MITOCHONDRIA

Bioenergetics, Biogenesis and Membrane Structure

Edited by

LESTER PACKER

ARMANDO GÓMEZ-PUYOU

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Lester Packer
Membrane Bioenergetics Group
Lawrence Berkeley Laboratory
University of California and the
Department of Physiology-Anatomy
Berkeley, California

Armando Gómez-Puyou
Departamento de Biología
Universidad Nacional Autónoma de México
México

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LIST OF CONTRIBUTORS

Diana S. Beattie
Department of Biochemistry, Mt. Sinai School of Medicine, The City University of New York, New York 10029

M. Beigel
Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico

Gerald P. Brierley
Department of Physiological Chemistry, College of Medicine, Ohio State University, Columbus, Ohio 43210

Aurora Brunner
Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico

Ernesto Carafoli
Laboratorium fur Biochemie, Eidgenossische Technische Hochschule, Zurich, Switzerland

Jorge Cerbón
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

G.S. Cobon
Department of Biochemistry, Monash University, Clayton, Victoria 3168, Australia

P.D. Crowfoot
Department of Biochemistry, Monash University, Clayton, Victoria 3168, Australia

A. Darszon
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

Sergio Estrada-O
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

P.A. George Fortes
Department of Biology, University of California, San Diego, La Jolla, California 92037

Carlos Gitler
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

Carlos Gómez-Lojero
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

A. Gómez-Puyou
Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico

M. Tuena de Gómez-Puyou
Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico

David E. Griffiths
Department of Molecular Sciences, University of Warwick, Coventry CV4 7AL, England

Peter C. Hinkle
Department of Biochemistry and Molecular and Cell Biology, Cornell University, Ithaca, New York 14853

Alec D. Keith
Department of Biophysics, Pennsylvania State University, University Park, Pennsylvania 16802

M. Klingenberg
Institut fur Physiologische Chemie und Physikalische Biochemie, Universitat Munchen, 8000 Munchen 15, Germany

Amira Klip
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

Kathryn F. LaNoue
Department of Physiology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, Pennsylvania 17033

A.W. Linnane
Department of Biochemistry, Monash University, Clayton, Victoria 3168, Australia

G.J.M. Lauquin
Laboratoire de Biochimie, Dept. de Recherche Fondamentale, Centre d'Etudes Nucleaires, 38041 Grenoble CEDEX, France

Henry R. Mahler
Department of Chemistry, Indiana University, Bloomington, Indiana 47401

S. Marzuki
Department of Biochemistry, Monash University, Clayton, Victoria 3168, Australia

R.J. Mehlhorn
Membrane Bioenergetics Group, Energy and Environment Division, Lawrence Berkeley Laboratory, University of California, Berkeley, Berkeley, California 94720

M. Montal
Departamento de Bioquimica, Centro de Investigacion y de Estudios Avanzados, Instituto Politecnico Nacional, Mexico 14, D.F., Mexico

Lester Packer
Membrane Bioenergetics Group, Energy and Environment Division, Lawrence Berkeley Laboratory, University of California, Berkeley, Berkeley, California 94720

Antonio Peña
Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico

A. Rendón
Department of Physiology-Anatomy, University of California, Berkeley, Berkeley, California 94720
On Leave From: Centre de Neurochimie, C.N.R.S., Strasbourg 6700, France

A. Scarpa
Johnson Research Foundation, University of Pennsylvania, Philadelphia, Pennsylvania 19174

Harold M. Tinberg
Physiology Research Laboratory, Veterans Administration Hospital, Martinez, California 94553

Marc E. Tischler
Department of Physiology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, Pennsylvania 17033

Alexander Tzagoloff
Public Health Research, Institute of the City of New York, New York, New York 10016

P.M. Vignais
Laboratoire de Biochimie, Dept. de Recherche Fondamentale, Centre d'Etudes Nucleaires, 38041 Grenoble CEDEX, France

P.V. Vignais
Laboratoire de Biochimie, Dept. de Recherche Fondamentale, Centre d'Etudes Nucleaires, 38041 Grenoble CEDEX, France

J.R. Williamson
Johnson Research Foundation, University of Pennsylvania, Philadelphia, Pennsylvania, 19174

PREFACE

The chapters in this book comprise the main lectures of an advanced course on the biogenesis, structure, and function of mitochondria that was sponsored by the Instituto de Biologia of the Universidad Nacional Autonoma de México in June, 1975. The lectures were imparted at the Instituto de Biología and at the Instituto de Investigaciones Biomédicas at the UNAM and at the Centro de Investigaciones y Estudios Avanzados, IPN in Mexico City.

It is now clear that only the joint efforts of researchers of a wide variety of disciplines will lead to a full understanding of mitochondria. The book is divided into three sections. Parts I and II cover many of the important approaches to the study of mitochondrial bioenergetics and biogenesis. These chapters are written to provide students of bioenergetics and other fields with an adequate background of the subject as well as with some of the more recent findings of the authors' laboratories. In Part III, membrane structure is emphasized.

During the two weeks of this course, it was recognized that a satisfactory comprehension of the molecular events that occur in mitochondria appears to be in sight. The basic questions are now well defined, and diffent and powerful methodologies are being applied to explore the various facets of the same problem. Therefore, it would seem that the answers to these questions will be the consequence of further experimentation, and in some cases of an improvement of present day methodology. In other words, a proper understanding of the molecular events that occur in mitochondria is now on the horizon.

The Editors are very much indebted to Dr. José Laguna for his encouragement and support in the developing of this course. We are also grateful to Dr. Antonio Peña for his collaboration in the organization of the meeting. We thank Ms. Yolanda Díaz D'Castro for her assistance in solving many of the administrative problems. We are also indebted to Ms. Sharon Anderson for faithfully and carefully assisting with the preparation of the chapters for publication, for editorial assistance, and for interfacing the contents with the publishers. We thank Dr. Alvaro Rendon for assisting in communications between the Editors and for his counsel with the assistance of Rosa Laura Oropeza-Rendón on the indexing of the book. The Editors also acknowledge the finan-

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Lester Packer
Armando Gómez-Puyou

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PART I
BIOENERGETICS

A substantial amount of effort has been expended in the past in attempts to ascertain the molecular mechanism of oxidative phosphorylation. While a completely satisfactory explanation for this process has not yet emerged, it has become apparent that phosphorylation is intimately related to numerous transport processes which take place across the inner membrane of the mitochondrion. Therefore, a complete picture of mitochondrial energy coupling must include not only a molecular mechanism for ATP formation, but also a mechanistic description of the transport reactions. In addition, the role of the transport reactions in metabolic regulation and communication between the mitochondrial and extra-mitochondrial compartments of the cell must be specified if we are to understand how mitochondrial oxidative phosphorylation is integrated into cellular metabolism

These objectives are currently being pursued by a number of laboratories and the variety of experimental approaches reflects the appeal of these questions to investigators in widely different disciplines. The chapters in this section illustrate the progress which has been made in establishing the characteristics of the transport reactions, in isolation and characterization of both transport and phosphorylation components, and in reconstitution of reactions from purified components.

MONOVALENT CATION TRANSPORT BY MITOCHONDRIA

Gerald P. Brierley

Although there is still no general consensus as to the mechanism of oxidative phosphorylation, it has become increasingly clear that the movement of ions across the mitochondrial membrane is intimately associated with the process of energy coupling. Mitochondria exchange substrate anions, inorganic phosphate (Pi), and adenine nucleotides across the inner membrane (Fig. 1) on a series of exchange-diffusion carriers [1] and the anion gradients thus produced, in conjunction with proton and cation movements, combine to provide a capacity for production of both pH gradients and potential differences between the mitochondrial matrix and extramitochondrial compartments [2,3]. If these gradients are not indeed the primary mode of energy coupling as suggested by Mitchell [2], they are at least in close communication with the primary coupling process. Early studies recognized that mitochondria could retain certain ions against concentration gradients and expend energy to accumulate others (see Ref. [4] for a review of the earlier literature), but recent intense interest in mitochondrial ion transport has stemmed largely from the predictions of the Mitchell hypothesis [2,3] and from a series of observations on mitochondrial divalent cation accumulation [4]. These studies revealed that impressive amounts of Ca^{+2}, Mn^{+2}, and Mg^{+2} could be accumulated at rapid rates and that the reaction was supported by an intermediate state or condition prior to the production of ATP in the phosphorylation process. A capacity for extensive uptake of monovalent cations upon the addition of inducing agents (ionophores), such as valinomycin, was demonstrated shortly thereafter (see [5] for a review), and much recent interest has centered on the high rates of monovalent cation uptake which result in the presence of these reagents. Rapid uptake of monovalent cations in the absence of ionophores can also be obtained when mitochondria are suspended in isotonic acetate or phosphate salts [6]. In addition to these ion uptake reactions, which are characterized by deposition of phosphate salts of divalent cations and by osmotic swelling when soluble ion pairs are accumulated, swollen mitochondria