



ADVANCED TOPICS IN SCIENCE AND TECHNOLOGY IN CHINA  
国家科学技术学术著作出版基金资助出版

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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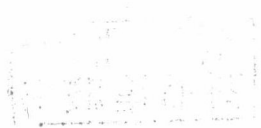
# **ADVANCED TOPICS IN SCIENCE AND TECHNOLOGY IN CHINA**

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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 subsequently 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.

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## 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 21<sup>st</sup> 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-tRNA<sup>Sec</sup>. 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 beneficial 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 transferases, and these artificial selenoenzymes 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  
May, 2011



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