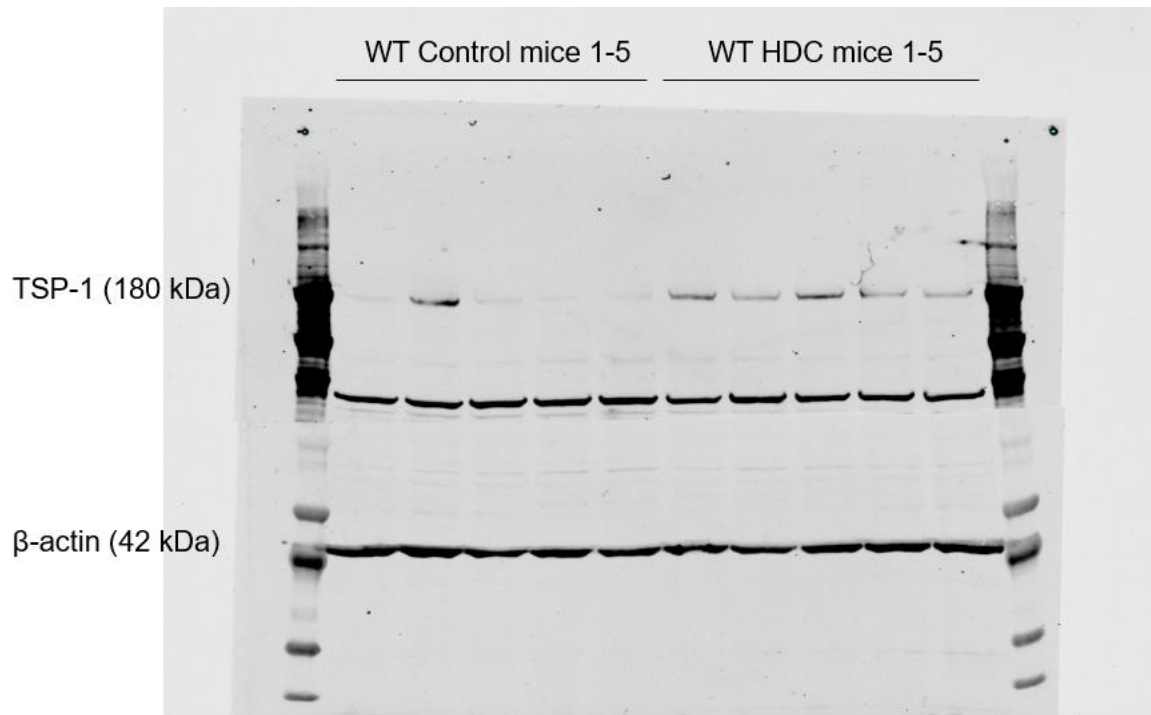
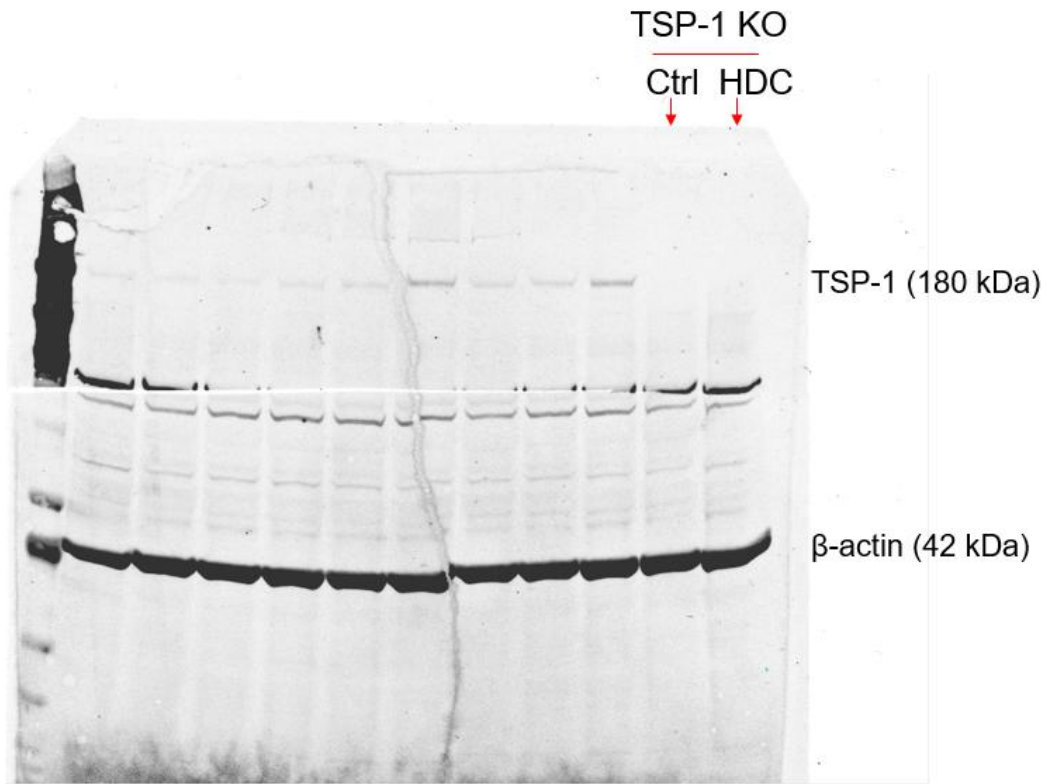


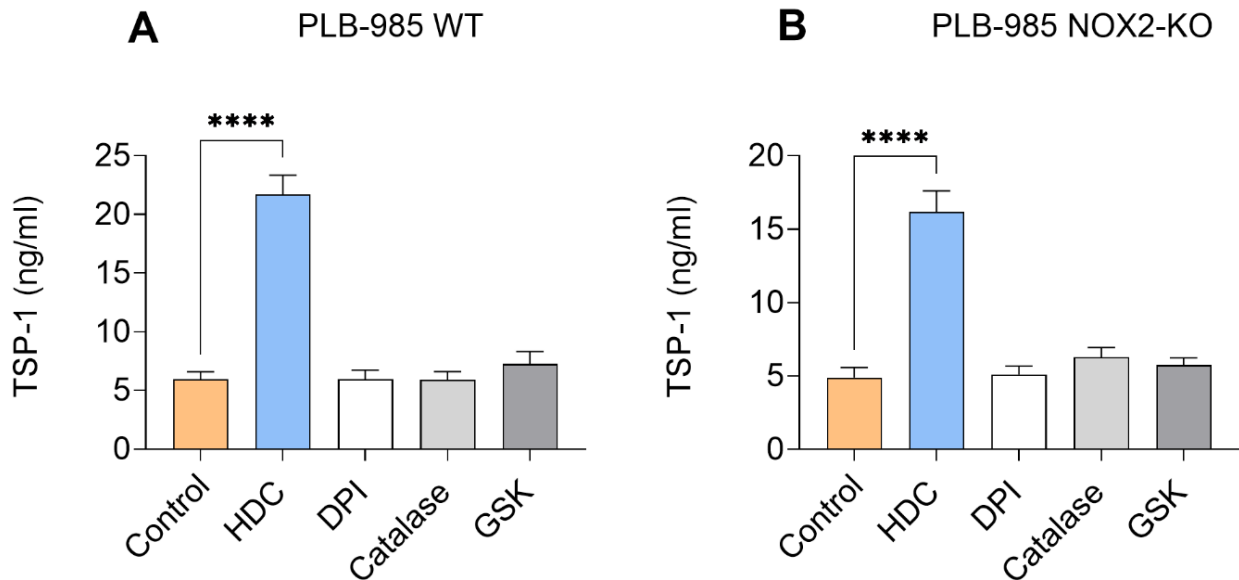
Supplementary Figure 1: Original uncropped western blots corresponding to Figure 1F. Lane identities are indicated above the blot. The positions of the TSP-1 and β -actin bands are shown on the left. The membrane was cut prior to antibody incubation for detection of TSP-1 and β -actin. Ctrl = control; HDC = histamine dihydrochloride.



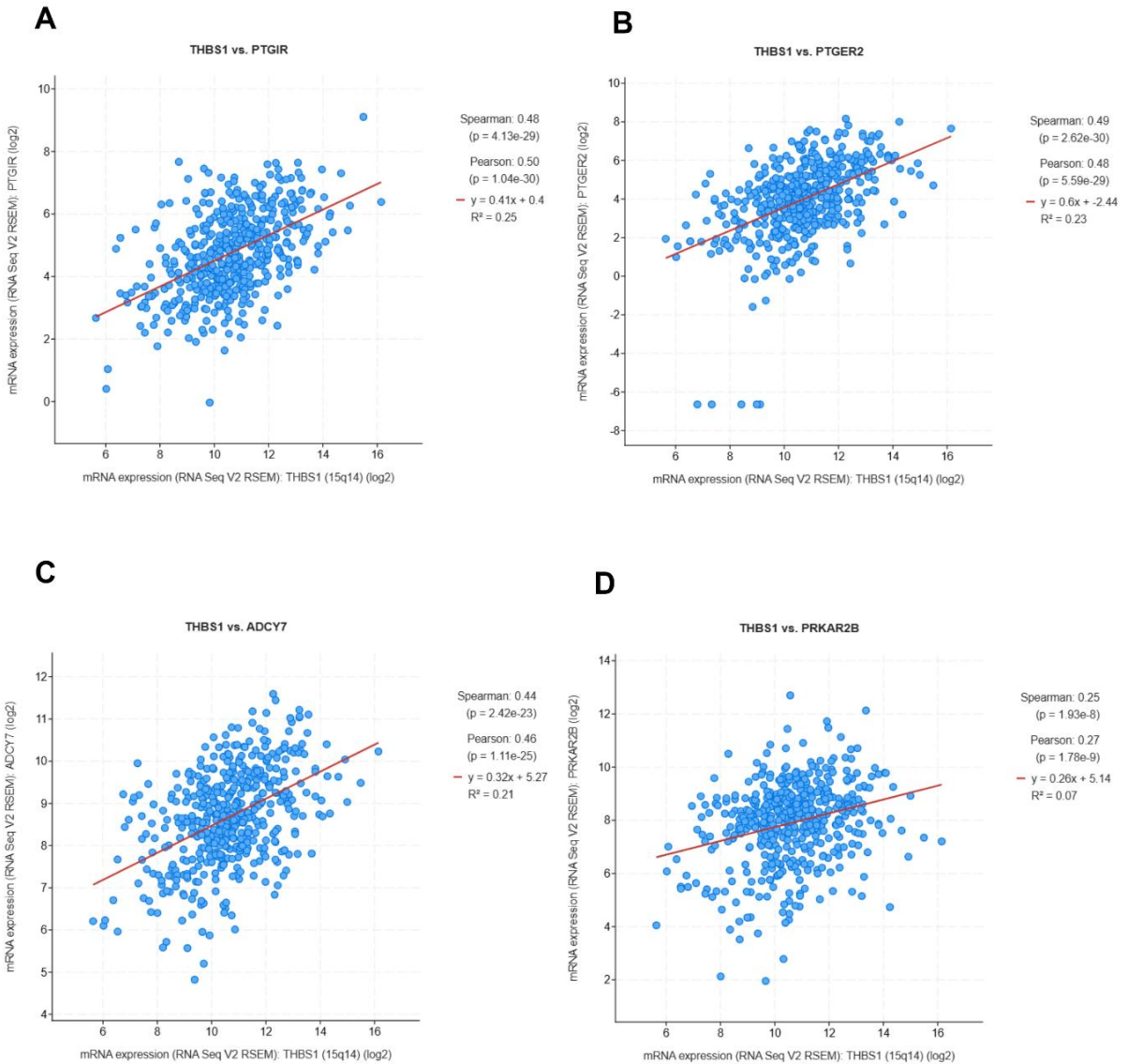
Supplementary Figure 2: Original uncropped western blots corresponding to Figure 3C. Lane identities are indicated above the blot. The positions of the TSP-1 and β -actin bands are shown on the left. The membrane was cut prior to antibody incubation for detection of TSP-1 and β -actin. Ctrl = control; HDC = histamine dihydrochloride.



Supplementary Figure 3: Original uncropped western blots corresponding to Figure 3C. Only the last 2 lanes were used and are indicated above the blot. The positions of the TSP-1 and β -actin bands are shown on the right. The membrane was cut prior to antibody incubation for detection of TSP-1 and β -actin. Ctrl = control; HDC = histamine dihydrochloride; TSP-1 KO = TSP-1 knockout mice.



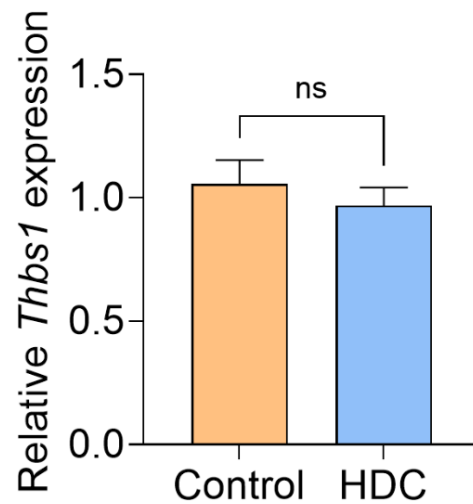
Supplementary Figure 4: Histamine dihydrochloride (HDC)-induced TSP-1 production is NOX2-independent. PLB-985 wild-type (WT) (**A**) and NOX2-KO (**B**) cells were stimulated with 100 μ M histamine dihydrochloride (HDC), 100 nM Diphenyleiodonium (DPI), 500U/ml Catalase or 1 μ M GSK2795039 and TSP-1 levels were determined by ELISA in the supernatant 8 hours later (n=6-9); one-way ANOVA followed by Holm-Šídák's test. Results are presented as mean \pm SEM. P-value is designated as follows; ****p < 0.0001.



Supplementary Figure 5: *THBS1* expression positively correlates with GPCR-cAMP-PKA pathway components in melanoma. Scatter plot showing the correlation between *THBS1* and genes associated with cAMP signaling in the TCGA– skin cutaneous melanoma (SKCM) cohort. **(A)** *PTGIR*, a prostaglandin I receptor, **(B)** *PTGER2*, a prostaglandin E receptor linked to cAMP/PKA activation, **(C)** *ADCY7*, encoding adenylyl cyclase 7 involved in cAMP synthesis, and **(D)** *PRKAR2B*, encoding a regulatory subunit of PKA. Expression values represent log₂

transformed RNA-Seq V2 RSEM data. Spearman and Pearson correlation coefficients are shown in each plot, with red lines indicating linear regression fits.

A



Supplementary Figure 6: Histamine dihydrochloride (HDC) does not induce long-lasting *Thbs1* mRNA expression *in vivo*, but only increases protein levels. (A) WT mice were treated with HDC or NaCl (control) one day before, and one and three days after intravenous inoculation of $1.0 - 1.5 \times 10^5$ B16F10 cells. Three weeks later, *Thbs1* mRNA levels in the lungs were determined (n=14-15 per group); Welch's unpaired t-test, ns = non-significant.