

**Table S6. Genes with the most significant expression changes among each subtype of kidney cells.**

Gene	Sepsis Average (log2)	Control Average (log2)	Fold Change	FDR P-value	Function
<b>Glomerulus</b>					
Interferon Induced Transmembrane protein 2 (IFITM2)	10.28	6.88	10.52	3.10E-09	Protein involved in pathways of cytokine signaling and innate immune system-can establish an innate immune state to eliminate pathogens efficiently (1).
Beta-2-Microglobulin (B2M)	10.84	8.65	4.56	1.18E-06	Protein associated with the MHC I heavy chain on the surface of nearly all nucleated cells. Elevated urinary B2M indicates subclinical tubular dysfunction in neonates with sepsis (2).
Lysozyme (LYZ)	8.39	6.36	4.07	1.00E-04	Enzyme whose natural substrate is the bacterial cell wall peptidoglycan, protecting against many species. Pegylated lysozyme reduces septic mortality by inhibiting LPS-mediated release of HMGB1 (3).
Vimentin (VIM)	7.5	5.88	3.08	1.91E-05	Type III intermediate filament protein maintaining integrity of the cytoplasm and stabilizing cytoskeletal interactions.
Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2)	8.03	6.45	2.98	2.06E-06	General repressor of translation by forming translationally inactive complexes.
Interferon Induced Transmembrane protein 3 (IFITM3)	8.38	6.97	2.66	2.48E-07	Interferon-induced membrane protein that helps confer immunity to several viruses. Upregulation of such protein is associated with HIV and Influenza infection (4, 5).
Annexin A2 (ANXA2)	8.6	7.23	2.59	2.69E-05	Protein for regulation of cellular growth and signal transduction. Inhibits pro-inflammatory response by regulating ROS and IL-17 signaling during sepsis (6).
Major Histocompatibility Complex, class II, DR Alpha (HLA-DRA)	8.17	6.8	2.58	4.00E-04	This class II molecule plays a central role in the immune system by presenting peptides derived from extracellular proteins. mRNA levels associated with sepsis in 183 patients (7).
Major Histocompatibility Complex, class I, E (HLA-E)	8.31	7.04	2.41	5.22E-07	This class I molecule binds a restricted subset of peptides derived from the leader peptides of other class I molecules.
S100 calcium binding protein A8 (S100A8)	7.39	6.16	2.35	5.67E-07	Protein regulator of a number of cellular processes such as cell cycle progression and differentiation. It may function in the inhibition of casein kinase and as a cytokine. Gene Expression Omnibus and KEGG pathway analysis reveal S100A8 to be one of the top 10 genes associated with Septic patients (8).
Cyclic Nucleotide Gated channel Beta 1 (CNGB1)	5.09	5.49	-1.32	2.09E-08	Regulates ion flow into the rod photoreceptor outer segment in response to light-induced alteration of the levels of intracellular cGMP.
Gap Junction protein alpha 5 (GJA5)	4.25	4.66	-1.33	3.23E-07	Component of gap junctions, which provide a route for the diffusion of low molecular weight materials from cell to cell.

Wilms Tumor 1 (WT1)	4.11	4.52	-1.33	2.30E-06	Transcription factor essential for normal development of the urogenital system. Decreases in nuclear WT-1 is associated with albuminuria via podocyte dysregulation (9).
Ficolin Collagen/Fibrinogen domain containing) 3 (FCN3)	5.15	5.58	-1.34	8.59E-08	Protein that can activate the complement pathway, aiding in host defense through the activation of the lectin pathway. Low FCN3 is associated with higher mortality in neonatal sepsis (10).
Apelin Receptor (APLNR)	4.31	4.76	-1.37	1.48E-07	Protein inhibiting adenylate cyclase activity and counter-regulating the pressure action of angiotensin II. Plays an integral role in fluid homeostasis in the setting of sepsis (11).
Tenascin C (TNC)	3.9	4.35	-1.37	2.42E-07	Extracellular matrix protein with a spatially and temporally restricted tissue distribution.
Integrin Beta 1 (ITGB1)	4.31	4.78	-1.38	5.78E-12	Subunit to membrane receptors involved in cell adhesion and recognition in a variety of processes including hemostasis, tissue repair, and immune response.
RAS-like, Estrogen-Regulated, Growth inhibitor (RERG)	3.48	3.96	-1.39	3.67E-08	Protein that inhibits cell proliferation and tumor formation.
Troponin I Type 1 (skeletal, slow) (TNNI1)	5.48	5.95	-1.39	3.08E-09	Protein that prevents muscle contraction by inhibiting calcium-mediated conformational changes in actin-myosin complexes.
P53-Responsive Gene 1 (PRG1)	4.1	4.65	-1.47	4.93E-08	This is an RNA Gene and it is affiliated with the lncRNA class.
<b>Proximal Convolutd Tubule</b>					
Chemokine (C-X-C motif) Ligand 8 (CXCL8)	5.99	3.43	5.89	5.00E-04	Mediator of inflammatory response secreted by neutrophils, serving as chemotactic factor to site of infection. During severe endotoxemia, it blunts PMN influx reducing tissue damage (12).
Metallothionein 2A (MT2A)	9.82	7.6	4.64	3.96E-07	Anti-oxidant proteins protecting against hydroxyl free radicals important in homeostatic control of metal in the cell. Implicated in first response to sepsis in the brain of young mice (13).
Potassium Channel, inwardly rectifying subfamily J, member 15 (KCNJ15)	6.49	4.33	4.48	5.14E-07	Integral membrane protein and inward-rectifier type potassium channel, allowing K to flow into the cell rather than out.
Glycerol Kinase (GK)	6.48	4.45	4.09	1.79E-06	Key enzyme in regulation of glycerol uptake and metabolism.
Ferritin, light Polypeptide (FTL)	10.76	8.89	3.64	5.19E-07	Major intracellular iron storage protein in prokaryotes and eukaryote. Target gene of NRF2 known to provide protection against sepsis in leukocytes by upregulating antioxidant genes (14).
Alanyl (membrane) Aminopeptidase (ANPEP)	7.59	5.81	3.42	2.34E-06	Found in small intestine and renal microvilli, involved in metabolism of regulatory proteins including granulocytes and macrophages.

Perilipin 2 (PLIN2)	7.15	5.44	3.26	3.37E-06	Lipid droplet surface membrane protein, involved in development and maintenance of adipose tissue. Found to upregulate glucose and lipid production during bacterial infection in periodontitis (15).
Microsomal Glutathione S-Transferase 1 (MGST1)	7.58	5.91	3.18	2.00E-04	Protein catalyzing the conjugation of glutathione to electrophiles and the reduction of lipid hydroperoxides.
Maltase-Glucoamylase (MGAM)	6.29	4.74	2.94	1.83E-07	Brush border membrane enzyme that plays a role in the final steps of digestion of starch.
Metallothionein 1L (gene/pseudogene)(MT1L)	6.97	5.71	2.4	4.00E-04	Pseudogene with a high content of cysteine residues that binds various heavy metals.
Deiodinase Iodothyronine Type I (DIO1)	4.54	4.87	-1.26	3.77E-05	Regulator protein of thyroid hormone, producing most of T3. Reduced activity in kidney after LPS-induced sepsis, reducing TH sensitivity (16).
Solute Carrier Family 13 Member 2 (SLC13A2)	5.08	5.44	-1.28	3.48E-07	Sodium-dependent dicarboxylate transporter regulated by cyclophilin b. It may play a role in the formation of kidney stones.
Solute Carrier Family 7 Member 13 (SLC7A13)	2.57	2.93	-1.29	1.57E-08	Anionic amino acid transmembrane transporter restricted to kidney expression.
Gastric Intrinsic Factor (GIF)	3.32	3.69	-1.3	7.16E-07	Glycoprotein secreted by parietal cells of the gastric mucosa required for vitamin B12 absorption. B12 deficiency is associated with increased susceptibility to bacterial infection (17).
Solute Carrier Family 22 Member 6 (SLC22A6)	5.44	5.81	-1.3	5.27E-08	Protein for sodium-dependent transport and excretion of organic anions, some of which are potentially toxic. Shows reduced expression during LPS-induced AKI (18).
Glycine Amidinotransferase (GATM)	4.24	4.65	-1.33	4.68E-08	L-Arginine:Glycine Amidinotransferase, a mitochondrial enzyme involved in creatine biosynthesis.
Solute Carrier Family 22 Member 7 (SLC22A7)	4.94	5.39	-1.37	8.06E-09	Sodium-independent transport and excretion of organic anions, localized to the basolateral membrane of the kidney. Suppressed during endotoxemia, impairing uptake of bile acids and bilirubin (19).
Solute Carrier Family 34 Member 1 (SLC34A1)	5.3	5.78	-1.4	3.43E-09	Type II sodium-phosphate cotransporter associated with hypophosphatemia and nephrolithiasis. Downregulated by tubular hypoxia that occurs during sepsis, functioning as a reliable marker for ARF progression (20).
Serine Hydroxymethyl-transferase 1 (SHMT1)	8.13	8.77	-1.55	1.15E-10	Soluble enzyme that catalyzes the reversible conversion of serine and tetrahydrofolate, important for amino acid and purine synthesis.
<b>Thick Ascending Limb</b>					
Acyl-CoA Synthetase Short-chain family member 1 (ACSS1)	5.47	5.49	-1.01	0.5013	This gene encodes a mitochondrial acetyl-CoA synthetase enzyme that plays an important role in the tricarboxylic acid cycle by catalyzing the conversion of acetate to acetyl CoA.
ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, Alpha 1 polypeptide (ATP1A1)	7.29	5.84	2.73	1.92E-08	This gene encodes an integral membrane protein responsible for establishing and maintaining the electrochemical gradients of Na and K ions across the plasma membrane.

ATPase, H <sup>+</sup> transporting, lysosomal 56/58kDa, V1 subunit B1 (ATP6V1B1)	5.49	5.46	1.03	0.2981	This gene encodes a component of vacuolar ATPase (V-ATPase), a multisubunit enzyme that mediates acidification of eukaryotic intracellular organelles.
CD24 molecule (CD24)	6.8	5.67	2.19	3.68E-07	This gene encodes a sialoglycoprotein that is expressed on mature granulocytes and B cells and modulates growth and differentiation signals to these cells. CD24 expression was associated with early prediction of sepsis in 3 different emergency and ICU cohorts (21).
Creatine Kinase, Brain (CKB)	6.26	5.97	1.23	2.00E-04	This gene encodes a cytoplasmic enzyme involved in energy homeostasis. It reversibly catalyzes the transfer of phosphate between ATP and various phosphogens such as creatine phosphate.
Claudin 10 (CLDN10)	3.43	3.19	1.18	0.0099	This gene encodes integral membrane proteins that serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets, and also play critical roles in maintaining cell polarity and signal transductions.
Claudin 16 (CLDN16)	4.45	4.9	-1.36	2.85E-09	This gene encodes an integral membrane protein which acts as either an intercellular pore or ion concentration sensor to regulate the paracellular resorption of magnesium ions.
Ribosomal Protein S18 (RPS18)	7.03	6.96	1.05	0.4063	This gene encodes a ribosomal protein that is involved in the binding of fMet-tRNA.
Ribosomal Protein S27A; microRNA 4426 (RPS27A)	5.96	5.7	1.2	7.00E-04	Fusion protein consisting of ubiquitin and ribosomal protein S27a.
Serine Peptidase Inhibitor, Kunitz Type 1 (SPINT1)	6.6	6.29	1.24	0.0016	Potent inhibitor specific for HGF activator thought to regulate proteolytic activation of HGF in injured tissues.
Serine/Threonine Kinase 24 (STK24)	6.25	5.64	1.53	8.85E-08	Functions upstream of mitogen-activated protein kinase (MAPK) signaling.
Synovial Apoptosis inhibitor 1, Synoviolin (SYVN1)	6.08	6.05	1.02	0.5815	Protein involved in endoplasmic reticulum (ER)-associated degradation.
Teratocarcinoma-Derived Growth Factor 1 (TDGF1)	4.38	4.73	-1.27	5.48E-07	Extracellular, membrane-bound signaling protein that plays an essential role in embryonic development and tumor growth.
Transmembrane protein 184B (TMEM184B)	5.84	5.83	1.01	0.8532	Protein that may activate the MAP kinase signaling pathway.
Tetraspanin 8 (TSPAN8)	2.95	3.15	-1.14	0.0025	Surface glycoprotein that mediates signal transduction events that important in the regulation of cell activation, growth and motility.
Ubiquitin C-terminal Hydrolase L1 (UCHL1)	4.82	4.85	-1.02	0.9424	Thiol protease that hydrolyzes a peptide bond at the C-terminal glycine of ubiquitin.
Zinc finger, MIZ-type containing 1 (ZMIZ1)	6.38	5.99	1.31	0.0016	Protein that regulates the activity of various transcription factors, including the androgen receptor, Smad3/4, and p53. It may also play a role in sumoylation.

<b>Distal Convolved Tubule</b>					
Aldolase, Fructose-bisphosphate B (ALDOB)	8.91	7.53	2.6	6.00E-04	Glycolytic enzyme that catalyzes reversible conversions, with different isozymes fluctuating through developmental cycle.
ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, Beta 1 polypeptide (ATP1B1)	7.44	6.42	2.02	7.86E-07	Integral membrane protein responsible for the electrochemical gradients of Na and K ions.
Ribosomal Protein S6 (RPS6)	5.15	4.55	1.51	6.85E-05	Component of the 40S subunit, and major substrate of protein kinases. Involved in cell growth and proliferation.
Defensin Beta1 (DEFB1)	5.66	5.1	1.47	4.00E-04	Antimicrobial peptide for resistance of epithelial surfaces. Genetic variations impact susceptibility and mortality in sepsis patients (22).
Uromodulin (UMOD)	6.08	5.69	1.31	0.0033	Constitutive inhibitor of calcium crystallization in renal fluids. Shows tubule dependent expression during sepsis (23), and reduced levels may be a risk factor for bacteremia (24).
Propionyl-CoA Carboxylase Alpha subunit (PCCA)	4.62	4.25	1.3	8.61E-05	Alpha subunit of the heterodimeric mitochondrial enzyme, often involved in metabolic diseases.
Chemokine (C-C motif) Ligand 3 (CCL3)	6.85	6.53	1.24	0.044	Macrophage inflammatory protein. Found to be essential for host resistance to bacterial sepsis in mice (25).
Calbindin 1 (CALB1)	4.69	4.47	1.17	0.0468	Protein buffering entry of calcium upon stimulation of glutamate receptors. Distinct marker for distal tubule, found to prevent autophagy-induced renal damage during sepsis (26).
Glucosidase Beta Acid (GBA)	6	5.89	1.08	0.019	Lysosomal membrane protein that cleaves an intermediate in glycolipid metabolism. Potential anti-inflammatory target, suppressing NFkB signaling and protecting against endotoxic shock (27).
Solute Carrier Family 12 Member 1 (SLC12A1)	3.87	3.76	1.08	0.0664	Kidney-specific sodium-potassium-chloride cotransporter key for concentrating urine. Downregulation occurs after LPS exposure, followed by infiltration of activated macrophages and increased iNOS expression which leads to ARF during sepsis (28).
Claudin 8 (CLDN8)	3.13	3.05	1.06	0.2517	Transmembrane protein functioning in tight junctions of DCT, important for maintaining signal transduction and cell polarity. Shows low mRNA expression during LPS-induced AKI (29).
Collagen type VI, Alpha 1 (COL6A1)	6.12	6.04	1.06	0.0684	Extracellular major structural protein component of microfibrils, important for maintaining tissue integrity.
Chloride Channel, voltage-sensitive KB (CLCNKB)	6.05	5.98	1.05	0.1602	Regulates cell volume, membrane potential, signal transduction and transepithelial transport, may be important for renal salt reabsorption.
Kininogen 1 (KNG1)	4.2	4.15	1.04	0.2235	This gene generates HMWK, essential for blood coagulation and assembly of the kallikrein-kinin system, and LMWK.
FXYD domain containing ion transport regulator 2 (FXYP2)	3.04	3.19	-1.11	0.0079	Encodes the sodium/potassium-transporting ATPase subunit gamma.
Solute Carrier Family 12 Member 3 (SLC12A3)	5.45	5.61	-1.12	0.1163	Renal thiazide-sensitive sodium-chloride co-transporter mediating NaCl reabsorption in the distal convoluted tubule.

Serpin Peptidase Anhibitor, Clade A Member 5 (SERPINA5)	4.96	5.17	-1.15	0.0101	Encodes a glycoprotein that inhibits serine proteases, aka Protein C Inhibitor. Found to attenuate disseminated intravascular coagulation that occurs during LPS-induced sepsis (30).
Kallikrein 1 (KLK1)	4.95	5.17	-1.16	0.002	Protein releasing the vasoactive peptide, Lys-bradykinin, from low molecular weight kininogen.
Secreted Frizzled-Related Protein 1 (SFRP1)	2.55	2.76	-1.16	0.0438	Silencing leads to deregulated activation of the Wnt-pathway which is associated with several inflammatory diseases. Antagonist to Wnt5 which is critical for macrophage inflammatory response during sepsis (31).
Myo-Inositol Oxygenase (MIOX)	5.54	5.78	-1.18	0.0072	Protein related to iron ion binding and oxido-reductase activity, acting on NAD(P)H.
Collecting Duct					
Thioredoxin Interacting Protein (TXNIP)	8.09	5.96	4.38	5.76E-08	Major regulator of cellular redox state and apoptosis. During LPS-induced septic shock, regulates iNOS expression (32); Role in attenuation of cardiac failure (33).
ZFP36 Ring Finger Protein (ZFP36)	9.2	7.11	4.28	4.68E-06	Protein for enzyme binding. Inflammatory factor regulating NFkB signaling during bacterial infection (34).
Kruppel-like Factor 6 (KLF6)	8.22	6.13	4.24	8.26E-10	Transcriptional activator and tumor suppressor. induced by LPS and IFN-γ for pathways critical to monocyte/macrophage activation (35).
H3 histone, family 3B (H3F3B)	8.17	6.17	3.99	4.96E-08	Nucleosome structure proteins in eukaryotes. Components of neutrophil extracellular traps with antimicrobial activity disrupting cell membranes (36).
6-Phosphofructo-2-Kinase/Fructose-2,6-Biphosphatase 3 (PFKFB3)	8.81	6.83	3.96	6.47E-09	Encodes a critical enzyme for glycolysis. Inhibition was found to suppress inflammation and apoptosis, reducing ALI during sepsis (37).
WD repeat and SOCS box containing 1 (WSB1)	6.78	4.96	3.52	2.53E-07	Unique protein involved in 2 pathways: Class I MHC antigen presentation and innate immunity.
BTG Family, Member 2 (BTG2)	7.67	5.95	3.29	1.20E-06	Anti-proliferative proteins involved in the regulation of the G1/S transition of the cell cycle.
Clusterin (CLU)	7.22	5.8	2.67	7.53E-08	Involved in cell death, tumor progression, and neurodegenerative disorders. Role as complement lysis inhibitor during bacterial infection (38).
Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells Inhibitor, Zeta (NFKBIZ)	6.16	4.76	2.65	2.79E-06	Role in inflammatory responses to LPS by interaction with NF-B proteins through ankyrin-repeat domains (39).
Cathepsin H (CTSH)	7.06	5.78	2.44	5.68E-07	Encodes a lysosomal cysteine proteinase important in the overall degradation of lysosomal proteins.
Keratin 75, Type II (KRT75)	4.39	4.66	-1.2	2.07E-06	The protein encoded by this gene is essential in hair and nail formation.

Aldehyde Dehydrogenase 1 Family, Member A3 (ALDH1A3)	5.24	5.52	-1.21	5.08E-09	Encodes an aldehyde dehydrogenase enzyme that uses retinal as a substrate.
MAL, T-cell differentiation protein (MAL)	4.38	4.65	-1.21	0.0043	Hydrophobic proteolipid found in T cells involved in signal transduction. Attenuates TLR2 expression reducing innate immune response and protecting against bacterial infection (40).
Serine Protease 12 (PRSS12)	4.42	4.7	-1.22	5.41E-07	Cleaves agrin protein, important for the formulation and maintenance of excitatory synapses.
Solute Carrier Family 4, Member 9 (SLC4A9)	5.05	5.34	-1.23	2.00E-04	Membrane protein for anion exchange, a sodium bicarbonate cotransporter.
C-type Lectin Domain Family 3, member B (CLEC3B)	5.59	5.91	-1.25	7.05E-07	Protein coding gene that is related to calcium ion and heparin binding.
Inositol Polyphosphate-5-phosphatase J (INPP5J)	5.07	5.42	-1.27	4.27E-07	Protein coding gene involved in signal transduction and osmoregulation.
Aldehyde Dehydrogenase 1 family, member A3 (ALDH1A3)	4.77	5.13	-1.28	3.56E-07	Encodes an aldehyde dehydrogenase enzyme that uses retinal as a substrate.
Intelectin 1 (ITLN1)	4.36	4.73	-1.3	2.62E-05	Protein for galacto-furanose binding. Elevated omentin levels have shown predictive value for ICU patient survival (41).
ST6 beta-Galactosamide Alpha-2,6-sialyltransferase 1 (ST6GAL1)	3.66	4.31	-1.57	1.58E-08	Type II membrane protein that catalyzes the transfer of sialic acid and also generates cell surface determinants.
Arylsulfatase E (chondrodysplasia punctata 1) (ARSE)	4.52	4.61	-1.06	0.0938	Arylsulfatase E is a member of the sulfatase family, which is essential for the correct composition of bone and cartilage matrix.
Chemokine (C-X-C motif) ligand 12 (CXCL12)	3.21	3.99	-1.72	2.62E-11	This antimicrobial gene encodes a ligand for the G-protein coupled receptor, chemokine (C-X-C motif) receptor 4, and plays a role in embryogenesis, immune surveillance, inflammation response, tissue homeostasis, and tumor growth and metastasis. CXCL12 predict mortality in patients with severe sepsis/shock (42).
Dual Specificity Phosphatase 9 (DUSP9)	4.75	4.94	-1.14	0.0767	This gene encodes phosphatases that inactivate their target kinases by dephosphorylating both the phosphoserine/threonine and phosphotyrosine residues.

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