Subcellular Biochemistry

Volume 6

Edited by

Donald B. Roodyn

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Aims and Scope

SUBCELLULAR BIOCHEMISTRY aims to bring together work on a wide range of topics in subcellular biology in the hope of stimulating progress towards an integrated view of the cell. In addition to dealing with conventional biochemical studies on isolated organelles, articles published so far and planned for the future consider such matters as the genetics, evolution, and biogenesis of cell structures, bioenergetics, membrane structure and functions, and interactions between cell compartments, particularly between mitochondria and cytoplasm and between nucleus and cytoplasm.

Articles for submission should be sent to Dr. D. B. Roodyn, Department of Biochemistry, University College London, Gower Street, London WCIE 6BT, U.K., and are best sent in the period February to April inclusive of each year. There are no rigid constraints as to the size of the articles and in general they should be between 9,000 and 36,000 words, with an optimum size of about 20,000 words. Although articles may deal with highly specialized topics, authors should try as far as possible to avoid specialist jargon and to make the article as comprehensible as possible to the widest range of biochemists and cell biologists. Full details of the preparation of manuscripts are given in a comprehensive Guide for Contributors which is available from the Editor or Publishers on request.

Preface

This volume continues the tradition of *SUBCELLULAR BIOCHEMISTRY* of trying to break down interdisciplinary barriers in the study of cell function and of bringing the reader's attention to less well studied, but nevertheless useful, biological systems.

We start with an extensive article by T. P. Karpetsky, M. S. Boguski and C. C. Levy on the structure, properties and possible functions of polyadenylic acid. Apart from revealing a general lack of appreciation of many important aspects of the chemical properties of polyadenylic acid, the literature also shows that there is a great gulf between those who study the biological role of polyadenylic acid and those who study its physicochemical properties. The article by Karpetsky and his colleagues is an attempt to overcome this lack of communication and to present an integrated view of the subject. The authors go into the subject in full detail and the more biologically inclined reader may on occasion have to reread his nucleic acid physical chemistry notes! However, the effort is worthwhile and the article is a timely reminder that we cannot treat nucleic acids as mere abstractions, but that they are complex organic macromolecules capable of equally complex, but nevertheless important, interactions.

The next article is by J. Steensgaard and N. P. Hundahl Møller and deals with computer simulation of density gradient centrifugation systems. From the rather early "hit and miss" bulk fractionation schemes, preparative centrifugal fractionation of cell homogenates has now developed into a rigorous and technically sophisticated discipline. The fact that many centrifugation procedures can now be accurately represented by computer models is a great advance. Apart from the convenience it provides of being able to carry out "dummy" runs without actually wasting precious biological material, the fact that the major parameters in the system can be quantified and handled in this way puts centrifugal fractionation on a much more sound theoretical basis. It is to be hoped that Steensgaard and Hundahl Møller's article will stimulate as much as it simulates.

The next article by U. C. Knopf deals with crown-gall tumors in general as well as the specific role of *Agrobacterium tumefaciens*. From relatively obscure beginnings, the subject is becoming more generally recognized as a most interesting experimental system for studying the induction of tumors. It is also becoming clear that there are some similarities between the processes involved in the action of *Agrobacterium tumefaciens* and of the nitrogen-fixing bacteria, particularly the *Rhizobia*. The famous root nodules of the nitrogen-fixing legumes are in fact "benign" nodules, perhaps different only in degree from the massive crown-galls. We thus have a most interesting comparative system of "benign" and "malignant" growth, and we can only hope, with the author, that the medical implications will not be lost just because the systems are found in plants and not in mice.

We next turn to another system that has only recently achieved the full interest and recognition that it deserves. This is the so-called "petite" mutation in yeast, and it is described in detail by P. A. Whittaker. Although the existence of "petites" was known for years amongst yeast geneticists, it was only with the explosive development of research in mitochondrial biogenesis in the last five years that the full significance of the "petite" mutation became widely appreciated. Mitochondrial genetics has now become a major discipline in its own right, with its own terminology and expertise. It is to be hoped that Whittaker's article will help to guide the reader through some of the intricacies of this new methodology.

The next article by G. Lenaz looks at some fundamental aspects of the role of lipids in cell membranes. In a detailed and extensive article, the author identifies five major roles for lipids in biomembranes. They act as binding surfaces for proteins, they are needed to separate aqueous compartments so as to allow vectorial processes to take place, they provide a hydrophobic milieu for reactions that require one, they are required for the formation of membranes from dissociated subunits, and finally they can act as modulators of membrane-bound enzymes. As with the article by Karpetsky and colleagues, this article delves into fundamental physicochemical aspects of the molecular entities involved and the reader is continually reminded that membranes are not abstractions but are made from very real molecules that have their own inherent chemical properties, a knowledge of which can greatly help in our understanding of the behavior of biological membranous assemblies.

The next article is by F. L. Crane, H. Goldenberg, D. J. Morré, and H. Löw and deals with the dehydrogenases of the plasma membrane. As the detailed tables presented by the authors clearly show, there is now overwhelming evidence for the existence of a range of dehydrogenases in plasma membranes isolated from a variety of cell types. Just as it took some time to appreciate the fact that the mitochondrial membrane is not the only site for linked respiratory activity and the "microsomal" respiratory chain is a complex system in its own right, so we must now generalize the picture even further, and think in terms of other membrane systems having bound respiratory enzymes, performing functions specific to the membrane in which they are found. The authors discuss several interesting ways in which plasma membrane dehydrogenases can act, for example, in redox control of the formation or breakdown of cyclic nucleotides. From primitive views of membrane-bound respiratory enzymes being solely involved in mitochondrial processes, we must now develop much more sophisticated attitudes toward the cellular role of "intrinsic" dehydrogenases, perhaps almost to the point of believing that the mitochondrion is really only a "special case" in which bound redox systems happen to be linked to the production of ATP.

The last article is by N. Lakshminarayanaiah and is entitled "Transport Processes in Membranes: A Consideration of Membrane Potential across Thick and Thin Membranes." Here we are hoping to bridge yet another unfortunate interdisciplinary gap, namely that between biophysicists and biochemists. One of the most important consequences of the famous chemi-osmotic theory of Mitchell is that biochemists have come to realize that the ion transport and membrane potential phenomena studied so eruditely and mathematically by biophysicists are in fact closely interconnected with the respiratory and bioenergetic properties of cell membranes. It is as if there has been a sudden realization that the term "membrane" as used by biophysicists is not some abstract concept or barrier, but refers in reality to *actual* membranes in real cells. Unfortunately, the mathematical rigor of the biophysical approach has not yet fully spilled over into biochemical membranology. Perhaps the phenomena under study are too complex to be represented by formal equations. Nevertheless, any attempt to propagate rigorous attitudes in cell biochemistry is surely to be encouraged, and it is to be hoped that Lakshminarayanaiah's article will demonstrate the remarkable extent to which "classical" physicochemical theory can be applied to the study of biomembranes.

As in previous volumes of *SUBCELLULAR BIOCHEMISTRY* we end with an account of recent books in cell biochemistry and biology. We discuss a number of texts in membrane research, organelle biochemistry, and plant biochemistry as well as some educational texts and once again hope that we are of some use in guiding the reader through the very extensive literature currently published in the overall field of cell biology.

D. B. Roodyn

London

Contents

Chapter 1

Structures, Properties, and Possible Biological Functions of Polyadenylic Acid

Timothy P. Karpetsky, Mark S. Boguski, and Carl C. Levy

Chapter 2

Computer Simulation of Density-Gradient Centrifugation

Jens Steensgaard and Niels Peter Hundahl Møller

Chapter 3

Crown-Gall and *Agrobacterium tumefaciens:* Survey of a Plant-Cell-Transformation System of Interest to Medicine and Agriculture

U. C. Knopf

Chapter 4

The Petite Mutation in Yeast

Peter A. Whittaker

Chapter 5

The Role of Lipids in the Structure and Function of Membranes

Giorgio Lenaz

Chapter 7

Transport Processes in Membranes: A Consideration of Membrane Potential across Thick and Thin Membranes

N. Lakshminarayanaiah

Chapter 1

Structures, Properties, and Possible Biologic Functions of Polyadenylic Acid

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1. INTRODUCTION

Our original interest in preparing this review lay in the fact that no one had presented a thorough examination of the topic, with particular attention to the *several* possible biological functions of polyadenylic acid [poly(A)]. However, as we scrutinized the literature, one point cropped up repeatedly: those engaged in research efforts aimed at clarifying the physiological significance of poly(A) did not make full use of the current body of knowledge concerning the chemical properties of the homopolymer. Similarly, results of experiments that clarify aspects of the physical nature of poly(A) were never interpreted in terms of intracellular functions. Thus, two vast bodies of literature exist in roughly equal proportions, one con-

The MEDLINE computer service of the National Library of Medicine, Bethesda, Maryland, and the CHEMCON data base (BRS, Inc., Schenectady, New York) were utilized to compile the initial bibliography on poly(A), consisting of articles published between 1966 and February 1977. The literature survey for this review was completed in July 1977.

Abbreviations used in this chapter: (CD) circular dichroism; (cDNA) complementary DNA; (DEAE) diethylaminoethyl; (DMSO) dimethylsulfoxide; (ESR) electron spin resonance; (HnRNA) nuclear heterogeneous RNA; (mRNA) messenger RNA; (mRNP) ribonucleoprotein complex; (NMR) nuclear magnetic resonance; [oligo(dT)] oligodeoxythymidylic acid; (ORD) optical rotatory dispersion; [poly(A)] polyadenylic acid; [poly(C)] polycytidylic acid; [poly(dT)] polydeoxythymidylic acid; [poly(G)] polyguanylic acid; [poly(U)] polyuridylic acid; (rRNA) ribosomal RNA; (SDS) sodium dodecyl sulfate; (tRNA) transfer RNA.