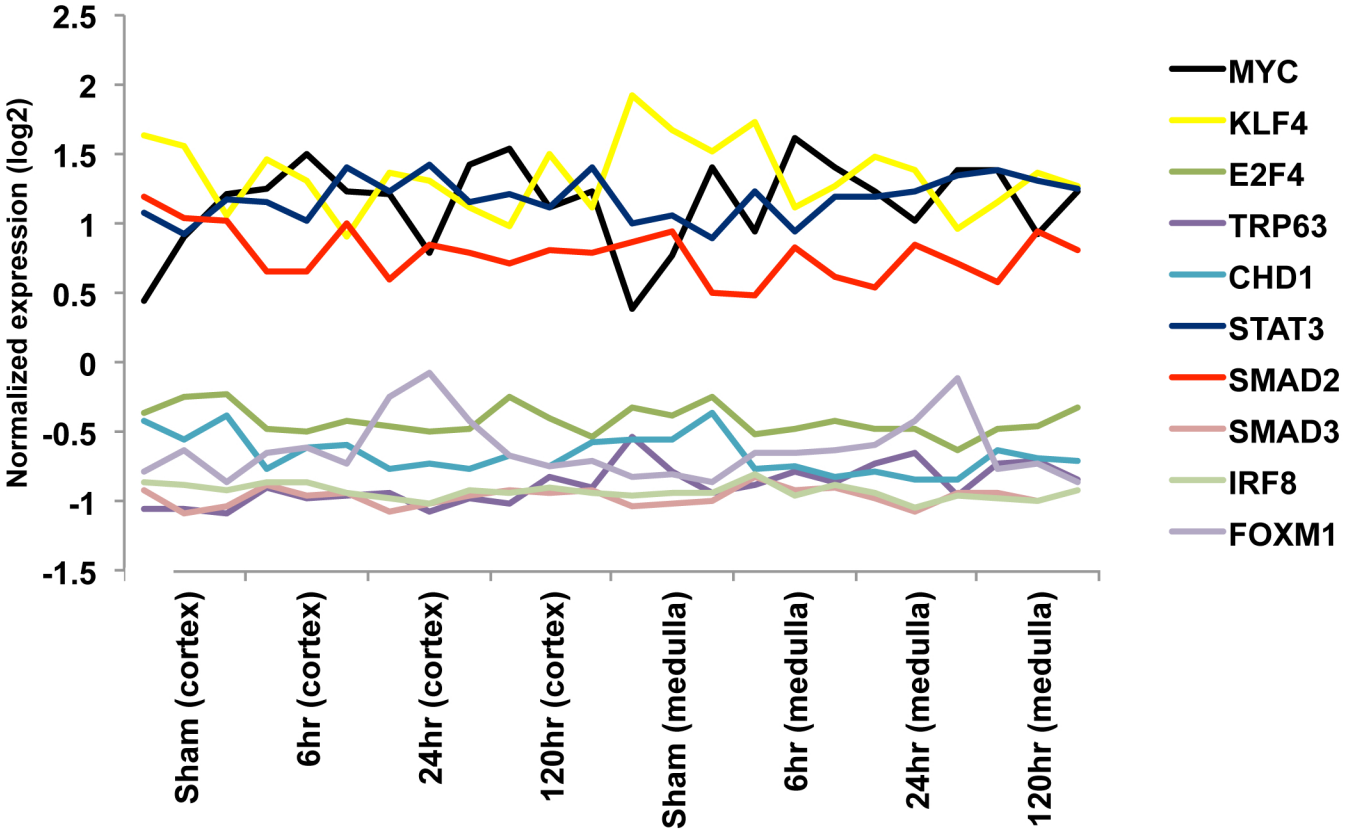
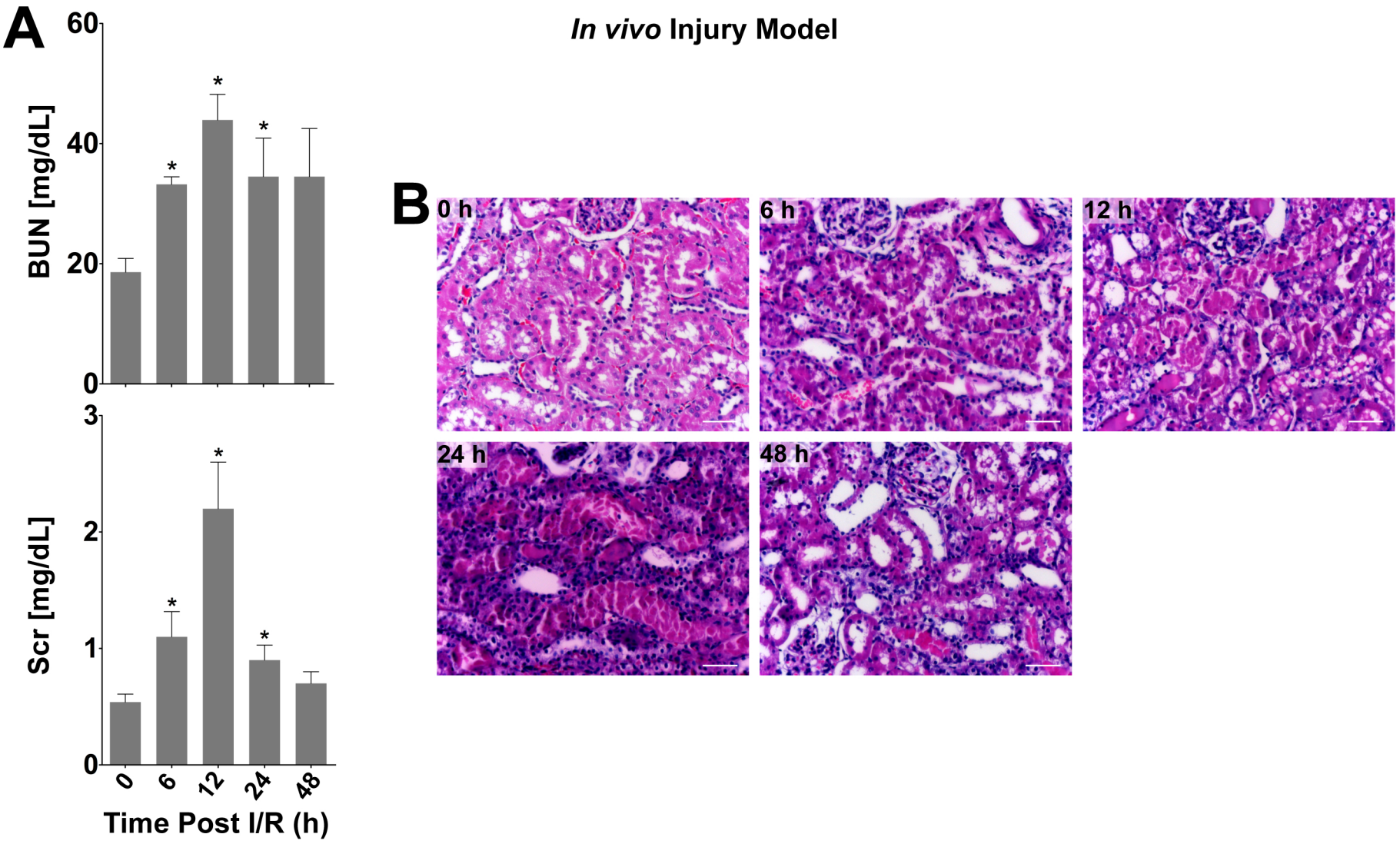
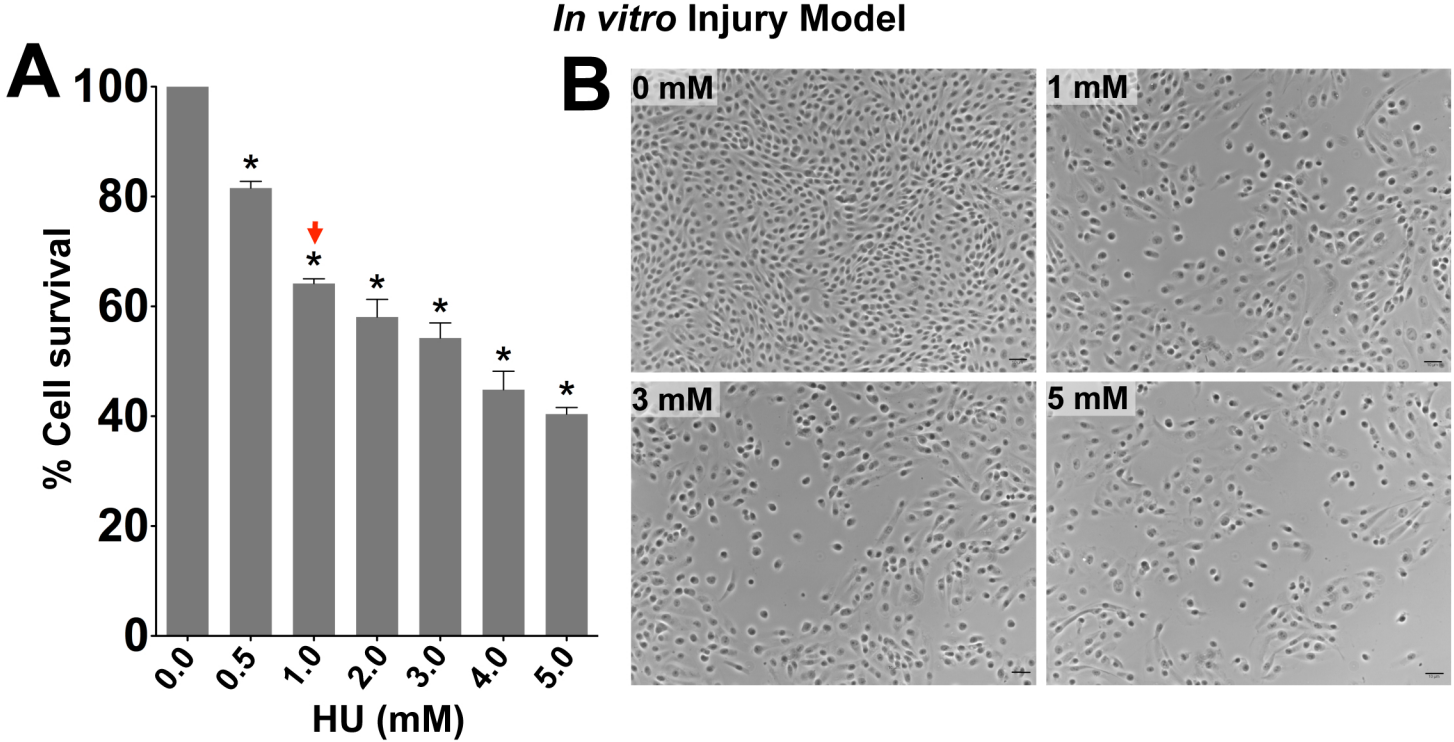


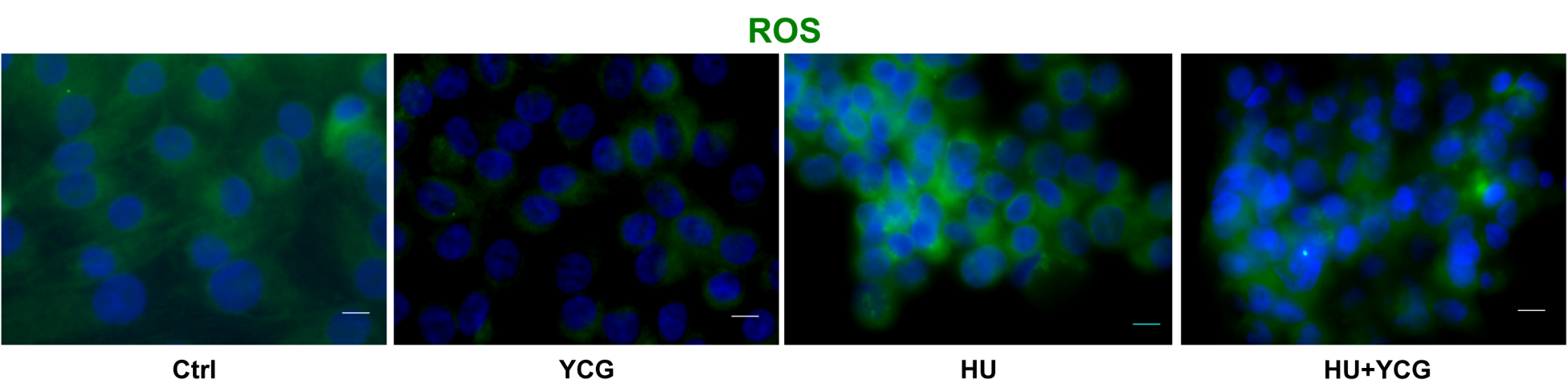
Supplementary Figure 1: Expression pattern of top 10 transcription factors across different time points in IRI model. Expression profiles of TF candidates discovered by SAM analysis were plotted for cortex and medulla for various time points following IRI.



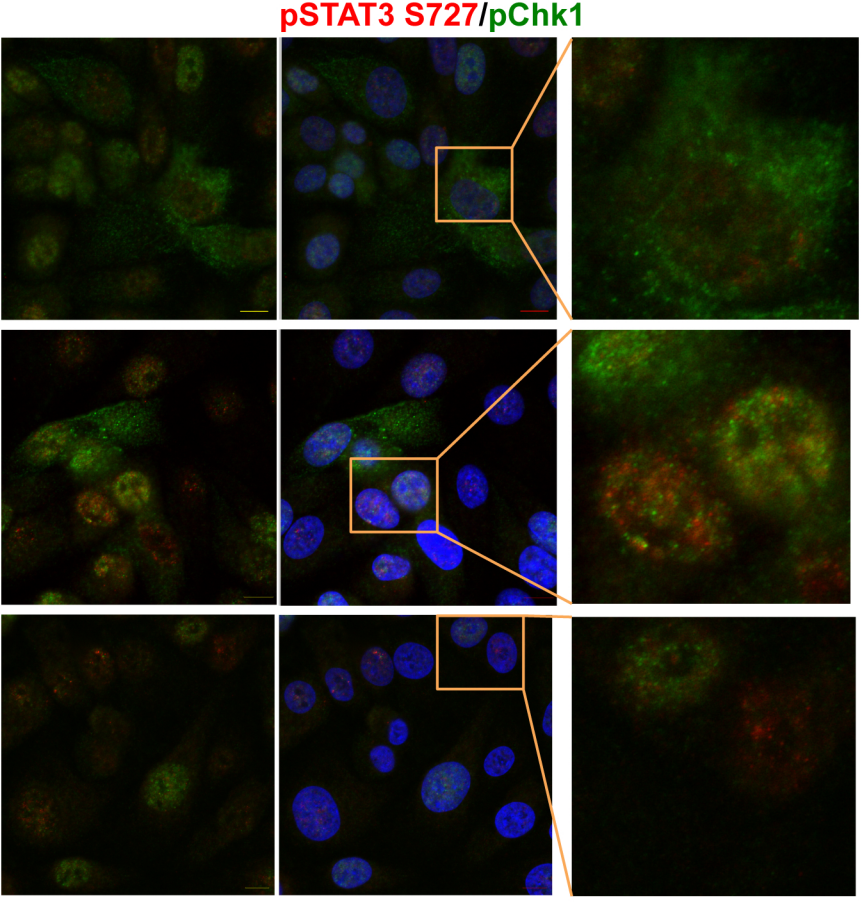
Supplementary Figure 2: Characterization of kidney dysfunction and tubular injury following bilateral renal ischemia/reperfusion injury (IRI). (**A**) Male Wistar rats were subjected to 30 min bilateral IRI. BUN and SCr were measured as kidney dysfunction. (**B**) Representative histological H&E stained images following IRI at 6h, 12h, 24h and 48 h showing proximal tubular necrosis as compared to sham. Bar represents 5 μm. '*' Represents significance as compared to sham ($p < 0.05$).



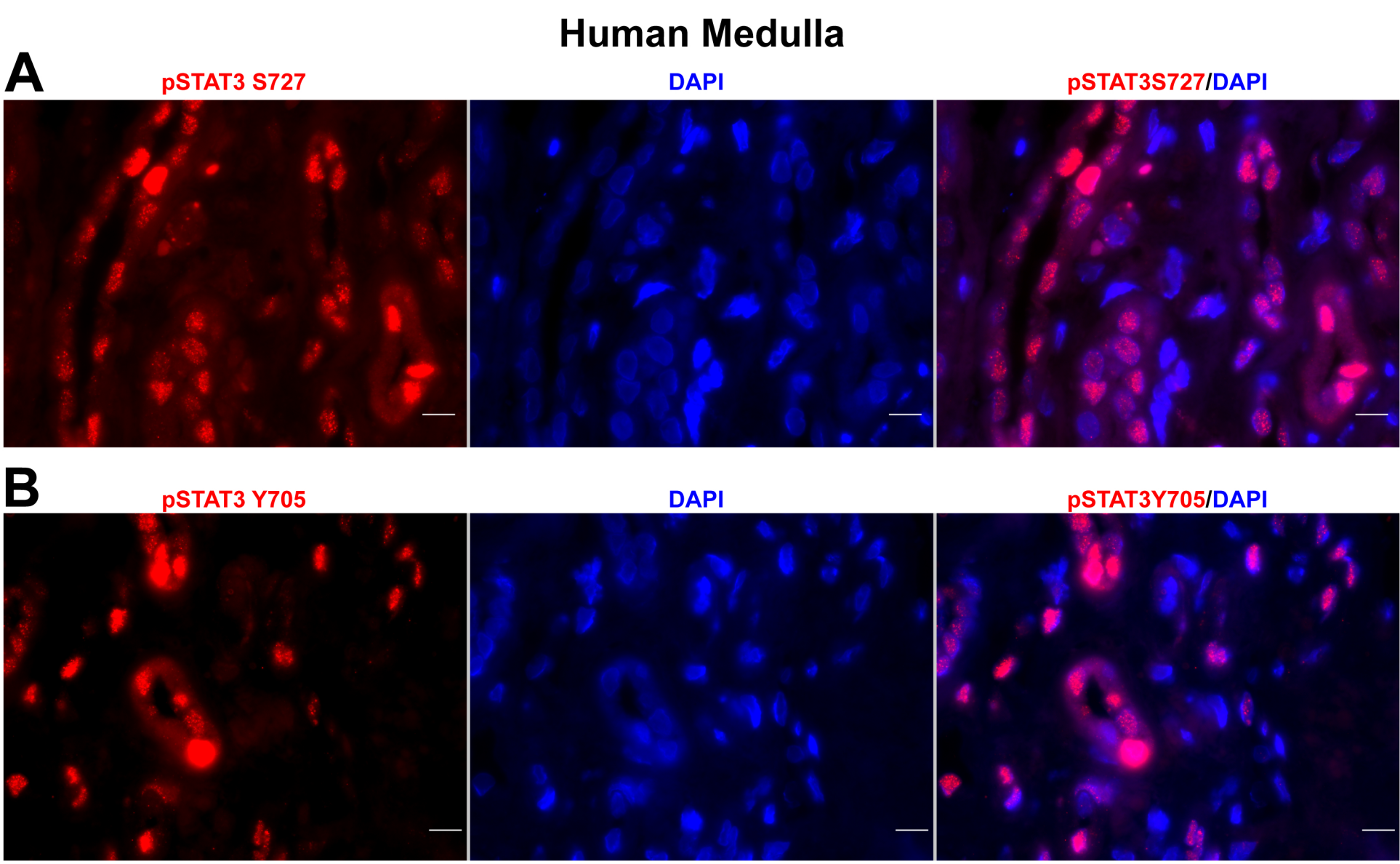
Supplementary Figure 3: Hydroxyurea (HU) treatment in human proximal tubular epithelial cells (HPTECs) results in dose-dependent cellular injury. HPTECs were treated with HU for 24 h and (**A**) MTT assay was performed. Arrow indicates HU dose used for further study. '*' Represents significantly different than control cells ($p < 0.05$). (**B**) Images were captured using Spot Advanced software on a Nikon microscope using Plan Flour 10X/0.3 NA objective. Bar represents 10 µm.



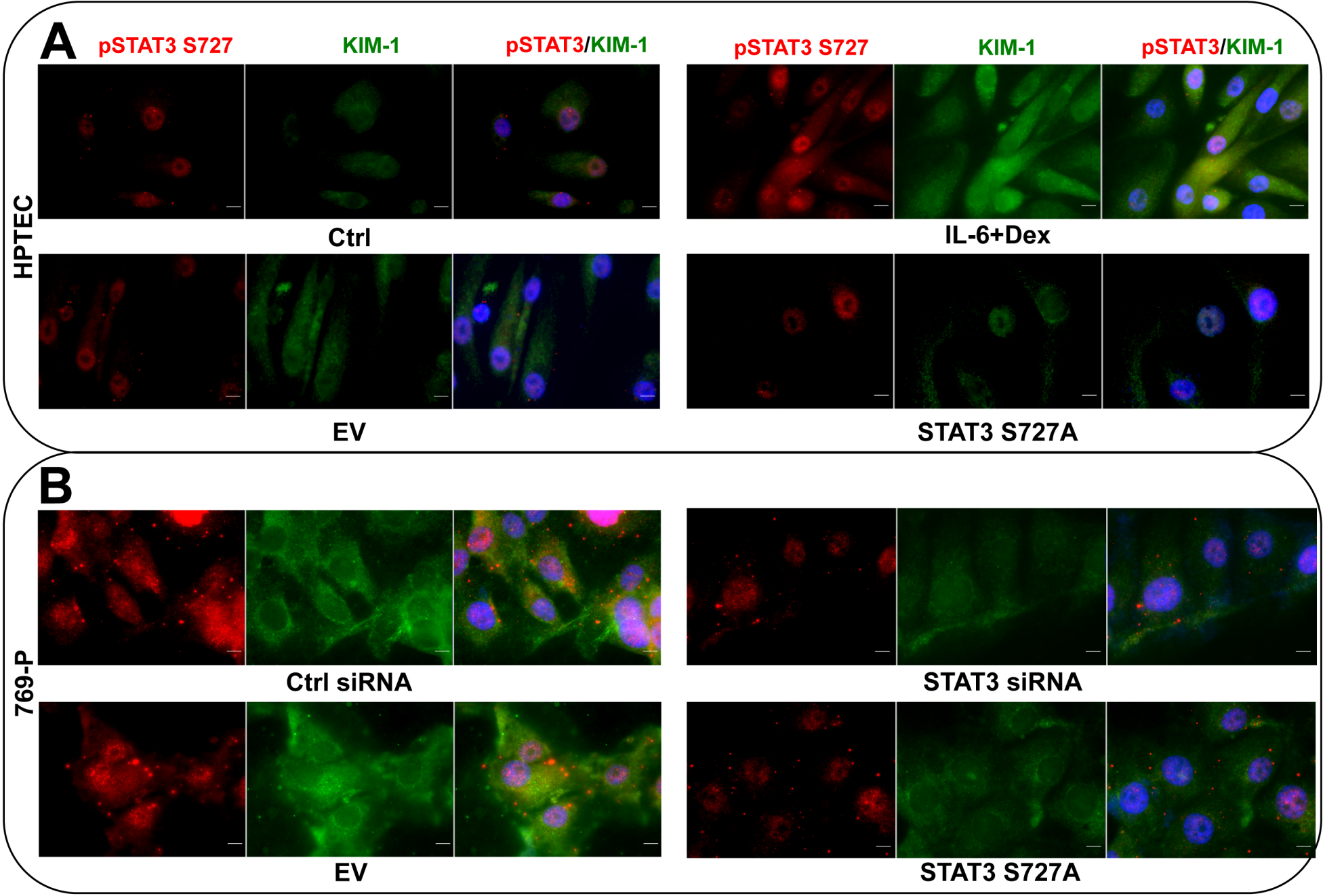
Supplementary Figure 4: ROS inhibitor YCG063 inhibits HU mediated ROS generation in human proximal tubular epithelial cells (HPTEC). HPTECs were pretreated 1h with YCG063 followed by treatment with HU and incubated for 24 h. Cells were incubated with DCFDA for 1 h and processed immediately for imaging. Bar represents 10 µm.



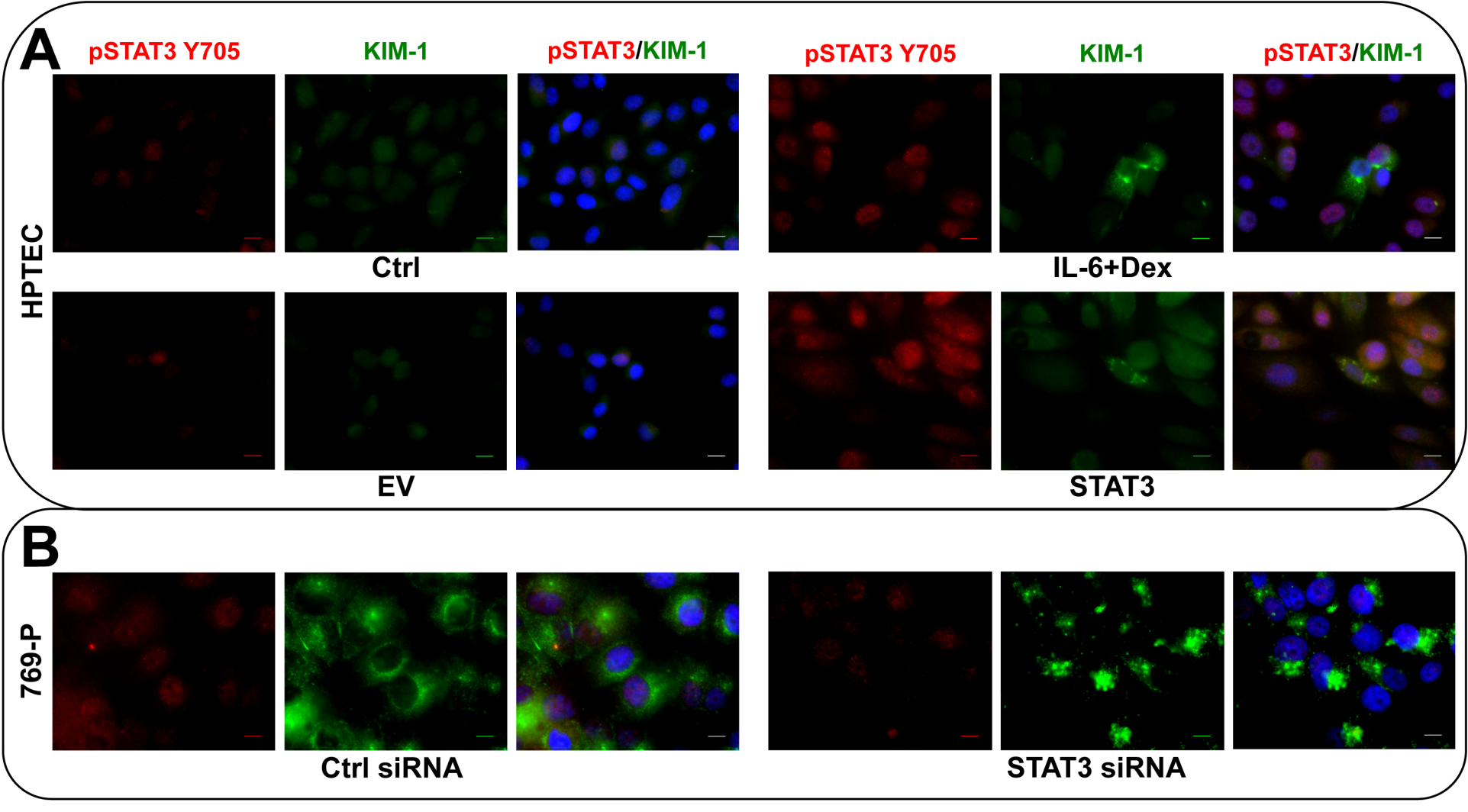
Supplementary Figure 5: pSTAT5727 and pChk1 co-localizes in the nucleus. Confocal images taken for HPTECs treated with HU or SB alone or in combination were stained with pSTAT3 727 and pChk1 antibodies. Bar represents 10 μm.



Supplementary Figure 6: Tubular epithelial cells of kidney medulla of patients with acute tubular injury express both S727 and Y705 phosphorylated STAT3. (**A**) Human kidney biopsies were immunostained for (**A**) pSTAT3 S727 or (**B**) pSTAT3 Y705. Bar represents 10 μm.



Supplementary Figure 7: Activated STAT3 expression (pSTAT3 S727) correlates with KIM-1 expression in HPTECs as well as in renal cell carcinoma cells (769-P). (**A**) HPTECs were treated with IL-6 and Dexamethasone or transfected with vector alone or STAT3_S727A plasmid and immunostaining was performed for pSTAT3 S727 and KIM-1. (**B**) 769-P cells were transfected with Ctrl, STAT3 siRNA or STAT3_S727A plasmid and immunostaining was performed for pSTAT3 S727 and KIM-1. Bar represents 10 µm.



Supplementary Figure 8: Activated STAT3 expression (pSTAT3 Y705) correlates with KIM-1 expression in human proximal tubular epithelial cells (HPTECs) as well as in renal cell carcinoma cells (769-P). (**A**) HPTECs were treated with IL-6 and Dexamethasone or transfected with vector alone or STAT3 plasmid and immunostaining was performed for pSTAT3 Y705 and KIM-1. (**B**) 769-P cells were transfected with Ctrl or STAT3 siRNA and immunostaining was performed for pSTAT3 Y705 and KIM-1. Bar represents 10 µm.

Supplementary table 1. List of top 10 TFs enriched with 203 probes identified by SAM analysis.

TF	Reference (Pubmed)	Target	p-Value	Genes
KLF4	18358816	57	8.28E-28	AACS, ADA, ANXA2, ANXA5, ATF3, BAK1, BTG2, CAPN2, CDC42EP2, CDCA7, CKS1B, CLDN4, CLIC1, COL4A1, CXCL16, CYR61, DUSP6, EDG5, EFEMP2, ELF3, FBLN1, FOSL1, GDF15, GMNN, H2AFX, HN1, IER2, JAK3, JUNB, KIF20A, KLF5, KRT8, KRTCAP2, LAMC2, LGALS3, LOX, LSM4, MAP3K1, MYC, NQO1, NRADD, NRM, PLEC1, PPP1R14B, PRKCDBP, PTGFRN, RAB3D, RIPK3, SCD2, TGIF, TMEM97, TUBB2A, TUBB5, UBE2C, UPP1, VASP, WFDC2
SMAD3	18955504	57	4.37E-25	ANGPTL4, ANXA1, ANXA2, ARHGAP11A, ARHGDIB, ATF3, BIRC3, BTG2, CCNB2, CD44, CD59, CLDN3, CLDN4, CLU, COL4A1, CRY1, CTPS, CYR61, DDX39, DUSP6, FOSL1, FSTL3, GLS, H2AFX, HN1, HSPB1, ITPKC, JUNB, KRT8, LAMC2, LDHA, LGALS3, MAP2K3, MED19, MYC, NFIL3, NME1, NPM3, PLEC1, PLP2, PRKCDBP, PRNP, PTGFRN, PTPRB, RFC2, RHOJ, RPL37, RUNX1, SERPINE1, SH2D4A, TAX1BP3, TGFA, TNFRSF12A, TOR3A, TUBB2A, UPP1, VIM
SMAD2	18955504	57	4.37E-25	ANGPTL4, ANXA1, ANXA2, ARHGAP11A, ARHGDIB, ATF3, BIRC3, BTG2, CCNB2, CD44, CD59, CLDN3, CLDN4, CLU, COL4A1, CRY1, CTPS, CYR61, DDX39, DUSP6, FOSL1, FSTL3, GLS, H2AFX, HN1, HSPB1, ITPKC, JUNB, KRT8, LAMC2, LDHA, LGALS3, MAP2K3, MED19, MYC, NFIL3, NME1, NPM3, PLEC1, PLP2, PRKCDBP, PRNP, PTGFRN, PTPRB, RFC2, RHOJ, RPL37, RUNX1, SERPINE1, SH2D4A, TAX1BP3, TGFA, TNFRSF12A, TOR3A, TUBB2A, UPP1, VIM
EKLF	21900194	37	1.48E-16	BAK1, BTG2, CD44, CDC20, CDCA7, CLIC1, CORO1A, DDX39, EIF4EBP1, EMP3, GNAI2, HMOX1, KRTCAP2, LCP1, LDHA, LGALS1, MYC, NQO1, NUBP2, PRNP, PSME2, RFC2, RPL10A, RPP21, RPS9, SCD2, SH3BGRL3, SLC16A3, SNRPA, SRM, SSR2, TUBB5, UBE2C, UMPS, VASP, VIM, ZNRD1
MYB	21317192	30	1.65E-14	BCL6, CAPN2, CASP3, DUSP6, EMP3, FXYD5, GNAI2, H2AFX, IRF1, JUNB, KLF5, LCP1, MAP2K3, MYC, NFIL3, PHLDA1, PLEK, PLP2,

				PRNP, RAB3D, RHOG, RHOJ, RRM2, RUNX1, SERTAD1, SLPI, SRM, SSR2, TMEM97, UMPS
FOXM1	23109430	18	3.91E-14	ARHGAP11A, AURKB, CCNB2, CDC20, CDKN3, H2AFX, HMGB2, HN1, IER5L, KIF20A, KIF23, LGALS1, LGALS3, PRC1, RND1, RRM2, TUBB2A, UBE2C
MYC	18555785	33	6.94E-14	ANGPTL4, BANF1, BZW2, CDCA7, CKS1B, CLDN4, CPZ, CSDA, CTPS, DDX39, EIF4EBP1, GDF15, GLS, H2AFX, HMOX1, KIF20A, LSM4, MRPL23, MRTO4, NME1, NPM3, NUBP1, NUBP2, PRC1, RPL10A, RPL27A, RPL37, RPS9, RRM2, SNRPA, TAF15, TMEM97, UMPS
TRP63	18441228	13	4.43E-12	AURKB, CKS1B, CNP1, COPEB, CYP3A13, ELF3, FOSL1, HMOX1, JUN, KIF23, PHLDA1, RRM2, VIM
IRF8	21731497	17	7.08E-12	AIF1, CD68, CD74, CDCA7, CNP1, CTSD, CTSS, EDG5, GDA, HMOX1, HTATIP2, PLEK, PSMB10, PSMB8, PSME2, RGS2, TAPBPL
STAT3	1855785	21	1.98E-11	ADA, BCL6, CLDN4, CNP1, EFEMP2, GLS, HMGB2, IER2, IRF1, JAK3, JUNB, LSM4, MAP3K1, MYC, NME1, SERPINE1, SPC24, SPSB1, TUBB5, UPP1, WFDC2

Supplementary table 2: List of primer pairs used to generate KIM-1 wild type and mutant luciferase plasmid

	F/R	Sequence
KIM-1 wild type promoter specific primers for cloning		
	F	5'-CCC GGG CTC GAG ATC TGC GAG TTT CAA AGA GAC CAG T
	R	5'-CCG GAA TGC CAA GCT ACT TTG TTT CCC CAC GGA GG
Primers used for site directed mutagenesis on KIM-1 promoter (red indicates mutated nucleotides)		
	F	5'- ATA AAT AAA ATA TGAA ACA CAC TTG CCC CGA GGA CCA CAG
	R	5'-CTG TGG TCC TCG GGG CAA GTG TGT TTC ATA TTT TAT TTA T