Nitric oxide promotes endothelial cell survival signaling through S-nitrosylation and activation of dynamin-2

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Endothelial cell-based angiogenesis requires activation of survival signals that generate resistance to external apoptotic stimuli, such as tumor necrosis factor-alpha (TNF-alpha), during pathobiologic settings. Mechanisms by which this is achieved are not fully defined. Here, we use a model in which the multifunctional cytokine nitric oxide counterbalances TNF-alpha-induced apoptosis, to define a role for membrane trafficking in the process of endothelial cell survival signaling. By perturbing dynamin GTPase function, we identify a key role of dynamin for ensuing downstream endothelial cell survival signals and vascular tube formation. Furthermore, nitric oxide is directly demonstrated to promote dynamin function through specific cysteine residue nitrosylation, which promotes endocytosis and endothelial cell survival signaling. Thus, these studies identify a novel role for dynamin as a survival factor in endothelial cells, through a mechanism by which dynamin S-nitrosylation regulates the counterbalances of TNF-alpha-induced apoptosis and nitric oxide-dependent survival signals, with implications highly relevant to angiogenesis.