

<https://doi.org/10.70200/RX202401021D>

NITRIC OXIDE, SUPEROXIDE AND PEROXYNITRITE – REDOX REGULATION OF THE CARDIOVASCULAR SYSTEM BY NITRO-OXIDATIVE STRESS AND S-NITROS(YL)ATION

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Oxidative stress is characterized by an excessive and prolonged formation of oxidants, causing an accumulating load of irreversible oxidative modifications of proteins, lipids, and nucleic acids that compromise cell integrity. This competes with the concept of redox regulation, combining the regulatory influence of nitric oxide ($\cdot\text{NO}$), superoxide ($\text{O}_2^{\cdot-}$), and their derivatives on redox-sensitive signaling pathways in the cell. The transition from redox regulation to oxidative stress is not only determined by the absolute amount of oxidants formed, but also by the respective intracellular site of formation, by the capacity of the defense machinery of the respective cell type, and by the ratio between $\cdot\text{NO}$ and $\text{O}_2^{\cdot-}$ that determines the nature of secondary radical species formed. Equimolar and concomitant fluxes of $\cdot\text{NO}$ and $\text{O}_2^{\cdot-}$, for instance, favor the formation of the oxidant peroxynitrite making $\text{O}_2^{\cdot-}$ an antagonist of $\cdot\text{NO}$ as well as an inhibitor of prostacyclin synthesis, while an excess of $\cdot\text{NO}$ over $\text{O}_2^{\cdot-}$ supports the formation of nitrosating species. Secondary $\cdot\text{NO}$ -derived species hence not only define cellular targets affected but also the nature of posttranslational modifications. A profound knowledge of redox regulation and the conditions supporting its fluent transition into oxidative stress is hence of outermost importance in molecular cardiovascular medicine. The present overview therefore aims to determine the spectrum of $\cdot\text{NO}$ -derived reactive species and the cellular conditions characteristic for reversible modifications and their modulation of cellular targets in redox regulation. The second objective is to define preconditions in cardiovascular cells culminating in an expenditure of the cellular antioxidant system and an accumulation of irreversible modifications that compromise cellular functions to a point of no return.

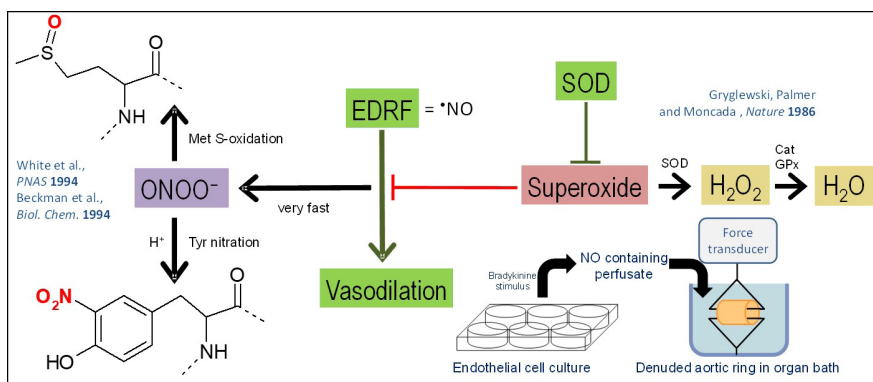


Figure 1. Superoxide anion-induced loss of “endothelium-derived relaxing factor (EDRF)” (Daiber et al. Redox Biol. 12:35-49, 2017).