Supplementary Figure 1. Effect of high glucose or TXNIP overexpression on TRX2 levels. Endothelial cells were treated with increasing glucose concentrations or an osmolar mannitol control with (A) TRX2 mRNA expression assessed by qPCR and (B) TRX2 protein levels assessed by Western blot. (C) Endothelial cells were transfected with plasmid encoding TXNIP, a TXNIP C247S mutant or empty plasmid (control) and TRX2 mRNA expression was assessed by qPCR.
Supplementary Figure 2. Elevated glucose concentration impairs endothelial cell function and induces TXNIP. HCAEC were treated with increasing glucose concentrations or an osmolar mannitol control. HCAEC angiogenic function was assessed by (A) migration in a modified Boyden chamber assay, (B) proliferation in an EdU incorporation assay, and (C) tubulogenesis in a growth factor-reduced Matrigel assay. Hyperglycemic modulation of the thio redoxin system was assessed by (D) qPCR of TXNIP mRNA levels, Western blot analysis of (E) TXNIP protein and (F) TRX1 protein, (G) qPCR of TRX2 mRNA levels, and (H) total TRX redox activity as assessed by the insulin disulfide reduction assay. * represents \( P<0.05 \) compared to 5 mM control.

Human coronary artery endothelial cells
Supplementary Figure 3. Gene silencing of TXNIP rescues impairment of endothelial cell dysfunction and angiogenesis induced by high glucose concentrations. HCAEC were transfected with siRNA to TXNIP (or scrambled “SCR” control siRNA) then treated with 5, 15 or 25 mM glucose. Angiogenic function of siRNA-transfected, glucose-treated HCAEC was assessed by (A) migration in a modified Boyden chamber assay, (B) proliferation in an EdU incorporation assay, and (C) tubulogenesis in a growth factor-reduced Matrigel assay. * represents $P<0.05$ compared to 5 mM mock transfection control.
**Supplementary Figure 4.** Gene silencing of TXNIP rescues impairment of endothelial cell dysfunction and angiogenesis induced by high glucose concentrations. Endothelial cells were transfected with siRNA to TXNIP (or scrambled “SCR” control siRNA) then treated with 5, 15 or 25 mM glucose then (A) eNOS protein and (B) nitric oxide levels assessed. Endothelial cells were transfected with plasmid encoding TXNIP, a TXNIP C247S mutant or empty plasmid (control) and (C) nitric oxide levels assessed by DAF fluorescence. (D) HCAEC were transfected with siRNA to TXNIP (or scrambled “SCR” control siRNA) and then treated with 5, 15 or 25 mM glucose ± human VEGF<sub>165</sub> (10 ng/mL) ± VEGF mAb (1 μg/mL), as indicated then analysed for VEGF-induced migration in a modified Boyden chamber assay. * represents \( P < 0.05 \) compared to 5 mM SCR siRNA control value, # represents \( P < 0.05 \) for TXNIP siRNA compared to SCR siRNA.