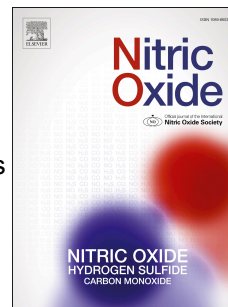


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The Discovery of Nitro-Fatty Acids as Products of Metabolic and Inflammatory Reactions and Mediators of Adaptive Cell Signaling

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Running title: *Nitro-fatty acid discovery and signaling actions*

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ABSTRACT

Foundational advances in eicosanoid signaling, the free radical biology of oxygen and nitric oxide and mass spectrometry all converged to enable the discovery of nitrated unsaturated fatty acids. Due to the unique biochemical characteristics of fatty acid nitroalkenes, these species undergo rapid and reversible Michael addition of biological nucleophiles such as cysteine, leading to the post-translational modification of low molecular weight and protein thiols. This capability has led to the present understanding that nitro-fatty acid reaction with the alkylation-sensitive cysteine proteome leads to physiologically-beneficial alterations in transcriptional regulatory protein function, gene expression and in vivo rodent model responses to metabolic and inflammatory stress. These findings motivated the preclinical and clinical development of nitro-fatty acids as new drug candidates for treating acute and chronic metabolic and inflammatory disorders.

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