SUPPLEMENTAL MATERIAL

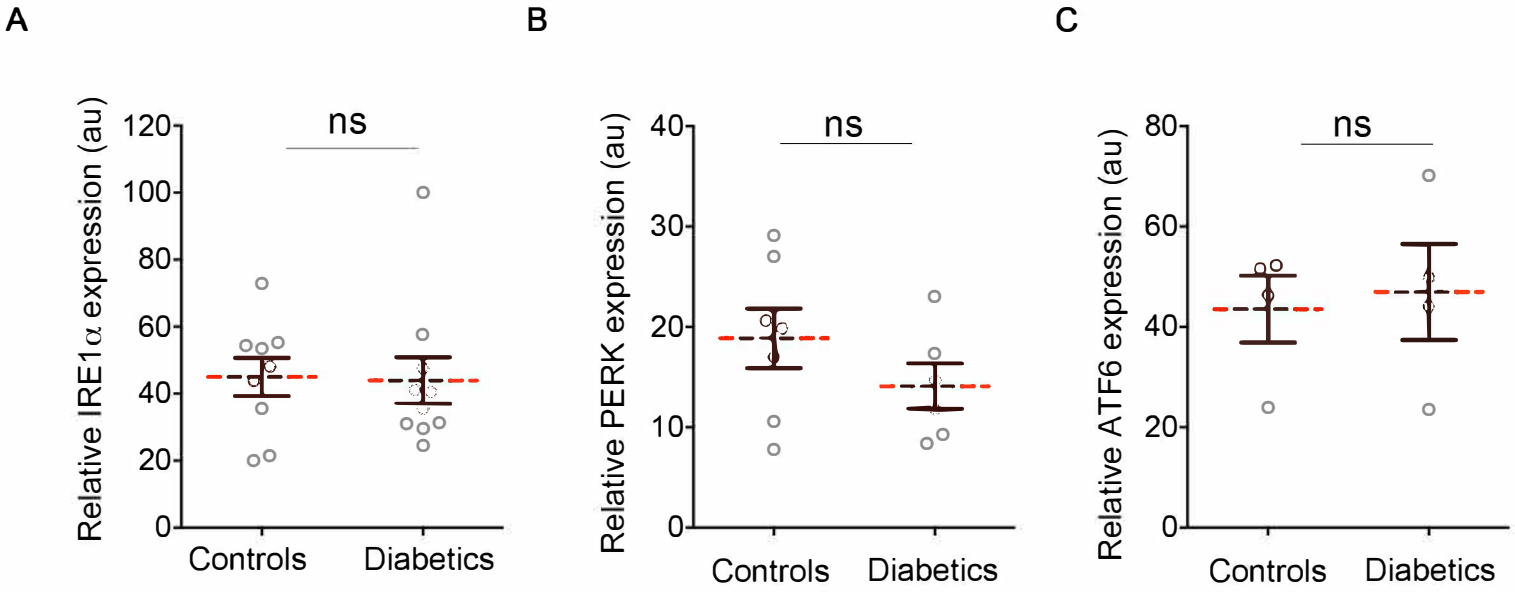

Figure S1. DM is not associated with changes in the expression of acute ER stress markers. Venous endothelial cells from diabetic and non-diabetic patients were freshly isolated as described in Materials and methods section of this article. Endothelial cells were identified by von Willebrand factor (vWF) staining and nuclear morphology. Total protein expression was determined by quantitative fluorescence and the use of specific antibodies against IRE1α **(A)**, PERK **(B)** and ATF6 **(C)**. Variables were compared using t-test.

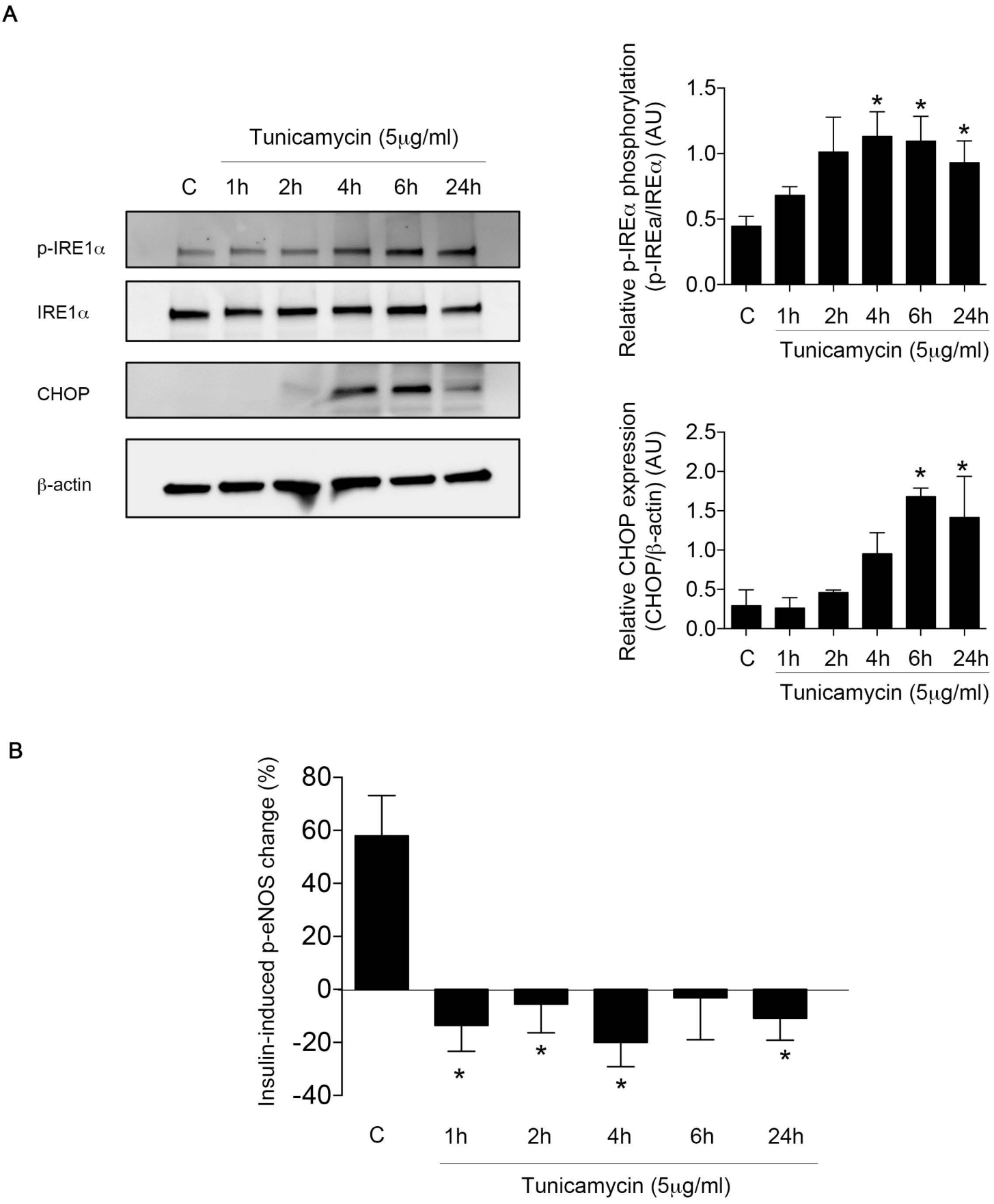

Figure S2. ER stress induction by tunicamycin impairs insulin-induced eNOS phosphorylation in endothelial cells in culture. A, Human aortic endothelial cells (HAECs) were incubated with tunicamycin for the indicated time points and ER stress activation was evaluated by an enhanced IRE1α phosphorylation and higher expression of CHOP. The blots shown are representative of at least 4 independent experiments that yielded equivalent results. The bar graph represents the mean±SEM of at least 4 independent experiments (n=9 for IRE1a phosphorylation, and n=4 for CHOP). **B,** Insulin-mediated endothelial nitric oxide (eNOS) activation was evaluated as eNOS phosphorylation at Ser1177, ER stress activation by tunicamycin impaired insulin-mediated changed in eNOS phosphorylation at Ser1177 (n=5). Variables were compared vs controls using paired t-test.

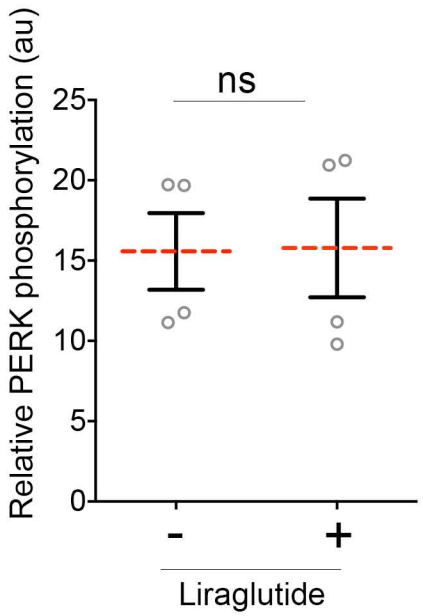

Figure S3. Liraglutide does not decrease PERK activation in endothelial cell from diabetic patients. Venous endothelial cells were isolated from diabetic patients and PERK activation was studied in the presence and absence of liraglutide. Pooled data showed that the PERK activation did not decrease after acute liraglutide treatment (n=4, P= 0.81, Cohen´s *d* = 0.133). Variables were compared using paired t-test.

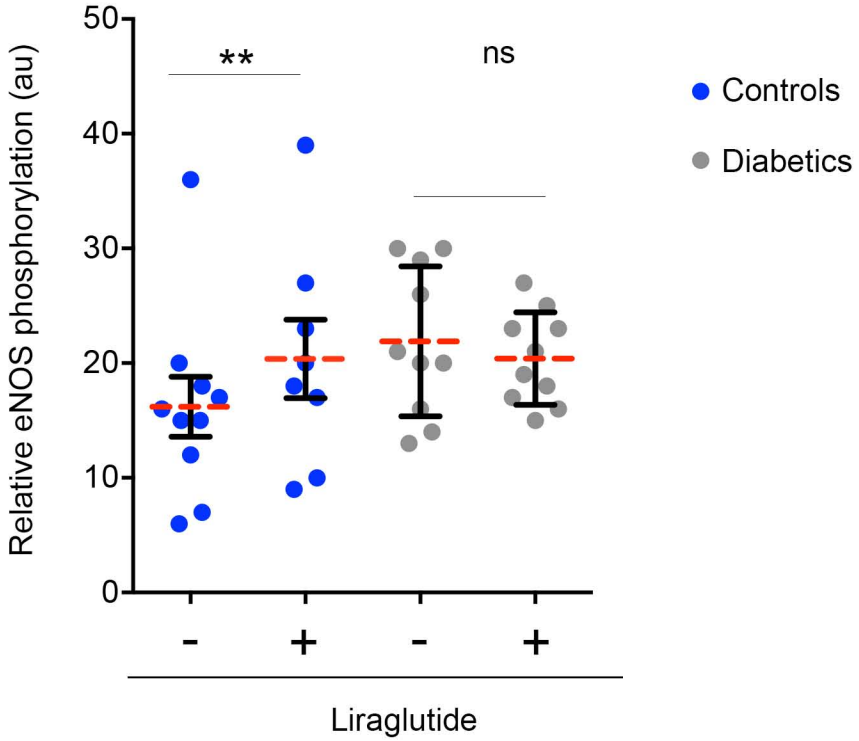

Figure S4. GLP-1 analogue, liraglutide, activates endothelial nitric oxide synthase in venous endothelial cells from non-diabetic patients. Venous endothelial cells were freshly isolated from diabetic and non-diabetic controls and eNOS activation was studied in the presence and absence of liraglutide. Pooled data showed that the liraglutide enhanced eNOS activation in endothelial cells isolated from non-diabetic patients (n=8, P= 0.006, Cohen´s *d* = 1.362), but it did not modify eNOS activation at its activation residue in endothelial cells isolated from patients with DM (n=10, P= 0.33, Cohen´s *d* = 0.324). Variables were compared using paired t-test.