PRINCIPLES OF MEDICAL BIOLOGY

Edited by

E. EDWARD BITTAR
NEVILLE BITTAR

CELL CHEMISTRY AND PHYSIOLOGY: PART I

Cell Chemistry and Physiology: Part I

PRINCIPLES OF MEDICAL BIOLOGY
A Multi-Volume Work, Volume 4

Editors: **E. EDWARD BITTAR,** *Department of Physiology,*
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Principles of Medical Biology
A Multi-Volume Work

Edited by **E. Edward Bittar,** *Department of Physiology, University of Wisconsin, Madison* and
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This work in 25 modules provides:

- A holistic treatment of the main medical disciplines. The basic sciences including most of the achievements in cell and molecular biology have been blended with pathology and clinical medicine. Thus, a special feature is that departmental barriers have been overcome.
- The subject matter covered in preclinical and clinical courses has been reduced by almost one-third without sacrificing any of the essentials of a sound medical education. This information base thus represents an integrated core curriculum.
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- There are increasing indications that the traditional education system in which the teacher plays the role of expert and the student that of a passive learner is undergoing reform in many medical schools. The trend can only grow.
- Medical biology as the new profession has the power to simplify the problem of reductionism.
- Over 700 internationally acclaimed medical scientists, pathologists, clinical investigators, clinicians and bioethicists are participants in this undertaking.

The next seven physical volumes are planned for Fall 1996.

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JAI PRESS, INC.

Greenwich, Connecticut *London, England*

Library of Congress Cataloging-in-Publication Data

Cell chemistry and physiology / edited by E. Edward Bittar, Neville
Bittar.
p. cm.—(Principles of medical biology ; v. 4)
Includes index.
ISBN 1-55938-805-6
1. Cytochemistry. 2. Cell physiology. I. Bittar, E. Edward.
II. Bittar, Neville. III. Series.
[DNLM: 1. Cells—chemistry. 2. Cells—physiology. QH 581.2 C392
1995]
QH611.C4214 1995
574.87—dc20
for Library of Congress 94-37215
CIP

55 Old Post Road No. 2
Greenwich, Connecticut 06836

JAI PRESS LTD.
The Courtyard
28 High Street
Hampton Hill, Middlesex TW12 1PD
England

ISBN: 1-55938-805-6

Library of Congress Catalogue Number: 95-33561

Manufactured in the United States of America

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PREFACE

This is the first of a 4-volume module that is an introduction to the study of cell chemistry and physiology. It is not intended to be encyclopedic in nature but rather a general survey of the subject with an emphasis on those topics that are central to an understanding of cell biology and those that are certain to become of increasing importance in the teaching of modern medicine.

We have followed what appeared to us to be the logical divisions of the subject beginning with proteins. Allewell and her colleagues stress the point that proteins fold spontaneously to form complex three-dimensional structures and that some of them unfold with the help of proteins called chaperones. Michaelis-Menten kinetics are shown by Nelsestuen to describe the behavior of enzymes in the test tube. The formalism is particularly useful in the search for agents of therapeutic value, as exemplified by methotrexate. Uptake by mammalian cells of substrates and their metabolic conversions are discussed by van der Vusse and Reneman. However, both Welch and Savageau expound the view that the cell is not simply a bagful of enzymes. The biologist is urged by Savageau to abandon Michaelis-Menten formalism and apply the Power Law. The biologist is also told that the approach to arriving at a theory of metabolic control would have to be one of successive approximations requiring the use of the computer. Information gained from comparative biochemistry is shown by Storey and Brooks to have shed new light on mechanisms of metabolic rate depression and freeze tolerance, and to be applicable to organ transplantation technology. We are reminded that enzyme adaptation is partly the result of the presence of a hydrating shell of vicinal water that stabilizes conformation of the enzyme. Vicinal water, according to Drost-Hansen and Singleton, lies adjacent to most solids and protein interfaces. The kinks or breaks observed in the slope of the Arrhenius plot are attributed to structural changes in vicinal water. Regulation of cell volume is shown by Hempling to involve regulation of cell water. It could be that the osmo-receptor or volume detection system is a protein that links the cytoskeleton to specific K and Cl channels. Additionally, it is interesting that aquaporins, which are water channel-forming membrane proteins, are now known to exist in both renal and extra-renal tissues. One of the renal porins is affected by vasopressin.

We then pass on to protein synthesis (Rattan) and other important topics including protein glycosylation (Hounsell), methylation (Clarke), ADP-ribosylation (Pearson) and prenylation (Gelb). Among the four types of lipids attached to membrane proteins are the prenyl groups. Ford and Gross in their chapter on lipobiology drive home the point that there is an accumulation of acyl carnitine and lysophospholipids during myocardial infarction.

It goes without saying that we owe these scientists a special debt of gratitude for their scholarly contributions. We also take this opportunity of thanking the editorial and production staff members of JAI Press for their courtesy and skill.

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Chapter 1

Proteins: An Introduction

NORMA M. ALLEWELL, VINCE J. LICATA, and XIAOLING YUAN

Principles of Medical Biology, Volume 4
Cell Chemistry and Physiology: Part I, pages 1–23

ISBN: 1-55938-805-6

INTRODUCTION

Functions of Proteins

Proteins are the molecular machines of the cell. Without enzymes and their cofactors, none of the reactions of cellular metabolism would occur on a time scale that could sustain life as we know it. Enzymes catalyze the reactions that generate the DNA and proteins of chromatin, the primary genetic material of the cell. They transcribe RNA from DNA and catalyze the synthesis of the lipids and proteins of cell membranes and the carbohydrates of the cell surface. Membrane proteins signal the presence of hormones and pump ions through membranes; they also recognize other cells, viruses, bacteria, and macromolecules, and trigger cellular responses to those recognition events. The proteins of the cytoskeleton serve both active and passive roles, moving cellular organelles and the cell itself, and forming the scaffold against which such movement is leveraged. DNA- and RNA-binding proteins regulate gene expression by binding to specific nucleotide sequences.

Often a single protein is responsible for the primary function of highly specialized cells; for example, actomyosin in muscle mediates muscle contraction, rhodopsin in the eye absorbs light, and hemoglobin in red blood cells binds and transports oxygen. Specific proteins on the surface of nerve cells recognize neurotransmitters and generate nerve impulses. Specific proteins on the surface of cells of the immune system bind foreign antigens and initiate the immune response.

Proteins need not be contained within a cell in order to play a physiological role. Extracellular proteins break down macromolecules in the intestine, and bind and transport materials in the blood. The proteins of the extracellular matrix provide the framework upon which tissues are laid down. Antibodies in blood recognize and bind foreign antigens. Viral coat proteins package the nucleic acids of viruses. Proteins secreted by foreign organisms sometimes trigger dramatic physiological reactions such as those produced by toxic shock protein and cholera toxin from bacteria.

The seemingly bewildering array of protein functions can be simplified by noting that proteins fall into a few major functional classifications:

1. *Enzymes* such as DNA polymerase, papain and other digestive enzymes, and all of the enzymes of intermediary metabolism.
2. *Binding proteins* such as hemoglobin and myoglobin, antibodies, and cell surface receptors.
3. *Signaling proteins* such as insulin and other polypeptide hormones.
4. *Structural proteins* such as collagen in connective tissue and keratin in hair and nails.