

Supplementary Information

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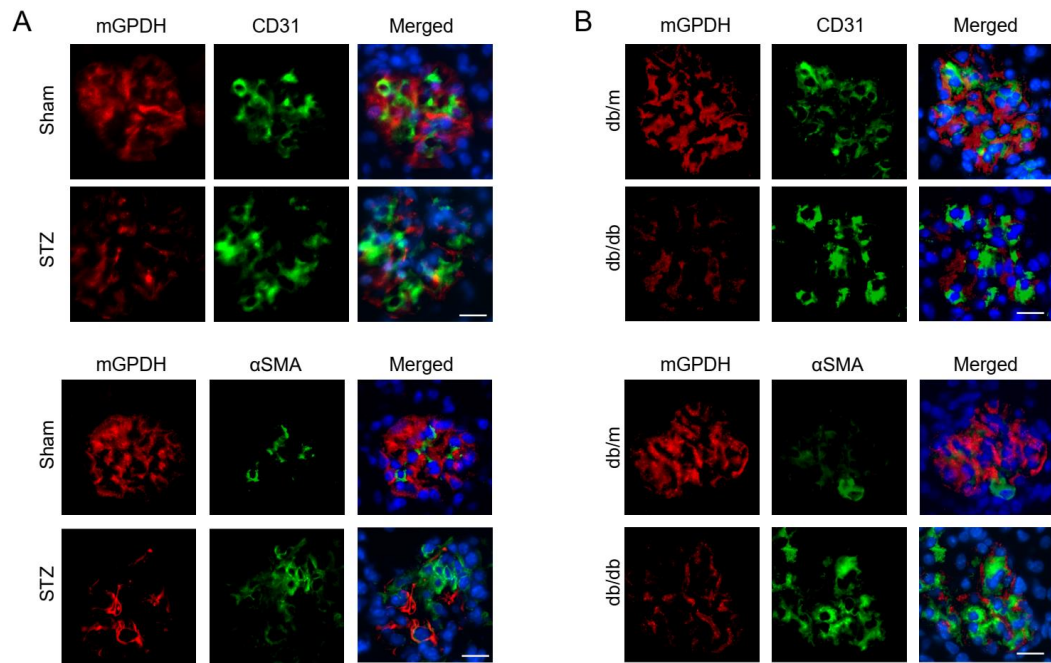
Supplementary Table 1. Clinical characteristics of DKD patients and healthy subjects

Supplementary Table 2. List of primers.

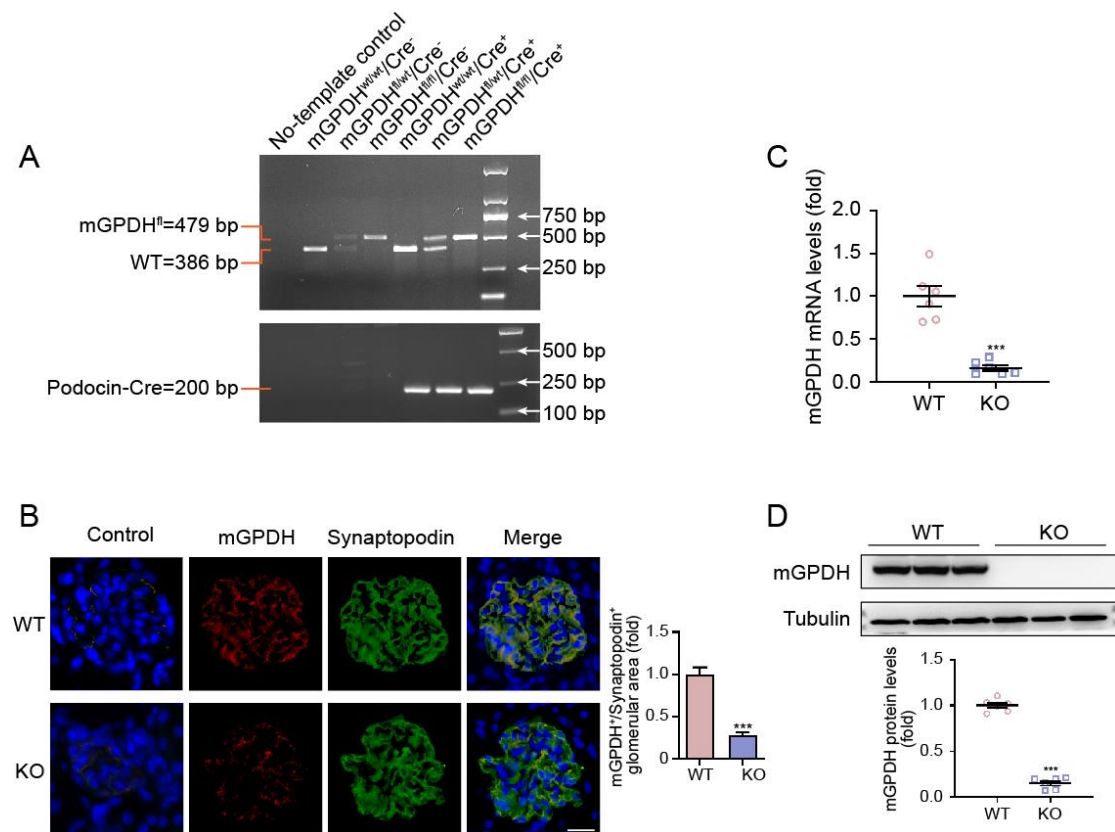
Supplementary Table 3. Differential expressed genes in glomeruli from diabetic mGPDH KO mice compared with WT mice.

Supplementary Table 4. Top 10 terms of KEGG analysis for differentially expressed genes in glomeruli from diabetic mGPDH KO mice compared with WT mice.

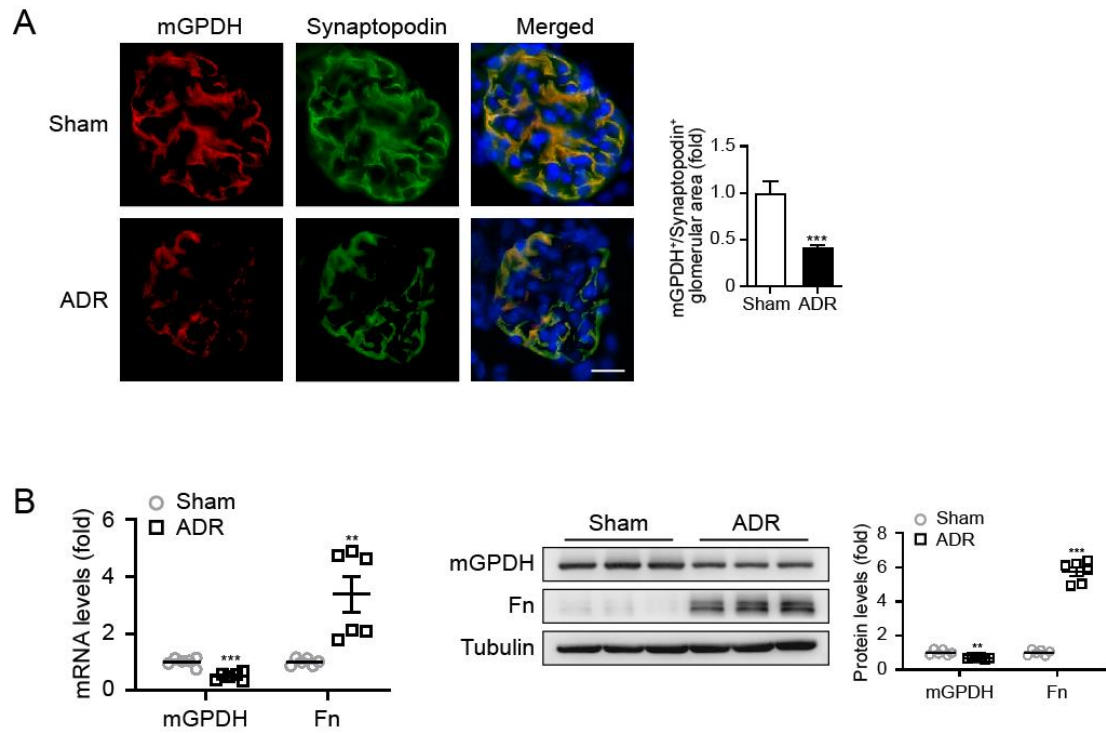
Supplementary Table 5. Top 10 terms of GO_BP analysis in glomeruli from diabetic mGPDH KO mice compared with WT mice.



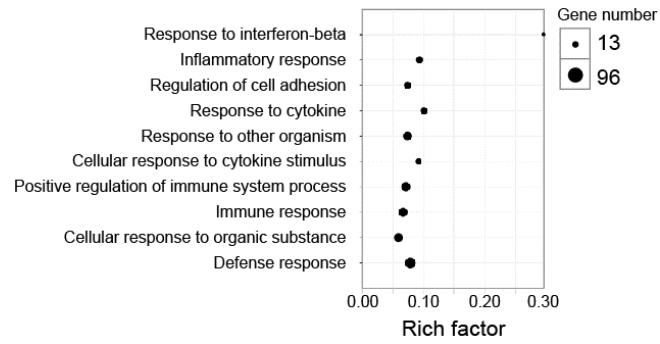
Supplementary Figure 1. mGPDH expression in glomerular cells from mice DKD models. Representative images of co-immunofluorescent staining of mGPDH with endothelial cell marker CD31 and mesangial cell marker α SMA in kidney cortical tissue from STZ-induced diabetic mice (A) and db/db mice (B). Scale bars: 20 μ m for A and B. n = 6 mice per group for A and B.



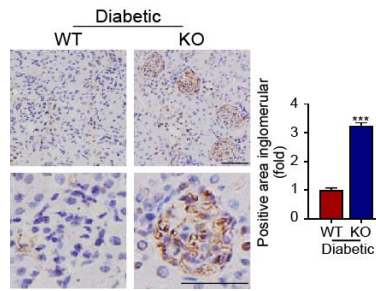
Supplementary Figure 2. Podocyte-specific deletion of mGPDH by using Cre-LoxP recombination system. (A) To generate podocyte-specific mGPDH deletion mice (KO) and their littermate control mice (WT), mGPDH^{fl/fl} mice were cross breeding with podocin-Cre mice, genotyping was conducted by tail at 3-4 weeks of age. (B) Representative images of co-immunofluorescent staining of mGPDH with podocyte marker synaptopodin were shown. (C and D) The mRNA and protein expression of mGPDH were assessed in isolated glomeruli from KO and WT mice. Scale bars: 20 μ m for B. n = 6 mice per group for B-D. Data are presented as the mean \pm S.E.M. ***P < 0.001.



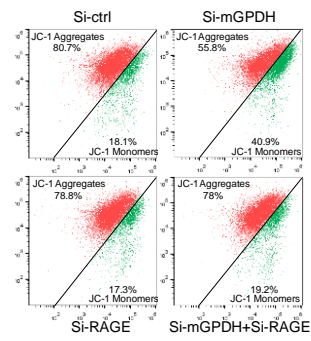
Supplementary Figure 3. mGPDH expression is decreased in glomerular cell from adriamycin (ADR)-induced podocyte injury mouse model. (A) Representative image of co-immunofluorescence staining of mGPDH with synaptopodin in kidney tissue from ADR-treated mice. (B) mRNA and protein expression of mGPDH from isolated glomeruli of ADR-injected mice. Scale bars: 20 μ m for A. n = 6 mice per group for A and B. Data are presented as the mean \pm S.E.M. **P < 0.01, ***P < 0.001.



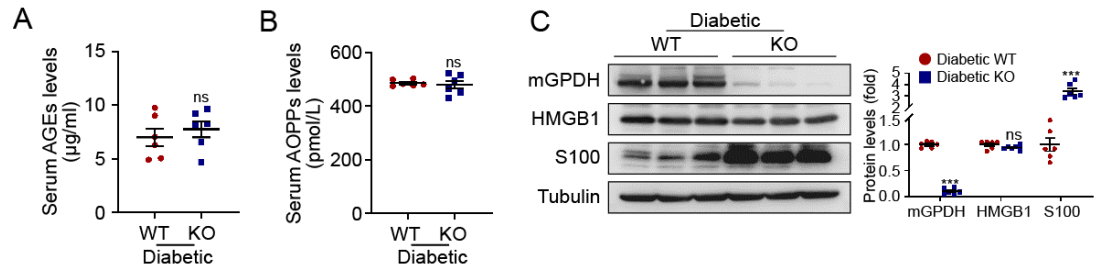
Supplementary Figure 4. KEGG pathway analysis among all significantly down-regulated genes. RNA-seq analysis were conducted in isolated glomeruli from diabetic KO and WT mice, and top 10 ranking terms of KEGG analysis in all significant down-regulated genes were shown. n = 3.



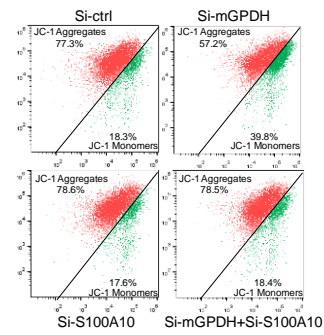
Supplementary Figure 5. Podocyte-specific mGPDH deletion increases RAGE expression in glomeruli. Representative immunohistochemistry images of RAGE in kidneys from diabetic mGPDH WT and KO mice. Scale bars: 50 μ m. n = 6 mice per group.



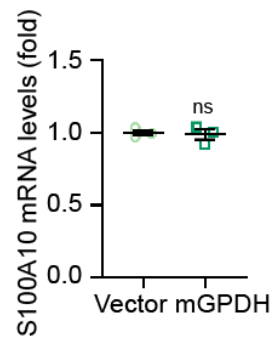
Supplementary Figure 6. MMP flow cytometry images of podocytes with knocking down mGPDH and RAGE. Podocytes were knocked down with mGPDH and (/or) RAGE with their specific siRNA and treated with high glucose (HG) for 48 hours, MMP was analyzed.



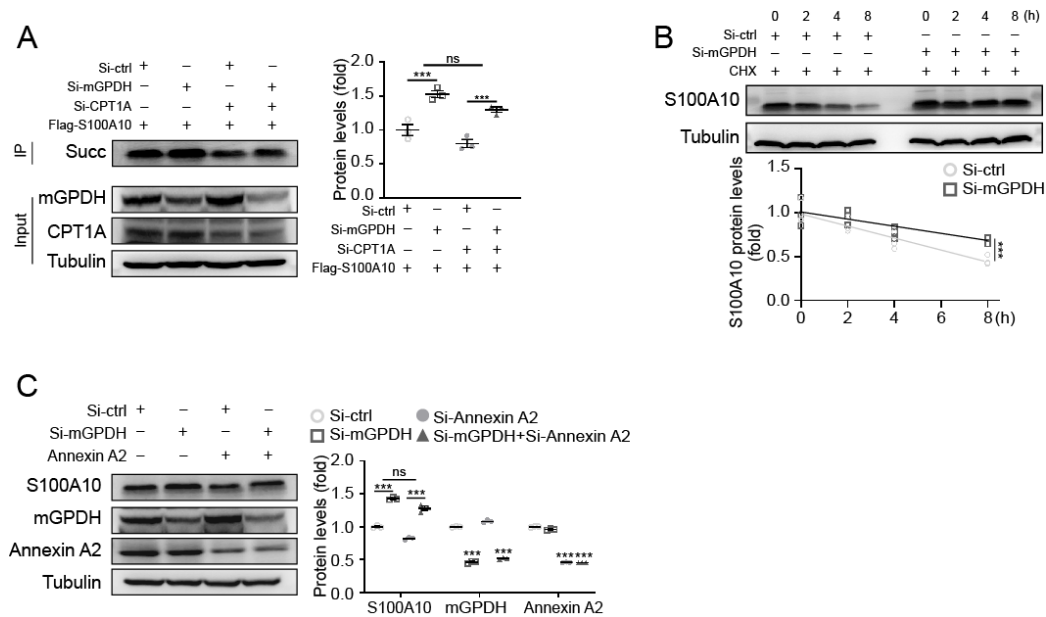
Supplementary Figure 7. Podocyte-specific mGPDH deletion increases S100 expression rather than AGEs, AOPPs and HMGB1. (A and B) Serum AGEs and AOPPs concentrations were detected by ELISA in diabetic KO and WT mice. (C) Expression of indicated protein in isolated glomeruli from diabetic KO and WT mice. n = 6 mice per group for A-C. Data are presented as the mean \pm S.E.M. ns, not significant.



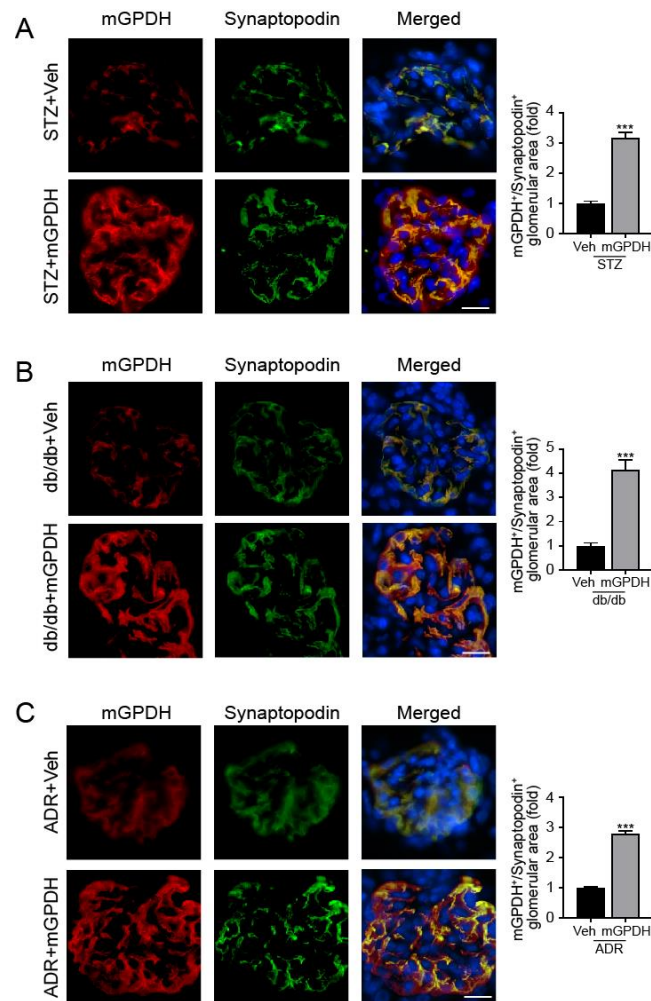
Supplementary Figure 8. MMP flow cytometry images of podocytes with knocking down mGPDH and S100A10. Podocytes were knocked down with mGPDH and (/or) S100A10 with their specific siRNA and treated with HG for 48 hours, MMP was analyzed.



Supplementary Figure 9. mGPDH overexpression has no effect on mRNA expression of S100A10. Differentiated podocytes were transfected with the mGPDH overexpression plasmid with 48 hours of HG treatment, and S100A10 mRNA expression is shown. $n = 3$.



Supplementary Figure 10. CPT1A and Annexin A2 may not involve in the regulation of mGPDH on S100A10. (A) Differentiated podocytes were knocked down with mGPDH and (/or) CPT1A with their specific siRNA and treated with HG for 48 hours, and S100A10 succinylation was detected. (B) Differentiated podocytes were transfected with mGPDH-specific siRNA, and the half-life of S100A10 protein was determined by pulse-chase assay with protein synthesis inhibitor CHX (25 μ M) administration. (C) Differentiated podocytes were knocked down with mGPDH and (/or) Annexin A2 with their specific siRNA and treated with HG for 48 hours, and the indicated protein expression was detected by immunoblotting. $n = 3$. The data are presented as the mean \pm S.E.M. *** $P < 0.001$; ns, not significant.



Supplementary Figure 11. AAV9-Nphs1-mGPDH leads to mGPDH overexpression in podocyte of glomeruli. Representative image of co-immunofluorescence staining of mGPDH with podocyte marker synaptopodin in STZ-induced diabetic mice (A), db/db mice (B) and ADR-injected mice. Scale bars: 20 μ m. n = 6 mice per group for A and B; n = 5-6 mice per group for C.