Emerging mechanisms for controlling nitric oxide function in health and disease: roles of hypoxia, nitrite and heme

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Nitric oxide has multiple functions including controlling vascular resistance and inflammation. Endogenous NO-formation in the vascular compartment is controlled by endothelial nitric oxide synthase and decreased NO-bioavailability is a contributor to numerous inflammatory diseases. Recent paradigms, discussed in this seminar, suggest that complementary and alternative pathways for NO-formation exist, especially during ischemic stress, a condition where enzymatic NO-generation is compromised. Specifically, we will discuss how NO-signaling may be affected via reduction of the inorganic anion, nitrite by oxygen sensitive heme proteins (including hemoglobin), how these novel pathways may control endogenous NO-signaling in the context of blood flow, how these go awry during acute inflammatory disease and how these paradigms are being developed in the next generation of NO-donor therapeutics to treat ischemic diseases.