



**Supplementary Fig. S6: RNA seq analysis of WT and GLS<sup>ECKO</sup> endothelial cells.** Murine pulmonary microvascular endothelial cells (MPMECs) were isolated from GLS *fl/fl* mice and transduced with either Ad-Cre or Ad-control. Deletion of GLS in MPMECs was confirmed by western blot analysis. RNAs were isolated from either WT (Ad-control) or GLS<sup>ECKO</sup> (Ad-Cre) endothelial cells and sent to BGI Inc. for sequencing and analysis using the Dr. Tom software. **(A)** Volcano plot of differentially expressed genes (DEG) in GLS<sup>ECKO</sup> versus WT. Red and green dots mark the upregulated and downregulated genes respectively in GLS<sup>ECKO</sup> compared to WT (n= 3 per group, FDR q-value < 0.05). **(B-C)** Bubble chart showing KEGG enrichment analysis of DEGs up **(B)** and DEGs down **(C)** comparing GLS<sup>ECKO</sup> with WT. Circle size represents the gene number while circle color represents the value of  $-\log_{10}(q_{\text{value}})$ . **(D)** The mean normalized enrichment score (NES) of the gene set enrichment analysis (GSEA) comparing to GLS<sup>ECKO</sup> to WT are represented by each bar. NES <0 and NES >0 represent downregulation and upregulation of specified pathways in GLS<sup>ECKO</sup> versus WT respectively. **(E-G)** Expression values of *Gls2*, *Vegfa*, *Kdr* (*Vegfr2*), *Tek* (*Tie2*), and *Leptin* (*Lep*) in GLS<sup>ECKO</sup> compared to WT. ns: not significant.