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Supplementary information

Phenotypic diversity and metabolic specialization of renal endothelial cells

In the format provided by the authors and unedited

Supplementary Table 1 | Renal endothelial cell marker genes and known functions				
Gene	**Protein**	**Compartment**	**Function**	**Ref.**
Abcc4	ATP binding cassette subfamily C member 4 (Multidrug resistance-associated protein 4)	Glomerular capillaries	Organic anion transporter	1,2
Ace	Angiotensin-converting enzyme	Large arteries	Conversion of angiotensin I into angiotensin II; involved in vasotone regulation	3,4
Adipor2	Adiponectin receptor 2	DVR	Adiponectin receptor; involved in vasotone regulation	5
Akr1b3	Aldo-keto reductase family 1 member B3	DVR papilla and AVR papilla	Reduction of glucose to sorbitol; maintenance of cell volume during hyperosmolarity	6
Aldoa	Fructose-bisphosphate aldolase A (also known as Aldolase 1)	AVR papilla	Glycolytic gene; conversion of fructose-1,6-bisphosphate to glyceraldehyde 3-phosphate and dihydroxyacetone phosphate	3,7,8
Alox12	Polyunsaturated fatty acid lipoxygenase ALOX12 (also known as Arachidonate 12-Lipoxigenase)	Cortical afferent arterioles and Glomerular distal afferent arterioles	Product of the arachidonate lipoxygenase; involved in vasotone regulation in response to angiotensin	3,9-11
Apln	Apelin	Cortical angiogenic capillaries and Medullary angiogenic capillaries	Involved in angiogenesis	3,12-14
Aplnr	Apelin Receptor	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	1,12,15
Apoe	Apolipoprotein E	Cortical peritubular capillaries type 1	Involved in lipid metabolism; internalization of lipoproteins or lipid complexes from the plasma to the cells by interacting with specific receptors	3,16
Aqp1	Aquaporin 1	DVR	Passive transport of water along an osmotic gradient; involved in urine concentration	1,3,17-20
Bmp4	Bone morphogenetic protein 4	Large arteries, cortical afferent arterioles and glomerular distal afferent arterioles	Secreted ligand of TGF-β; involved in elastic fiber assembly	1,3,21
Calca	Calcitonin gene-related peptide 1	Cortical efferent arterioles and glomerular distal efferent arterioles	Involved in vasotone regulation; potent renal vasodilator	3,22
Car2	Carbonic anhydrase 2	AVR papilla	Reversible conversion of carbon dioxide and water into carbonic acid; involved in urine concentration by interacting with AQP1	3,23
Cd36	Platelet glycoprotein 4 (Fatty acid translocase)	mRECs; medullary capillaries	Uptake of long-chain fatty acids from the circulation; renal deficiency linked to a higher risk for spontaneous hypertension	3,24-26

Cd9	CD9 antigen (Tetraspanin-29)	Cortical veins and AVR papilla	Osmolarity-induced gene; also involved in immune cell adhesion and extravasation	3,27,28
Cldn5	Claudin-5	Large arteries, cortical afferent arterioles, glomerular distal afferent arterioles and DVR	Endothelial tight junction; expression restricted in arteries and absent in capillaries and veins in the kidney	1,3,12,17,29
Col4a1	Collagen alpha-1 (IV) chain	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,12,13
Col4a2	Collagen alpha-2 (IV) chain	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,13
Crip1	Cysteine-rich protein 1	DVR papilla and AVR papilla	Stress response factor; cytoprotective	3,30
Cryab	Alpha-crystallin B chain	Cortical efferent arterioles, glomerular distal efferent arterioles and AVR papilla	Part of the small heat shock protein family; hyperosmolarity-induced gene regulated by NFAT5	3,31,32
Cxcl12	Stromal cell-derived factor 1 (also known as C-X-C motif chemokine 12)	DVR and cortical afferent arterioles	Ligand for CxCr4 and CxCr7; important in development of the renal vasculature	3,33,34
Cxcr4	C-X-C Chemokine Receptor type 4 (also known as stromal cell-derived factor 1 receptor)	Glomerular afferent arterioles and JGA	Chemokine receptor; expressed by ECs in contact with renin-positive cells at the JGA	34
Cyp4b1	Cytochrome P450 4B1	gRECs	Monooxygenase	3
Edn1	Endothelin-1	Large arteries, cortical afferent arterioles, glomerular distal afferent arterioles and DVR	Vasotone regulation; potent vasoconstrictor	3,12,35,36
Ehd3	EH domain-containing protein 3	Glomerular capillaries	Regulation of endocytic recycling of VEGFR2	1,3,37,38
Eng	Endoglin	Glomerular capillaries	Associated with the TGF-β–BMP signaling pathway; important in vascular development and disease	3,39,40
Eln	Elastin	Large arteries	Elastic fiber assembly	1,3,12,41
Esm1	Endothelial cell-specific molecule 1	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,12-14

Fbln5	Fibulin-5	Large arteries, cortical afferent arterioles, cortical efferent arterioles, glomerular distal afferent arterioles, glomerular afferent arterioles JGA, glomerular efferent arterioles JGA, glomerular distal efferent arterioles, DVR and DVR papilla	Elastic fiber assembly	1,3,12,42,43
Fgf1	Fibroblast growth factor 1	Glomerular capillaries	Growth factor; regulation of renal blood pressure	1,44
Flt1	Vascular endothelial growth factor receptor 1	Cortical peritubular capillaries type 1, cortical interferon activated capillaries, cortical angiogenic capillaries, medullary capillaries, medullary interferon activated capillaries, and medullary angiogenic capillaries	VEGF receptor	3
Flt4	Vascular endothelial growth factor receptor 3	Lymphatics	VEGF receptor	45
Fscn1	Fascin	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,13
Fxyd2	Na(+)/K(+) ATPase subunit gamma	AVR papilla	Hyperosmolarity-induced gene; regulation of the Na^+/K^+ ATPase activity	3,31
Fxyd5	FXYD domain-containing ion transport regulator 5	DVR papilla and AVR papilla	Hyperosmolarity-induced gene; regulation of Na^+/K^+ ATPase activity	3,46
Fxyd6	FXYD domain-containing ion transport regulator 6	AVR	Regulation of Na^+/K^+ ATPase activity	3
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase	AVR papilla	Glycolytic gene; conversion of glyceraldehyde 3-phosphate to D-glycerate 1,3-bisphosphate	3,7,8
Gas6	Growth arrest-specific protein 6	Cortical veins, glomerular efferent arterioles JGA and AVR	Regulation of endothelial permeability	3,47
Gata5	Transcription factor GATA 5	gRECs	Transcription factor; crucial for gREC identity	1,3,24
Gja4	Gap junction alpha-4 protein	Cortical afferent arterioles, glomerular distal afferent arterioles, DVR and DVR papilla	Connexin 37; present in ECs from afferent arterioles but not efferent arterioles	3,33,48
Gja5	Gap junction alpha-5 protein	Glomerular afferent arterioles JGA and large arteries	Connexin 40; regulation of renin release to regulate communication between the endothelium and the granular cells in the JGA	3,12,49-51
Gpihbp1	Glycosylphosphatidylinositol-anchored high density lipoprotein-binding protein 1	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,13

Hipk2	Homeodomain-interacting protein kinase 2	Glomerular capillaries	Transcription factor; regulation of TGF-β-dependent angiogenesis during embryonic development	[3,52]
Hpgd	15-hydroxyprostaglandin dehydrogenase	DVR	Vasotone regulation; involved in prostaglandin metabolism	[3,53]
Ifi203	Interferon-activable protein 203	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Ifi204	Interferon-activable protein 204	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Ifit1	Interferon-induced protein with tetratricopeptide repeats 1	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Ifit2	Interferon-induced protein with tetratricopeptide repeats 2	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Ifit3	Interferon-induced protein with tetratricopeptide repeats 3	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Ifit3b	Interferon-induced protein with tetratricopeptide repeats 3B	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Igfbp3	Insulin-like growth factor-binding protein 3	cRECs	Insulin growth factor binding protein	[3,55,56]
Igfbp7	Insulin-like growth factor-binding protein 7	mRECs	Insulin growth factor binding protein; urinary marker of renal injury and predictor of renal recovery after acute kidney injury	[3,57]
Insr	Insulin receptor	Cortical peritubular capillaries type 1, cortical interferon activated capillaries and cortical angiogenic capillaries	Insulin growth factor binding receptor	[3]
Irf7	Interferon regulatory factor 7	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Isg15	Ubiquitin-like protein ISG15	Cortical interferon activated capillaries and medullary interferon activated capillaries	Interferon-stimulated gene	[3,54]
Jag1	Jagged1	Large arteries	Notch ligand; EC expression important for vascular smooth muscle cells in development	[3,58]
Jup	Junction plakoglobin	Cortical postcapillary venules and medullary postcapillary venules	Regulation of endothelial permeability by interacting with VE-Cadherin	[3,59,60]

Kcnn4	Intermediate conductance calcium-activated potassium channel protein 4	Cortical afferent arterioles, glomerular distal afferent arterioles and large arteries	Potassium channel activated by intracellular calcium	1
Kdr	Vascular endothelial growth factor receptor 2	Cortical peritubular capillaries type 1, cortical interferon activated capillaries, cortical angiogenic capillaries, glomerular capillaries, medullary capillaries, medullary interferon activated capillaries, medullary angiogenic capillaries, cortical postcapillary venules and medullary postcapillary venules	VEGF receptor	3
Klf4	Kruppel-like factor 4	Cortical efferent arterioles and glomerular distal efferent arterioles	Shear stress-induced gene; protective effect in acute kidney injury and regulation of proteinuria	3,61
Ldha	L-lactate dehydrogenase A chain	AVR papilla	Glycolytic gene; conversion of lactate to pyruvate	3,7,8
Lpl	Lipoprotein lipase	Glomerular capillaries	Involved in lipid metabolism; extracellular enzyme on the luminal side of the vascular endothelial surface; degradation of circulating triglycerides in the bloodstream	3,12,62,63
Ltbp4	Latent-transforming growth factor beta-binding protein 4	Large arteries	Elastic fiber assembly by interacting with fibulin-5	1,3,64
Lyve1	Lymphatic vessel endothelial hyaluronan receptor 1	Lymphatics	Hyaluronan receptor	65
Mapt	Microtubule-associated protein tau	Glomerular capillaries	Promotion of microtubule assembly and stability	3,66
Mgp	Matrix Gla protein	Large arteries	Suppression of vascular calcification likely by inhibiting BMP2 and BMP4 signaling	3,12,67
Nostrin	Nostrin (also known as nitric oxide synthase trafficker)	Glomerular capillaries	Triggering of eNOS translocation from the plasma membrane to vesicle-like subcellular structures, attenuating nitric oxide production	24,68
Npr3	Atrial natriuretic peptide receptor 3	cRECs	Regulates blood volume and sodium excretion	3,69,70
Nr2f2	COUP transcription factor 2	Cortical veins; cortical postcapillary venules; medullary postcapillary venules; AVR and AVR papilla	Vein transcription factor	3,12,71
Nrgn	Neurogranin	DVR papilla and AVR papilla	Calmodulin-binding protein	3

Nrp1	Neuropilin-1	Cortical peritubular capillaries type 1, cortical interferon activated capillaries, cortical angiogenic capillaries, medullary capillaries, medullary interferon activated capillaries and medullary angiogenic capillaries	VEGF receptor	3
Pdpn	Podoplanin	Lymphatics	Mucin-type protein; the most reliable marker in humans for lymphatic ECs	72-74
Pi16	Peptidase inhibitor 16	gRECs	Shear stress-induced gene	3,12,75
Plat	Tissue-type plasminogen activator	gRECs	Involved in the breakdown of blood clots; conversion of plasminogen to plasmin, a fibrinolytic enzyme	3,12
Plk2	Serine/threonine-protein kinase PLK2	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,76
Plpp3	Phospholipid phosphatase 3	Medullary capillaries and cortical peritubular capillaries type 1	Involved in lipid metabolism; catalyses the dephosphorylation of several lipid substrates; crucial role in vascular development	3,77
Plvap	Plasmalemma vesicle-associated protein	Cortical peritubular capillaries, cortical interferon activated capillaries, cortical angiogenic capillaries, AVR and AVR papilla	PV-1; present in fenestrated ECs with diaphragms	1,3,78
Prox1	Prospero homeobox protein 1	Lymphatics	Transcription factor; required for development of the murine lymphatic system	79
Ptprr	Receptor-type tyrosine-protein phosphatase R	Glomerular efferent arterioles JGA	Hyperosmolarity-responsive gene	3,31
S100a4	Protein S100-A4 (also known as S100 calcium-binding protein A4)	DVR papilla	Hyperosmolarity responsive-gene; NFAT5 target gene	3,46
S100a6	Protein S100-A6 (also known as S100 calcium-binding protein A6)	DVR papilla and AVR papilla	Hyperosmolarity responsive-gene; NFAT5 target gene	3,46
S1pr1	Sphingosine-1-phosphate receptor 1	Large arteries, cortical afferent arterioles and glomerular distal afferent arterioles	Vascular tone regulation by activating eNOS	3,80
Scin	Adseverin (also known as Scinderin)	DVR	Formation of a multiprotein complex, presumably for AQP-2 trafficking	3,81
Scn7a	Sodium channel protein type 7 subunit alpha	Glomerular capillaries	Voltage-gated sodium channel protein; linked to hypertension	1,24,82

Sema3g	Semaphorin-3G	Large arteries, cortical afferent arterioles and cortical efferent arterioles	Control of endothelial and smooth muscle cell functions in an autocrine and paracrine manner; positive angiogenesis regulator	3,83
Sema5a	Semaphorin-5A	Glomerular capillaries	Crucial in vascular development by promoting angiogenesis	1,24,84
Slc14a1	Urea transporter 1 (also known as UT-B)	DVR	Urea transporter; necessary for urine concentration	1,3,17,85,86
Slc2a1	Solute carrier family 2 member 1 (also known as GLUT-1)	Cortical peritubular capillaries type 1, cortical interferon activated capillaries and cortical angiogenic capillaries	Glucose transporter; glucose reabsorption in the blood stream	1,87
Slc26a10	Solute carrier family 26 member 10	Glomerular afferent arterioles JGA	Pseudogene	3
Slc5a3	Sodium/myo-inositol cotransporter	DVR	Myoinositol transporter; maintenance of cell volume during hyperosmolarity; NFAT5 target gene	1,88
Slc6a6	Sodium- and chloride-dependent taurine transporter	Cortical efferent arterioles and glomerular distal efferent arterioles	Taurine transporter; maintenance of cell volume during hyperosmolarity	1,3
Slc8a1	Sodium/calcium exchanger 1	Cortical afferent arterioles, glomerular distal afferent arterioles and large arteries	Na^+/Ca^{2+} exchanger	1
Smad6	MAD homolog 6 (also known as SMAD family member 6)	Glomerular capillaries	Associated with the TGF-β–BMP signalling pathway; overexpression might prevent excessive TGF-β signalling and glomerular dysfunction	3,39
Smad7	MAD homolog 7 (also known as SMAD family member 7)	Glomerular capillaries	Associated with the TGF-β–BMP signalling pathway; overexpression might prevent excessive TGF-β signalling and glomerular dysfunction	3,39
Sox17	Transcription factor SOX-17	Large arteries, cortical afferent arterioles, cortical efferent arterioles, glomerular distal afferent arterioles, glomerular afferent arterioles JGA, glomerular efferent arterioles JGA, glomerular distal efferent arterioles, DVR and DVR papilla	Arterial transcription factor	1,3,12,89
Tbx3	T-box transcription factor TBX3	gRECs	Transcription factor; crucial for gREC identity	1,3,24
Tek	Angiopoietin-1 receptor	AVR	Angiopoietin-1 receptor; necessary for maintaining medullary vascular bundles and for urine concentration	3,90
Thrsp	Thyroid hormone-inducible hepatic protein	Cortical peritubular capillaries type 1	Involved in lipid metabolism for the de novo synthesis of fatty acids	3,91
Tnxb	Tenascin X	Cortical postcapillary venules and medullary postcapillary venules	Extracellular matrix protein; binding of VEGFA and VEGFB	3,92

Trp53i11	Tumor protein p53-inducible protein 11	Cortical angiogenic capillaries and medullary angiogenic capillaries	Involved in angiogenesis	3,12,13
Tspan7	Tetraspanin-7	gRECs	Present in stalk cells in angiogenesis	3,13
Vegfa	Vascular endothelial growth factor A	Glomerular capillaries	Maintenance of vascular homeostasis in adults	1,93
Xiap	E3 ubiquitin-protein ligase XIAP (also known as X-linked inhibitor of apoptosis protein)	Glomerular capillaries	Apoptosis inhibitor; upregulated by TGF-β	3,94

AVR, ascending vasa recta; cRECs, cortical renal endothelial cells; DVR, descending vasa recta; eNOS, endothelial nitric oxide synthase; gRECS, glomerular renal endothelial cells; JGA, juxtaglomerular apparatus; NFAT5, Nuclear Factor Of Activated T Cells 5 (also known as TonEBP); mRECS, medullary renal endothelial cells; PV-1, plasmalemmal vesicle associated protein-1; TGF-β, transforming growth factor beta; VEGF, vascular endothelial growth factor.

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