Methods in ENZYMOLOGY

Volume 269

Nitric Oxide

Part B

Physiological and Pathological Processes

Edited by

Lester Packer

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Preface

The realization that nitric oxide (NO·), a free radical that is generated in biological systems, plays a pivotal role in physiology, pathology, and pharmacology has led to an explosion of new research. The recognition that the endothelial relaxing factor (ERDF) is actually NO· has been important in revolutionizing our thinking about how the vasculature is regulated. The physiological functions of NO· in signaling by the activation of guanylate cyclase and the existence of a multitude of other targets have now been identified for NO· in biological systems.

NO· is a free radical species, and therefore reactive as such. However, it reacts with the superoxide anion with a rate constant of about 6.7×10^9 M^{-1} sec^{-1} forming peroxynitrite ($ONOO^-$), a species more reactive toward lipids, DNA, and proteins, leading to their chemical modification and to pathological effects.

Overcoming difficulties in accurately assessing its generation, detection, and characterization in biological systems was the impetus for seeking contributions to these two *Methods in Enzymology* volumes on nitric oxide (268 and 269). They provide a comprehensive and detailed account of the methodology relating to four areas. In this volume methods and assays relevant to the effects of NO· in cells and tissues and the pathological and clinical aspects of NO· are included. The articles in Section I focus on the reactivity of NO· and tissue-specific effects of NO· as well as on its effects in cell signaling mechanisms. The emphasis of Section II is on the pathological action of NO· recognized by reactions of nitrosylation and nitration and on the interaction of NO· with membranes, proteins, and nucleic acids. Methods for detecting the action of peroxynitrite, tissue and cell toxicity, and clinical aspects of NO· inhalation therapy are included. Volume 268 covers methods relating to the generation of NO·. In Section I the chemistry and biology of NO·, methods for its detection, and NO· donors are covered. Section II covers NO· synthase—its purification, assay of the activity of endogenous and inducible forms of NO· synthase, its hemoprotein homology, the tissue distribution of NO· synthase, and its molecular cloning and expression.

In bringing these volumes to fruition, credit must be given to experts in various specialized fields of NO· research who provided contributions and to those who helped select the authors to provide the state of the art methodology. The topics and methods included in these volumes were chosen on the excellent advice of the volume advisors, Bruce N. Ames, Joseph Beckman, Enrique Cadenas, Victor Darley-Usmar, Bruce Freeman,

Barry Halliwell, Louis J. Ignarro, Hiroe Nakazawa, William Pryor, and Helmut Sies, to whom I extend my sincere thanks and most grateful appreciation.

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