Endothelial cells utilize a number of specialized mechanosensory systems to sense fluid shear stress, signal, and respond to maintain hemodynamic homeostasis. A stabilization pathway is activated by steady shear and is characterized by high expression of the transcription factors KLF2/4, whereas inflammation and remodeling responses are initiated upon altered shear and are characterized by activation of NF-kB and SMAD2/3 signaling. Dr. Coon’s recent research advances with the Schwartz Lab team related to how shear regulates the KLF2 pathway include newly identified regulatory genes and a biochemical mechanism linking oxidative stress, mitochondrial dynamics, and proteostasis. In parallel, he will discuss the dynamic cellular responses to shear involving Klf2/4 induction and Klf2/4 suppression.