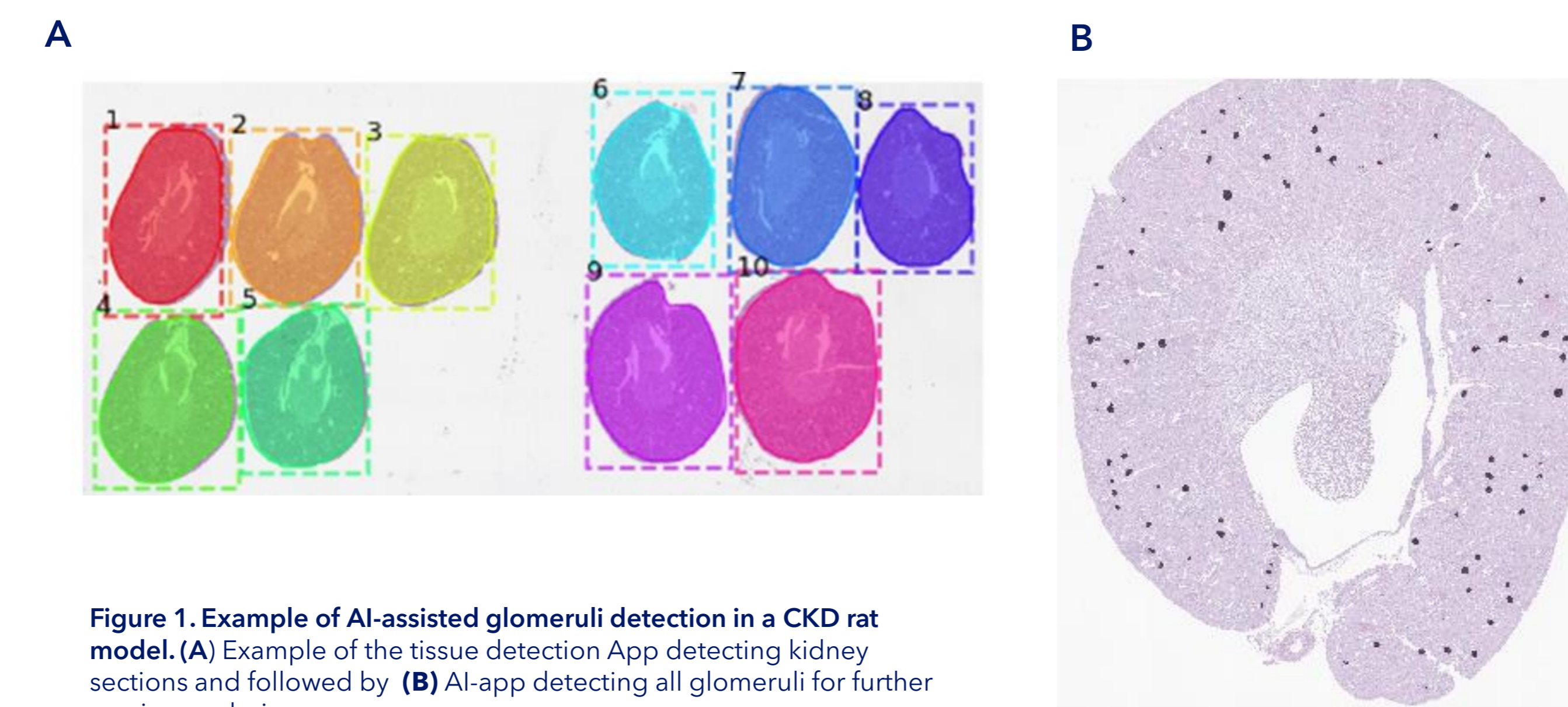


Figure 1. Example of AI-assisted glomeruli detection in a CKD rat model. (A) Example of the tissue detection App detecting kidney sections and followed by (B) AI-app detecting all glomeruli for further scoring analysis.

2 AI-Assisted App for scoring of glomerulosclerosis severity

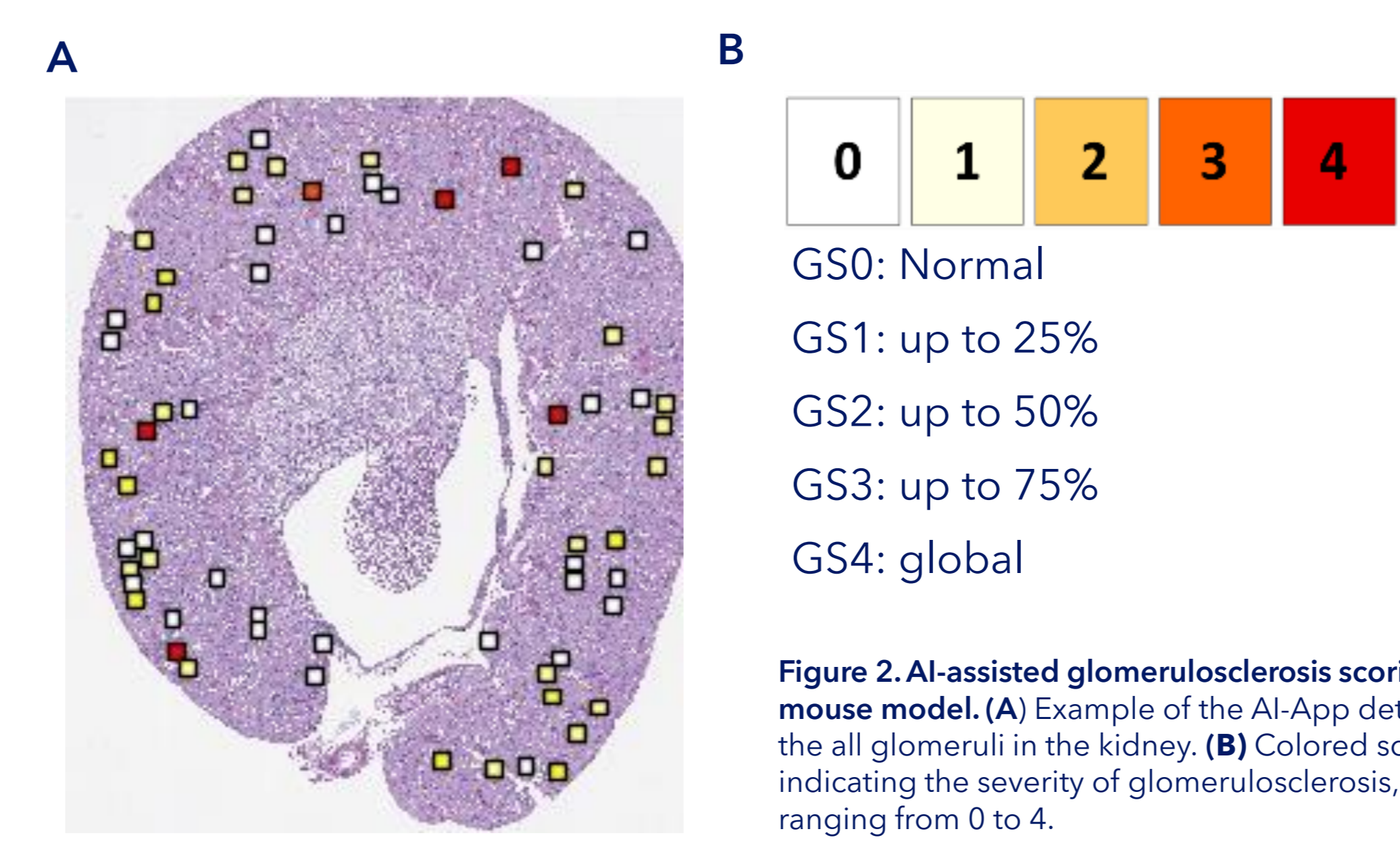


Figure 2. AI-assisted glomerulosclerosis scoring in Anti-GBM mouse model. (A) Example of the AI-App detecting and scoring the all glomeruli in the kidney. (B) Colored score system indicating the severity of glomerulosclerosis, with scoring ranging from 0 to 4.

3 Representative images of glomerulosclerosis severity according to AI-assessed scores

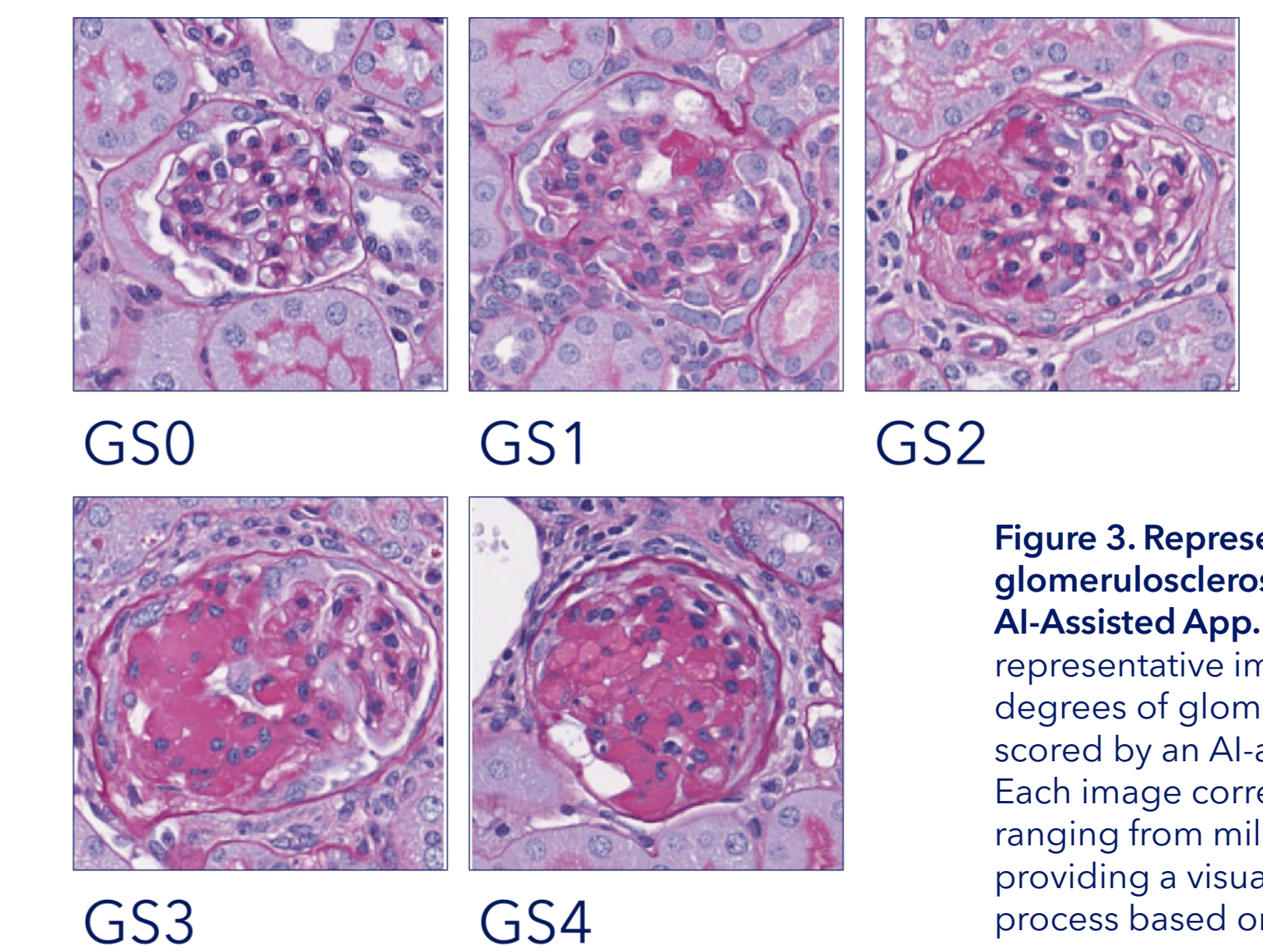


Figure 3. Representative images of glomerulosclerosis scores generated by AI-Assisted App. This figure displays representative images illustrating different degrees of glomerulosclerosis severity, scored by an AI-assisted application. Each image corresponds to a specific score, providing a visual reference for the scoring process based on glomerular damage.

4 Overview of rodent CKD models applied

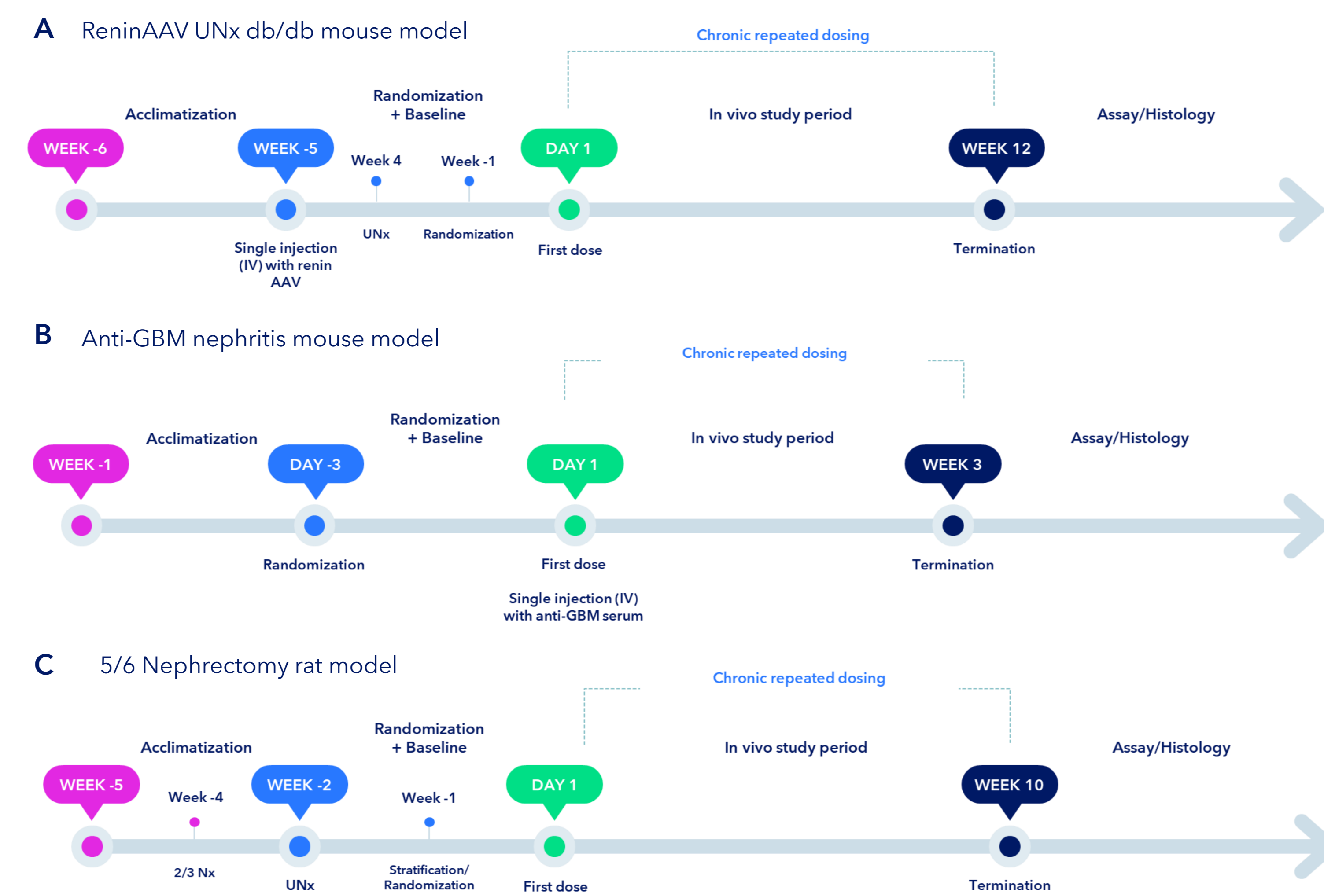


Figure 4. Individual study outlines for characterizing glomerulosclerosis severity in three different rodent models of CKD. (A) Diabetic kidney disease (ReninAAV-UNx db/db mouse). (B) Glomerulonephritis (anti-GBM mouse model). (C) Severe CKD (5/6 Nx rat model).

5 Validation of AI-assisted glomerulosclerosis scoring

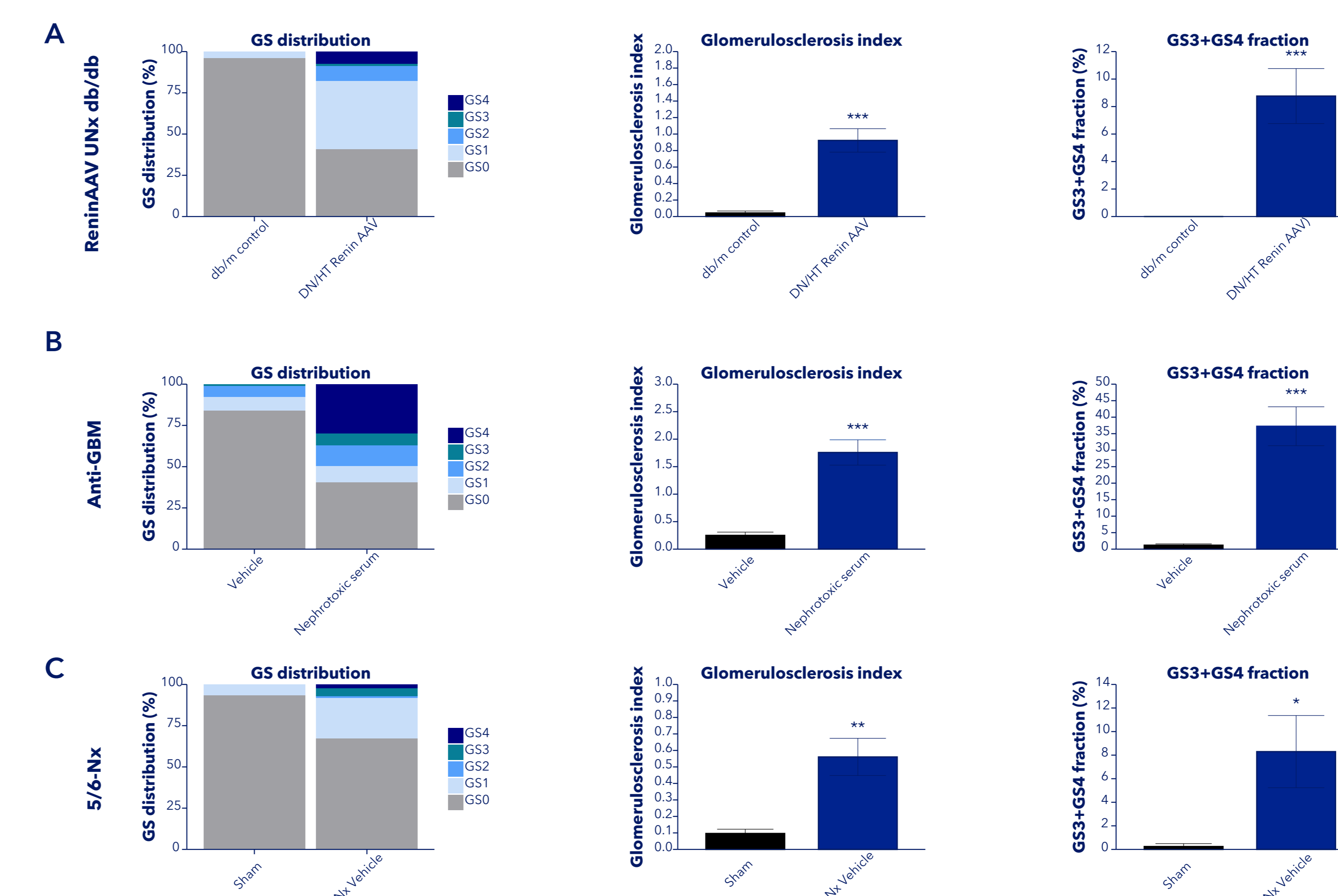


Figure 5. Comparative analysis of glomerulosclerosis across three rodent models of CKD. This figure presents three sets of plots for different rodent models of glomerulosclerosis in (A) ReninAAV UNx db/db, (B) anti-GBM and (C) 5/6-Nx model. Distribution of Glomerulosclerosis Scores shows the distribution of glomerulosclerosis severity across the groups, categorized by scores from GS0 to GS4. Glomerulosclerosis Index represents the average burden of the disease across groups. Percentage of Severe Glomerulosclerosis (% of GS3 and GS4) highlights the proportion of severely affected glomeruli in each model.

Authors

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Background & Aim

Glomerulosclerosis is a hallmark of chronic kidney disease (CKD) and involves the formation of glomerular scar tissue.

Accurate histopathological evaluation of glomerulosclerosis is crucial for assessing the diagnosis, prognosis and treatment CKD patients. Several rodent models of CKD shows glomerulosclerosis and are highly instrumental in preclinical target discovery and drug development. To accelerate the objective and efficient assessment of glomerulosclerosis, we have designed, validated and implemented an AI-powered histopathological scoring system applicable for both mouse and rat models of CKD.

Methods

A deep learning AI-model was trained on a large sample test set (4293 glomeruli images) of mouse and rat PAS-stained kidney sections and compared to expert histopathologist-verified manual glomerulosclerosis scoring. AI model performance was validated using an independent kidney sample set from three different rodent models of CKD:

- (1) Diabetic kidney disease** induced by adeno-associated virus-mediated renin overexpression in uninephrectomized (ReninAAV-UNx) diabetic *db/db* mice
- (2) Glomerulonephritis** induced by immunization with-glomerular basement membrane (GBM) antibody in the mouse
- (3) Severe CKD** induced by 5/6 nephrectomy (Nx) in the rat.

Conclusion

- + Our AI-based glomerulosclerosis scoring method offers unbiased, accurate and automated glomerulosclerosis assessment in rodent models of CKD.
- + The pipeline is optimized to accommodate both mouse and rat kidney sections, highlighting the applicability to the wide range of rodent models of CKD used in preclinical drug discovery.

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