SIGNAL TRANSDUCTION AND THE GASOTRANSMITTERS

SIGNAL TRANSDUCTION AND THE GASOTRANSMITTERS

NO, CO, and H₂S in Biology and Medicine

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DEDICATION

To Lily, Jennifer, Jessica, and Clover:

You are my source of inspiration.

Rui Wang, MD, PhD, FAHA

The current era of biological investigation is among the most transformational in history. The genuine emergence of genomic strategies and the rapid follow-on of proteomic and information technologies have provided scientists with unprecedented opportunities for discovery. The frontiers of knowledge are simply falling back. With this amazing revolution in understanding of the molecular underpinnings of cellular, tissue, and organismic homeostasis, a greater appreciation for the complexity of signals, networks, and linkages has crystallized. Regulation of biological functions rests not only with transcriptional, translational, and post-translational modifications of proteins, but also in the orchestral harmony of ligands and receptors, cell adhesive systems, cytoskeletal organization, ion channel function, membrane dynamics, and a range of transmitters.

Typically, transmitters have been categorized as those participating in neural functions or as humoral amines. In *Signal Transduction and the Gasotransmitters: NO, CO, and H₂S in Biology and Medicine*, Dr. Rui Wang and the sterling group of contributors he has assembled provide a paradigm-shifting assessment of the new category of transmitters, the gasotransmitters. Although nitric oxide was discovered approximately 20 years ago, it has only recently been appreciated that this famous molecule is among a whole group of substances that play critical roles in cell signaling and regulation, arising either environmentally or endogenously. These diverse molecules include, but are not limited to, nitric oxide, carbon monoxide, and hydrogen sulfide. Considering the now-identified roles of these three gasotransmitters in physiology and toxicology, it is understandable that the contributions are accordingly organized in sections corresponding to each. The origin, quantities, and interactions among these transmitters determine their impact on ionic fluxes, the excitability of muscle and nerve, and metabolism. There is an interesting and perhaps not surprising range of availability of any given gasotransmitter that conveys either physiological benefit or toxicological adversity, even when the gases arise endogenously. Individual chapters clearly frame the spectrum of their disease-related and physiological roles.

Like all nascent fields of study, it is often difficult to predict the full magnitude of importance of certain discoveries. Although the discovery of the role of nitric oxide in biological function deserved the Nobel Prize, and nitric oxide is now known to be a pivotal molecule in many organ systems, it is tempting to speculate that knowledge of the role of endogenous gases in a broader scale, especially as it relates to the homeostatic balancing act or that of other species, is barely coming into its own. Dr. Wang is to be congratulated on bringing the subject of gasotransmitters into coherence. I believe that biologists from many fields will welcome the knowledge that is captured here.

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The endogenous production and physiological function of many gaseous molecules including, but not limited to, nitric oxide (NO), carbon monoxide (CO), and hydrogen sulfide (H₂S), have been increasingly recognized in recent years. These gaseous molecules, defined as gasotransmitters, share common chemical features and biological action modes, but distinguish themselves from classical neurotransmitters and humoral factors. The concept of gasotransmitters has found its application across a wide spectrum of biological systems. Recent advances in the novel and challenging field of gasotransmitter biology and medicine—encompassing biomedical and clinical issues, health services, and population health studies—are dazzling. Gasotransmitters are important endogenous signaling molecules. Among many cellular and molecular targets of gasotransmitters, membrane ion channels are the key signal transduction link regulated by gasotransmitters. The regulation of ion channels by gasotransmitters can result from the activation of different second messengers or the direct interactions between gasotransmitters and ion channel proteins. The latter is a novel mechanism and has attracted great attention from researchers in every field of biomedical studies.

Many books have been published that focus on neurotransmitters and other classical signal transduction pathways. *Signal Transduction and the Gasotransmitters: NO, CO, and H₂S in Biology and Medicine* reviews the biology and medicine of gasotransmitters with an emphasis on signaling transduction mechanisms in general, and ion channel regulation in particular. Following an account of the historical evolution of the gasotransmitter concept, the endogenous metabolisms of gasotransmitters and their regulation, the comparison of the toxicological profiles and biological actions, and interactions among gasotransmitters in terms of their production and effects are discussed. The physiological roles of NO, CO, and H₂S in the regulation of cardiovascular, neuronal, and gastrointestinal systems, as well as of cell metabolism are reviewed. The interaction of gasotransmitters with K_{Ca} channels, KATP channels, voltage-gated Ca²⁺ channels, voltage-gated Na⁺ channels, and cyclic nucleotide-gated ion channels are presented. Included in the array of different mechanisms for the interaction of NO, CO, and H₂S are channel phosphorylation, S-nitrosylation, carboxylation, sulfuration, and altered cellular redox status. Guidance and suggestions can be found for exploring and characterizing lesser known gasotransmitters.

Signal Transduction and the Gasotransmitters: NO, CO, and H₂S in Biology and Medicine should serve as a summary and a standard reference source concerning signal transduction mechanisms underlying the physiological functions of gasotransmitters. Clinical scientists and physicians as well as other professional health workers should be excited by the advances in gasotransmitter research described in this book. The authors hope that scientists from both basic biology and health science disciplines find this book useful, interesting, and inspiring.

Rui Wang, MD, PhD, FAHA

CONTENTS

Foreword	vii
Preface	ix
Contributors	xiii

PART I. GASOTRANSMITTERS: PAST, PRESENT, AND FUTURE

- 1 The Evolution of Gasotransmitter Biology and Medicine: *From Atmospheric Toxic Gases to Endogenous Gaseous Signaling Molecules* 3
Rui Wang
- 2 Interactions Between Gasotransmitters 33
Ray J. Carson, Gunter Seyffarth, Rubina Mian, and Helen Maddock

PART II. THE EMERGENCE OF THE FIRST GASOTRANSMITTER: NITRIC OXIDE

- 3 Nitric Oxide: *Synthesis and Metabolism, Tissue Stores, and the Relationship of Endothelium-Derived Nitric Oxide to Endothelium-Dependent Hyperpolarization* 59
Chris R. Triggle, Hong Ding, Ella S. M. Ng, and Anthie Ellis
- 4 Chemical Interaction of Nitric Oxide With Protein Thiols: *S-Nitrosylation Signaling* 95
Allan Doctor and Benjamin M. Gaston
- 5 Nitric Oxide and Adenosine Triphosphate-Sensitive Potassium Channels: *Their Different Properties But Analogous Effects on Cellular Protection* 109
Shoji Sanada, Jiyoong Kim, and Masafumi Kitakaze
- 6 Interactions of Nitric Oxide and Related Radical Species With K_{Ca} Channels 123
Yanping Liu and David D. Gutterman
- 7 Nitric Oxide and Voltage-Gated Ca^{2+} Channels 137
Claudio Grassi, Marcello D'Ascenzo, and Gian Battista Azzena
- 8 Interactions of Nitric Oxide and Cardiac Ion Channels 157
Zhao Zhang, Kathryn A. Glatter, and Nipavan Chiamvimonvat
- 9 S-Nitrosylation of Cyclic Nucleotide-Gated Channels 169
Marie-Christine Broillet

PART III. STORY OF A SILENT KILLER: THE RESURGENCE OF CARBON MONOXIDE AS THE SECOND GASOTRANSMITTER

- 10 Synthesis and Metabolism of Carbon Monoxide 187
Stefan W. Ryter and Augustine M. K. Choi
- 11 Interaction of Carbon Monoxide With K^+ Channels in Vascular Smooth Muscle Cells 205
Rui Wang

12	Modulation of Multiple Types of Ion Channels by Carbon Monoxide in Nonvascular Tissues and Cells	219
	Rui Wang	
13	The Molecular Mechanisms Underlying the Effects of Carbon Monoxide on Calcium-Activated K ⁺ Channels	231
	Lingyun Wu	
14	Carbon Monoxide and Signal Transduction Pathways	249
	Patty J. Lee and Leo E. Otterbein	
15	Carbon Monoxide-Induced Alterations in the Expression of K _{Ca} Channels in Pulmonary Artery Smooth Muscle Cells	259
	Eric Dubuis, Prem Kumar, Pierre Bonnet, and Christophe Vandier	
PART IV. GAS OF THE ROTTEN EGG: HYDROGEN SULFIDE AS THE THIRD GASOTRANSMITTER		
16	Hydrogen Sulfide Production and Metabolism in Mammalian Tissues	275
	Kenneth N. Maclean and Jan P. Kraus	
17	Toxicological and Environmental Impacts of Hydrogen Sulfide	293
	Sheldon H. Roth	
18	Hydrogen Sulfide and the Regulation of Neuronal Activities	315
	Hideo Kimura	
19	The Role of Hydrogen Sulfide as an Endogenous Vasorelaxant Factor	323
	Rui Wang, Youqin Cheng, and Lingyun Wu	
20	Hydrogen Sulfide and Visceral Smooth Muscle Contractility	333
	Philip K. Moore	
21	Interaction of Hydrogen Sulfide and Adenosine Triphosphate-Sensitive Potassium Channels in Vascular Smooth Muscle Cells	345
	Rui Wang	
PART V. GASOTRANSMITTERS, OTHER GASEOUS MOLECULES, AND CELL METABOLISM		
22	Gasotransmitters as a Novel Class of Metabolic Regulators: <i>Nitric Oxide</i> , <i>Carbon Monoxide</i> , and <i>Nitrous Oxide</i>	359
	Misato Kashiba	
	Index	371

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