OXIDATIVE STRESS IN VERTEBRATES AND INVERTEBRATES

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Molecular Aspects of Cell Signaling

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"Live as if you were to die tomorrow. Learn as if you were to live forever."

Mohandas Karamchand Gandhi

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PREFACE

All oxygen-utilizing animals and organisms have to deal with reactive oxygen species (ROS), which include superoxide anions, hydroxyl, alkoxyl, and peroxyl radicals, and hydrogen peroxide. These radicals are common products of life in an aerobic environment, and they are responsible for oxygen toxicity. Proteins, lipids, and nucleic acid are targets for ROS attack, and modification of these molecules can increase the risk of chronic neurodegenerative diseases, visceral diseases, and cancer. "Oxidative Stress in Vertebrates and Invertebrates: Molecular Aspects of Cell Signaling" provides readers with a comprehensive description of the latest research on oxidative stress and antioxidant defenses in vertebrate and invertebrate systems. In biological systems, cells respond to mild oxidative stress by inducing antioxidant defenses and other protective systems. The antioxidant capacities of tissues are well matched to the rates of oxygen consumption and radical production. In vertebrate and invertebrate systems a variety of endogenous antioxidants (reduced glutathione) and antioxidant enzymes (superoxide dismutase, glutathione peroxidase, glutathione reductase, and catalase) act in a concerted manner to protect tissues against oxidative damage. The balance among oxidants and antioxidant enzyme systems, levels of antioxidants, and endogenous antioxidant mechanisms may be of major importance in the protection against oxidative stress-mediated cell injury. Under normal conditions, the rate of production of oxidants is balanced by the rate of oxidant elimination. However, an imbalance between prooxidants and antioxidants results in oxidative stress. Increase in ROS production has a substantial impact cellular metabolism and may lead to either defective cellular function and aging or chronic neurodegenerative and visceral diseases. Therefore, a better understanding of the roles of ROS-mediated signaling in normal cellular function as well as in disease is necessary for the development of therapeutic agents for oxidative stress-related chronic diseases.

Unlike other edited books that focus on oxidative stress in mammals, this unique book provides a comparative account of oxidative stress and antioxidant defenses in vertebrates and invertebrates, dealing not only with basic mechanisms and biomarkers but also with oxidative stress-mediated chronic diseases. This edited book is a valuable source of information for both basic scientists and clinicians who are interested in basic mechanism and oxidative stress-associated diseases. In this book, chapters are organized into two sections: (1) oxidative stress in vertebrates (Chapters 1–17) and (2) oxidative stress in invertebrates (Chapters 18–26), followed by a perspective (Chapter 27).

In Part I, Chapters 1 and 2 deal with the generation of ROS in the brain and their signaling associated with neural cell survival, cell suicide, and diseases. Chapters 3 and 4 discuss mitochondrial DNA mutation-induced oxidative stress underlying biochemical and pathological consequences and redox therapy in mitochondrial diseases and changes in kainic acid-induced neurotoxicity, which can be implicated in the pathogenesis of neurotraumatic and neurodegenerative diseases. Chapter 5 covers the historical aspects of the discovery of NF-E2-related factor 2 (Nrf2), recent advances in molecular aspects of its function, and updates involving Nrf2 association with various pathological conditions. Chapter 6 discusses modulation of oxidative stress by caloric restriction, suggesting that a calorie-restricted diet and the composition of diet may significantly improve ROS homeostasis both in single cells as well as in the whole body. Chapters 7–10

deal with the contribution of oxidative stress and inflammation to the pathogenesis of neurodegenerative diseases (Alzheimer disease, Parkinson disease). Chapter 11 summarizes free radical contribution to the development of cardiovascular diseases and discusses the applicability of antioxidant therapy based on data from clinical trials. Chapter 12 provides a comparison between vertebrates and invertebrates with regard to oxidative stress and aging. Chapter 13 addresses various environmental stressor-induced toxicities in experimental animals like rats and humans to elucidate the molecular mechanisms underlying oxidative stress. Chapter 14 discusses the role of selenoproteins in cellular redox regulation and signaling. Chapter 15 gives a clinical demonstration of the effectiveness of antioxidant administration in different diseases. Chapter 16 demonstrates that grape-derived bioactive polyphenolic components from wine effectively protect against the onset and progression of Alzheimer disease phenotypes, suggesting that moderate wine consumption may have preventive and/or therapeutic value in Alzheimer disease. Finally, Chapter 17 discusses pharmacological and therapeutic properties of propolis, a resinous mixture that honeybees collect from tree buds, sap flow, and other botanical sources, which is very beneficial for human health because of its richness in phenolic compounds.

In Part II, Chapter 18 reviews the endocrine control of oxidative stress in insects. Chapter 19 focuses on oxidative stress and innate immune system in airway epithelial cells of the fruit fly *Drosophila melanogaster*. Chapter 20 explores the molecular mechanisms of antioxidant protective processes in the honeybee *Apis mellifera*. Chapter 21 describes a hypothetical mechanism associated with iron-induced oxidative stress, implicating ROS production in olfactory dysfunction in the honeybee brain. Chapter 22 covers cutting-edge information on the Keap1/Nrf2 system in flies as well as its implications in combating human diseases. Chapter 23 is devoted to orchestration of oxidative stress responses in *Drosophila melanogaster* and promoter analysis study of circadian regulatory motifs. Chapter 24 deals with the protective role of sestrins (a unique family of proteins that is critically involved in cellular defense) against chronic target of rapamycin complex activation and oxidative stress in *Drosophila*. Chapter 25 explores current advances in the studies of oxidative stress and age-related memory impairment in the nematode *C. elegans*. Chapter 26 elegantly reviews oxidative challenge and redox sensing in mollusks by focusing on effects of natural and anthropic stressors. Finally, Chapter 27 provides readers with an in-depth perspective on current progress on our understanding of oxidative stress. It also presents readers and researchers with information that will be important for future research dealing with oxidative stress.

Biochemists, neuropharmacologists, toxicologists, and clinicians will find this book useful for understanding basic mechanisms of oxidative stress in vertebrate and invertebrate systems. It is hoped that "Oxidative Stress in Vertebrates and Invertebrates: Molecular Aspects of Cell Signaling" will further stimulate young and senior scientists to perform research on oxidative stress and oxidative stress-associated diseases.

Tahira Farooqui
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FOREWORD

Oxidative stress is a cytotoxic process that occurs in cells when antioxidant mechanisms are overwhelmed by reactive oxygen species (ROS). This imbalance not only causes damage to important biomolecules (lipids, proteins, and nucleic acids) in cells, but also has an impact on functional activities in both vertebrates and invertebrates. This new volume entitled "Oxidative Stress in Vertebrates and Invertebrates: Molecular Aspects of Cell Signaling" brings together important information from expert researchers in the oxidative stress-mediated cell signaling area in both vertebrate and invertebrate systems. Accumulation of high levels of ROS and significant reduction in cellular redox systems are common processes associated with acute and chronic visceral and neurodegenerative diseases, including hypertension, preeclampsia, arteriosclerosis, acute renal failure, diabetes, and Alzheimer and Parkinson diseases. This well-organized book presents up-to-date and comprehensive information on oxidative stress-related signaling events in vertebrates and invertebrates. The text is clear, concise, and easily accessible. Subject matter is divided into a vertebrate section (17 chapters) and an invertebrate section (10 chapters). The editors are known for their work on oxidative stress and neurodegeneration. They have done a commendable job in putting together this volume, and have contributed 5 chapters. These editors have taken great care in selecting the topics and describing progress that has been recently made in this field. The authors of this book also tried to ensure uniformity and mode of presentation in a simple and clear manner.

Topics addressed in the vertebrate section include the generation of ROS and their roles in cell survival and suicide; ROS-induced signal transduction and human diseases; biochemical and pathological consequences and redox therapy; pathogenesis of neurotraumatic and neurodegenerative diseases; oxidative stress mediated by caloric restriction; the role of oxidative stress and neuroinflammation in Alzheimer disease and Parkinson disease; selenoproteins in cellular redox regulation and signaling; antioxidant therapy and its effectiveness in oxidative stress-mediated disorders; pharmacological and therapeutic properties of propolis; comparison of oxidative stress in aging between vertebrates and invertebrates; and finally, oxidative stress-mediated signaling pathways by environmental stressors. The invertebrate section includes oxidative stress-induced signaling in three important phyla, namely, arthropoda, annelida, and mollusca. Topics addressed in this section include effect of oxidative stress on insect endocrine control; the innate immune system in airway epithelial cells of *Drosophila*; age-related memory impairment in *C. elegans*; olfactory learning and memory in *Apis mellifera*; Keap1/Nrf2 signaling in *Drosophila*; circadian rhythm in *Drosophila*; molecular antioxidant protective processes in *Apis mellifera*; protective role of sestrins against chronic TOR; and oxidative challenge and redox sensing in mollusks.

The subject matter in this book develops logically and progresses from one topic to another with an extensive bibliography along with major primary references. These references will help readers in pursuing their areas of interest. In order to facilitate better understanding and easier reading, this book also contains a large number of figures and line diagrams of signal transduction pathways. This book fills the gap between basic science and

clinical studies and provides the reader with the skills to apply basic science to clinical settings of chronic diseases associated with oxidative stress.

This book is essential reading material for a broad range of individuals, including researchers, clinicians, graduate and medical students, as well as the many health-conscious individuals who wish to know more about the emerging field of oxidative stress in vertebrate and invertebrate systems. It can be used as a supplemental text for a range of biology courses. It is anticipated that senior neuroscientists may also find some inspiration from this book to overcome problems encountered in their research on oxidative stress in vertebrate and invertebrate systems.

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