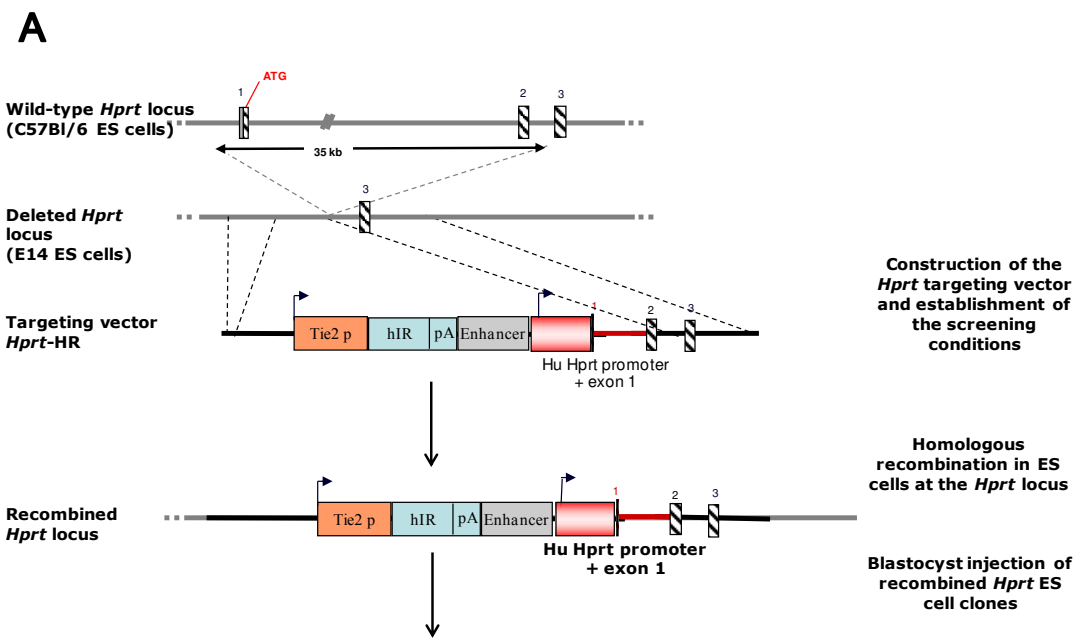
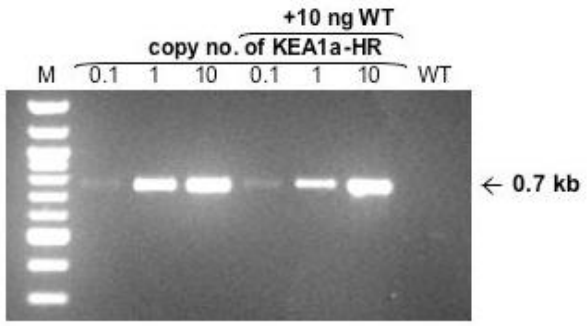
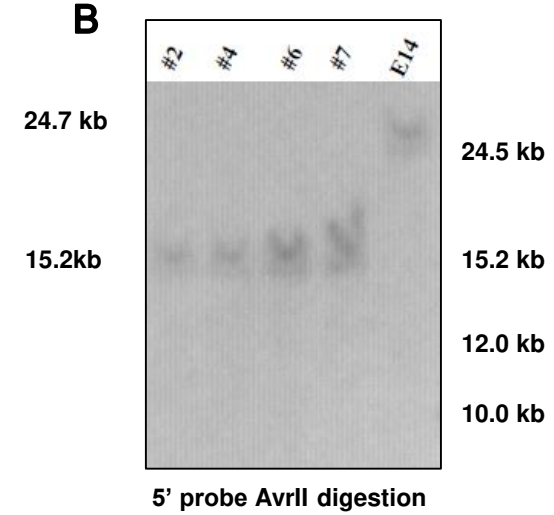
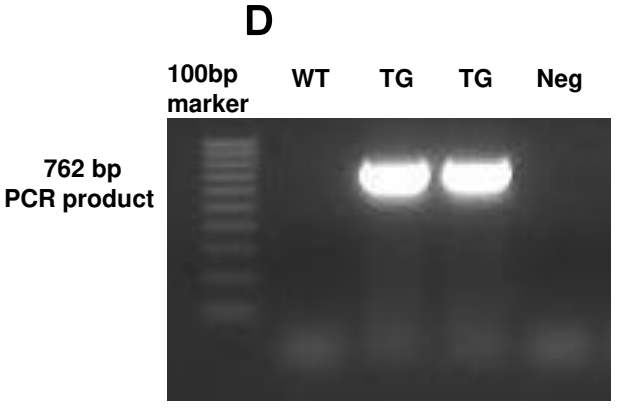
Supplemental Figure I



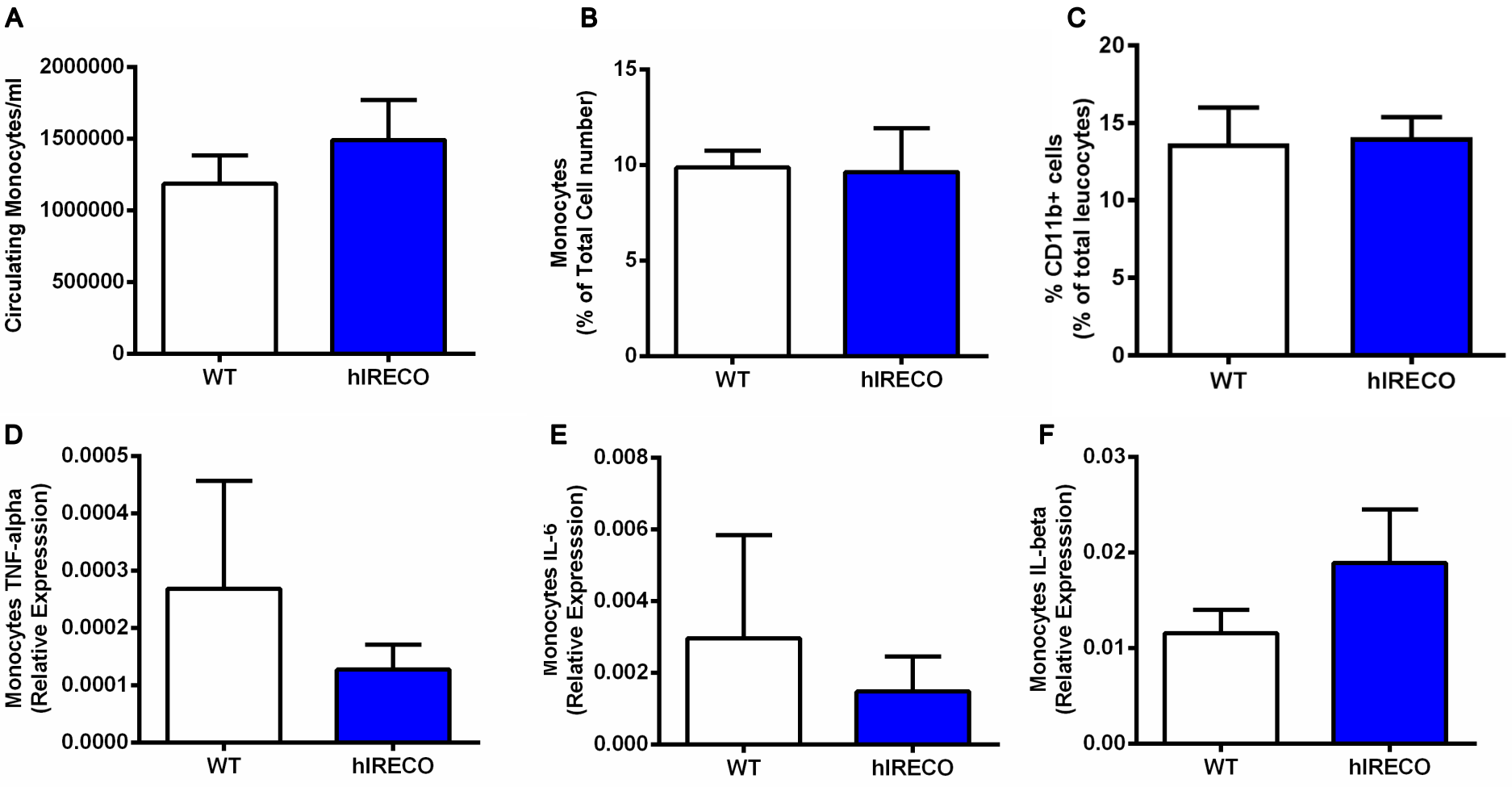






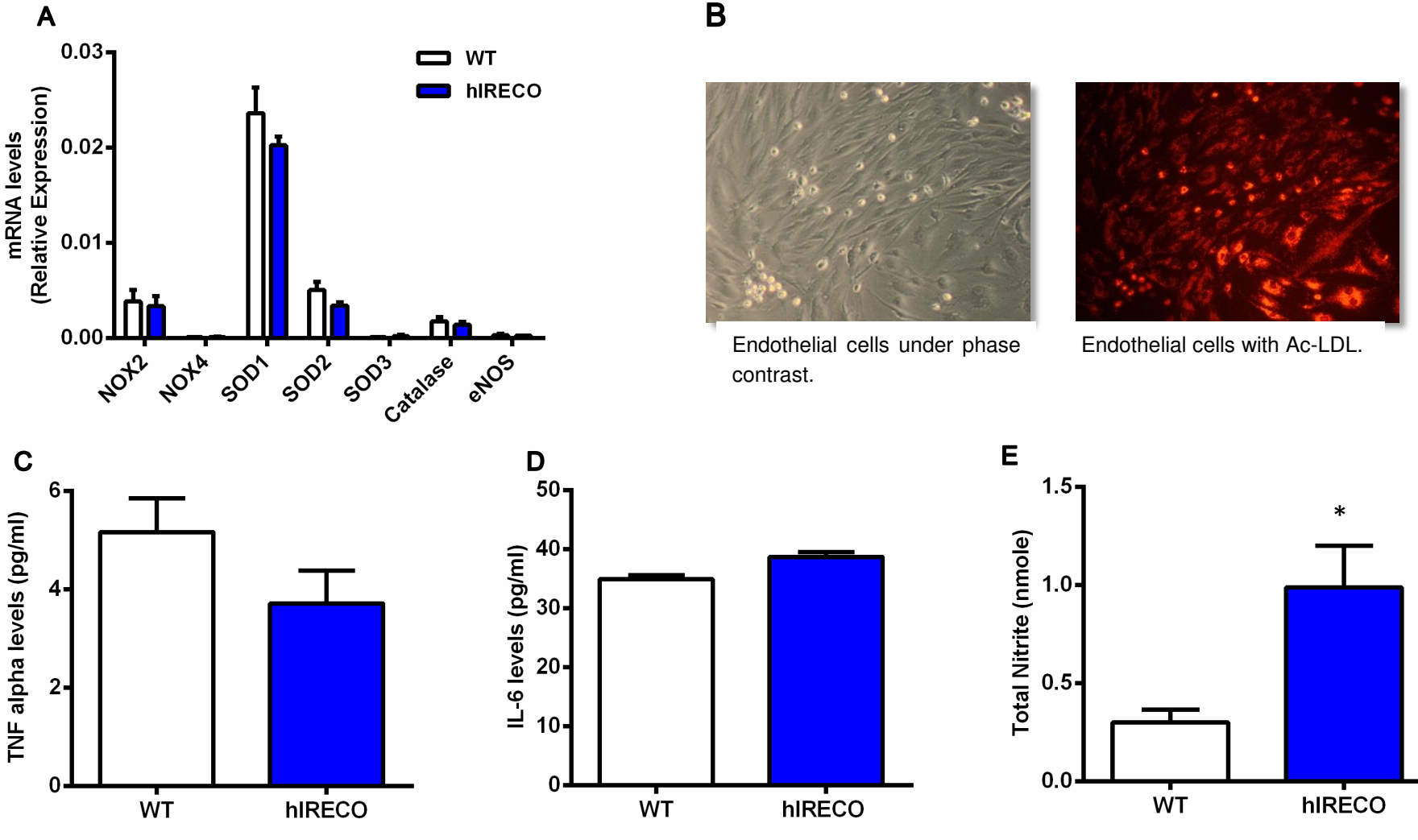
Supplemental Figure I. A) Construction of targeting vector to generate mice with endothelium-specific transgenic expression of human insulin receptor. **B)** Southern blot validated the correct heterozygous status of 4 of 7 tested F1 females, by detecting the15.2kb sized AvrII fragment of the C57BL/6 Hprt wild type allele and the 9.8kb sized AvrII fragment of the reconstituted Hprt allele. **C)** Genotyping protocol validated the multiple copies of transgene. **D**) PCR product using isolated DNA,showing no human insulin receptor gene expression in wild type (WT) and in hIRECO (TG) ear notches. Neg denotes negative control, using water as template.

Supplemental Figure II



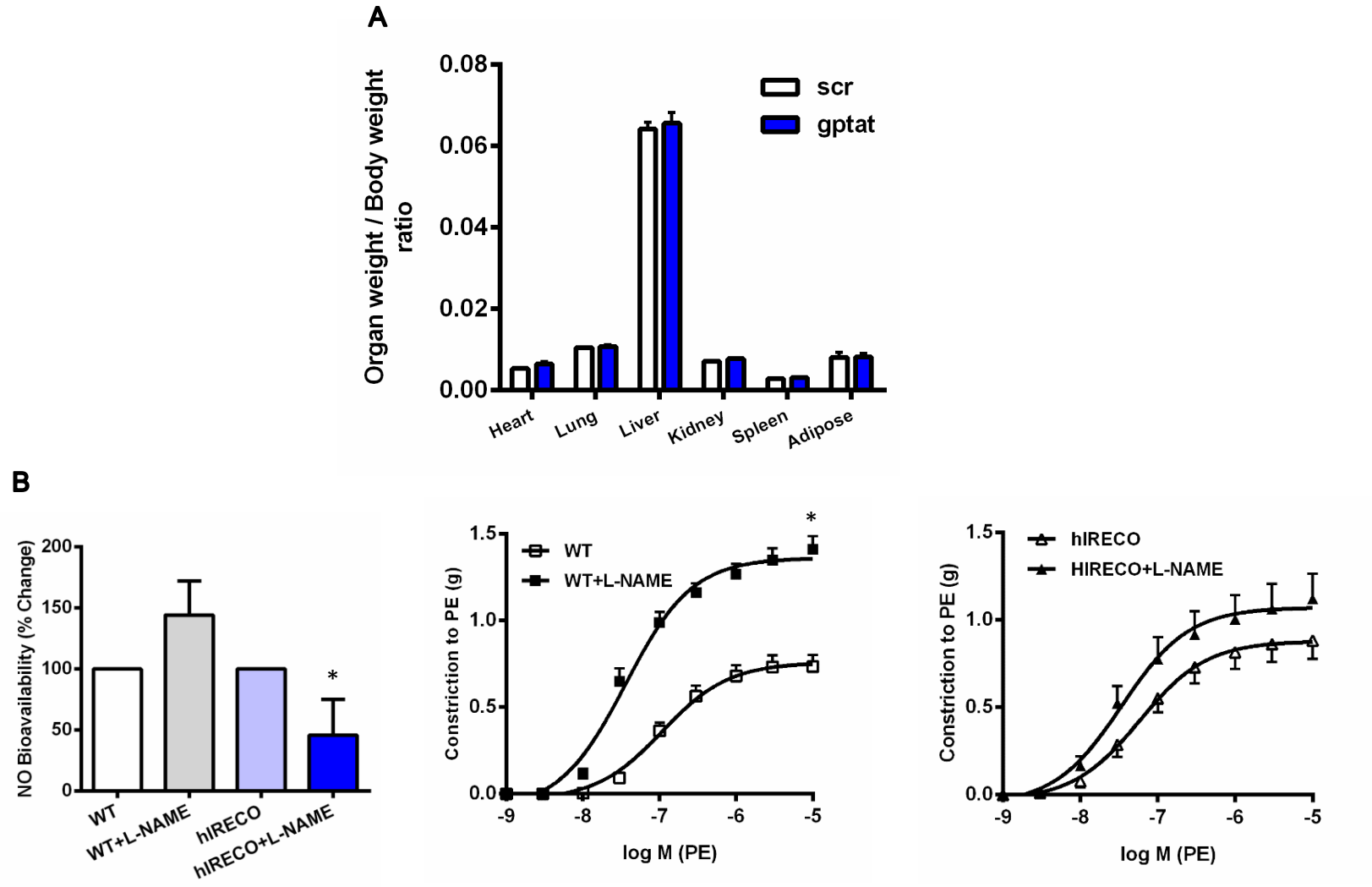
Supplemental Figure II. A) No difference in monocyte count in mice with endothelial cell specific over-expression of the human insulin receptor (hIRECO). **B)** No difference in monocyte as percent of circulating cells in hIRECO. **C)** No difference in CD11b expression in monocytes from hIRECO. **D)** No difference in TNF-alpha mRNA expression in monocytes from hIRECO. **E)** No difference in IL-16 mRNA expression in monocytes from hIRECO **F)** No difference in IL-1Beta mRNA expression in monocytes from hIRECO (Data presented as mean ± SEM. All experiments n=5 mice WT denotes wild type).

Supplemental Figure III



Supplemental Figure III. A) No difference in mRNA expression of Nox2 NADPH oxidase (Nox2), Nox4 NADPH oxidase (Nox4) in superoxide dismutase 1,2 and 3 (SOD), catalase and endothelial NO synthase in pulmonary endothelial cells from mice with endothelial cell specific over-expression of the human insulin receptor (hIRECO). **B)** Isolated pulmonary endothelial cells under phase contrast microscopy and upon staining with DiI-conjugated Acetylated LDL (Ac-LDL) C**)** No difference in circulating plasma TNF-alpha in hIRECO. **D)** No difference in circulating plasma IL-6 in hIRECO **E**) Total nitrite levels are significantly higher in the hIRECO plasma compared to WT (all experiments n=5 mice WT denotes wild type).

Supplemental Figure IV



Supplemental Figure IV. A) Chronic pharmacological inhibition of Nox2 NADPH oxidase with gp91ds-tat to hIRECO mice via osmotic mini-pump for 28 days had no effect on organ mass. **B**) Basal NO production in response to isometric tension assessed by measuring the constrictor response to the NO synthase inhibitor, L-NMMA was reduced in hIRECO mice (left). PE constrictor response in the WT with and without L-NMMA (centre). PE constrictor response in hIRECO mice aorta with and without L-NMMA (right). % Change means the change from maximal constriction to PE after L-NMMA (Data presented as mean ± SEM. All experiments n=5 mice WT denotes wild type).

Supplemental Table I. Primer sequences used for quantitative PCR for mRNA levels

Gene	Forward primer	Reverse primer
Beta-Actin	CGTGAAAAGATGACCCAGATCA	TGGTACGACCAGAGGCATACAG
NOX2	GGTTCCAGTGCGTGTTGCT	GCGGTGTGCAGTGCTATCAT
NOX4	GGAGACTGGACAGAACGATTCC	TGTATAACTTAGGGTAATTTCTAGAGTGAATGA
SOD1	GGACCTCATTTTAATCCTCACTCTAAG	GGTCTCCAACATGCCTCTCTTC
SOD2	CACACATTAACGCGCAGATCA	GGTGGCGTTGAGATTGTTCA
SOD3	GGGATGGATCTAGAGCATTAAGGA	ACACCTTAGTTAACCCAGAAATCTTTTC
eNOS	CTGGAGCACCCCACGCT	AGCGGTGAGGGTCACACAG
Catalase	GCTGAGAAGCCTAAGAACGCAAT	CCCTTCGCAGCCATGTG
Human Insulin Receptor	GTCATCAACGGGCAGTTTG	GGTGCAGCCGTGTGACTTAC
Mouse Insulin Receptor	CTT GAT GTG CAC CCC ATG TCT	TCG GAT GTT GAT GAT CAG GCT
Mouse ve-Cadherin	TCAACGCATCTGTGCCAGAGAT	CACGATTTGGTACAAGACAGTG
Mouse TNF-alpha	Taqman probes: mm00443258_m1	
Mouse IL-6	Taqman probes: mm00446190_m1	
Mouse IL-1beta	Taqman probes: mm00434228_m1	