

Supplementary Table 5: Pathway enrichment analysis of the tubulointerstitium dataset. Signaling pathway related to the DE gene, TFs, and kinase of the tubulointerstitium network were determined. Adj. P-value \leq 0.05 was considered as statistical significance threshold.

Pathways	adj. p-value
Signaling by the B Cell Receptor (BCR)	6.28043E-24
Interleukin receptor SHC signaling	6.28043E-24
FBXL7 down-regulates AURKA during mitotic entry and in early mitosis	6.28043E-24
RET signaling	6.28043E-24
Gastrin-CREB signalling pathway via PKC and MAPK	6.28043E-24
Signaling by Insulin receptor	6.28043E-24
Insulin receptor signalling cascade	6.28043E-24
Cell Cycle Checkpoints	6.28043E-24
DNA Replication	6.28043E-24
Regulation of DNA replication	6.28043E-24
Removal of licensing factors from origins	6.28043E-24
Cell Cycle, Mitotic	6.28043E-24
CDT1 association with the CDC6:ORC:origin complex	6.28043E-24
Ub-specific processing proteases	6.28043E-24
UCH proteinases	6.28043E-24
Deubiquitination	6.28043E-24
MAPK family signaling cascades	6.28043E-24
Defective CFTR causes cystic fibrosis	6.28043E-24
NIK-->noncanonical NF-kB signaling	6.28043E-24
RAF/MAP kinase cascade	6.28043E-24
TNFR2 non-canonical NF-kB pathway	6.28043E-24
Regulation of RAS by GAPs	6.28043E-24
C-type lectin receptors (CLRs)	6.28043E-24
CLEC7A (Dectin-1) signaling	6.28043E-24
Dectin-1 mediated noncanonical NF-kB signaling	6.28043E-24
Signaling by Hedgehog	6.28043E-24
VEGFR2 mediated cell proliferation	6.28043E-24
Interleukin-3, 5 and GM-CSF signaling	6.28043E-24
Degradation of DVL	6.28043E-24
Degradation of AXIN	6.28043E-24
Asymmetric localization of PCP proteins	6.28043E-24
Regulation of mitotic cell cycle	6.28043E-24
Regulation of mRNA stability by proteins that bind AU-rich elements	6.28043E-24
AUF1 (hnRNP D0) binds and destabilizes mRNA	6.28043E-24
Signaling by Interleukins	6.28043E-24
VEGFA-VEGFR2 Pathway	6.28043E-24
PCP/CE pathway	6.28043E-24
Beta-catenin independent WNT signaling	6.28043E-24
ABC-family proteins mediated transport	6.28043E-24
NCAM signaling for neurite out-growth	6.28043E-24
Metabolism of polyamines	6.28043E-24
Regulation of ornithine decarboxylase (ODC)	6.28043E-24
Autodegradation of the E3 ubiquitin ligase COP1	6.28043E-24
FCERI mediated NF-kB activation	6.28043E-24
FCERI mediated MAPK activation	6.28043E-24
Signaling by Leptin	6.28043E-24
Mitotic Metaphase and Anaphase	6.28043E-24
Separation of Sister Chromatids	6.28043E-24
Fc epsilon receptor (FCERI) signaling	6.28043E-24
IRS-related events triggered by IGF1R	6.28043E-24
IGF1R signaling cascade	6.28043E-24
DAP12 signaling	6.28043E-24
Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	6.28043E-24
Cellular responses to stress	6.28043E-24

Cellular response to hypoxia	6.28043E-24
DAP12 interactions	6.28043E-24
Regulation of activated PAK-2p34 by proteasome mediated degradation	6.28043E-24
Downstream TCR signaling	6.28043E-24
TCR signaling	6.28043E-24
TCF dependent signaling in response to WNT	6.28043E-24
Signaling by Wnt	6.28043E-24
Degradation of beta-catenin by the destruction complex	6.28043E-24
Signaling by VEGF	6.28043E-24
Signalling to p38 via RIT and RIN	6.28043E-24
Signalling to ERKs	6.28043E-24
NGF signalling via TRKA from the plasma membrane	6.28043E-24
Signaling by PDGF	6.28043E-24
Downstream signal transduction	6.28043E-24
Vif-mediated degradation of APOBEC3G	6.28043E-24
Vpu mediated degradation of CD4	6.28043E-24
SHC1 events in EGFR signaling	6.28043E-24
GRB2 events in EGFR signaling	6.28043E-24
APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint	6.28043E-24
Signaling by EGFR	6.28043E-24
Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins	6.28043E-24
APC/C:Cdc20 mediated degradation of mitotic proteins	6.28043E-24
Regulation of APC/C activators between G1/S and early anaphase	6.28043E-24
Cdc20:Phospho-APC/C mediated degradation of Cyclin A	6.28043E-24
APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1	6.28043E-24
APC/C:Cdc20 mediated degradation of Securin	6.28043E-24
APC/C-mediated degradation of cell cycle proteins	6.28043E-24
SCF-beta-TrCP mediated degradation of Emi1	6.28043E-24
ARMS-mediated activation	6.28043E-24
Frs2-mediated activation	6.28043E-24
Prolonged ERK activation events	6.28043E-24
Innate Immune System	6.28043E-24
Signalling to RAS	6.28043E-24
Host Interactions of HIV factors	6.28043E-24
Signaling by SCF-KIT	6.28043E-24
Cytokine Signaling in Immune system	6.28043E-24
Cross-presentation of soluble exogenous antigens (endosomes)	6.28043E-24
Antigen processing-Cross presentation	6.28043E-24
ER-Phagosome pathway	6.28043E-24
Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha	6.28043E-24
Regulation of Hypoxia-inducible Factor (HIF) by oxygen	6.28043E-24
Activation of NF-kappaB in B cells	6.28043E-24
Downstream signaling events of B Cell Receptor (BCR)	6.28043E-24
SOS-mediated signalling	6.28043E-24
IRS-mediated signalling	6.28043E-24
Class I MHC mediated antigen processing & presentation	3.01819E-17
Antigen processing: Ubiquitination & Proteasome degradation	3.01819E-17
Synthesis of active ubiquitin: roles of E1 and E2 enzymes	3.01819E-17
Protein ubiquitination	3.01819E-17
Post-translational protein modification	3.01819E-17
Metabolism of proteins	3.01819E-17
Immune System	3.01819E-17
Adaptive Immune System	3.01819E-17
Th17 cell differentiation	1.76393E-13
Factors involved in megakaryocyte development and platelet production	2.02934E-13
Kinesins	2.02934E-13
Transport to the Golgi and subsequent modification	2.02934E-13
Mitotic Prometaphase	2.02934E-13
COPI-independent Golgi-to-ER retrograde traffic	2.02934E-13

COPI-mediated anterograde transport	2.02934E-13
RHO GTPases Activate Formins	2.02934E-13
RHO GTPases activate IQGAPs	2.02934E-13
Protein folding	2.02934E-13
Chaperonin-mediated protein folding	2.02934E-13
Post-chaperonin tubulin folding pathway	2.02934E-13
Formation of tubulin folding intermediates by CCT/TriC	2.02934E-13
Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding	2.02934E-13
Recruitment of NuMA to mitotic centrosomes	2.02934E-13
Centrosome maturation	2.02934E-13
Recruitment of mitotic centrosome proteins and complexes	2.02934E-13
Resolution of Sister Chromatid Cohesion	2.02934E-13
MHC class II antigen presentation	2.02934E-13
ER to Golgi Anterograde Transport	2.02934E-13
Transport of connexons to the plasma membrane	2.02934E-13
Gap junction assembly	2.02934E-13
Microtubule-dependent trafficking of connexons from Golgi to the plasma membrane	2.02934E-13
Gap junction trafficking	2.02934E-13
Gap junction trafficking and regulation	2.02934E-13
Translocation of GLUT4 to the plasma membrane	2.02934E-13
Hemostasis	2.02934E-13
FoxO signaling pathway	8.21666E-13
CD209 (DC-SIGN) signaling	3.41279E-12
MAPK targets/ Nuclear events mediated by MAP kinases	3.41279E-12
CREB phosphorylation	3.41279E-12
ERK/MAPK targets	3.41279E-12
Nuclear Events (kinase and transcription factor activation)	3.41279E-12
AGE-RAGE signaling pathway in diabetic complications	8.39824E-11
Wnt signaling pathway	1.00197E-10
Adherens junction	2.07436E-10
MAPK signaling pathway	3.63208E-10
Focal adhesion	6.08886E-10
Thyroid hormone signaling pathway	3.13688E-09
O-glycosylation of TSR domain-containing proteins	3.42568E-09
O-linked glycosylation	3.42568E-09
Defective B3GALTL causes Peters-plus syndrome (PpS)	3.42568E-09
Diseases associated with O-glycosylation of proteins	3.42568E-09
Diseases of glycosylation	3.42568E-09
Disease	3.42568E-09
Cell cycle	5.9193E-09
Recycling pathway of L1	3.23407E-08
L1CAM interactions	3.23407E-08
Interferon gamma signaling	1.21298E-07
Th1 and Th2 cell differentiation	2.17982E-07
IRAK2 mediated activation of TAK1 complex upon TLR7/8 or 9 stimulation	2.33762E-07
MyD88 dependent cascade initiated on endosome	2.33762E-07
TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation	2.33762E-07
TRAF6 mediated induction of TAK1 complex	2.33762E-07
TRIF-mediated TLR3/TLR4 signaling	2.33762E-07
IKK complex recruitment mediated by RIP1	2.33762E-07
Activation of IRF3/IRF7 mediated by TBK1/IKK epsilon	2.33762E-07
Regulation of TLR by endogenous ligand	2.33762E-07
IRAK4 deficiency (TLR2/4)	2.33762E-07
MyD88 deficiency (TLR2/4)	2.33762E-07
Diseases associated with the TLR signaling cascade	2.33762E-07
Caspase activation via extrinsic apoptotic signalling pathway	2.33762E-07
Diseases of Immune System	2.33762E-07
TRIF-mediated programmed cell death	2.33762E-07
Toll Like Receptor 2 (TLR2) Cascade	2.33762E-07

Toll-Like Receptors Cascades	2.33762E-07
Toll Like Receptor TLR6:TLR2 Cascade	2.33762E-07
Toll Like Receptor 7/8 (TLR7/8) Cascade	2.33762E-07
Toll Like Receptor TLR1:TLR2 Cascade	2.33762E-07
Toll Like Receptor 3 (TLR3) Cascade	2.33762E-07
Toll Like Receptor 9 (TLR9) Cascade	2.33762E-07
MyD88-independent TLR3/TLR4 cascade	2.33762E-07
MyD88:Mal cascade initiated on plasma membrane	2.33762E-07
Activated TLR4 signalling	2.33762E-07
Toll Like Receptor 4 (TLR4) Cascade	2.33762E-07
Ligand-dependent caspase activation	2.33762E-07
PI3K-Akt signaling pathway	3.10742E-07
Signaling pathways regulating pluripotency of stem cells	8.39382E-07
Axon guidance	1.65612E-06
Sphingolipid signaling pathway	1.89951E-06
Neutrophil degranulation	3.01632E-06
Interleukin-4 and 13 signaling	4.9624E-06
Interleukin-10 signaling	4.9624E-06
Platelet activation	5.65449E-06
IL-17 signaling pathway	6.03235E-06
Osteoclast differentiation	6.47348E-06
Gap junction	7.36104E-06
Neurotrophin signaling pathway	9.00301E-06
Response to elevated platelet cytosolic Ca ²⁺	9.58875E-06
Disinhibition of SNARE formation	9.58875E-06
Long-term potentiation	1.06086E-05
Formation of the cornified envelope	1.43845E-05
Keratinization	1.43845E-05
Developmental Biology	1.43845E-05
Phagosome	1.46729E-05
ErbB signaling pathway	1.91926E-05
Regulation of actin cytoskeleton	2.20261E-05
Prolactin signaling pathway	2.55587E-05
Apoptosis	2.97138E-05
Antigen processing and presentation	3.70117E-05
Oxytocin signaling pathway	3.93962E-05
Activation of the AP-1 family of transcription factors	4.73919E-05
TP53 regulates transcription of additional cell cycle genes whose exact role in the p53 pathway remain uncertain	5.35978E-05
TP53 Regulates Transcription of Cell Cycle Genes	5.35978E-05
Deadenylation of mRNA	5.35978E-05
Deadenylation-dependent mRNA decay	5.35978E-05
Transcriptional Regulation by TP53	5.35978E-05
Chemokine signaling pathway	6.16943E-05
GnRH signaling pathway	7.90804E-05
p53 signaling pathway	9.04514E-05
Endocytosis	0.00011384
Platelet degranulation	0.0001457
Progesterone-mediated oocyte maturation	0.000188012
T cell receptor signaling pathway	0.00021586
NOD-like receptor signaling pathway	0.000231561
Cell adhesion molecules (CAMs)	0.00030561
Fc epsilon RI signaling pathway	0.00030977
Rap1 signaling pathway	0.000327757
Regulation of TP53 Expression and Degradation	0.000416377
Regulation of TP53 Degradation	0.000416377
Regulation of TP53 Activity	0.000416377
KSRP (KHSRP) binds and destabilizes mRNA	0.00042258
PERK regulates gene expression	0.00042258
ATF4 activates genes	0.00042258

Generation of second messenger molecules	0.00042258
B cell receptor signaling pathway	0.000645314
Oocyte meiosis	0.000876249
Cyclin A/B1 associated events during G2/M transition	0.000888089
HuR (ELAVL1) binds and stabilizes mRNA	0.000888089
TGF-beta receptor signaling activates SMADs	0.000888089
Downregulation of TGF-beta receptor signaling	0.000888089
Interactions of Rev with host cellular proteins	0.000888089
NEP/NS2 Interacts with the Cellular Export Machinery	0.000888089
Export of Viral Ribonucleoproteins from Nucleus	0.000888089
Rev-mediated nuclear export of HIV RNA	0.000888089
Protein processing in endoplasmic reticulum	0.000888641
Downregulation of ERBB2 signaling	0.000947433
Signaling by PTK6	0.000947433
ERBB2 Activates PTK6 Signaling	0.000947433
ERBB2 Regulates Cell Motility	0.000947433
PI3K events in ERBB2 signaling	0.000947433
GRB2 events in ERBB2 signaling	0.000947433
Downregulation of ERBB2:ERBB3 signaling	0.000947433
GRB7 events in ERBB2 signaling	0.000947433
Nuclear signaling by ERBB4	0.000947433
SHC1 events in ERBB4 signaling	0.000947433
PI3K events in ERBB4 signaling	0.000947433
SHC1 events in ERBB2 signaling	0.000947433
Signaling by ERBB4	0.000947433
Signaling by ERBB2	0.000947433
SUMOylation of RNA binding proteins	0.001045166
SUMO E3 ligases SUMOylate target proteins	0.001045166
SUMOylation of DNA damage response and repair proteins	0.001045166
SUMOylation	0.001045166
Cellular Senescence	0.001045166
Oxidative Stress Induced Senescence	0.001045166
Antigen Presentation: Folding, assembly and peptide loading of class I MHC	0.00106206
Insulin resistance	0.001518524
Circadian Clock	0.001627753
BMAL1:CLOCK,NPAS2 activates circadian gene expression	0.001627753
RORA activates gene expression	0.001627753
TNF signaling pathway	0.001801132
Inhibition of adenylate cyclase pathway	0.00236097
Activation of GABAB receptors	0.00236097
GABA B receptor activation	0.00236097
Platelet activation, signaling and aggregation	0.00236097
Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding	0.00236097
G alpha (s) signalling events	0.00236097
Incretin synthesis, secretion, and inactivation	0.00236097
Signal amplification	0.00236097
ADP signalling through P2Y purinoceptor 12	0.00236097
Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1)	0.00236097
Peptide hormone metabolism	0.00236097
G-protein activation	0.00236097
Adenylate cyclase inhibitory pathway	0.00236097
PLC beta mediated events	0.00236097
G-protein mediated events	0.00236097
Opioid Signalling	0.00236097
Interferon Signaling	0.002596513
NS1 Mediated Effects on Host Pathways	0.002596513
Influenza Infection	0.002596513
Host Interactions with Influenza Factors	0.002596513
Antiviral mechanism by IFN-stimulated genes	0.002596513

ISG15 antiviral mechanism	0.002596513
Inflammatory mediator regulation of TRP channels	0.002703184
Toll-like receptor signaling pathway	0.002846288
Hippo signaling pathway	0.003300545
RNA Polymerase II Transcription Initiation And Promoter Clearance	0.004081855
RNA Polymerase II Transcription Initiation	0.004081855
RNA Polymerase II Transcription Pre-Initiation And Promoter Opening	0.004081855
RNA Polymerase II Promoter Escape	0.004081855
Regulation of TP53 Activity through Phosphorylation	0.004081855
RNA Polymerase II HIV Promoter Escape	0.004081855
HIV Transcription Initiation	0.004081855
Leukocyte transendothelial migration	0.004755329
CRMPs in Sema3A signaling	0.004971413
Semaphorin interactions	0.004971413
HIF-1 signaling pathway	0.005324622
MyD88 cascade initiated on plasma membrane	0.005437394
Uptake and actions of bacterial toxins	0.005437394
Uptake and function of anthrax toxins	0.005437394
JNK (c-Jun kinases) phosphorylation and activation mediated by activated human TAK1	0.005437394
MAP kinase activation in TLR cascade	0.005437394
Toll Like Receptor 5 (TLR5) Cascade	0.005437394
Toll Like Receptor 10 (TLR10) Cascade	0.005437394
YAP1- and WWTR1 (TAZ)-stimulated gene expression	0.005533448
NF-kappa B signaling pathway	0.006023459
Autophagy	0.00702112
Apelin signaling pathway	0.00752721
mTOR signaling pathway	0.009298888
Fc gamma R-mediated phagocytosis	0.009585428
Estrogen signaling pathway	0.00986996
TRAIL signaling	0.010303802
Death Receptor Signalling	0.010303802
Dimerization of procaspase-8	0.010303802
TP53 Regulates Transcription of Death Receptors and Ligands	0.010303802
Regulation of necroptotic cell death	0.010303802
TP53 Regulates Transcription of Cell Death Genes	0.010303802
CASP8 activity is inhibited	0.010303802
Regulated Necrosis	0.010303802
RIPK1-mediated regulated necrosis	0.010303802
Regulation by c-FLIP	0.010303802
Cell surface interactions at the vascular wall	0.010303802
Listeria monocytogenes entry into host cells	0.01128247
InlB-mediated entry of Listeria monocytogenes into host cell	0.01128247
Negative regulation of MET activity	0.01128247
Signaling by MET	0.01128247
EGFR downregulation	0.01128247
Extracellular matrix organization	0.015445513
Degradation of the extracellular matrix	0.015445513
Syndecan interactions	0.016161666
Dopaminergic synapse	0.017811067
ECM-receptor interaction	0.020378073
DCC mediated attractive signaling	0.020927102
EPHB-mediated forward signaling	0.020927102
Nephrin interactions	0.020927102
Netrin-1 signaling	0.020927102
EPH-Ephrin signaling	0.020927102
eNOS activation and regulation	0.020927102
NOSTRIN mediated eNOS trafficking	0.020927102
Metabolism of nitric oxide	0.020927102
Adipocytokine signaling pathway	0.021149708

Tight junction	0.026440954
Fatty acid, triacylglycerol, and ketone body metabolism	0.027235529
Regulation of lipid metabolism by Peroxisome proliferator-activated receptor alpha (PPARalpha)	0.027235529
Transcriptional regulation of white adipocyte differentiation	0.027235529
PPARA activates gene expression	0.027235529
TGF-beta signaling pathway	0.028180307
Longevity regulating pathway	0.028553227
VEGF signaling pathway	0.036574608
PECAM1 interactions	0.038788655
Signal transduction by L1	0.0395926
SEMA3A-Plexin repulsion signaling by inhibiting Integrin adhesion	0.0395926
Sema3A PAK dependent Axon repulsion	0.0395926
Neurophilin interactions with VEGF and VEGFR	0.0395926
RHO GTPases Activate WASPs and WAVES	0.045168574
Regulation of actin dynamics for phagocytic cup formation	0.045168574
Fcgamma receptor (FCGR) dependent phagocytosis	0.045168574
RHO GTPase Effectors	0.045168574
Gene Expression	0.045425788
Generic Transcription Pathway	0.045425788