

COENZYME Q:

Molecular Mechanisms in
Health and Disease

Edited by

Valerian E. Kagan
Peter J. Quinn

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CRC Press

Boca Raton London New York Washington, D.C.

Library of Congress Cataloging-in-Publication Data

Coenzyme Q: molecular mechanisms in health and disease / edited by Valerian E. Kagan and Peter J. Quinn.

p. cm.

Includes bibliographical references and index.

ISBN 0-8493-8732-9

1. Ubiquinones. I. Kagan, Valerian E. II. Quinn, Peter J.

QP801.U24 C645 2000

612'.0151—dc21

00-034234

CIP

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International Standard Book Number 0-8493-8732-9

Library of Congress Card Number 00-034234

Printed in the United States of America 1 2 3 4 5 6 7 8 9 0

Printed on acid-free paper

Preface

Since its discovery in 1957 by Crane and associates, coenzyme Q (CoQ, ubiquinone Q₁₀) has become the subject of extensive studies in bioenergetics. This resulted in the discovery of its unique and remarkable role in energy production in mitochondria. The ubiquitous presence of CoQ in essentially all types of intracellular membranes and lipoproteins suggests that there are additional roles for CoQ in cellular biochemical pathways associated with its redox properties. One such role is that, in its reduced form, CoQ acts as an electron donor to reduce reactive chain-initiating and chain-propagating radicals, i.e., functions as a radical scavenger or chain-breaking antioxidant. Later findings implicated CoQ in extramitochondrial electron-transport systems, demonstrating its utility as a universal redox component. Since a variety of biological functions depend on CoQ, the question of deficiency or dysregulation leading to pathological states can be raised. Because of this, an emphasis was put on tissue levels of CoQ in maintaining health and its possible roles in disease.

This volume attempts to summarize the latest developments in these very different areas of CoQ research. It covers a broad spectrum of different fields in which CoQ represents a subject of investigation—from physical chemistry and biophysics through biochemistry, molecular biology, and cell biology to nutritional sciences, medical applications, and geriatrics. Not surprisingly, levels and depth of mechanistic understanding and description of CoQ's different effects are radically different in these different fields and this is reflected in the chapters into which this book has been divided.

Another specific feature of the book is the widespread geography of contributing authors, with all corners of the globe being represented. This reflects not only a wide-ranging geographic interest in research on CoQ, but also provides a number of the heterogeneous approaches and styles reflected in the chapters in the volume. An international team of experts joined forces to produce a work that addresses the major facets of CoQ research and creates a must-have resource for researchers in the field. With this understanding, the editors did not attempt to make the volume more uniform at the expense of losing the bright and colorful originality furnished by selected contributors—all experts in their respective fields. Instead, the editors believed that the most essential goal is a balanced approach encompassing the most important achievements in the field.

Hands-on experts describe in detail the key findings, discoveries, and concepts in different aspects of CoQ research. Therefore, the reader will find chapters describing the topography and behavior of CoQ in membranes (P. Quinn and G. Lenaz) as well as its most essential antioxidant chemical properties (K. Mukai). This is followed by wonderfully presented contemporary ideas on the bioenergetic mechanisms for CoQ in mitochondria (P.L. Dutton et al.). New concepts on extramitochondrial functions of CoQ (in plasma membranes and lysosomes) are discussed in two chapters (P. Navas et al. and H. Nohl and L. Gille). Recent discoveries in biosynthetic pathways for CoQ based on molecular genetic approaches are presented in the chapter by C. Clarke and T. Jonassen. Several chapters are dedicated to detailed descriptions of the antioxidant mechanisms of CoQ in membranes. These include considerations of antioxidant dynamics of CoQ in membranes (E. Niki), its special role in antioxidant protection of lipoproteins (S.R. Thomas and R. Stocker), and its antioxidant interactions with vitamin E (V. Kagan et al.). The chapter by H. Nohl et al. demonstrates that, despite an almost unequivocally accepted antioxidant role for CoQ, there is still enough room for further research as it identifies conditions under which CoQ may become a source of reactive oxygen species rather than their scavenger. A special chapter is focused on biochemical and pharmacological properties of CoQ analogs (A. Mordente et al.)

As a transition to the health effects of CoQ, C. Weber reviews issues related to dietary intake and sources of CoQ. Important methodological information on assays and handling of samples for CoQ analysis can be obtained in the chapter presented by Rousseau et al.. Additionally, three chapters are focused on plasma levels of CoQ as potential markers of abnormal status of the organism, i.e., disease. In fact, chapters by A. Kontush, Y. Yamamoto and S. Yamashita, and J.B. Ubbink describe the potential use of CoQ measurements as diagnostic predictors of disease.

Several chapters discuss health effects of CoQ in experimental conditions (animal studies) or in clinical settings (chapters by D. Das and H. Otani, Alho et al., A. Gvozdjakova and K. Jarmila, and G.P. Littaru and M. Battino). The role of CoQ in liver diseases is presented in two chapters discussing alcohol-induced liver injury (S. Eaton et al.) and liver carcinogenesis (P. Stal and J.M. Olsson).

Special attention was paid to an issue of potential benefits that CoQ supplementation may offer in sport and physical exercise (C. Malm and M. Svensson, T.J. Vasankari and Ahotupa, and J. Faff). Finally, relationships between CoQ and longevity are the subject of the chapter written by H. Alho and K. Lonrot.

While studies of CoQ mechanisms in mitochondrial energy production have been recognized by Peter Mitchell's 1978 Nobel Prize for chemistry, many essential mechanistic details have become more evident now. Some of the earlier outstanding contributors to the subject, such as Karl Folkers and Lars Ernster, have now left the field to be replaced by new talents striving to discover and learn about other functions of CoQ. It is this still-incomplete knowledge of biosynthesis, transport, delivery, biochemical pathways, and pathological dysregulation of CoQ that limits its effective use in health and disease. We hope that the summary of CoQ research contained in this volume will contribute to furthering our understanding of its role and functions and stimulate further research critical for future applications.

Valerian Kagan and Peter Quinn

About the Editors

Valerian E. Kagan received his Ph.D. degree in biochemistry and biophysics from M.V. Lomonosov Moscow State University, and his D.Sc. degree from the USSR Academy of Sciences, Moscow. In 1983, Dr. Kagan was awarded the State Prize of the USSR for science. From 1976 through 1983, Dr. Kagan was an associate research professor at M.V. Lomonosov Moscow State University in Moscow, and from 1983 to 1989 he was a research professor and head of the Membrane Biostabilization Group in the Institute of Physiology Sofia (Bulgaria). Dr. Kagan was an associate research biochemist in the Department of Molecular and Cell Biology at the University of California, Berkeley, and a visiting scientist at Lawrence Berkeley Laboratory. Since 1992, Dr. Kagan has been an associate professor of environmental and occupational health, and of pharmacology at the University of Pittsburgh. He is also a member of the University of Pittsburgh Cancer Institute and holds a visiting professorship at King's College, London.

Dr. Kagan's research interests are focused on free radicals and antioxidants in biology and medicine, genotoxicity of free radicals, oxidative stress mechanisms in apoptosis, and biochemistry of nitric oxide. He has published more than 300 papers in peer-reviewed journals.

Peter J. Quinn, Ph.D., is currently professor of biochemistry at King's College, London, where he heads a research team using a range of biophysical methods to investigate the structure of biological membranes and their constituents. One of Dr. Quinn's particular interests is in the interaction of coenzyme Q and vitamin E with the membrane lipid matrix. His undergraduate degree was obtained from the University of Melbourne, and his postgraduate degrees from the University of Sidney and London University. He holds a visiting professorship at the University of Pittsburgh and Robert Gordon University.

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PART 1

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