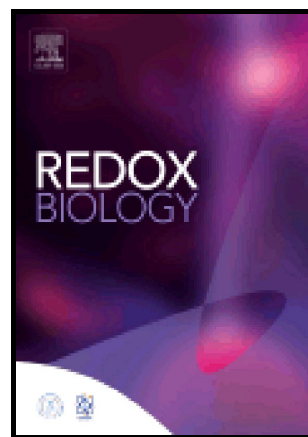


# Author's Accepted Manuscript

Fundamentals on the Biochemistry of Peroxynitrite  
and Protein Tyrosine Nitration

Silvina Bartesaghi, Rafael Radi



www.elsevier.com/locate/redox

PII: S2213-2317(17)30621-3  
DOI: <http://dx.doi.org/10.1016/j.redox.2017.09.009>  
Reference: REDOX754

To appear in: *Redox Biology*

Received date: 16 August 2017  
Revised date: 6 September 2017  
Accepted date: 15 September 2017

Cite this article as: Silvina Bartesaghi and Rafael Radi, Fundamentals on the Biochemistry of Peroxynitrite and Protein Tyrosine Nitration, *Redox Biology*, <http://dx.doi.org/10.1016/j.redox.2017.09.009>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**Fundamentals on the Biochemistry of Peroxynitrite and Protein****Tyrosine Nitration****Silvina Bartesaghi<sup>a,b,1</sup>, Rafael Radi<sup>a,b,1</sup>**<sup>a</sup>Departamento de Bioquímica<sup>b</sup>Center for Free Radical and Biomedical Research, Facultad de Medicina, Universidad de la República, Avda. General Flores 2125, Montevideo 11800, Uruguay

sbartesa@fmed.edu.uy

rradi@fmed.edu.uy

**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 ( $O_2^{\cdot-}$ ) and nitric oxide ( $\cdot NO$ ). This process is in competition with the enzymatic dismutation of  $O_2^{\cdot-}$  and the diffusion of  $\cdot NO$  across cells and tissues and its reaction with molecular targets (*e.g.* guanylate cyclase). Understanding the kinetics and compartmentalization of the  $O_2^{\cdot-}$  /  $\cdot NO$  interplay is critical to rationalize the shift of  $\cdot NO$  from a physiological mediator to a cytotoxic intermediate. Once formed, peroxynitrite ( $ONOO^-$  and  $ONOOH$ ;  $pK_a = 6,8$ ) 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  $\cdot NO$ -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  $\cdot NO$ -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

---

<sup>1</sup> To whom correspondence should be addressed

Download English Version:

<https://daneshyari.com/en/article/8286726>

Download Persian Version:

<https://daneshyari.com/article/8286726>

[Daneshyari.com](https://daneshyari.com)