Vascular endothelial dysfunction can initiate oxidative stress, i.e. superoxide (SO) overproduction, during ischemia/reperfusion (I/R). Endothelial dysfunction is characterized by an increase of oxidative stress, leading to an increase in blood hydrogen peroxide (H2O2) and a decrease in endothelial-derived nitric oxide (NO) bioavailability. Leukocyte NADPH oxidase is well studied; however, endothelial NADPH oxidase contributing to I/R injury is not well characterized. Previous studies using Gö 6983, a broad-spectrum protein kinase C inhibitor that can inhibit NADPH oxidase activity, has attenuated blood H2O2 levels during femoral I/R *in vivo* (1,2). A selective NADPH oxidase inhibitor, apocynin, interrupts the intracellular assembly of the enzyme by preventing the translocation to the cell membrane. Specifically, apocynin blocks the Cys196 residue interaction between endothelial NADPH oxidase subunits p47phox and p22phox (Fig. 3). This in turn inhibits SO release from endothelial NADPH oxidase, which further enhances endothelial-derived NO release both of which may reduce oxidative stress in I/R injury.