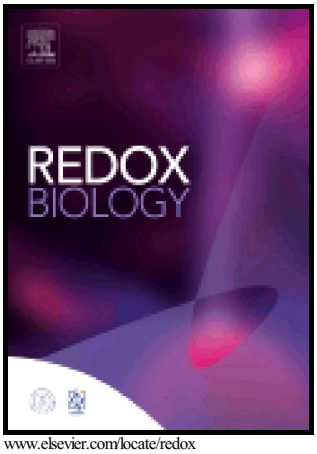

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Fundamentals on the Biochemistry of Peroxynitrite and Protein Tyrosine Nitration

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Abstract:

In this review we provide an analysis of the biochemistry of peroxynitrite and tyrosine nitration. Peroxynitrite is the product of the diffusion-controlled reaction between superoxide ($O_2^{\bullet-}$) and nitric oxide ($^{\bullet}NO$). This process is in competition with the enzymatic dismutation of $O_2^{\bullet-}$ and the diffusion of $^{\bullet}NO$ across cells and tissues and its reaction with molecular targets (*e.g.* guanylate cyclase). Understanding the kinetics and compartmentalization of the $O_2^{\bullet-}$ / $^{\bullet}NO$ interplay is critical to rationalize the shift of $^{\bullet}NO$ from a physiological mediator to a cytotoxic intermediate. Once formed, peroxynitrite ($ONOO^-$ and ONOOH; pKa = 6,8) behaves as a strong one and two-electron oxidant towards a series of biomolecules including transition metal centers and thiols. In addition, peroxynitrite anion can secondarily evolve to secondary radicals either *via* its fast reaction with CO_2 or through proton-catalyzed homolysis. Thus, peroxynitrite can participate in *direct* (bimolecular) and *indirect* (through secondary radical intermediates) oxidation reactions; through these processes peroxynitrite can participate as cytotoxic effector molecule against invading pathogens and/or as an endogenous pathogenic mediator. Peroxynitrite can cause protein tyrosine nitration *in vitro* and *in vivo*. Indeed, tyrosine nitration is a hallmark of the reactions of $^{\bullet}NO$-derived oxidants in cells and tissues and serves as a biomarker of oxidative damage. Protein tyrosine nitration can mediate changes in protein structure and function that affect cell homeostasis. Tyrosine nitration in biological systems is a free radical process that can be promoted either by peroxynitrite-derived radicals or by other related $^{\bullet}NO$-dependent oxidative processes. Recently, mechanisms responsible of tyrosine nitration in hydrophobic biostructures such as membranes and lipoproteins have been assessed and involve the parallel occurrence and connection with lipid peroxidation. Experimental

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