ADVANCED TOPICS IN SCIENCE AND TECHNOLOGY IN CHINA

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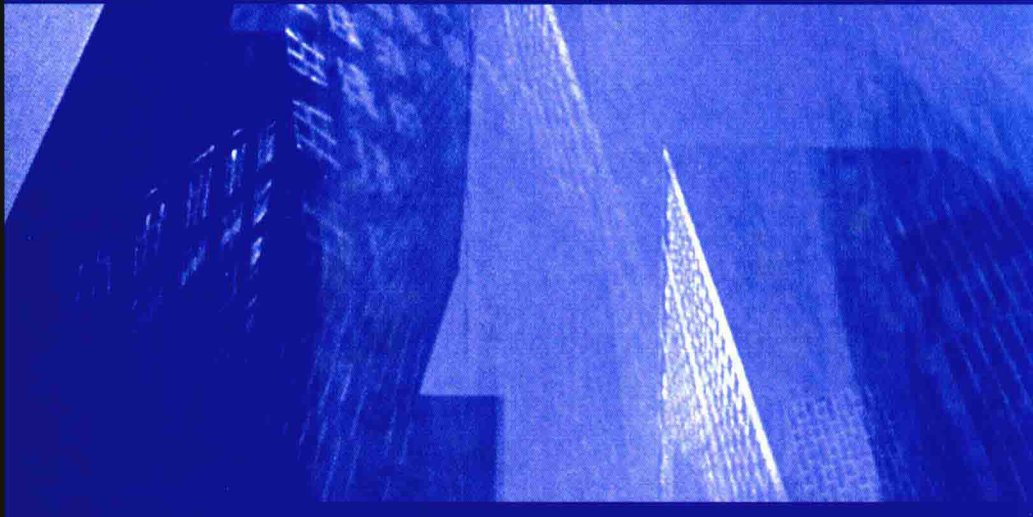
Junqiu Liu • Guimin Luo • Ying Mu
Editors

Selenoproteins and Mimics



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With 120 figures, 28 of them in color

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Zhejiang University is one of the leading universities in China. In Advanced Topics in Science and Technology in China, Zhejiang University Press and Springer jointly publish monographs by Chinese scholars and professors, as well as invited authors and editors from abroad who are outstanding experts and scholars in their fields. This series will be of interest to researchers, lecturers, and graduate students alike.

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Foreword

The research area of selenoproteins has seen considerable progress in recent years. The initial identification of selenium as an essential trace element was followed by the characterization of glutathione peroxidases as selenoproteins, which subsequnetly resulted in a wealth of information on various other selenoproteins. Early on, organic selenium compounds were identified as mimics of glutathione peroxidase activities. The current state of knowledge in these two research fields is brought together in this volume.

Regarding selenoproteins, following their identification and the study of their structure and characterization of their function and regulating, there have been efforts to bring their role into perspective in terms of physiology and pathology. An early landmark was Keshan disease, and current aspects are presented here on various exciting topics.

Selenoprotein mimics have been associated with the functioning of compounds capable of carrying out the reduction of hydroperoxides, a domain of glutathione peroxidases. The present volume contains valuable information on current knowledge in this field, addressing chemically new types of compounds and their potential in therapeutic applications. As not all functions of selenoproteins are uncovered yet, further types of selenoprotein mimics can be expected in the future.

It is noteworthy that the editor, Professor Junqiu Liu, and his other colleagues from China have contributed to this research area with highly interesting work in recent years, so that one can truly formulate that there is a tradition in Chinese research in the field of selenium and selenoproteins, stemming from the initial observation of the role of the trace element in Keshan disease to the current research fronts in the 21st century. Congratulations to this and to a fine book which hopefully will lead to further projects and research excitement.

Helmut Sies
Professor of Biochemistry and Molecular Biology
Heinrich-Heine-University Dusseldorf
Germany
sies@uni-duesseldorf.de

Preface

The element selenium was first discovered in 1817 by Berzelius and was recognized as an essential nutrient in the late 1950s. However, the biochemical role of selenium was not established until 1973 with the discovery of the selenoprotein, glutathione peroxidase (GPx). In 1973, selenium was indentified as an essential component of the active site of selenoenzyme GPx. From this year the biochemical and biological role of selenium began to be established. One important advance in this area is the investigation of selenoproteins. Selenoproteins exist in all major forms of life, eukaryote, bacteria and others. They are proteins which includes selenocysteine residues. Selenoproteins are important constituents of a number of enzymes with a range of functions including antioxidant function, thyroid hormone metabolism, male fertility and immune mechanisms. Selenium occurs in selenoproteins as specifically incorporated selenocysteine, and selenocysteine is recognized as the 21st amino acid. There is a rather complicated pathway of selenocysteine biosynthesis and specific incorporation into selenoproteins. The biosynthesis of selenocysteine is regulated by four genes and begins with the aminoacylation of the amino acid serine by the enzyme serine synthetase to produce Ser-tRNASec. Research suggests that the mammalian genome encodes 25 selenoprotein genes, while more than 40 selenoprotein genes may exist in different tissues. Thus, the number of selenoproteins indentified has grown substantially in recent years although the functions of only about half of these selenoproteins are understood. Conventionally, iodothyronine deiodinases, thioredoxin reductases, selenophosphate synthetase, selenoprotein P, selenoprotein W and the well-known glutathione peroxidases represent important classes of selenoproteins, and recent indentified selenoproteins includes selenoproteins Sel15, SelH, SelI, SelK, SelM, SelN, SelO, SelR, SelS, SelT, SelU, SelV, SelX, and SelZ. Their functions may be less understood or even unknown.

It is well known that selenium associate with human health and disease. For selenium-related disease, typical example includes Keshan disease, a selenium deficiency disease, which was first described in the early 1930s in China. Observational studies show that selenium can be benefical for immune system, reducing the cardiovascular and cancer mortality. Recent studies indicate that selenium shows important influence on asthma, arthritis, male infertility and HIV/AIDS.

To explore the functional importance of selenium in selenoproteins, significant

efforts have directed toward the development of biomimetic chemistry of selenoproteins. In this regard, the main progress focus on the simulation of the behaviors of selenium in selenoenzyme GPx. Up to now, a number of organoselenium/tellurium compounds and artificial selenoproteins were designed to mimic the natural GPx. A typical example is ebselen (2-phenyl-1,2-benzisoselenazol- 3[2*H*]-one), this "small molecular selenoenzyme" has been widely investigated as an artificial GPx from abundant experiments to clinic trials. Important progress has been made recently for the design of selenoantibody and seleno/telluro-glutathione tansferases, and these artificial selenoenzmes show amazed catalytic behaviors rivaling natural ones!

In this book, we combine the introduction of the recent development of selenoproteins with the advance in their functional imitation. Thus the book associates crossed subjects including biology, chemistry and medical science. This book consists of two parts with 20 chapters. The first part which was titled "Selenoproteins" describes major aspects of the identified selenoproteins with identified functions, these selenoproteins include glutathione peroxidases, thyroid hormone deiodinase. Thioredoxin reductases, selenophosphate synthetase, selenoprotein P, selenoprotein W, deiodinase, thioredoxin and selenoprotein T. The biosynthesis mechanism of selenoproteins is also discussed in this Part. The introduction of the bioinformatics of selenoproteins will help us to obtain insights into selenium utilization, distribution and the discovery of new selenoproteins. The description of main diseases such as cancers, brain diseases and heart diseases, and the occurrence of different forms of selenium in foods will give us a rough picture of the relationship of selenoproteins with human health. The second part which was titled "Selenoprotein mimics" presents the recent progress of biomimetic chemistry of selenoprotein. This part provides an overview for the reasonable design and synthesis of artificial models with selenoenzyme activity. Thus, a series of ideas and approaches for the design of artificial selenoproteins including chemical and biological methods has been described.

We hope that the biomimetic chemistry of selenoproteins will enrich both pharmaceutical and academic aspect of selenium and selenoproteins and also hope that the two part of this book will facilitate each other. The progress of selenoproteins would facilitate the design and preparation of artificial selenoproteins, and at the same time the functional imitation of selenoproteins would increase the understanding for the structures and functions of selenoproteins, and also for their further application in human health. This book provides a new review of selenoproteins, their mimetic chemistry and their varied aspects of health. Research in these directions is in progress although there are still many unanswered questions. It provides a platform for the scientists, researchers and students in the field of selenoproteins, their mimetic chemistry and others. This book should be suitable for wide readers in chemistry, biology and medical science.

Junqiu Liu, Guimin Luo
Changchun, China
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Contributors

Björn Åkesson
Biomedical Nutrition, Pure and Applied Biochemistry, Lund University, POBox 124, Lund, Sweden and Department of Clinical Nutrition, Lund University Hospital, Lund, Sweden

Christine Allmang
Architecture et Réactivité de l'ARN—Université de Strasbourg, Centre National de la Recherche Scientifique, Institut de Biologie Moléculaire et Cellulaire, 67084 Strasbourg, France

Youssef Anouar
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Sébastien Arthaud
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Frederick P. Bellinger
Department of Cell and Molecular Biology, John A Burns School of Medicine, University of Hawaii at Manoa, Honolulu HI 96813, USA

Marla J. Berry
Department of Cell and Molecular Biology, John A Burns School of Medicine, University of Hawaii at Manoa, Honolulu HI 96813, USA

Krishna P. Bhabak
Department of Inorganic and Physical Chemistry, Indian Institute of Science Bangalore, 560012, India

Abdeslam Chagraoui
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Leonidas H. Duntas
Endocrine Unit, Evgenidion Hospital, University of Athens, Greece

Leopold Flohé
Otto-von-Guericke-Universität, Universitätsplatz 2, D-39106 Magdeburg, and MOLISA GmbH, Brenneckestrasse 20, D-39118 Magdeburg, Germany

Yan Ge
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun, 130012, China

Tien Hoac
Biomedical Nutrition, Pure and Applied Biochemistry, Lund University, POBox 124, Lund, Sweden

Jin Huang
Graduate University of Chinese Academy of Sciences, Beijing, 100049, China

Kaixun Huang
Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan, 430074, China

Xin Huang
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun, 130012, China

Daewon Jeong
Department of Microbiology, Yeungnam University College of Medicine, Daegu 705-717, Korea

Liang Jiang
College of Life Sciences, Shenzhen University, Shenzhen, 518060, China

Jean Joss
Biological Sciences, Macquarie University, Sydney, NSW 2109, Australia

Ick Young Kim
Laboratory of Cellular and Molecular Biochemistry, School of Life Sciences and Biotechnology, Korea University, Seoul 136-701, Korea

Alain Krol
Architecture et Réactivité de l'ARN - Université de Strasbourg, Centre National de la Recherche Scientifique, Institut de Biologie Moléculaire et Cellulaire, 67084 Strasbourg, France

Isabelle Lihrmann
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Junqiu Liu
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun, 130012, China

Qiong Liu
College of Life Sciences, Shenzhen University, Shenzhen, 518060, China

Xiaoman Liu
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun, 130012, China

Thomas Lundh
Department of Occupational and Environmental Medicine, Lund University Hospital, Lund, Sweden

Guimin Luo
Key Laboratory for Molecular Enzymology and Engineering of the Ministry of Education, Jilin University, Changchun, 130012, China

Destiny-Love Manecka
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Barry Moore
Eccles Institute of Human Genetics, Department of Human Genetics, University of Utah, Salt Lake City, UT 84112, USA

Ying Mu
Research Center for Analytical Instrumentation, Institute of Cyber-Systems and Control, State Key Laboratory of Industrial Control Technology, Zhejiang University, Hangzhou, 310058, China

Govindasamy Mugesh
Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore, 560012, India

Gunilla Önning
Biomedical Nutrition, Pure and Applied Biochemistry, Lund University, POBox 124, Lund, Sweden

Jun Panee
Department of Cell and Molecular Biology, John A Burns School of Medicine, University of Hawaii at Manoa, Honolulu HI 96813, USA

Yoshiro Saito
Department of Medical Life Systems, Faculty of Medical and Life Sciences, Doshisha University, Kyotanabe, Kyoto, Japan

Jiacong Shen
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, China

Helmut Sies
Institut fr Physiologische Chemie I, Heinrich-Heine-Universita¨t Duesseldorf, D-40001 Duesseldorf, Germany

Peter P.A. Smyth
UCD School of Medicine and Medical Science, University College Dublin, Ireland

Kazuhiko Takahashi
Department of Nutritional Biochemistry, Hokkaido Pharmaceutical University School of Pharmacy, Otaru, Hokkaido, Japan

Yannick Tanguy
INSERM U982, Neuronal and Neuroendocrine Differentiation and Communication Laboratory, University of Rouen, 76821 Mont-Saint-Aignan, France

Huibi Xu
Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan, 430074, China

Jiayun Xu
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun, 130012, China

Yawei Xu
Key Laboratory for Molecular Enzymology and Engineering of the Ministry of Education, Jilin University, Changchun, 130023, China

Fei Yan
Key Laboratory for Molecular Enzymology and Engineering of the Ministry of Education, Jilin University, Changchun, 130012, China

Wei Zhang
State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, China

Liangwei Zhong
Graduate University of Chinese Academy of Sciences, Beijing, 100049, China

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