

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1: Podocyte specific knockdown of *Klf15* in *Podocin-Cre Klf15^{flox/flox}* mice was confirmed. (A) Primary glomerular epithelial cells (PGECs) were isolated from 12-week old *Podocin-Cre Klf15^{flox/flox}* and *Podocin-Cre Klf15^{+/+}* mice and cultured at 37°C for 1 week. Real-time PCR was performed for *Nephrin*, *Podocin*, *Synaptopodin*, and *Wt1* mRNA expression (n=6, ***p<0.001, Mann-Whitney test). (B) Real-time PCR was performed for *Klf15* mRNA expression (n=6, *p<0.05, Mann-Whitney test). (C) Protein was also extracted and western blot analysis for *Klf15* was performed. The representative blot of three independent experiments is shown in the top panel. The bottom panel shows the quantification of *Klf15* by densitometry (n=3, *p<0.05, Mann-Whitney test). (D) Immunofluorescence staining for *Klf15* and *Wt1* was performed in 12-week old *Podocin-Cre Klf15^{flox/flox}* and *Podocin-Cre Klf15^{+/+}* mice. Representative images from four mice in each group are shown in the left panel (X 20). Arrows show colocalization of *Klf15* and *Wt1*. Arrowheads show a lack of colocalization. Asterisk demonstrates nonspecific *Wt1* staining. “R” represents autofluorescence from RBCs. In the right panel, a total of 30 glomeruli were selected in each mouse and quantification of *Klf15* staining in the podocytes was determined by the ratio of *Klf15*⁺ and *Wt1*⁺ cells to *Wt1*⁺ cells (n=6 mice, **p<0.01, unpaired *t* test).

Supplementary Figure 2: LPS treated *Podocin-Cre Klf15^{flox/flox}* mice exhibit a lack of recovery in proteinaceous casts and tubular dilatation after DEX administration. *Podocin-Cre Klf15^{flox/flox}* and *Podocin-Cre Klf15^{+/+}* mice were concurrently treated with either DEX or vehicle after LPS treatment. All mice were sacrificed and renal cortex fixed for histology. (A-B) Periodic acid-Schiff (PAS) and hematoxylin and eosin (H&E) were performed to evaluate for glomerular or tubulointerstitial changes (X10, X 40). The representative images from 6 mice in each group are shown. Arrows show tubular dilatation and proteinaceous casts. No glomerulosclerosis or inflammatory exudate was observed.

Supplementary Figure 3: The pattern of inflammatory markers is similar between *Podocin-Cre Klf15^{+/+}* and *Podocin-Cre Klf15^{flox/flox}* mice after concurrent LPS and DEX treatment. *Podocin-Cre Klf15^{flox/flox}* and *Podocin-Cre Klf15^{+/+}* mice were concurrently treated with either DEX or vehicle after LPS treatment. All mice were sacrificed, glomeruli isolated, and RNA extracted for real-time PCR. (A) *Tnfa* (n=6, **p<0.01, Kruskal-Wallis test with Dunn’s post-test), (B) *Il-6* (n=6, *p<0.05, **p<0.01, Kruskal-Wallis test with Dunn’s post-test), (C) *Il-1β* (n=6, *p<0.05, Kruskal-Wallis test with Dunn’s post-test), and (D) *Infγ* mRNA expression levels are shown relative to untreated mice (n=6, *p<0.05 versus DEX only treatment, Kruskal-Wallis test with Dunn’s post-test). (E-F) Renal cortex from all mice was fixed for histology and immunostaining was performed for F4/80 and Gr-1. Quantification was performed by counting the number of cells with +F4/80 or +Gr-1 per high power field (HPF, X20). A total of 30 HPF were selected in each mouse for quantification (n=6 mice, *p<0.05, Kruskal-Wallis test with Dunn’s post-test).

Supplementary Figure 4: shRNA-mediated *KLF15* knockdown reduced survival and actin stress fiber formation in differentiated human podocytes. *KLF15* knockdown in human podocytes was performed using lentiviral shRNAmir system with the following constructs, *KLF15-shRNA33* and *KLF15-shRNA32*. *EV-shRNA* serves as the empty vector control. (A) Western blot was performed to confirm *KLF15* knockdown with quantification by densitometry (n=3, *p<0.05, Kruskal-Wallis test with Dunn’s post-test). (B) Human podocytes were transferred from 33°C to 37°C to induce cell differentiation. Cell survival was determined by counting the number of cells at 4, 7, 10, 14 days in 37°C (n=3, **p<0.01, ***p<0.001, Kruskal-Wallis test with Dunn’s post-test). (C) Phalloidin and hoechst staining was performed in surviving *EV-shRNA* and *KLF15-shRNA32* cells at 14 days post differentiation in 37°C. The representative images from 3 independent experiments are shown. A total of 100 cells were selected in each group and the cells were classified into the percentage of cells in type A, type B, or type C (n=3, *p<0.05, **p<0.01, unpaired *t* test). (D) Immunofluorescence staining for *Wt1* was performed in 12-week old *Podocin-Cre Klf15^{flox/flox}* and *Podocin-Cre Klf15^{+/+}* mice. A total of 30 glomeruli were selected in each mouse for quantification of podocyte number (n=6 mice, *p<0.05, unpaired *t* test).

Supplementary Figure 5: Overexpression of KLF15 increases actin stress fiber formation. We initially overexpressed KLF15 in human podocytes using lentiORF-*KLF15* clone under permissive conditions (33°C). **(A)** Western blot was performed to confirm the increased expression of KLF15 after transfection in human podocytes. Subsequently, lentiORF-*KLF15* and LentiORF-*RFP* human podocytes were grown to 80% confluency in permissive conditions. **(B)** Phalloidin and hoechst staining was performed to assess for changes in actin stress fiber formation. In addition to Figure 5B-C, supplementary representative images from 3 independent experiments are shown.

Supplementary Figure 6: Reduced KLF15 expression in GC-nonresponsive primary glomerulopathies. Immunofluorescence for Hoechst and KLF15 was performed in renal biopsy specimens from 16 healthy donor nephrectomies, 15 GC-responsive, and 20 GC-nonresponsive patients. In addition to the representative images and quantification provided in Figure 6 and 7, supplementary representative images of KLF15 staining in the glomeruli are provided. Each set of images with Hoechst and KLF15 staining are from distinct human biopsies.

Supplementary Figure 7: Reduced Synaptopodin and Nephtrin expression in GC-nonresponsive primary glomerulopathies. Immunofluorescence for Nephtrin and Synaptopodin was performed in renal biopsy specimens from 16 healthy donor nephrectomies, 15 GC-responsive, and 20 GC-nonresponsive patients. ImageJ was used to quantify the intensity of **(A)** Synaptopodin and **(B)** Nephtrin expression in the glomerulus in all three groups. The glomerular region was selected, and optical density (OD) was measured and quantified as a relative fold change to healthy subjects in the lower panel (* $p < 0.05$, ** $p < 0.01$, Kruskal-Wallis test with Dunn's post-test).

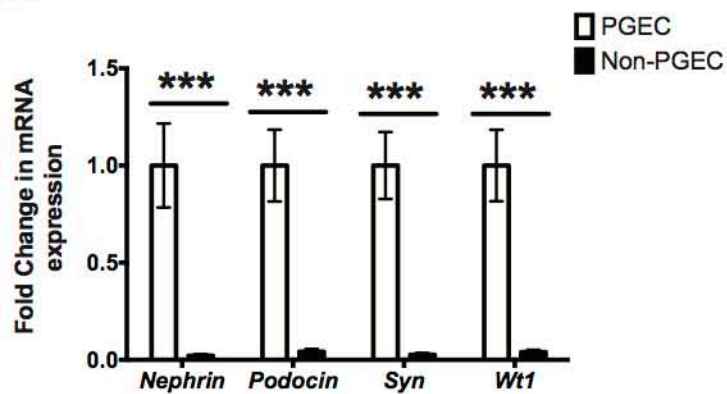
Supplementary Figure 8: KLF4 expression is unchanged with dexamethasone treatment. Cultured human podocytes were initially differentiated for 14 days and subsequently treated with either dexamethasone (DEX) or vehicle (VEH) for 12 hours. RNA was extracted and real-time PCR was performed. **(A)** *KLF4* and *KLF15* mRNA expression was compared between cultured human podocytes treated with and without DEX. ($n=6$, ** $p < 0.01$, Mann-Whitney test). **(B)** Immunofluorescence staining for Klf4 was performed in wildtype mice treated with DEX, LPS, LPS/DEX. The representative images of three independent experiments are shown in the left panel (X 20). In the right panel, the intensity of KLF4 expression was quantified ($n=3$, * $p < 0.05$, Kruskal-Wallis test with Dunn's post-test). **(C)** Immunofluorescence for Hoechst and KLF4 was performed in renal biopsy specimens from 16 healthy donor nephrectomies, 15 GC-responsive, and 20 GC-nonresponsive patients. Representative images of KLF4 staining in the glomeruli are provided (left panel) in all three groups. In the right panel, the intensity of KLF4 expression was quantified and presented as fold change relative to the healthy donor nephrectomies (** $p < 0.01$, Kruskal-Wallis test with Dunn's post-test).

Supplementary Table 1: Primer Sequences for Real-Time PCR

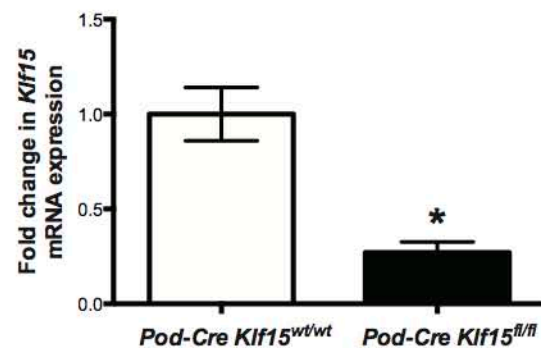
Gene	Forward primer	Reverse primer
Human <i>KLF15</i>	GTTGGGTATCTGGGTGATAGGC	TGAGAGTCGGGACTGGAACAG
Mouse <i>Nephrin</i>	TGGTCAACTGTGTGTCTGGG	TTATCTGAGCTCCGGGGTGT
Mouse <i>Podocin</i>	CCAAATCCTCCGGCTTAGGG	GAAGCAGATGTCCCAGTCGG
Mouse <i>Klf15</i>	AGAGCAGCCACCTCAAGGCCCA	TCACACCCGAGTGAGATCGCCGGT
Mouse <i>Il-6</i>	GACAAAGCCAGAGTCCTTCAGAGAG	CTAGGTTTGCCGAGTAGATCTC
Mouse <i>Il1-β</i>	CAGGATGAGGACATGAGCACC	CTCTGCAGACTCAAACCTCCAC
Mouse <i>Tnfa</i>	ATGAGCACAGAAAGCATGATC	TACAGGCTTGTCACTCGAATT
Mouse <i>Infy</i>	TCAAGTGGCATAGATGTGGAAGAA	TGGCTCTGCAGGATTTTCATG

Supplementary Figure 1

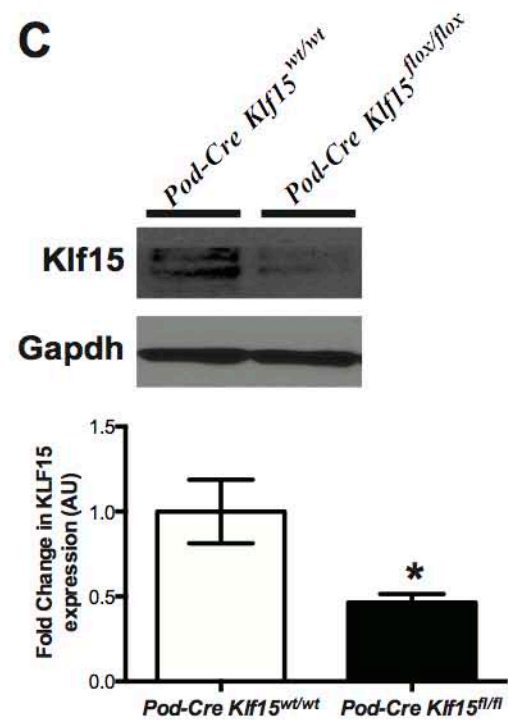
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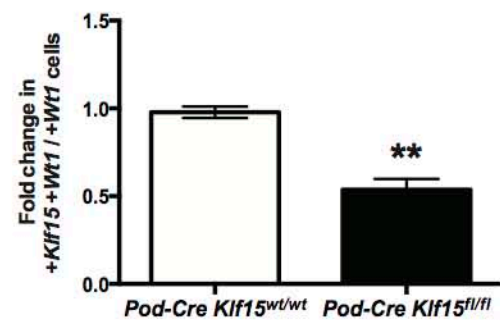
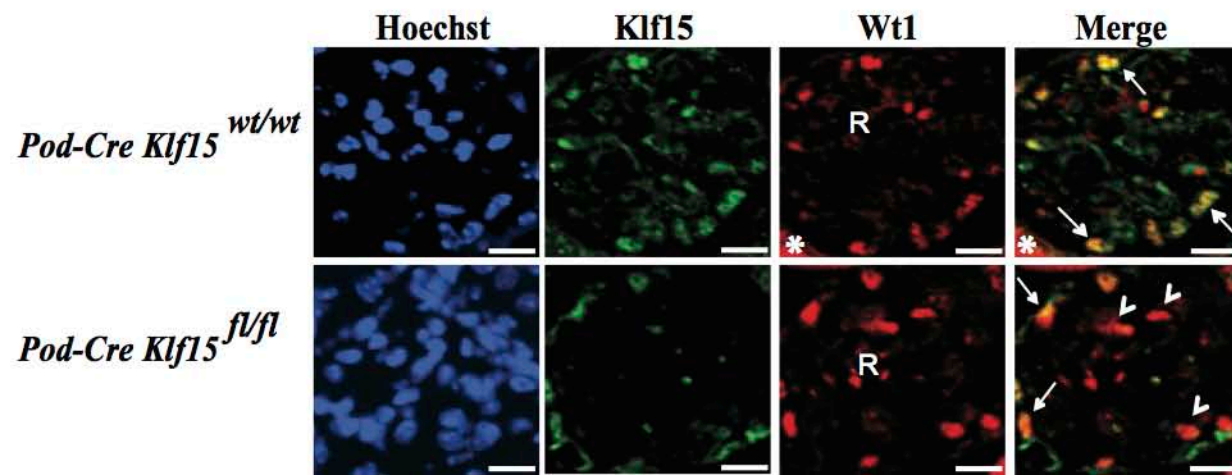
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C

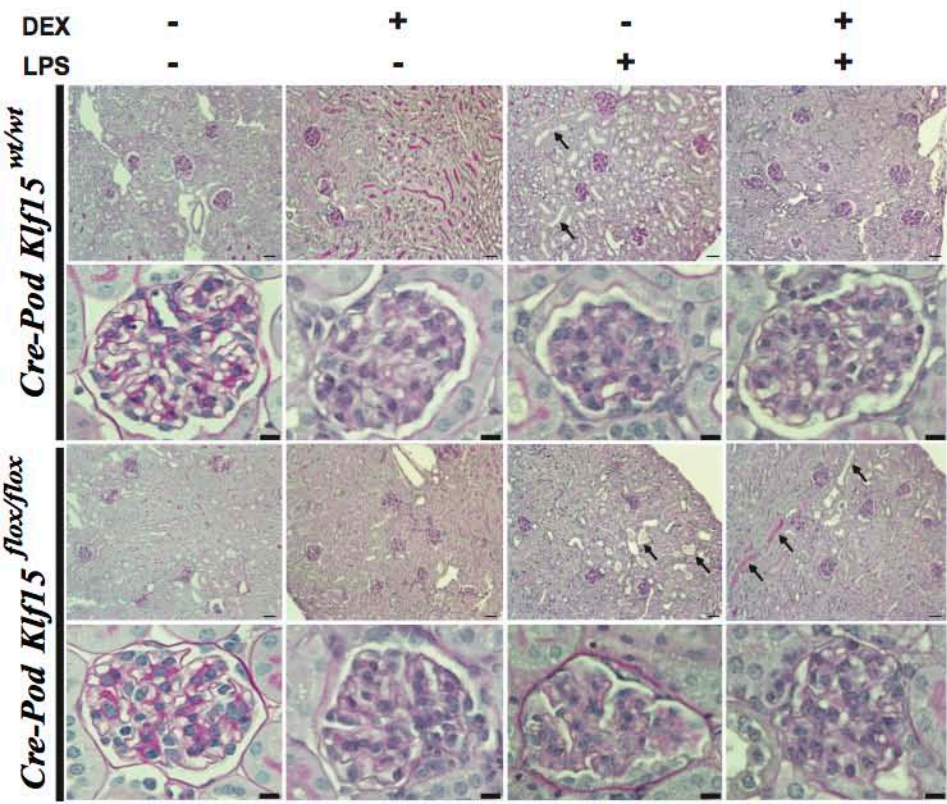


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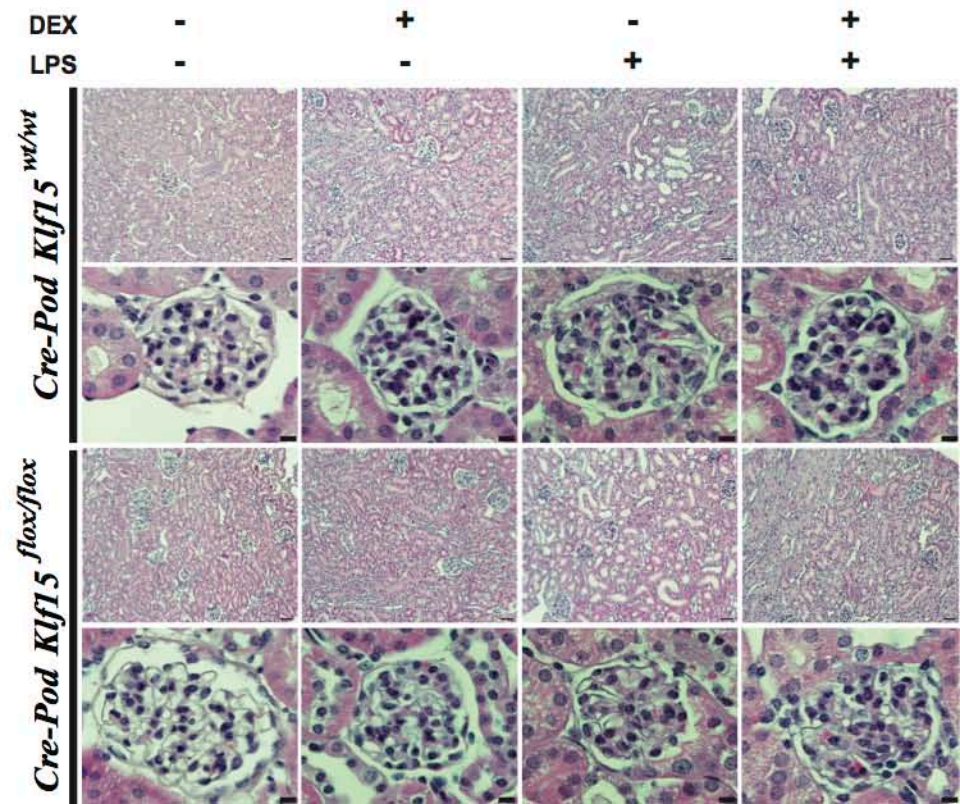


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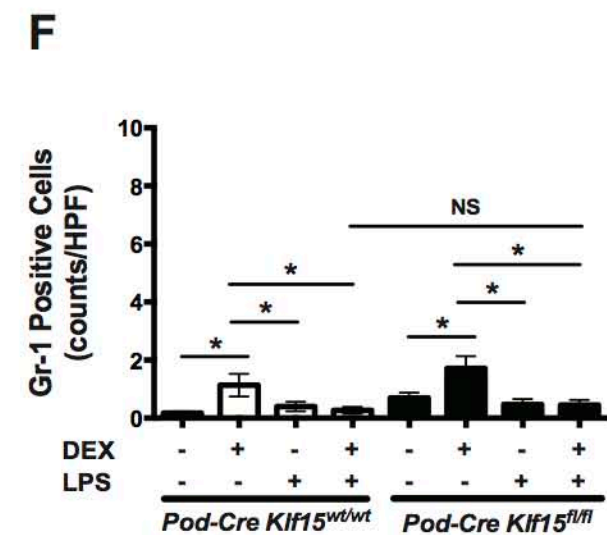
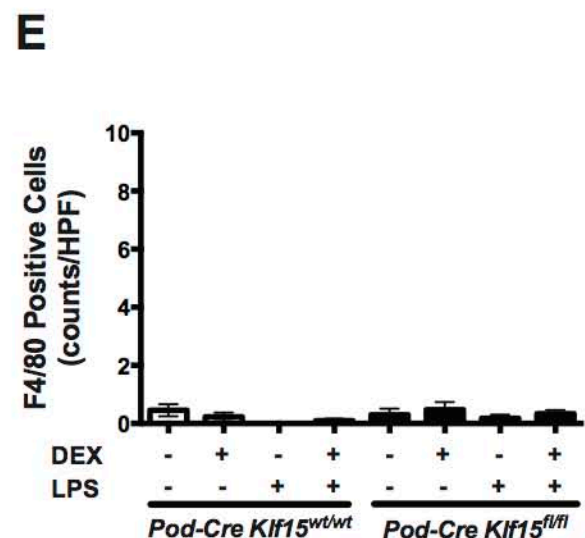
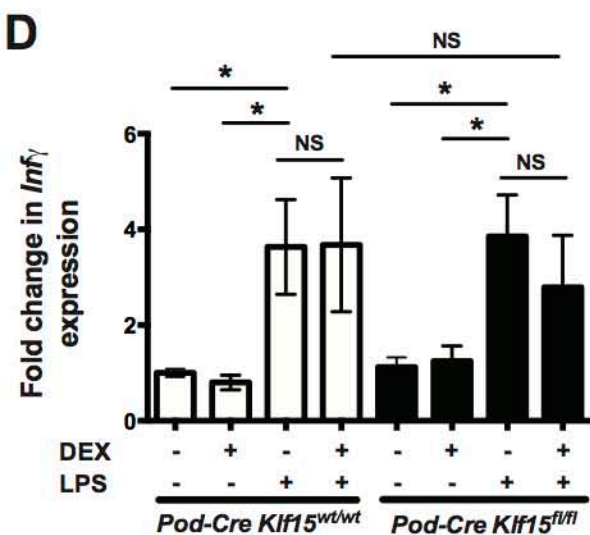
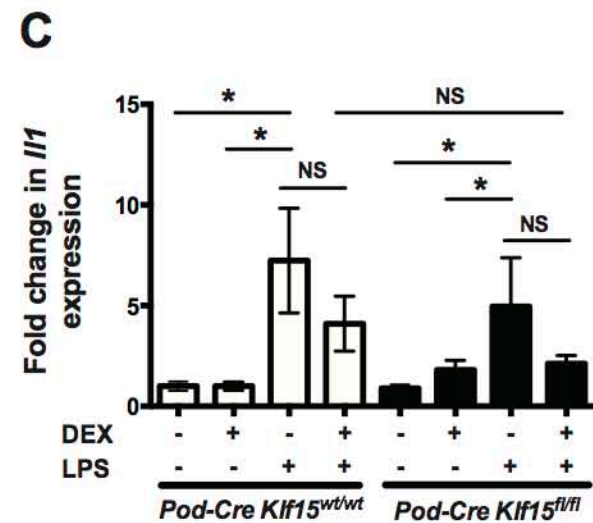
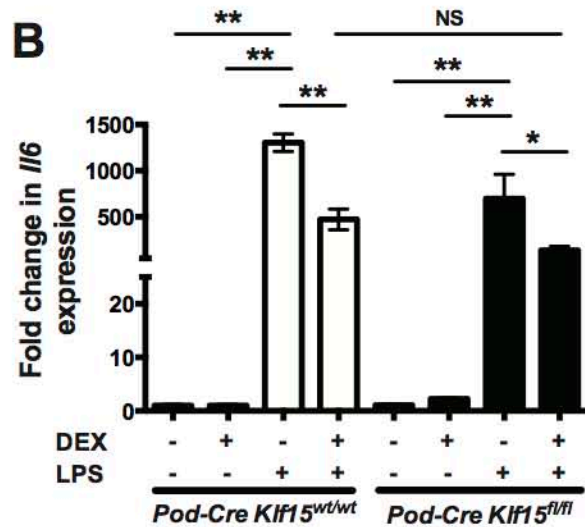
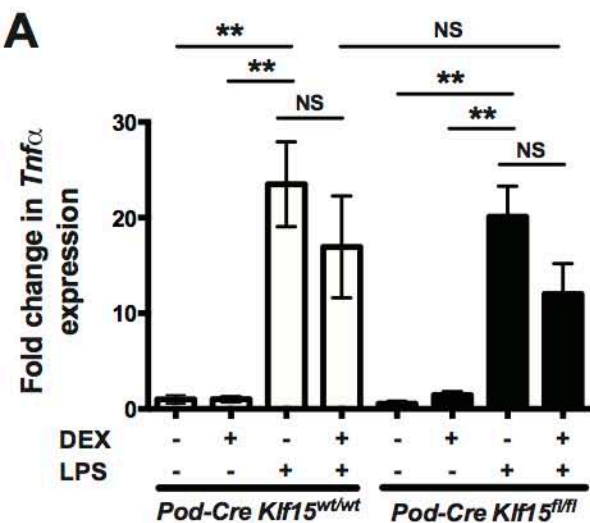
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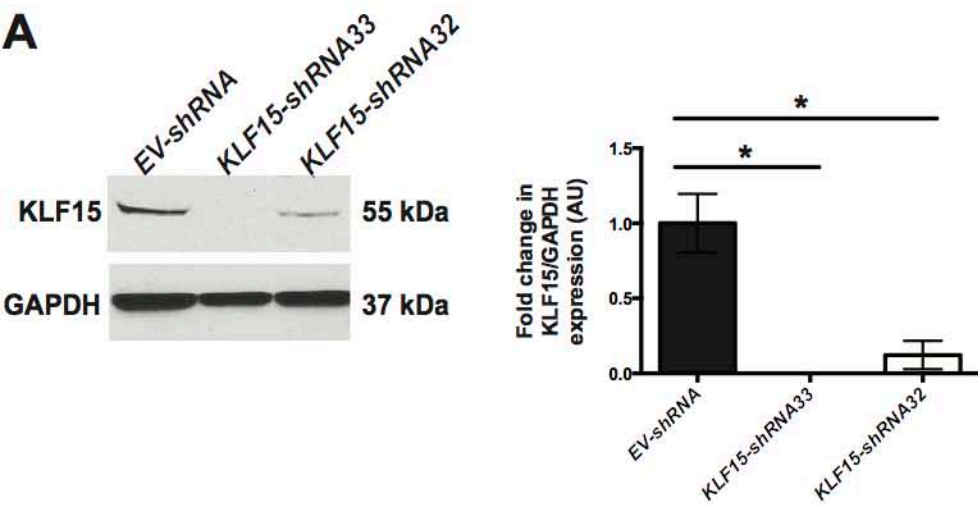


Supplementary Figure 3

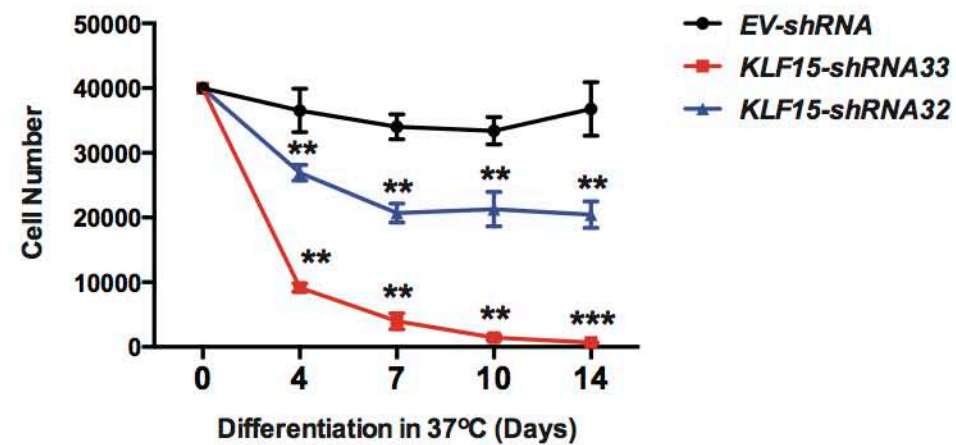


Supplementary Figure 4

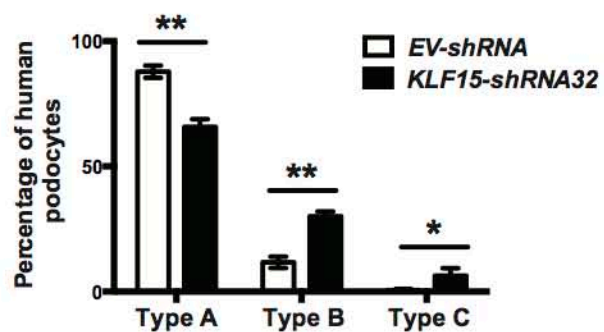
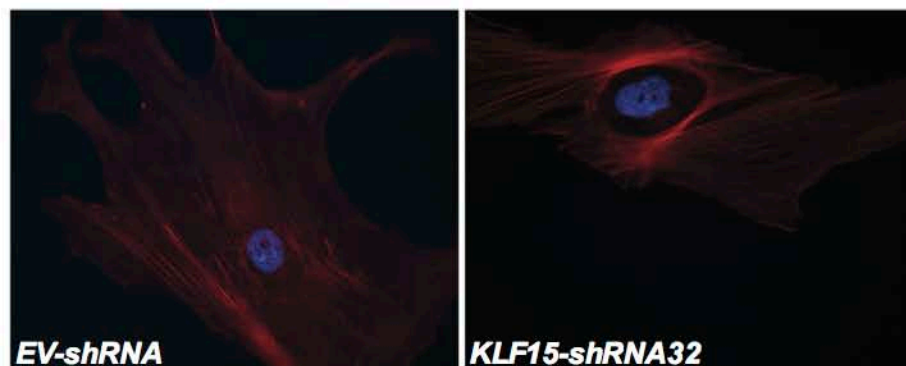
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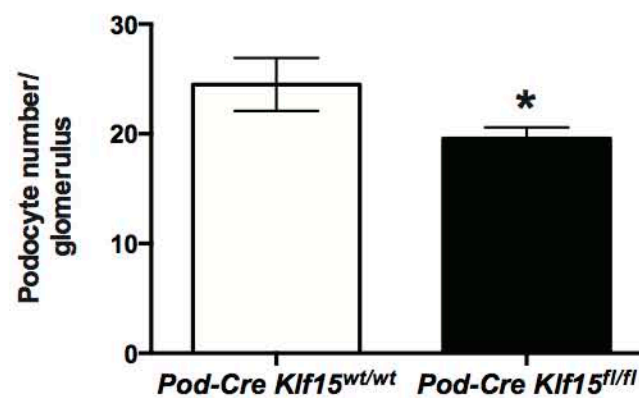
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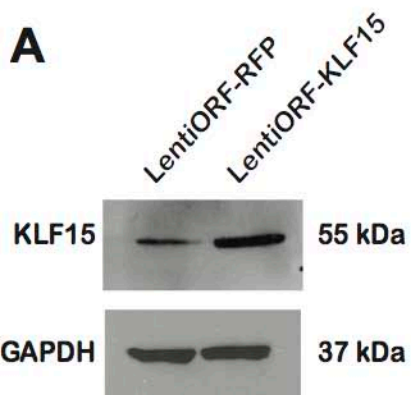


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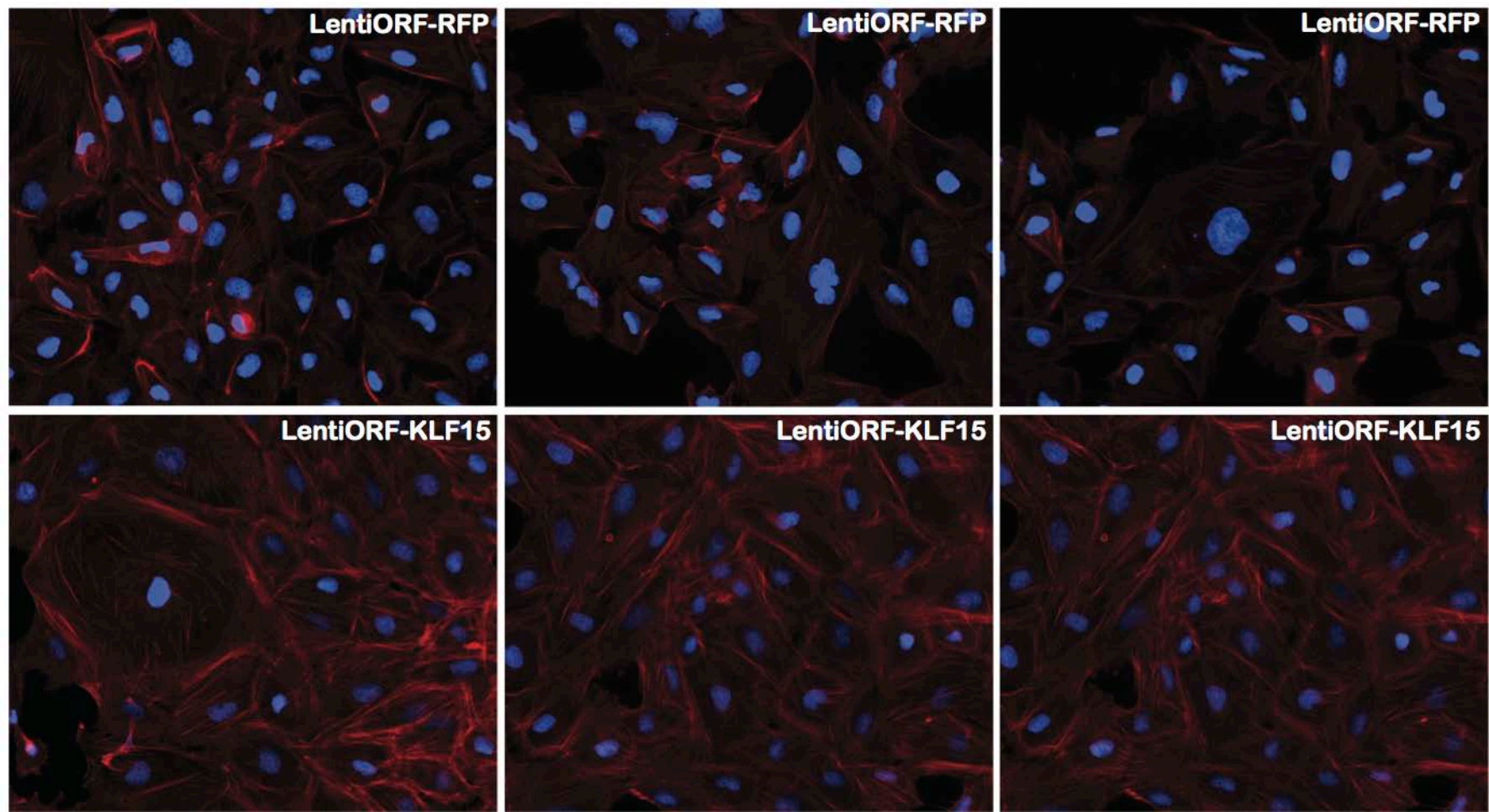


Supplementary Figure 5

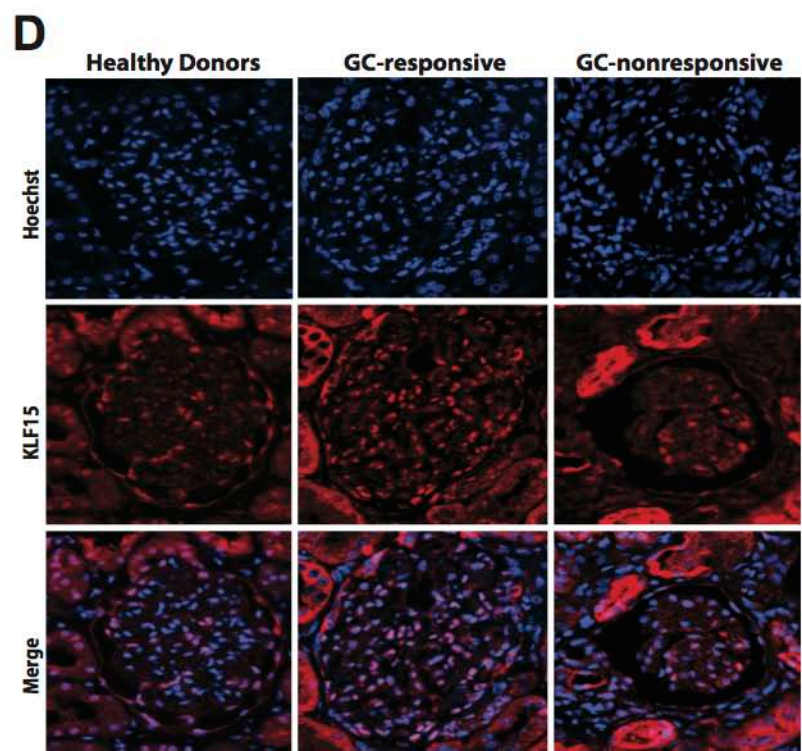
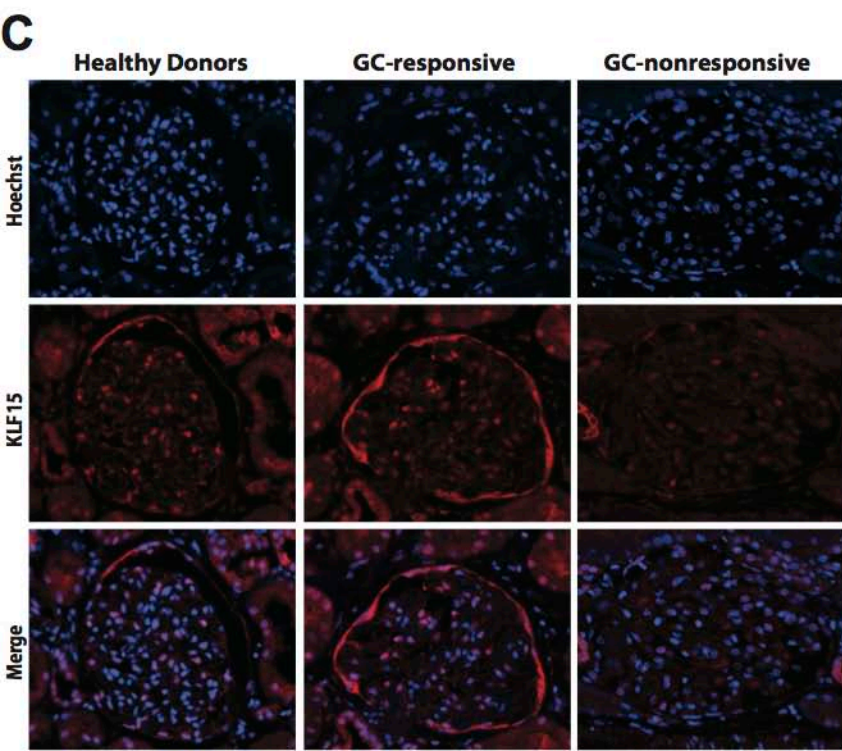
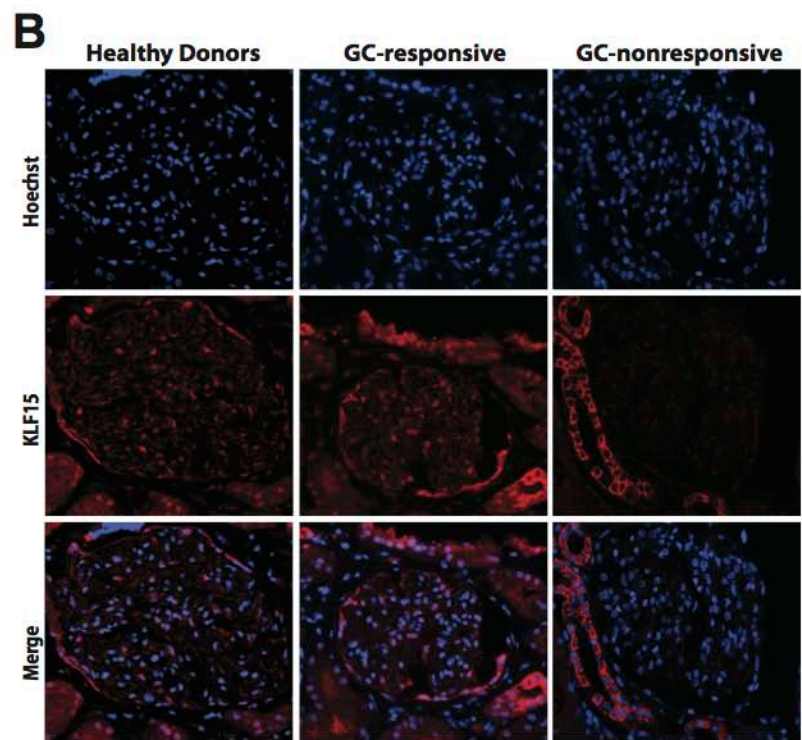
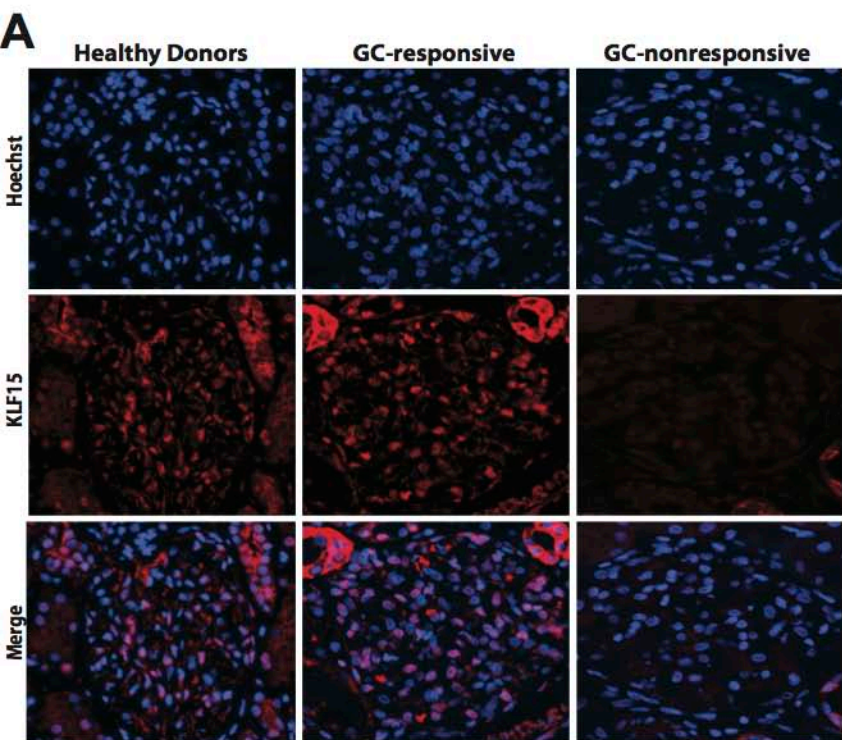
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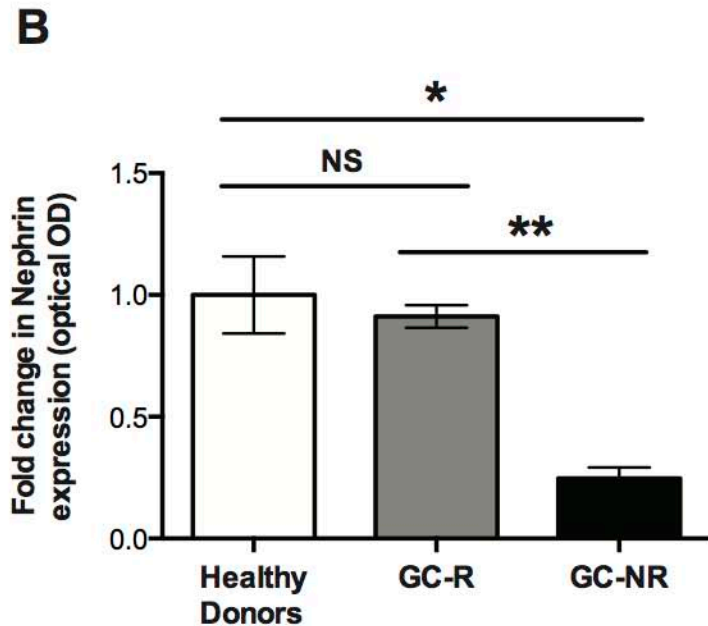
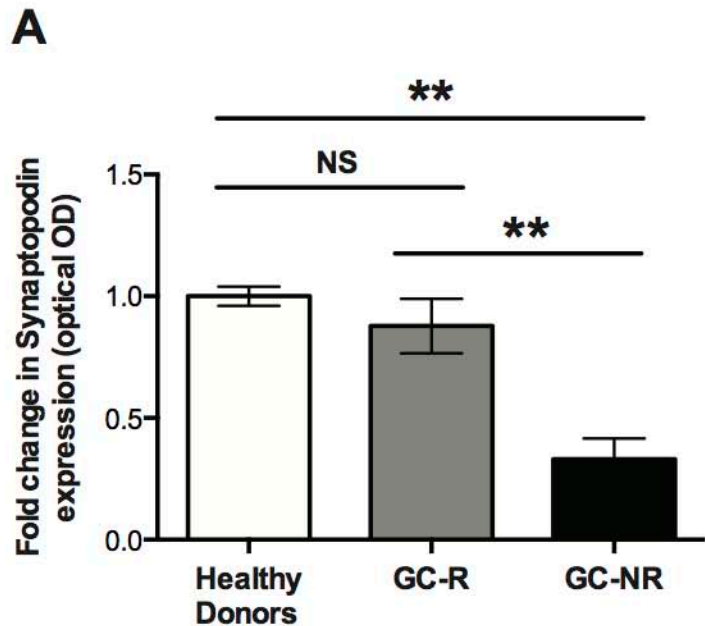
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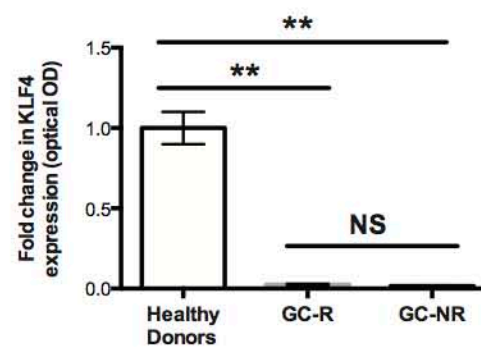
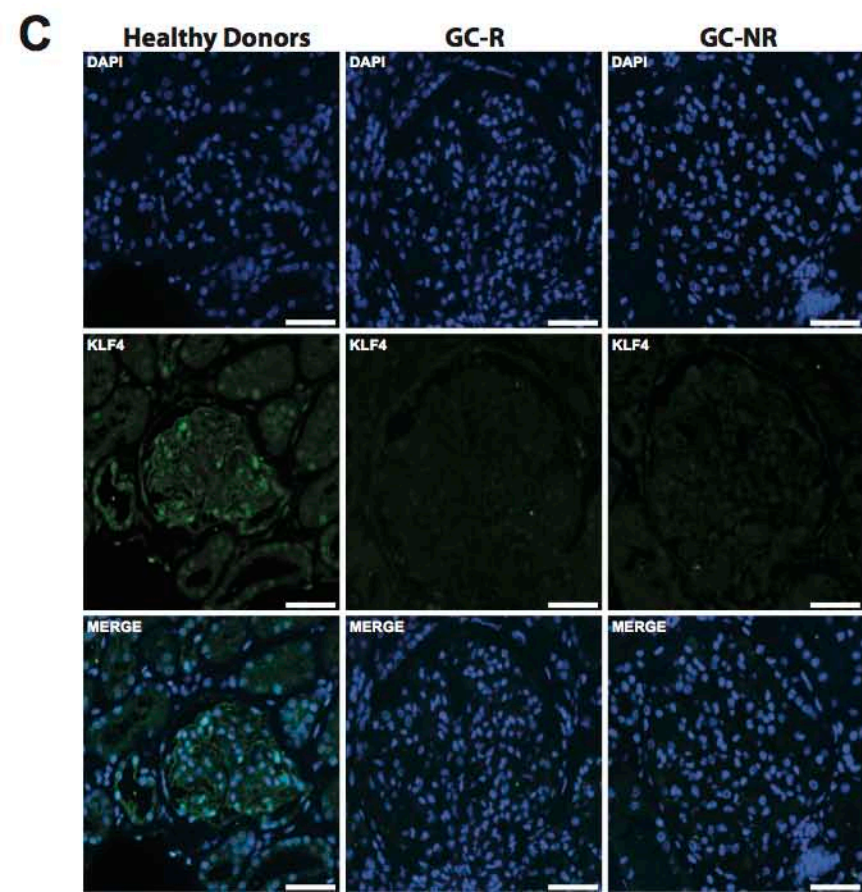
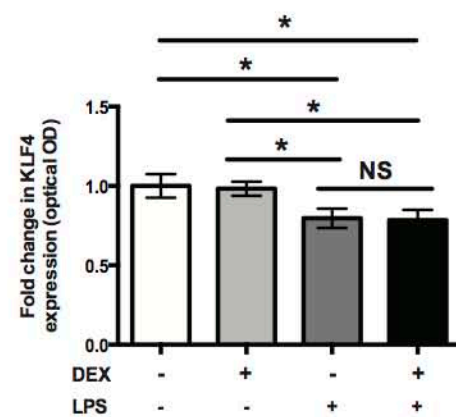
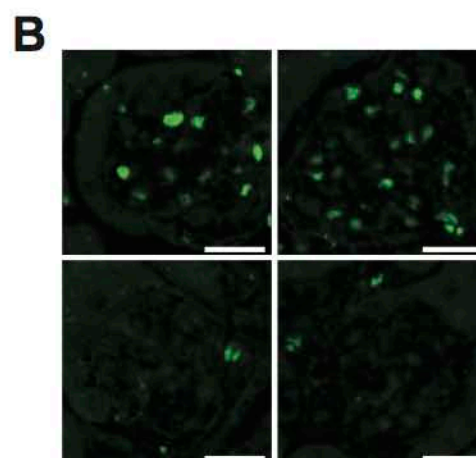
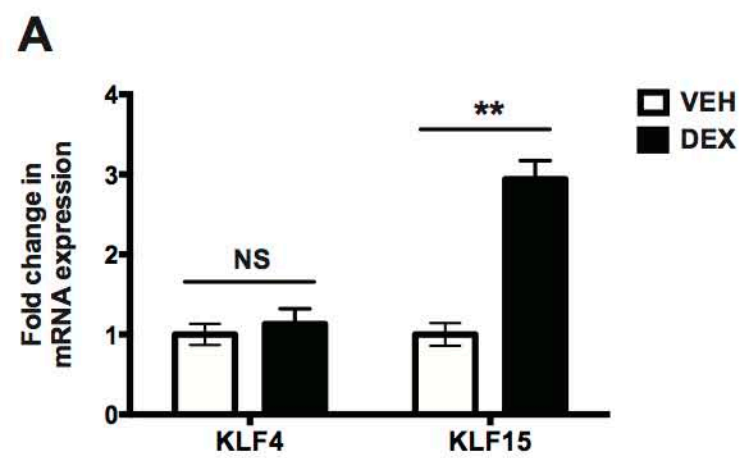
Supplementary Figure 6



Supplementary Figure 7



Supplementary Figure 8



Gene Name	Binding sites
CTCF	233
PARD3	55
KCNQ2	50
C8orf58	45
PDE9A	40
PPAP2C	40
TCF7L2	39
KCNMA1	36
CACNA1G	33
GAA	33
C17orf76-AS1	32
METTL23	28
ZBTB24	26
DDIT3	24
DPEP1	24
MYLK	24
CACNA1C	23
DISC1	23
KCNAB2	22
GSN	21
JOSD2	20
PCID2	20
RNPC3	20
MEIS2	19
TP53	19
ERBB2IP	18
IRF3	18
KLF11	18
MFSD11	18
RAP1GDS1	18
TP73	18
WDR47	18
ECI2	17
C8orf33	16
FAM213B	16
ITGB2	16
KCNK7	16
MEG3	16
NFKBIL1	16
RNH1	16
TSNAX-DISC1	16
BBIP1	15

CLN8	15
CPSF3L	15
FERMT2	15
FOLH1	15
NPHS1	15
PAX2	15
RNF38	15
SYNCRIP	15
ZGPAT	15
ATP2A3	14
BEAN1	14
BRSK2	14
BTBD2	14
COL6A1	14
DNAJB5	14
NUDT8	14
RBFA	14
ZFYVE28	14
ZNF419	14
ZXDC	14
ARFRP1	13
OPRL1	13
TCF7	13
ADAM8	12
ADRM1	12
AKIP1	12
AKR1E2	12
BAG6	12
CHCHD7	12
CHRNA4	12
CIRBP	12
CXCL12	12
GCNT3	12
GNL3	12
HNRNPF	12
KAT6A	12
KCNC4	12
KTN1	12
LAMTOR2	12
LSS	12
MEF2A	12
MYADM	12
NCAPH2	12

NIPA2	12
NMRK1	12
NR4A3	12
NT5C3L	12
PCMT1	12
PEG10	12
PTCH1	12
PTPN2	12
RCAN3AS	12
RNF170	12
SERPINA1	12
SEZ6L2	12
SIRT2	12
SNAP91	12
TEX264	12
TRPC4	12
TVP23C	12
TVP23C-CDRT4	12
URM1	12
WDR45L	12
CCDC112	11
CTDSP1	11
HDLBP	11
LIMS2	11
NFATC1	11
ACVR1	10
BCL2L13	10
BZRAP1-AS1	10
CACNA1A	10
CD8B	10
CHRD	10
CSK	10
DAP3	10
DCAF4	10
DGCR2	10
DNAJC16	10
DNMT3B	10
EWSR1	10
EZH2	10
FBXO44	10
FGD5-AS1	10
FOXP1	10
GPRASP2	10

LRRC20	10
MAPK9	10
NPRL3	10
PRSS21	10
PTGER3	10
RAD54L	10
RNF146	10
SFI1	10
SMAD2	10
ANAPC10	9
ATAD3A	9
BLNK	9
CCNT2	9
DERL3	9
FGFRL1	9
GPR64	9
IFT81	9
IGSF1	9
KLK6	9
MARVELD3	9
NAA10	9
NCOR2	9
NFIC	9
NOVA1	9
OPRM1	9
PHF1	9
PICALM	9
PPARD	9
RNF145	9
RNF212	9
RTN2	9
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TCF4	9
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ARHGEF18	8
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DRD2	8
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JAKMIP2	8
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LEF1	8
LRTOMT	8
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FGFR1	6
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FOXP4	6
FRS2	6
GCFC2	6
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GDI2	6
GLYCK	6
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PHACTR3	6
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