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Supplemental Table 1. Primer sequences. Shown are sequences of primer sets used for the expression analysis of the indicated genes by RT-PCR.

Gene	Forward Primer Reverse Primer
<i>Kim1</i> (mouse)	5'-AAACCAGAGATTCCCACACG-3' 5'-GTCGTGGGTCTTCCTGTAGC-3'
<i>Loxl2</i> (mouse)	5'-GATCTTCAGCCCCGATGGA-3' 5'-CAAGGGTTGCTCTGGCTTGT-3'
<i>Tgfβ1</i> (mouse)	5'-TGGCGAGCCTTAGTTTGGGA-3' 5'-TCGACATGGAGCTGGTGAAA-3'
<i>Acta2</i> (mouse)	5'-CCTGACGCTGAAGTATCCGATAG-3' 5'-TTTTCCATGTCGTCCCAGTTG-3'
<i>Pgk1</i> (mouse)	5'-CAAACAACCAAAGGATCAAGG-3' 5'-CCCAAGATAGCCAGGAAGG-3'
<i>Pdk1</i> (mouse)	5'-GTTAGGGATAGGGTTGGAGATCTTT-3' 5'-TCACAGGATGGTTGGTTCTTTCT-3'
<i>Ldha</i> (mouse)	5'-CGTCTCCCTGAAGTCTCTTAACC-3' 5'-CCCACACCATCTCAACACC-3'
<i>Kdr</i> (mouse)	5'-ACTGCAGTGATTGCCATGTTCT-3' 5'-TCATTGGCCCGCTTAACG-3'
<i>Emcn</i> (mouse)	5'-TGCAACCACTCCATCAACCA-3' 5'-CGCGATAACCACAGGCAAA-3'
<i>Vcam1</i> (mouse)	5'-TAGAGTGCAAGGAGTTCGGG-3' 5'-CCGGCATATACGAGTGTGAA-3'
<i>Icam1</i> (mouse)	5'-TGGATACCTGAGCATCACCA-3' 5'-CTGCTACCTGCACTTTGCC-3'
<i>Cxcl1</i> (mouse)	5'-GCAGACCATGGCTGGGATT-3' 5'-CCTGAGGGCAACACCTTCAA-3'

<i>Cxcl2</i> (mouse)	5'-GCGCCCAGACAGAAGTCATAG-3' 5'-AGGGTCAAGGCAAACCTTTTTGA-3'
<i>Tnfa</i> (mouse)	5'-GCTGAGCTCAAACCCTGGTA-3' 5'-CGGACTCCGCAAAGTCTAAG-3'
<i>VCAM1</i> (human)	5'-GCTTCAGGAGCTGAATACCC-3' 5'-AAGGATCACGACCATCTTCC-3'
<i>IRF-1</i> (human)	5'-TTTCGCTGTGCCATGAACTC-3' 5'-TGTTCCCTGCTCTGGTCTTTCAC-3'

Supplemental Figure 1. Validation of *Cdh5-Cre* driven recombination of the *Phd2* flox allele in the kidney. Recombination analysis of *Phd2* flox allele in genomic DNA isolated from kidneys of *EC-Phd2* mice or their *Cre-* littermate controls. Primers used, amplify the conditional (2-lox) and the recombined (1-lox) allele.

Supplemental Figure 2. Endothelial *Phd2* ablation does not alter serum BUN levels 1 day following bilateral IRI. Shown are serum BUN levels in *EC-Phd2* mice or their *Cre-* littermate controls at day 1 after bilateral IRI (n=16-17; P>0.5, 2-tailed Student's t-test). ns, not statistically significant

Supplemental Figure 3. Endothelial *Phd2* deletion does not alter post-ischemic kidney stabilization of HIF at day 3 post unilateral renal IRI. (A) Shown is immunoblot analysis of HIF-1 α and HIF-2 α in post-ischemic kidneys from *EC-Phd2* and *Cre-* controls at day 3 post unilateral renal IRI. Ponceau S staining was used to assess for equal protein loading. Nuclear kidney extracts from a mouse treated with an oral PHD inhibitor served as positive control (+Co). Right graphs show densitometric analyses of HIF-1 α and HIF-2 α normalized to Ponceau. (B) Representative images of immunofluorescence detection of HIF-1 on kidney cryosections from *EC-Phd2;mT/mG* and *EC;mT/mG* mice at day 3 following unilateral renal artery clamping compared to uninjured kidneys. Shown are merged images of mTomato (red), EGFP (green) and HIF-1 staining (white) with (top 2 rows) or without DAPI (bottom 2 rows). Non-recombined cells express membrane-bound mTomato while recombined cells express membrane-bound EGFP. In the *EC-Phd2;mT/mG* mice, EGFP⁺ cells represent *Phd2* deficient ECs whereas in the *EC;mT/mG* controls, EGFP⁺ cells correspond to ECs competent for *Phd2*. Insets, top 2 rows: higher magnification views from dashed square marked areas showing ECs without evidence of HIF

staining. Overall, at day 3 post IRI the staining for HIF-1 was rare and there was no difference in endothelial HIF-1 between mutants and controls. Yellow arrows indicate HIF-1 stained nuclei. Scale bars indicate 50 μ m.

Supplemental Figure 4. Single cell transcriptomic analysis of *Phds/Eglns* in kidney endothelial cells. The *t*-distributed stochastic neighbor embedding (tSNE) map demonstrates 16 distinct cell types revealed by unsupervised clustering. Right panel shows the magnified endothelial cell cluster, which consisted 2.29% of 43,745 analyzed cells. Bottom panel depicts heatmap showing the expression levels of *Egln1* (*Phd2*), *Egln2* (*Phd1*) and *Egln3* (*Phd3*) in kidney endothelial cells. The color scheme is based on z-score distribution.

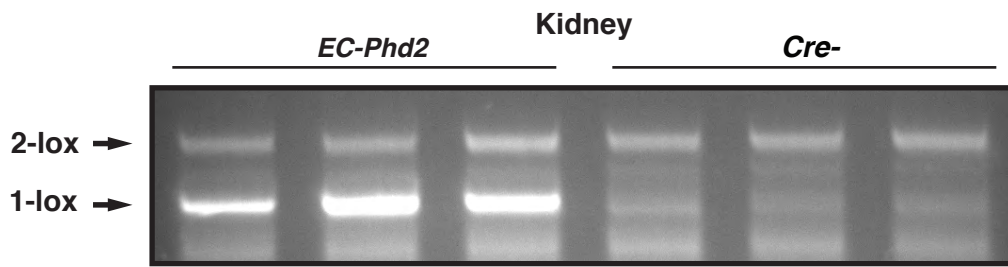
Supplemental Figure 5. Concurrent endothelial *Phd2* and *Hif2* deletion does not alter post-ischemic kidney mRNA levels of *Il-1b* and *Il-6* at day 3 post unilateral renal IRI. Shown are mRNA levels of *Il-1b* and *Il-6* in post-ischemic and contralateral kidneys of *EC-Phd2Hif2* mice and their *Cre-* controls at day 3 post unilateral IRI (n=8; P>0.05, 1-way ANOVA with Sidak correction for multiple comparisons).

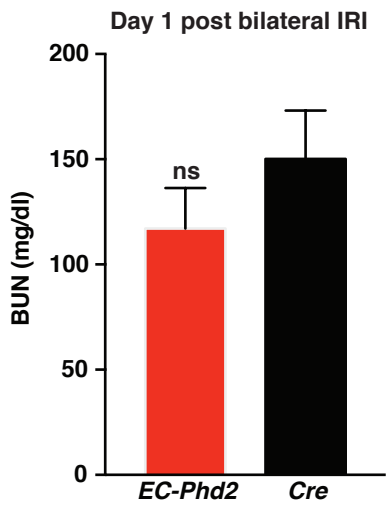
Supplemental Figure 6. Inducible endothelial specific inactivation of *Phd2* attenuates histological kidney injury at day 3 following renal IRI. (A) Background autofluorescence indicated by the percentage of GFP⁺ cells in bone marrow of *Cre-* (*mT/mG*) mice. (B) Recombination analysis of *Phd2* flox allele in genomic DNA isolated from kidney, lung, liver and heart following tamoxifen treatment of *iEC-Phd2* and *Cre-* mice. (C) Acute injury scores in post-

ischemic kidneys of tamoxifen treated *iEC-Phd2* and *Cre-* mice at day 3 following kidney IRI (n=5-4; P=0.0446, 2-tailed Student's t-test).

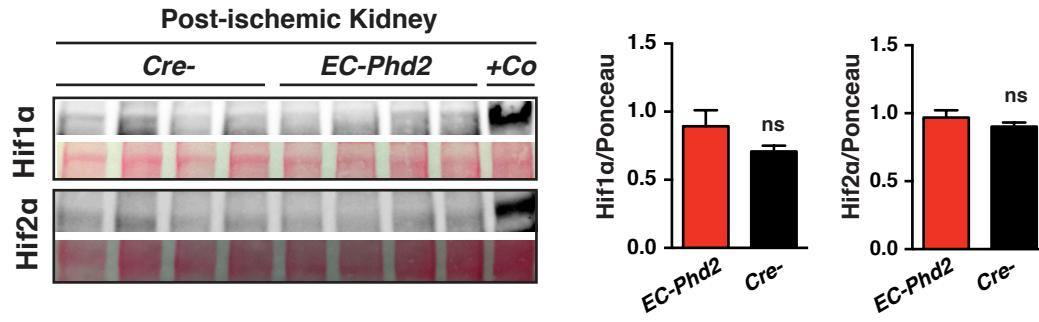
Supplemental Figure 7. Endothelial *Phd2* ablation does not influence serum kynurenic acid and α -ketoglutarate levels. Serum kynurenic acid and α -ketoglutarate levels for *EC-Phd2* and *Cre-* mice measured by LC/MS and GC/MS respectively (n=8, P>0.05, 2-tailed Student's t-test).

Supplemental Figure 1

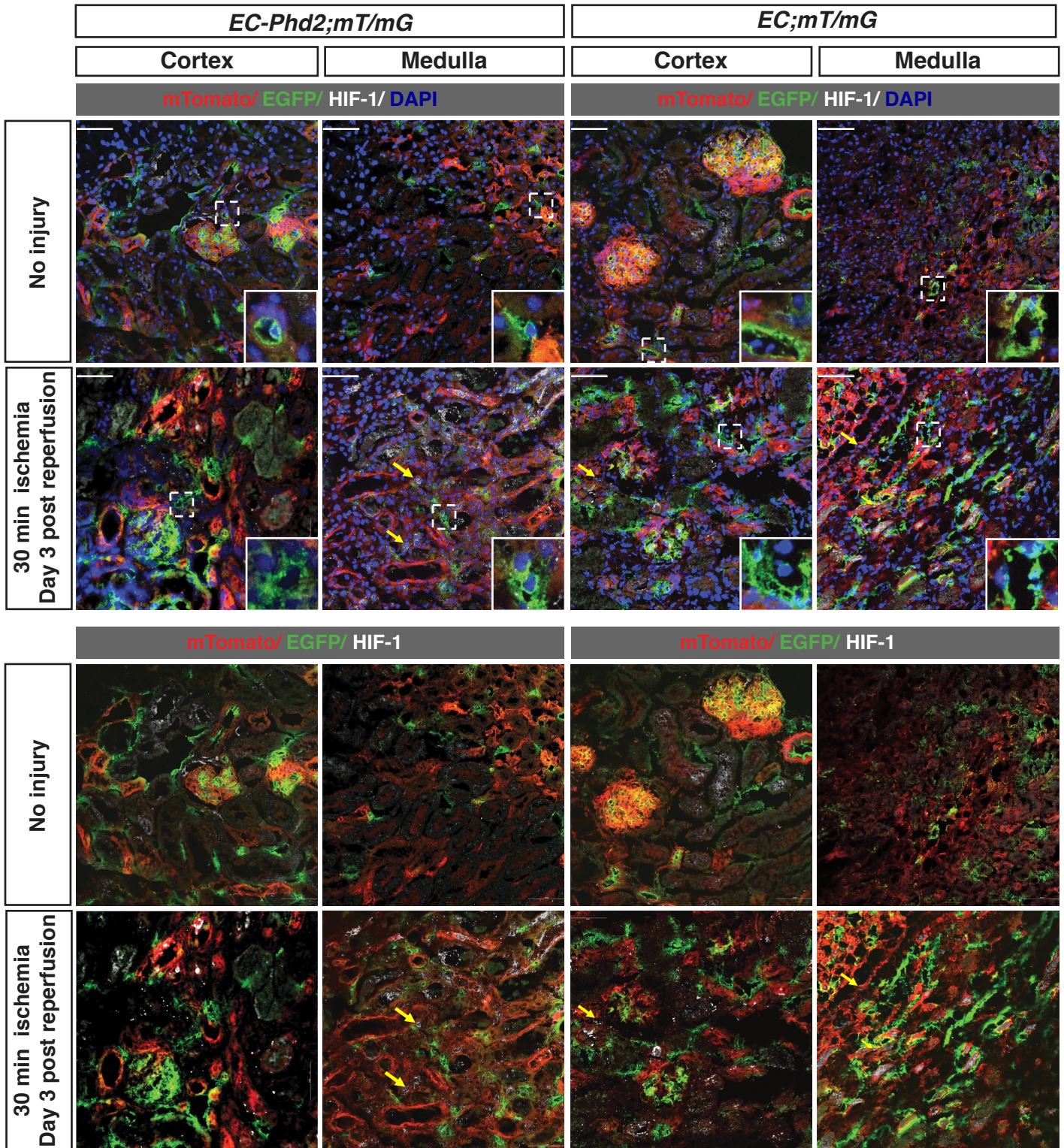


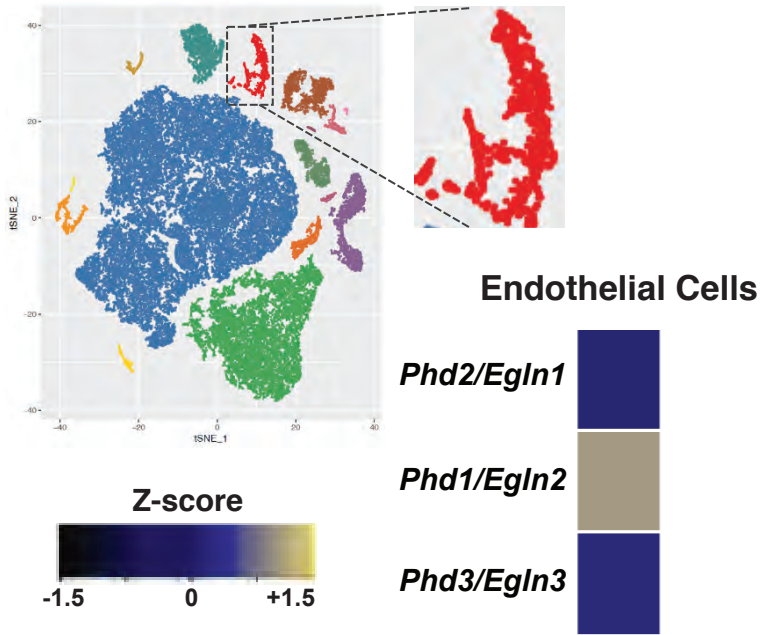


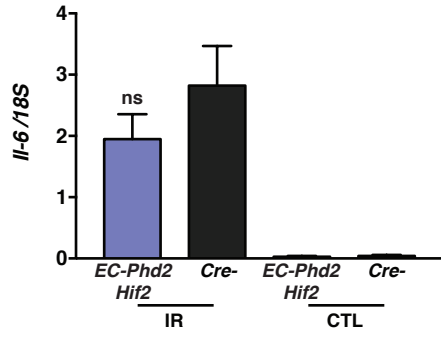
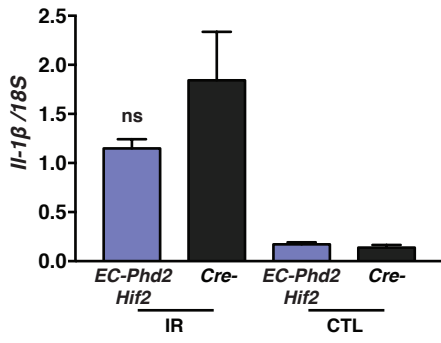
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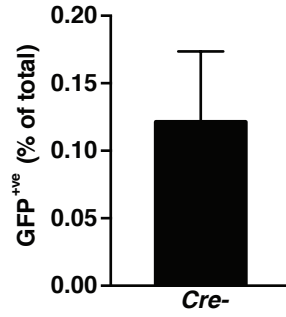
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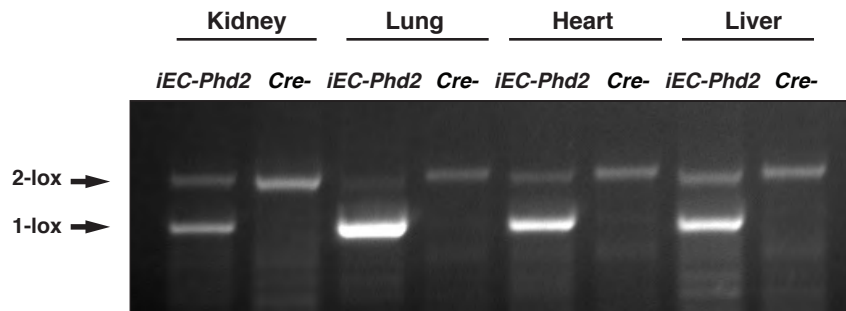




A.



B.



C.

