Silvina Bartesaghi
Universidad de la República de Uruguay | UdelaR · Departamento de Bioquímica
Ph.D.

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nisms of Oxidative Inactivation of Human Glutamine Synthetase

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olás Campolo · Mauricio Mastrogiovanni · Michele Mariotti · [...] · Rafael Radi

nitrite-Mediated Oxidative Modifications of Nerve Growth Factor (NGF)

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ntific methodology course for advanced medical students: an eight-year perspective

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ound: Exponential increases in the development of medical knowledge, the expansion of areas where ne develops its activities, the emergence of new pathologies (e.g., COVID-19), novel diagnostic ds and therapeutic strategies, together with the appearance of multiple communication and information logies, determined that the ed...

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ysis Studies of Oxidation and Nitration of Tyrosine and Some Other Biological Targets by nitrite-Derived Radicals

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a K. Folkes · Silvina Bartesaghi · Madia Trujillo · [...] · Rafael Radi

despread interest in free radicals in biology extends far beyond the effects of ionizing radiation, with attention largely focusing on reactions of free radicals derived from peroxynitrite (i.e., hydroxyl, nitrogen e, and carbonate radicals). These radicals can easily be generated individually by reactions of tically-produ...

sed proteasomal cleavage at nitrotyrosine sites in proteins and peptides

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istiane Ott · Florencia Tomasina · Nicolás Campolo · [...] · Rafael Radi

al of moderately oxidized proteins is mainly carried out by the proteasome, while highly modified s are no longer degradable. However, in the case of proteins modified by nitration of tyrosine residues rotyrosine (NO2Y), the role of the proteasome remains to be established. For this purpose, degradation and mass spectrome...

fects of nitric oxide or oxygen on the stable products formed from the tyrosine phenoxyl radical

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a K Folkes · Silvina Bartesaghi · MadiaTrujillo · [...] · Rafael Radi

ne is a critical component of many proteins and can be the subject of oxidative posttranslational cations. Furthermore, the oxidation of tyrosine residues to phenoxyl radicals, sometimes quite stable, is ial for some enzymatic functions. The lifetime and fate of tyrosine radicals in biological systems is driven by the avai...

otyrosine and related derivatives in proteins: precursors, radical intermediates and impact in function

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020

olás Campolo · Federico Issoglio · Dario Estrin · [...] · Rafael Radi

ive post-translational modification of proteins by molecular oxygen (O2)- and nitric oxide (•NO)-derived e species is a usual process that occurs in mammalian tissues under both physiological and ogical conditions and can exert either regulatory or cytotoxic effects. Although the side chain of several acids is prone to expe...

putational investigation of the reactions of tyrosyl, tryptophanyl, and cysteinyl radicals with nitric and molecular oxygen

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018

lerico N Pedron · Silvina Bartesaghi · Dario Estrin · [...] · Ari Zeida

s are main targets of oxidants in biological systems. This oxidation may occur in the protein backbone as in certain amino acid side chains, depending on the oxidant and amino acid intrinsic reactivity. ver, many enzymes are capable of generating stable amino acid radicals, such as tyrosyl, tryptophanyl steinyl radicals. T...

sed proteasome cleavage rates at nitrotyrosine sites in proteins and peptides

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018

ina Bartesaghi · Cristiane Ott · Florencia Tomasina · [...] · Rafael Radi

ve post-translational modifications to proteins can lead to conformationally altered and/or ctional proteoforms. Removal of moderately oxidized proteins is mainly carried out by the proteasome ighly modified proteins are no longer degradable. However, in the case of proteins modified by nitration sine residues to 3-nitrot...

s into the mechanisms of peroxynitrite-mediated inactivation of human glutamine synthetase

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018

ina Bartesaghi · Nicolás Campolo · Mauricio Mastrogiovanni · [...] · Rafael Radi

ine synthetase (GS) is a key metabolic enzyme that catalyzes the ATP-dependent synthesis of ine from glutamate and ammonia. In the CNS, it is mainly located in the cytosol of astrocytes, playing ortant role in detoxification of ammonia and excess glutamate. Alterations in GS activity and oxidative nslational modifications h...

mistry of Peroxynitrite and Protein Tyrosine Nitration

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018

ardo Ferrer-Sueta · Nicolás Campolo · Madia Trujillo · [...] · Rafael Radi

nitrite is a short-lived and reactive biological oxidant formed from the diffusion-controlled reaction of e radicals superoxide (O2•−) and nitric oxide (•NO). In this review, we first analyze the biochemical ce for the formation of peroxynitrite in vivo and the reactions that lead to it. Then, we describe the al reactions...

nentals on the Biochemistry of Peroxynitrite and Protein Tyrosine Nitration

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ina Bartesaghi · Rafael Radi

review we provide an analysis of the biochemistry of peroxynitrite and tyrosine nitration. Peroxynitrite is duct of the diffusion-controlled reaction between superoxide (O2(•)(-)) and nitric oxide ((•)NO). This s is in competition with the enzymatic dismutation of O2(•-) and the diffusion of (•)NO across cells and s and i...

mistry of Nitric Oxide and Peroxynitrite: Sources, Targets and Biological Implications

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016

ián Aicardo · Débora M. Martinez · Nicolás Campolo · [...] · Rafael Radi

oxide (•NO) is a relatively stable free radical generated biologically that participates in a series of signal ucing and physiological processes in human biology. Enzymatic as well as non-enzymatic sources of ve been reported in vivo. In circumstances where •NO is overproduced and/or in the context of a pro- t environment, i...

ive Inactivation of Human Glutamine Synthetase: Biochemical and Computational Studies

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ina Bartesaghi · Nicolás Campolo · Federico Issoglio · [...] · Rafael Radi

ine synthetase (GS) is a key metabolic enzyme that catalyzes the ATP-dependent synthesis of ine from glutamate and ammonia. In the central nervous system, it is mainly located in the cytosol of ytes, playing an important role in ammonia detoxification and prevention of glutamate-dependent oxicity. Alterations in GS activity...

ng the Catalytic Mechanism of Human Glutamine Synthetase by Computer Simulations

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016

lerico Issoglio · Nicolás Campolo · Ari Zeida · [...] · Silvina Bartesaghi

ıine synthetase is an important enzyme which catalyzes the ATP-dependent formation of glutamine lutamate and ammonia. In mammals it has a key role preventing excitotoxicity in the brain and ying ammonia in the liver. In plants and bacteria, it is fundamental for nitrogen metabolism, being for the organism survival. In the...

f 20S proteasome in the fate of oxidized and tyrosine nitrated proteins

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ıe-Nitrated Proteins: Proteomic and Bioanalytical Aspects

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los Batthyany · Silvina Bartesaghi · Mauricio Mastrogiovanni · [...] · Rafael Radi

cance: "Nitroproteomic" is under active development, as 3-nitrotyrosine in proteins constitutes a nt left by the reactions of nitric oxide-derived oxidants that are usually associated to oxidative stress ons. Moreover, protein tyrosine nitration can cause structural and functional changes, which may be of hysiological re...

nitrite-Dependent Nitration of Human Glutamine Synthetase: Biochemical and Computational Studies

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ina Bartesaghi · Nicolas Campolo · Federico Issoglio · [...] · Rafael Radi

noglobin is nitrated in functional legume nodules in a tyrosine residue within the heme cavity by a peroxide-dependent mechanism

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015

ria Martha Sainz · Laura Calvo-Begueria · Carmen Pérez-Rontomé · [...] · Manuel Becana

ı Tyr nitration is a post-translational modification yielding 3-nitrotyrosine (NO2-Tyr). Formation of NO2- generally considered as a marker of nitroxidative stress and is involved in some human hysiological disorders, but it has been poorly studied in plants. Leghemoglobin (Lb) is an abundant rotein of legume nodules that pla...

catalyzed protein tyrosine nitration in biological systems

e

014

olás Campolo · Silvina Bartesaghi · Rafael Radi

ı tyrosine nitration is an oxidative postranslational modification that can affect protein structure and ın. It is mediated in vivo by the production of nitric oxide-derived reactive nitrogen species (RNS), ng peroxynitrite (ONOO(-)) and nitrogen dioxide ((•)NO2). Redox-active transition metals such as iron opper (Cu), and...

. Tyrosine Nitration in Membranes is Connected to Lipid Peroxidation: Influence of Molecular ıLevels

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013

ina Bartesaghi · Rafael Radi

: and mechanistic considerations to assess the biological fate of peroxynitrite

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13

astian Carballal · Silvina Bartesaghi · Rafael Radi

nitrite, the product of the reaction between superoxide radicals and nitric oxide, is an elusive oxidant of alf-life and low steady-state concentration in biological systems; it promotes nitroxidative damage. We nsider kinetic and mechanistic aspects that allow rationalizing the biological fate of peroxynitrite from otaine...

s of oxidation of tyrosine by a model alkoxyl radical

e

012

a K Folkes · Silvina Bartesaghi · Madia Trujillo · [...] · Peter Wardman

ion of tyrosine moieties by radicals involved in lipid peroxidation is of current interest; while a rate nt has been reported for reaction of lipid peroxyl radicals with a tyrosine model, little is known about the n between tyrosine and alkoxyl radicals (also intermediates in the lipid peroxidation chain reaction). In udy,...

ular basis of intramolecular electron transfer in proteins during radical-mediated oxidations: Computer tion studies in model tyrosine-cysteine peptides in solution

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eroxidation and Protein Tyrosine Nitration Are Mechanistically Connected: Model Studies With ne-Containing Transmembrane Peptide

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r Nitrite in Nitric Oxide Biology: A Redox Interplay with Implications for Pathophysiology and eutics

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cently, nitrite has been considered a stable and inert metabolite of nitric oxide (•NO) metabolism. This now changing as it has been shown that nitrite can be reduced back to •NO and thus one may consider sible interaction regarding ˙NO:nitrite couple. Not only physiological regulatory actions have been ed to nitrite bu...

r nitrite in nitric oxide biology: a redox interplay with implications for pathophysiology and eutics

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bara S Rocha · Bruno Gago · Cassilda Pereira · [...] · João Laranjinha

cently, nitrite has been considered a stable oxidation inert metabolite of nitric oxide ((·)NO) olism. This view is now changing as it has been shown that nitrite can be reduced back to (·)NO and ne may consider a reversible interaction regarding (·)NO:nitrite couple. Not only physiological regulatory s have been assigned t...

s of reduction of tyrosine phenoxyl radicals by glutathione

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011

a K Folkes · Madia Trujillo · Silvina Bartesaghi · [...] · Peter Wardman

cation of tyrosine (TyrOH) is used as a marker of oxidative and nitrosative stress. 3,3'-Dityrosine ion, in particular, reflects oxidative damage and results from the combination of two tyrosyl phenoxyl s (TyrO·). This reaction is in competition with reductive processes in the cell which 'repair' tyrosyl s: possible reduct...

ne-Lipid Peroxide Adducts from Radical Termination: Para Coupling and Intramolecular Diels-Alder ation

e

010

nan Shchepin · Matias Moller · hye-young hong Kim · [...] · Ned A Porter

dical co-oxidation of polyunsaturated lipids with tyrosine or phenolic analogues of tyrosine gave rise to eroxide-tyrosine (phenol) adducts in both aqueous micellar and organic solutions. The novel adducts olated and characterized by 1D and 2D NMR spectroscopy as well as by mass spectrometry (MS). The al data suggest that...

vity of hydrogen sulfide with peroxynitrite and other oxidants of biological interest

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astian Carballal · Madia Trujillo · Ernesto Cuevasanta · [...] · Beatriz Alvarez

gen sulfide (H(2)S) is an endogenously generated gas that can also be administered exogenously. It ates physiological functions and has reported cytoprotective effects. To evaluate a possible antioxidant e investigated the reactivity of hydrogen sulfide with several one- and two-electron oxidants. The rate nt of the direct re...

rosine: Quantitative Analysis, Mapping in Proteins, and Biological Significance

ter

010

é M. Souza · Silvina Bartesaghi · Gonzalo Peluffo · Rafael Radi

uction Foundation of 3-Nitrotyrosine Formation Tyrosine Analogs as Probes for Following Nitration and ion Reactions Methods for Quantification of 3-Nitrotyrosine in Biological Samples Mapping 3-rosine in Proteins Conclusions and Perspectives Acknowledgements References

eroxyl Radicals Mediate Tyrosine Dimerization and Nitration in Membranes

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010

ina Bartesaghi · Jorge Wenzel · Madia Trujillo · [...] · Rafael Radi

tyrosine dimerization and nitration by biologically relevant oxidants usually depend on the intermediate ion of tyrosyl radical ((*)Tyr). In the case of tyrosine oxidation in proteins associated with hydrophobic partments, the participation of unsaturated fatty acids in the process must be considered since they ly constit...

r Twelve. Tyrosine Nitration, Dimerization, and Hydroxylation by Peroxynitrite in Membranes as d by the Hydrophobic Probe N-t-BOC-l-tyrosine tert-Butyl Ester

e

008

ina Bartesaghi · Gonzalo Peluffo · Hao Zhang · [...] · Rafael Radi

tyrosine oxidation mechanisms in hydrophobic biocompartments (i.e., biomembranes, lipoproteins) to nitrated, dimerized, and hydroxylated products are just starting to be appreciated. This chapter on the use of the hydrophobic tyrosine analog N-t-BOC-l-tyrosine tert-butyl ester (BTBE) incorporated sphatidyl choline lipo...

r 12 Tyrosine Nitration, Dimerization, and Hydroxylation by Peroxynitrite in Membranes as Studied by drophobic Probe N- t-BOC- l-tyrosine tert-Butyl Ester

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008

ina Bartesaghi · Gonzalo Peluffo · Hao Zhang · [...] · Rafael Radi

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oration of the Hydrophobic Probe N - t -BOC- l -tyrosine tert -Butyl Ester to Red Blood Cell Membranes dy Peroxynitrite-Dependent Reactions

e

007

alia Romero · Gonzalo Peluffo · Silvina Bartesaghi · [...] · Rafael Radi

ve previously demonstrated that red blood cells (RBC) are an important sink of intravascularly generated nitrite even in the presence of physiological concentrations of CO2 or other plasmatic biotargets. Once erythrocytes, peroxynitrite reacts fast with oxyhemoglobin (oxyHb; k2=2 x 10(4) M(-1) s(-1) at 37 s C and pH 7.4) and...

n tyrosine nitration in hydrophilic and hydrophobic environments

e

007

ina Bartesaghi · Gerardo Ferrer-Sueta · Gonzalo Peluffo · [...] · Rafael Radi

review we address current concepts on the biological occurrence, levels and consequences of protein e nitration in biological systems. We focused on mechanistic aspects, emphasizing on the free radical nisms of protein 3-nitrotyrosine formation and critically analyzed the restrictions for obtaining large e nitration yield...

nship between tyrosine nitration in hydrophobic environments and lipid radical dependent processes

erence Paper

007

ina Bartesaghi · Madia Trujillo · Gonzalo Peluffo · [...] · Rafael Radi

nistic Studies of Peroxynitrite-Mediated Tyrosine Nitration in Membranes Using the Hydrophobic N-t-BOC-l-tyrosine tert-Butyl Ester†

e

06

ina Bartesaghi · Valeria Valez · Madia Trujillo · [...] · Rafael Radi

f the mechanistic studies of tyrosine nitration have been performed in aqueous solution. However, protein tyrosine residues shown to be nitrated in vitro and in vivo are associated to nonpolar rtments. In this work, we have used the stable hydrophobic tyrosine analogue N-t-BOC-L-tyrosine tert- ster (BTBE) incorporated into pho...

nitrite-derived carbonate and nitrogen dioxide radicals readily react with lipoic and dihydrolipoic acid

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005

dia Trujillo · Lisa Folkes · Silvina Bartesaghi · [...] · Rafael Radi

ipoic acid (LA) and dihydrolipoic acid (DHLA) may have a role as antioxidants against nitric oxide- l oxidants. We previously reported that peroxynitrite reacts with LA and DHLA with second-order rate nts of 1400 and 500 M(-1) s(-1), respectively, but indicated that these direct reactions are not fast n to protect against per...

ons of desferrioxamine with peroxynitrite-derived carbonate and nitrogen dioxide radicals

e

004

ina Bartesaghi · Madia Trujillo · Ana Denicola · [...] · Rafael Radi

n chelating agent desferrioxamine inhibits peroxynitrite-mediated oxidations and attenuates nitric oxide ygen radical-dependent oxidative damage both in vitro and in vivo. The mechanism of protection is ndent of iron chelation and has remained elusive over the past decade. Herein, stopped-flow studies d that desferrioxamin...

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Neil Hogg
Medical College of Wisconsin

Leonor Thomson
Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Christine Winterbourn
University of Otago

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Ana Denicola
Universidad de la República de Uruguay

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Thomas von Woedtke
Leibniz Institute for Plasma Science and Technology

Renaud Brouquisse
French National Institute for Agriculture, Food, and Environment (INRAE)

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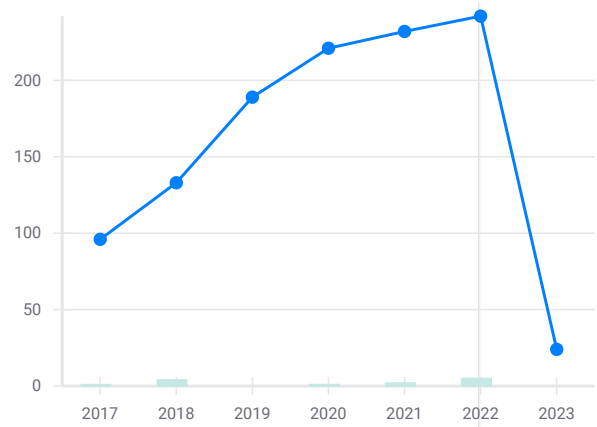

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