Supplementary Table 1. Signaling pathways involved in kidney diseases

Signaling pathway	CRD	TMA (HUS) P-ECL	DN	CGN	IgAN	MPGN	LN	AKI	CKD	Anti-GBM GN	FSGS
VEGF-A											
In vitro studies and animal model	↓ During glomerular development, causing loss of GFB and reduction of survival [7]	↓ In P-ECL, due to excessive sFlt1 [10,11]	A delicate balance of the signal intensity ↑ In the early angiogenic stage [14–17] ↓ Accelerates renal damage [18]								
Human studies		↓ Due to elevated sFlt1in P-ECL and anti-VEGF therapy [12,13]	In tubulointerstitial compartments, a significant inverse correlation between VEGF-A and proteinuria [19]	↑ In serum and urine [20]		↑ Inducing MC proliferation [21]					
ET-1											
In vitro studies and animal model			↑ Deletion of ETAR and ETBR avoid D-FSGS and podocyte loss [33]				↑ GECs production of ET-1 by PCM-LN, ECM-PCM-LN induces nephrin loss in podocyte. Anti-ETAR antibody blocks the effect [34]				↑ Release of ET-1 by podocyte and enhance ETAR expression in GECs through activating TGF-β [35,36]
Human studies							Correlation between the FPW and the pathological score of GEC damage [34]				
ANGPTs											
In vitro studies and animal model	↓ Deletion of ANGPT1 before (E) 12.5 leads to early embryonic death. Deletion at E10.5 showed vascular abnormalities [53]		↓ ANGPT1 worsens DN, ↑ ANGPT1 delays DN progression [54]							↓ ANGPT1, ↑ ANGPT2 results in glomerular capillaries loss [55]	

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Supplementary Table 1. Continued

Signaling pathway	CRD	TMA (HUS) P-ECL	DN	CGN	IgAN	MPGN	LN	AKI	CKD	Anti-GBM GN	FSGS
CXCL12/CXCR4/CXCR7											
In vitro studies and animal model	CXCL12 or CXCR4 or CXCR7 leads to deficit nephro-genesis [61,62]		Protective or aggra-vate effect on DN progres-sion [63]				↑ CXCL12/CXCR4 axis causes LN progression via ACSs-mediated autoantibodies deposits, T cell, and PerB1a lym-phocyte infiltra-tion [63]	↑ CXCL12/ CXCR4 axis con-tributes to AKI regenera-tion [68]			
IL-6											
In vitro studies and animal model			IL-6 induces insu-lin resistance. Hyperglycemia triggers podo-cyte, MC, inter-stitial tissue, and tubules to generate IL-6 [73]		↑ MC production by ImmC, and CC. Promoting MC prolifer-ation and IC recruit-ment [73]		↑ In serum, urine, and glomeruli. IL-6 deficiency or inhibi-tion IL-6 Trans-sig ameliо-rate LN [73].	↑ In isch-emia and nephro-toxin AKI [73].	IL-6 injection exacerbates atheroscle-rosis [73]		
Human studies			↑ In early stage of type I D. Correla-tion be-tween IL-6 and autoimmune diabetes [73] ↑ In type II D. Associated with atherosclerosis development [73]				↑ In serum, urine, and glomeruli. Correlation with the activity of LN [73]		↑ In plasma, accelerates the CVD and CKD progres-sion [73]		
EVs											
In vitro studies and animal model	EVs from GECs undergoing EndMT cause podocytes' EMT [85]. EPC-derived EVs protect podocyte and GEC against complement- and cytokine-induced damage [86].										

AKI, acute kidney injury; ANGPT, angiopoietin; Anti-GBM GN, anti-glomerular basement membrane glomerulonephritis; ASCs, antibody-secreting cells; CC, comple-ment component; CGN, cres-centic glomerulonephritis; CKD, chronic kidney disease; CRD, congenital renal diseases; CVD, the chronic vascular disease; D, diabetes; DN, diabetic nephropathy; D-FSGS, diabetic FSGS; ECM-PCM-LN, endothelial-conditioned medium stimulated with PCM-LN; EMT, epithelial-to-mesenchymal transition; EndMT, endothelial-to-mesenchymal transition; EPCs, endothelial progenitor cells; EVs, extracellular vesicles; ET-1, endothelin-1; ETAR, endothelin receptor type A; ETBR, endothelin receptor type B; FSGS, focal segmental glomerular sclerosis; FPW, width of the foot process; GECs, glomerular endothelial cells; GFB, glomerular fil-tration barrier; HUS, hemolytic uremic syndrome; IC, inflammatory cell; IgAN, IgA nephropathy; IL-6, interleukin-6; ImmC, immune cells; LN, lupus nephritis; MC, mesangial cell; MPGN, membranoproliferative glomerulonephritis; P-ECL, preeclampsia; PCM-LN, podocyte-conditioned medium stimulated with IgG from LN patients; Per-B1a, peritoneal B1a; sFlt1, soluble form of VEGF receptor-1; TMA, thrombotic microangiopathy; Trans-sig, trans-signaling; VEGF-A, vascular endothelial growth fac-tor A.