

Supplemental Table S1. Hypoxia-regulated miRNAs in HUVEC

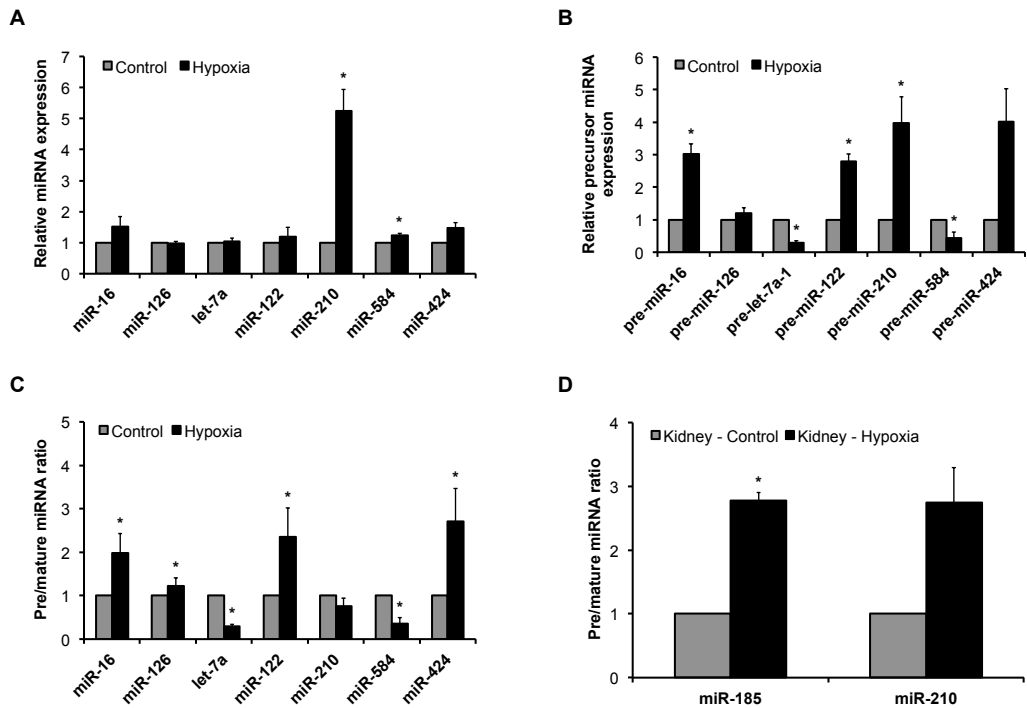
HUVEC hypoxia-regulated miRNAs

miRNA	Average fold change at 24 hr hypoxia	Statistical significance
hsa-miR-138-1*	0.64	1.28E-03
hsa-miR-146b-3p	0.57	1.62E-03
hsa-miR-185	0.57	2.54E-03
hsa-miR-193b*	0.63	6.23E-03
hsa-miR-210	2.46	1.28E-03
hsa-miR-302d*	0.58	1.71E-03
hsa-miR-30c-2*	0.57	4.22E-03
hsa-miR-32*	0.66	7.24E-03
hsa-miR-374b*	0.72	3.09E-03
hsa-miR-490-3p	0.63	6.03E-03
hsa-miR-494	0.54	5.99E-03
hsa-miR-498	0.76	5.74E-03
hsa-miR-505*	0.72	6.16E-03
hsa-miR-509-3-5p	0.65	2.42E-04
hsa-miR-509-5p	0.60	3.78E-03
hsa-miR-513a-5p	0.50	9.05E-05
hsa-miR-516b	0.68	5.01E-03
hsa-miR-549	0.67	1.47E-04
hsa-miR-551b	0.63	3.47E-04
hsa-miR-576-3p	0.53	8.18E-03
hsa-miR-583	0.58	8.27E-04
hsa-miR-620	0.55	2.27E-03
hsa-miR-620	0.64	6.27E-03
hsa-miR-658	0.60	7.75E-04
hsa-miR-665	0.54	1.73E-03
hsa-miR-765	0.56	7.76E-04
hsa-miR-877	0.76	7.63E-03
hsa-miR-886-5p	0.54	2.53E-04
hsa-miR-920	0.62	4.71E-03
hsa-miR-921	0.57	1.56E-03
hsa-miR-922	0.66	6.21E-03
hsa-miR-939	0.60	9.33E-03
miRPlus_17848	0.65	4.69E-03
miRPlus_28431	0.60	5.08E-03
miRPlus_42487	0.50	4.12E-04
miRPlus_42793	0.68	4.12E-04

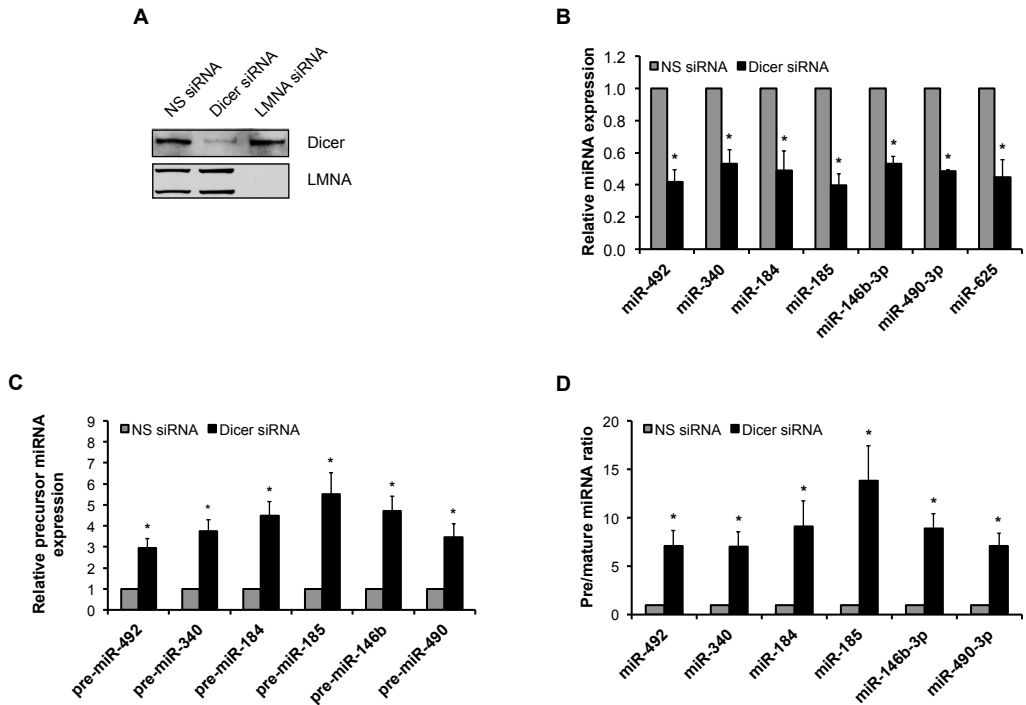
* Total no. of hypoxia-regulated miRNAs in HUVEC ($p < 0.01$) = **36**

* Up-regulated miRNAs (highlighted in grey) = **1**

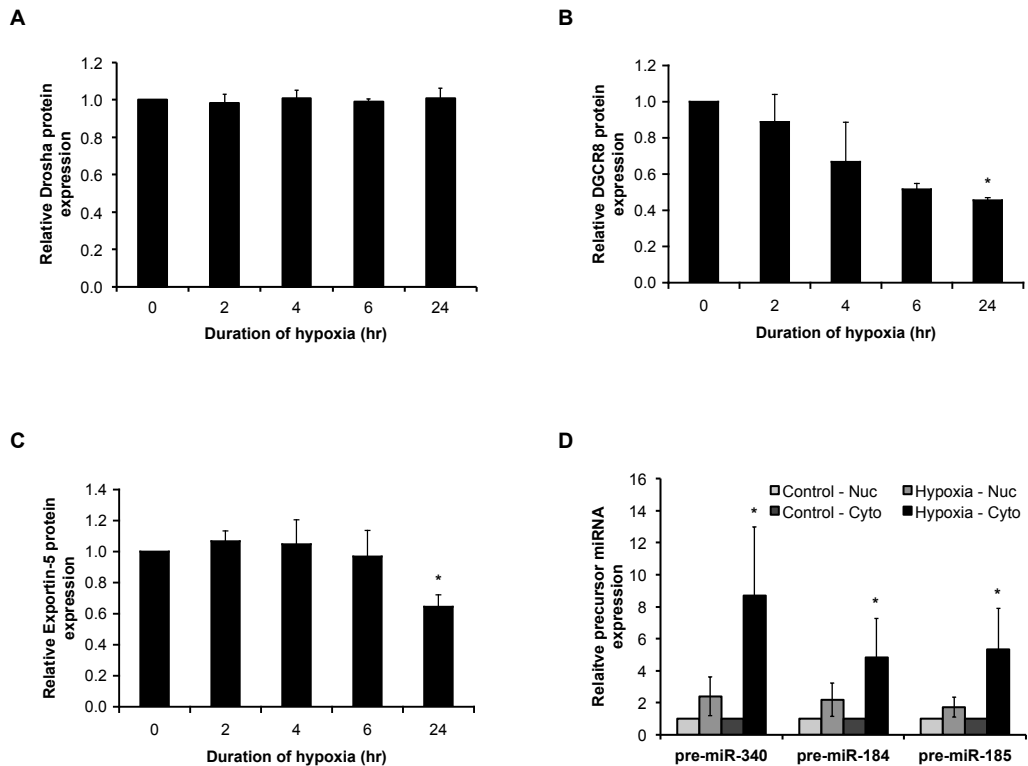
* Down-regulated miRNAs = **35**



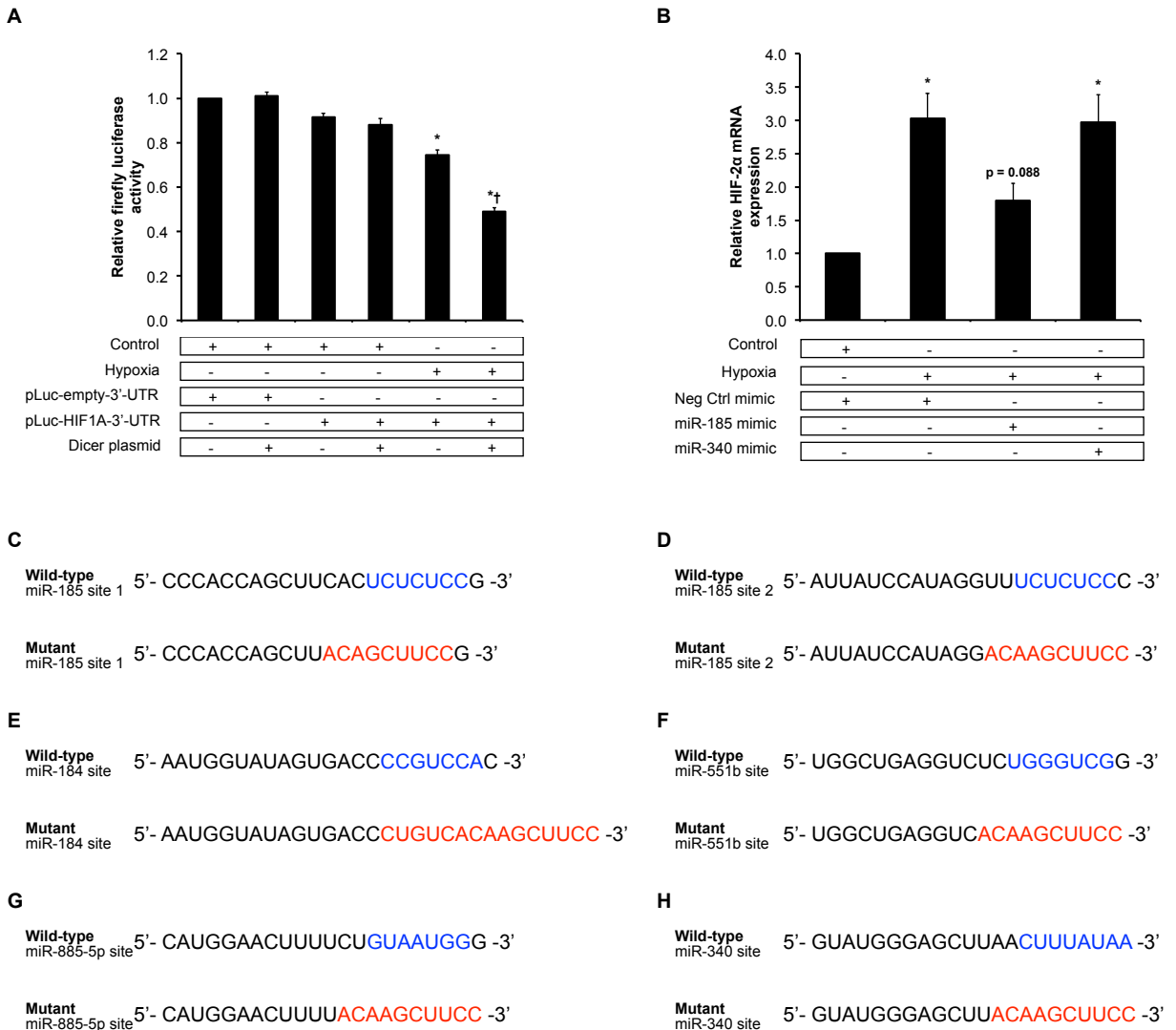
Supplemental Figure S1. Effect of chronic hypoxia on microRNA expression in endothelial cells. Expression levels of (A) miRNAs that did not change in chronic hypoxia or are known to be hypoxia-induced in most human cell types (i.e. miR-210), (B) corresponding precursor miRNAs, and (C) the ratio of precursors to their mature counterparts in control versus 24 hr hypoxic HUVEC. Data represent mean \pm SEM (n=3). * denotes statistical significance (p<0.05) compared to the respective Control. (D) Ratio of precursor to mature miR-185 and miR-210 in 24 hr hypoxic mouse kidney. Data represent mean \pm SEM (n=4). * denotes statistical significance (p<0.05) compared to Kidney - Control.



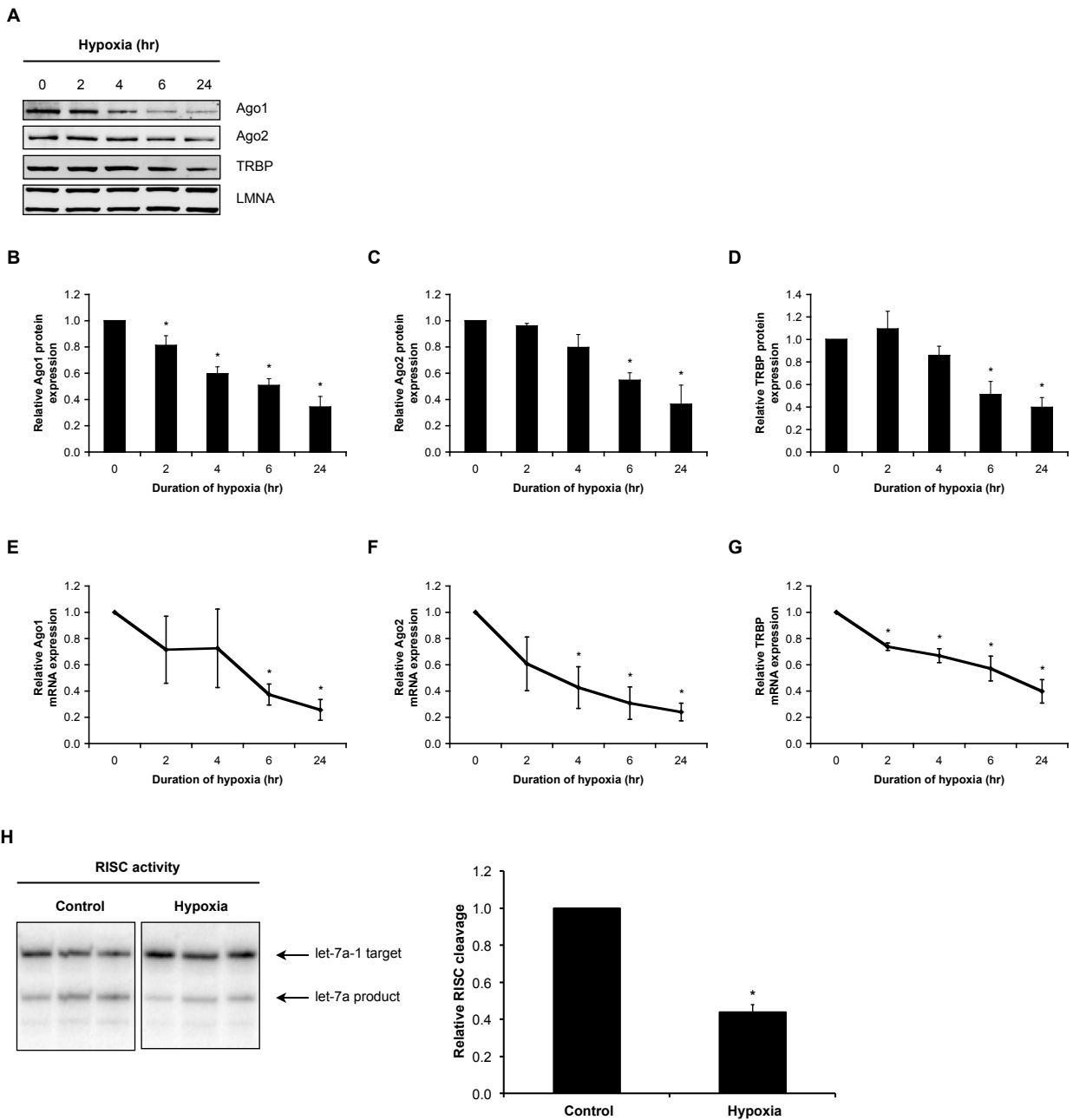
Supplemental Figure S2. Effect of Dicer knockdown on microRNA expression in endothelial cells. (A) Representative immunoblots of Dicer siRNA knockdowns in normoxic HUVEC. Expression levels of (B) representative microRNAs, (C) corresponding precursor microRNAs, and (D) the ratio of precursor microRNAs to their mature counterparts under Dicer knockdown conditions. Data represent mean \pm SEM (n=3). * denotes $p < 0.05$ compared to non-silencing (NS) siRNA control.



Supplemental Figure S3. Effect of hypoxia on the expression and function of microRNA pathway components in endothelial cells. Quantification of (A) Drosha, (B) DGCR8 and (C) Exportin-5 immunoblots (see Fig. 2A). Data represent mean \pm SEM (n=3). * denotes statistical significance ($p < 0.05$) compared to 0 hr. (D) HIF-targeting miRNA precursor levels in nuclear (Nuc) and cytoplasmic (Cyto) fractions of control versus 24 hr hypoxic HUVEC. Data represent mean \pm SEM (n=3). * denotes $p < 0.05$ compared to Hypoxia - Nuc.



Supplemental Figure S4. Effect of chronic hypoxia on 3'-UTR function of HIF- α isoforms. **(A)** Relative firefly luciferase activity. Data represent mean \pm SEM (n=3). * and † denote $p < 0.05$ compared to control and 24 hr hypoxic non over-expressing HUVEC, respectively, with pLuc-HIF1A-3'-UTR. **(B)** HIF-2 α mRNA levels in control versus 24 hr hypoxic HUVEC that had been transfected with miRNA mimics. Data represent mean \pm SEM (n=3). * denotes $p < 0.05$ compared to Control/Neg Ctrl mimic. Schematics of **(C, D)** miR-185, **(E)** miR-184, **(F)** miR-551b, **(G)** miR-885-5p, and **(H)** miR-340 wild-type and mutant binding sites in HIF-2 α 3'-UTR. Seed and mutant sequences are highlighted in blue and red, respectively.



Supplemental Figure S5. Effect of hypoxia on the expression and function of RISC components in endothelial cells. (A) Representative immunoblots of hypoxic HUVEC. Quantification of (B) Ago1, (C) Ago2, and (D) TRBP immunoblots. mRNA levels of (E) Ago1, (F) Ago2, and (G) TRBP in hypoxic HUVEC. Data represent mean \pm SEM (n=3). * denotes $p < 0.05$ compared to 0 hr. (H) Representative gel (left panel) and quantification (right panel) of RISC activity in control versus 24 hr hypoxic HUVEC. Data represent mean \pm SEM (n=3). * denotes $p < 0.05$ compared to Control.

Supplemental Table S2. Hypoxia-regulated miRNAs in mouse kidney**Mouse kidney hypoxia-regulated miRNAs**

miRNA	Average fold change at 24 hr hypoxia	Statistical significance
mmu-miR-1264-5p	0.28	0.012
mmu-miR-126-5p	0.57	0.000
mmu-miR-129-1-3p	0.20	0.001
mmu-miR-133b	0.51	0.048
mmu-miR-138	2.65	0.036
mmu-miR-16	0.57	0.043
mmu-miR-183	0.35	0.015
mmu-miR-1839-5p	0.35	0.013
mmu-miR-1899	0.22	0.001
mmu-miR-190	0.48	0.004
mmu-miR-1902	0.11	0.000
mmu-miR-193	0.39	0.041
mmu-miR-1933-5p	0.28	0.011
mmu-miR-1939	0.26	0.006
mmu-miR-1944	0.39	0.019
mmu-miR-1956	1.84	0.047
mmu-miR-1958	0.36	0.043
mmu-miR-1963	0.15	0.001
mmu-miR-1964-3p	0.42	0.010
mmu-miR-1970	0.51	0.038
mmu-miR-1983	0.37	0.011
mmu-miR-19b	0.49	0.015
mmu-miR-200c	0.51	0.024
mmu-miR-201	0.35	0.020
mmu-miR-205	0.30	0.015
mmu-miR-2142	0.53	0.032
mmu-miR-2144	0.47	0.022
mmu-miR-216a	0.14	0.001
mmu-miR-2182	5.57	0.020
mmu-miR-22	0.39	0.004
mmu-miR-293	0.11	0.002
mmu-miR-29c	0.56	0.021
mmu-miR-301b	0.49	0.030
mmu-miR-3062	0.20	0.010
mmu-miR-3066	0.13	0.002
mmu-miR-3069-3p	0.30	0.047
mmu-miR-3069-5p	0.36	0.046
mmu-miR-3070b-3p	0.29	0.002
mmu-miR-3073-3p	0.10	0.001
mmu-miR-3074-2-3p	0.37	0.047

mmu-miR-3074-5p	0.20	0.013
mmu-miR-3075	0.18	0.004
mmu-miR-3078	0.11	0.001
mmu-miR-3079-3p	0.22	0.004
mmu-miR-3080-3p	0.27	0.016
mmu-miR-3080-5p	0.26	0.006
mmu-miR-3082-5p	0.23	0.009
mmu-miR-3084	0.16	0.002
mmu-miR-3091-3p	0.36	0.013
mmu-miR-3093-5p	0.32	0.019
mmu-miR-3094	0.22	0.009
mmu-miR-3095-3p	0.21	0.003
mmu-miR-3095-5p	0.20	0.007
mmu-miR-3096-5p	0.23	0.012
mmu-miR-3100-5p	0.24	0.006
mmu-miR-3101	0.21	0.007
mmu-miR-3104-3p	0.26	0.026
mmu-miR-3105-3p	0.22	0.016
mmu-miR-3109	0.25	0.007
mmu-miR-3112	0.23	0.022
mmu-miR-3113	7.04	0.015
mmu-miR-32	0.26	0.003
mmu-miR-322	0.45	0.049
mmu-miR-324-5p	0.42	0.036
mmu-miR-325	0.12	0.001
mmu-miR-327	0.24	0.011
mmu-miR-329	0.29	0.000
mmu-miR-331-3p	0.34	0.020
mmu-miR-337-3p	0.15	0.001
mmu-miR-338-5p	0.49	0.014
mmu-miR-339-3p	0.02	0.000
mmu-miR-340-3p	0.21	0.007
mmu-miR-342-5p	0.31	0.039
mmu-miR-343	0.09	0.001
mmu-miR-344e	0.23	0.009
mmu-miR-344f-3p	0.17	0.011
mmu-miR-344f-5p	0.05	0.000
mmu-miR-3470b	0.18	0.001
mmu-miR-3472	0.24	0.016
mmu-miR-3474	0.15	0.003
mmu-miR-3475	0.37	0.045
mmu-miR-34b-3p	0.19	0.006
mmu-miR-350	0.21	0.007

mmu-miR-362-3p	0.13	0.001
mmu-miR-363-3p	0.41	0.016
mmu-miR-380-5p	0.20	0.001
mmu-miR-383	0.29	0.028
mmu-miR-412-5p	0.23	0.017
mmu-miR-425	10.91	0.005
mmu-miR-429	0.37	0.011
mmu-miR-434-3p	0.16	0.002
mmu-miR-448-5p	0.20	0.008
mmu-miR-449c	0.23	0.012
mmu-miR-453	0.30	0.050
mmu-miR-455	0.19	0.006
mmu-miR-464	0.32	0.037
mmu-miR-465a-3p	0.11	0.000
mmu-miR-466b-3p	0.19	0.001
mmu-miR-466c-3p	0.12	0.000
mmu-miR-466i-5p	0.08	0.000
mmu-miR-466p-3p	0.15	0.000
mmu-miR-483	0.34	0.038
mmu-miR-488	0.25	0.039
mmu-miR-497	0.29	0.004
mmu-miR-505-3p	0.21	0.008
mmu-miR-505-5p	0.22	0.010
mmu-miR-509-5p	0.18	0.009
mmu-miR-511-3p	0.29	0.031
mmu-miR-511-5p	0.17	0.001
mmu-miR-540-3p	0.11	0.000
mmu-miR-540-5p	0.16	0.003
mmu-miR-541	0.27	0.023
mmu-miR-546	0.26	0.037
mmu-miR-582-3p	0.26	0.040
mmu-miR-590-3p	0.40	0.035
mmu-miR-592	0.18	0.008
mmu-miR-669a-5p	0.32	0.015
mmu-miR-669j	0.14	0.001
mmu-miR-669p	0.24	0.004
mmu-miR-673-3p	0.08	0.001
mmu-miR-674	0.36	0.018
mmu-miR-675-3p	0.32	0.021
mmu-miR-676	0.24	0.007
mmu-miR-677	0.30	0.009
mmu-miR-679-3p	0.19	0.003
mmu-miR-679-5p	0.22	0.009

mmu-miR-688	0.20	0.013
mmu-miR-696	0.36	0.020
mmu-miR-697	0.28	0.007
mmu-miR-700	0.28	0.025
mmu-miR-701	0.32	0.017
mmu-miR-704	0.15	0.001
mmu-miR-706	0.22	0.020
mmu-miR-710	0.17	0.002
mmu-miR-712	0.21	0.010
mmu-miR-720	0.31	0.008
mmu-miR-741	0.24	0.018
mmu-miR-743b-5p	0.15	0.001
mmu-miR-763	0.37	0.035
mmu-miR-764-5p	0.24	0.000
mmu-miR-804	0.12	0.000
mmu-miR-871-3p	0.26	0.007
mmu-miR-871-5p	0.37	0.038
mmu-miR-876-5p	0.24	0.004
mmu-miR-878-3p	0.31	0.020
mmu-miR-883a-5p	0.15	0.002
mmu-miR-92a	0.31	0.007
mmu-miR-99a	0.72	0.036

* Total no. of hypoxia-regulated miRNAs in mouse kidney ($p < 0.05$) = **148**

* Up-regulated miRNAs (highlighted in grey) = **5**

* Down-regulated miRNAs = **143**

Supplemental Table S3. qRT-PCR primer sequences

qRT-PCR primer sequences (Unless otherwise stated, all primer sequences are for human genes.)

Gene	Forward Primer	Reverse Primer
Drosha	5'- GGC CCA CCC TGA CCG ACT TCA TGA T -3'	5'- TTG CCT TTG CGC TGC ATT TGC AGA GT -3'
DGCR8	5'- GCT GCC CGA GCT ACA CTG GAA ATC -3'	5'- CAG CCC AGC CTT GCT GGT CAG -3'
Exportin-5	5'- TCC GCC GCA CAG ACT GCT GAT G -3'	5'- GCC CAG CGC ACA CAA CAC CTG AC -3'
Dicer	5'- ACG TTT TCC CAC CAT ATG T -3'	5'- CTG CAT TTA GGA GCT AGA TGA -3'
Dicer pre-mRNA	5'- ATG GCA ACA AGA AGC AAT TC -3'	5'- GAG GCC TGA AAG GGT AAA T -3'
Dicer (mouse)	5'- TCT CCC CAG CAT ACT GTA TC -3'	5'- TTC CAC CCG AAG TCT AAG TT -3'
TRBP	5'- TGG CCC TCA AAC ACC TCA AA -3'	5'- TGT CCT CAG GCA GTG AAG AGT CTA G -3'
Ago1	5'- GCG CCC TGC CAT GTG GAA GA -3'	5'- TGA GGG GCT TGG GCT GCT CAT CTA -3'
Ago2	5'- CTT CCC CTG GAG GTC TGT AAC A -3'	5'- CTT CGC ATC AAT TTG CTA ATC TCT T -3'
HIF-1 α	5'- AGG CCG CTC AAT TTA TGA AT -3'	5'- TTT GGC AAG CAT CCT GTA CT -3'
HIF-2 α	5'- TGG CGA CAT GAT CTT TCT GTC A -3'	5'- ATG GTC GCA GGG ATG AGT GA -3'
GLUT1	5'- CAC CAC CTC ACT CCT GTT ACT T -3'	5'- CAA GCA TTT CAA AAC CAT GTT TCT A -3'
BNIP3L	5'- CTG CAC AAA CTT GCA CAT TG -3'	5'- TAA TTT CCA CAA CGG GTT CA -3'
VEGFA	5'- GCA GAC CAA AGA AAG ATA GAC CAA G -3'	5'- CGC CTC GGC TTG TCA CAT -3'
VEGFR1	5'- AAG ATT CAG GCA CCT ATG -3'	5'- TCG CAG GAG GTA TGG -3'
sVEGFR1	5'- AAG ATT CAG GCA CCT ATG -3'	5'- AAT TTG GAG ATC CGA GA -3'
VEGFR2	5'- TTA CTA TTC CCA GCT ACA TGA TCA G -3'	5'- AGA CGG ACT CAG AAC CAC ATC ATA A -3'
CXCR4	5'- CCA GTA GCC ACC GCA TCT -3'	5'- ATA GTC CCC TGA GCC CAT TT -3'
18S	5'- AGG AAT TGA CGG AAG GGC AC -3'	5'- GGA CAT CTA AGG GCA TCA CA -3'
Luciferase	5'- ACT CCT CTG GAT CTA CTG GTC -3'	5'- GTA ATC CTG AAG GCT CCT CA -3'
Pri/pre-miR-16	5'- GCC TTA GCA GCA CGT AAA TAT -3'	5'- CTT CAG CAG CAC AGT TAA TAC TG -3'
Pri/pre-miR-122	5'- CAA TGG TGT TTG TGT CTA AAC TAT CA -3'	5'- GCC TAG CAG TAG CTA TTT AGT GTG A -3'
Pri/pre-miR-126	5'- GGC GAC GGG ACA TTA TTA C -3'	5'- TCA CGG TAC GAG TTT GAA GTG -3'
Pri/pre-miR-146b	5'- CCT GGC ACT GAG AAC TGA -3'	5'- GGG CAC CAG AAC TGA GTC -3'
Pri/pre-miR-184	5'- TCA CGT CCC CTT ATC ACT -3'	5'- TCA CCT ACC CTT ATC AGT TCT -3'
Pri/pre-miR-185	5'- GGG GGC GAG GGA TTG -3'	5'- TGG GAG GGA AGG ACC AGA G -3'
Pri/pre-miR-210	5'- ACC CGG CAG TGC CTC C -3'	5'- GCT GCC CAG GCA CAG ATC -3'
Pri/pre-miR-340	5'- GTA CCT GGT GTG ATT ATA A -3'	5'- CCC ACA AAC GAC ATA -3'
Pri/pre-miR-424	5'- ACA GCA GCA ATT CAT GTT TTG A -3'	5'- CAG CGC CTC ACG TTT TG -3'
Pri/pre-miR-490	5'- GGA GGC CTT GCT GGT TT -3'	5'- GTC CGC TGC TTG TGA ACA -3'
Pri/pre-miR-492	5'- GCG GGA CAA GAT TCT TGG -3'	5'- GCA GCC AGT TGA GCA TTG -3'
Pri/pre-miR-584	5'- TTT GCC TGG GAC TGA G -3'	5'- TTG GCC TGG AAC TGA C -3'
Pri/pre-let-7a(1)	5'- TGG GAT GAG GTA GTA GGT T -3'	5'- AGG AAA GAC AGT AGA TTG TAT AGT TA -3'
Pri/pre-miR-16(1) (mouse)	5'- TCA GCG GTG CCT TAG CA -3'	5'- TCA GCA GCA CAG TCA ATA CT -3'
Pri/pre-miR-185 (mouse)	5'- AAA GGC AGT TCC TGA TGG T -3'	5'- AGC CAG CCC CTG GGA G -3'
Pri/pre-miR-200c (mouse)	5'- TAC CCA GCA GTG TTT GG -3'	5'- TTA CCC GGC AGT ATT AGA G -3'
Pri/pre-miR-210 (mouse)	5'- TTG CTC CGG ACC CAC TGT G -3'	5'- CGC TGC CCA GGG ACA GAT C -3'
Pri/pre-miR-293 (mouse)	5'- ATC TGT GGT ACT CAA ACT G -3'	5'- ATC GGC AAC ACT ACA AAC -3'
Pri/pre-miR-324 (mouse)	5'- TGC CTC CTC GCA TCC CCT A -3'	5'- TGG GGC AGT GGG TCT CC -3'
Pri/pre-miR-325 (mouse)	5'- AGT GCT TGG TTC CTA GTA G -3'	5'- GCA CAG TGC TTG ATT GAT A -3'
Pri/pre-miR-425 (mouse)	5'- TTG AGT GGG CAC CCA AGA A -3'	5'- TGG GCG GAC ACG ACA TT -3'