

Supplementary Figures

Figure S1:

Transendothelial transport of insulin and glucose to muscle interstitium. **(A)** In the normal state, insulin (blue) and glucose (green) must travel from the blood stream across endothelial cells (red) and potentially pericytes (yellow) to reach the muscle interstitium and activate insulin signaling in myocytes. The basal flow rate is depicted by the horizontal arrow. **(B)** Insulin induces vasodilation of muscle vasculature, which is thought to increase nutritive blood flow, which increases transport of insulin and glucose to the muscle interstitium. **(C)** In insulin resistant situations, insulin exerts only vasoconstriction signals, which decreases nutritive flow, leading to reduced glucose and insulin transendothelial transport. **(D)** Loss of pericytes is thought to increase muscle vessel permeability and transendothelial transport.

Figure S2:

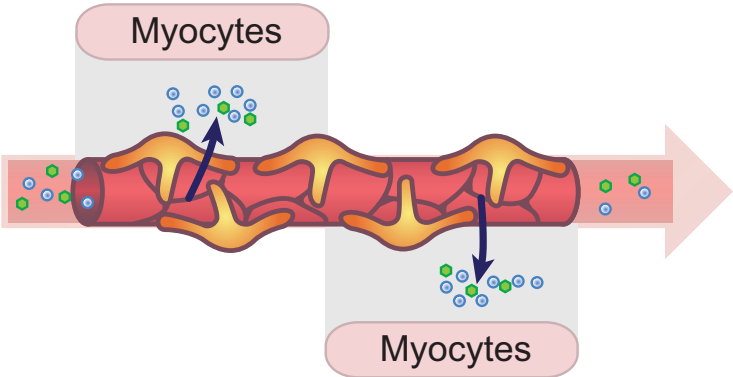
Insulin-induced vasodilation and vasoconstriction signaling in endothelial cells and pericytes. **(A)** Insulin signaling in endothelial cells results in increased NO production and secretion, which stimulates in dephosphorylation of myosin in pericytes and vSMCs and results in vasorelaxation. Note that signaling events that increase vasodilation are shown in green and those that increase vasoconstriction are shown in red. **(B)** Conversely, insulin also stimulates endothelin-1 production, which stimulates myosin phosphorylation and results in vasoconstriction.

Figure S3:

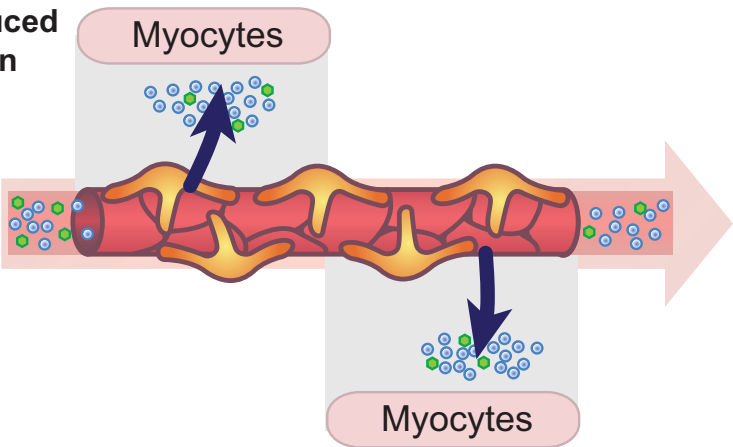
Increased pericyte hypertrophy with obesity. **(A-B)** Islet α -smooth muscle actin staining (red) increases from lean (+/+) **(A)** to *ob/ob* mice **(B)**, suggesting that islet pericytes are acquiring more vSMC-like characteristics with obesity. Endothelial cells (PECAM-1 antibody) are stained in green and β -cells (insulin antibody) are stained in blue for **(A-B)**. **(C-D)** Islet NG-2 staining (green) also increases from lean **(C)** to *ob/ob* mice **(D)**, which is characteristic of islet pericyte hypertrophy. Endothelial cells are stained in red and β -cells are stained in blue for **(C-D)**. Scale bar = 50 μ m.

Supplementary Figure 1

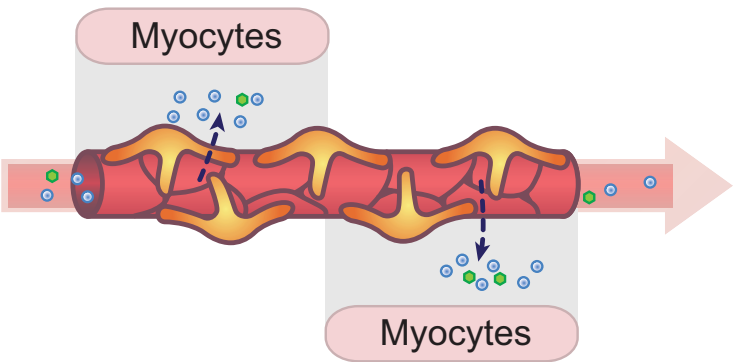
A. Normal



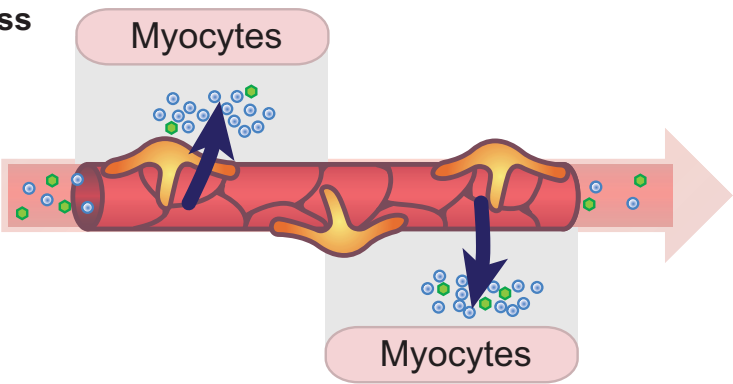
B. Insulin Induced Vasodilation



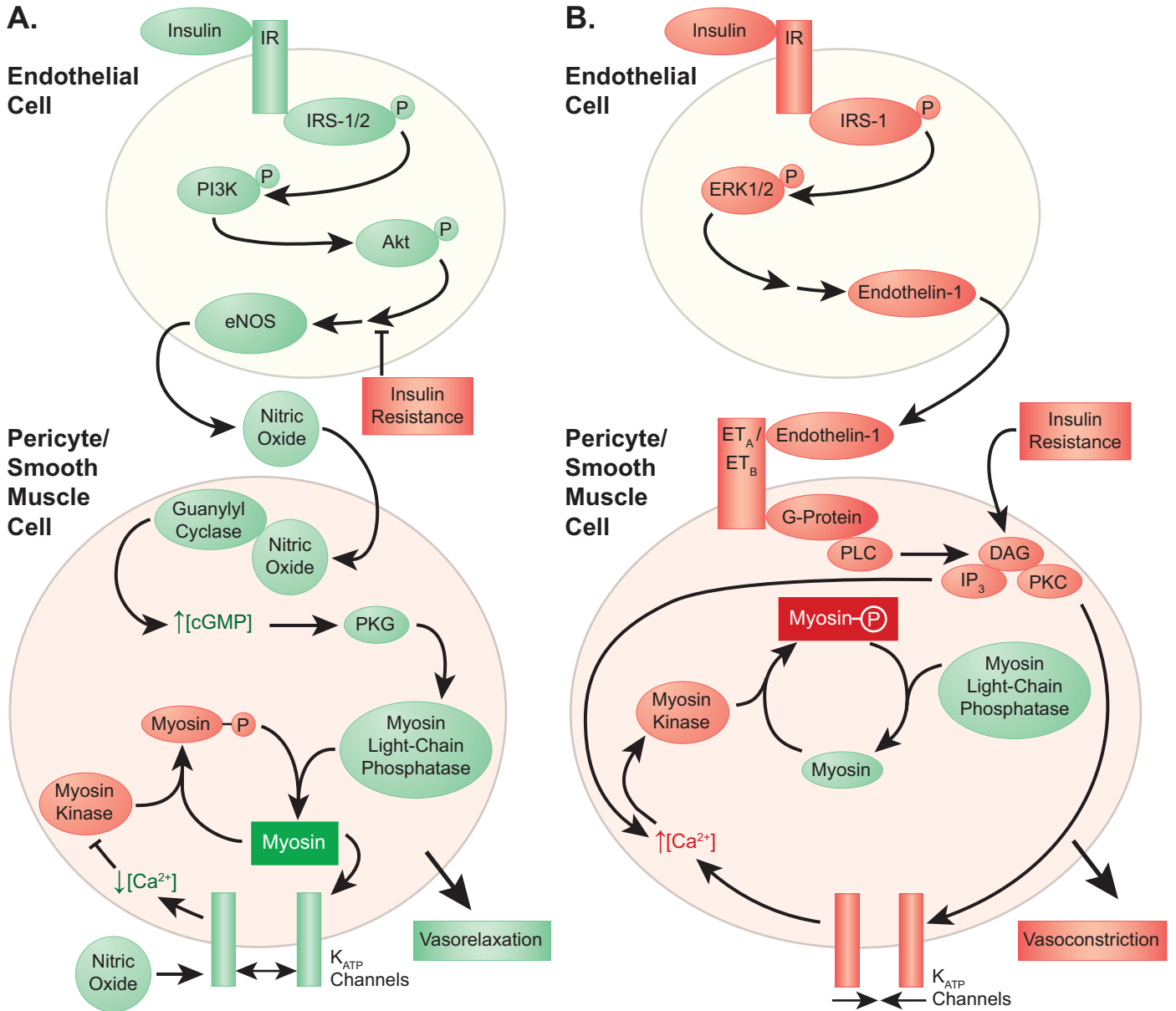
C. Insulin Resistance



D. Pericyte Loss



Supplementary Figure 2



Supplementary Figure 3

