

CELL PHYSIOLOGY OF NEOPLASIA

*A Collection of Papers Presented at the Fourteenth Annual
Symposium on Fundamental Cancer Research, 1960*

PUBLISHED FOR
THE UNIVERSITY OF TEXAS M. D. ANDERSON
HOSPITAL AND TUMOR INSTITUTE



UNIVERSITY OF TEXAS PRESS, AUSTIN

CELL PHYSIOLOGY OF NEOPLASIA

A Collection of Papers Presented at the Symposium on
Neoplasia and Tumor Biology, Houston, Texas, 1960

EDITED BY

THE UNIVERSITY OF TEXAS M. D. ANDERSON HOSPITAL
AND TUMOR INSTITUTE

Library of Congress Catalog Card No. 60-53251
© 1960 by The University of Texas M. D. Anderson Hospital
and Tumor Institute, Houston, Texas

Manufactured in the United States of America
by the Printing Division of The University of Texas

**CELL PHYSIOLOGY
OF
NEOPLASIA**

Acknowledgment

The staff of The University of Texas M. D. Anderson Hospital and Tumor Institute gratefully acknowledges the assistance of the National Science Foundation; the American Cancer Society, Texas Division; the Bertner Foundation; the Heuermann Foundation; and the State of Texas Department of Health, for providing funds for support and publication of this symposium.

Gratitude is expressed also to the members of the 1960 symposium committee for their efforts in arranging the program. Members of the committee were T. C. Hsu, chairman, T. S. Painter, honorary chairman, Joe E. Boyd, Jr., Jeffrey P. Chang, Leon L. Dmochowski, Felix L. Haas, Saul Kit, and H. Grant Taylor.

This symposium volume was edited and arranged for publication by the following members of the Publications Department: Russell W. Cumley, Marilyn Abbott, and Joan McCay.

The book was produced by Joan McCay.

Finally, the staff acknowledges The University of Texas Press and the Printing Division of The University of Texas for their fine cooperation in the publication of this volume.

Table of Contents

Introduction	3
<u>R. LEE CLARK, JR.</u>	
<i>The Nucleus</i>	
Chromosome Behavior in Tumors: Readjustments to Boveri's Theory	9
P. C. KOLLER	
Discussion	38
K. BAYREUTHER	
Sex Chromosomes in Malignancy, Transplantability of Growths, and Aberrant Sex Determination	49
GEORGE YERGANIAN, REI KATO, MARY J. LEONARD, HENRY J. GAGNON, and LULU A. GRODZINS	
Experimental Studies on Malignant Nucleoli	97
M. J. KOPAC	
Electron Microscopy of the Nuclear Envelope	129
MICHAEL L. WATSON	
<i>The Cytoplasm</i>	
Morphology and Physiology of the Golgi Complex	161
ALBERT J. DALTON	

Morphology of Cell Constituents in Tumors of Viral Origin	185
L. DMOCHOWSKI, C. E. GREY, SARAH E. STEWART, BERNICE E. EDDY, BEN R. BURMESTER, and WILLARD G. WALTER	

Enzyme Localization in Tumor Cells	219
ALEX B. NOVIKOFF	

Relations Between Nucleus and Cytoplasm in Normal and Malignant Growth	269
TORBJÖRN CASPERSSON, LORE VOGT-KÖHNE, and OLLE CASPERSSON	

Nucleic Acids

Deoxyribonucleic Acid (DNA) Variations in Neoplastic and Virus-Infected Cells: A Cytochemical and Cytopatho- logical Study	295
CECILIE LEUCHTENBERGER and RUDOLF LEUCHTEN- BERGER	

Studies on the Structure, Composition, and Metabolism of Tumor RNA	337
SAUL KIT	

The Biochemistry of Ribonucleotides and Ribonucleic Acid in Normal and Malignant Cells	374
WILLIAM S. BECK	

Biological Activity of Ribonucleic Acids of Viral Origin	407
JOHN S. COLTER and KAY A. O. ELLEM	

Bertner Foundation Lecture

The Lives of Cancer Cells	435
E. V. COWDRY	

Cell Growth and Cell Development

Histochemical Study of Enzymatic Behavior in Cells of Rat Livers During the Early Stage of Carcinogenesis Induced by 3'-Methyl-4-Dimethylaminoazobenzene and N-2-Flu- orenyldiacetamide	471
JEFFREY P. CHANG	

Nuclear Physiology in Adenocarcinoma of the Amphibia WILLIAM R. DURYEE	501
Growth and Chromosome Studies on Drug Resistant Lines of Cells in Tissue Culture	524
MORGAN HARRIS and FRANK H. RUDDLE	
Duplication of Chromosomes and Related Events in the Cell Cycle	547
J. HERBERT TAYLOR	
Mitosis and Cytodifferentiation	576
RIOJUN KINOSITA and SUSUMU OHNO	
An Attempt to Determine the Developmental Potentialities of the Cancer Cell Nucleus by Means of Transplantation .	591
THOMAS J. KING and ROBERT GILMORE MCKINNELL	
<i>Summary and Perspectives</i>	
Problems and Perspectives in Cellular Biology . . .	621
M. J. KOPAC	
Index	639

CELL PHYSIOLOGY OF NEOPLASIA

Introduction

R. LEE CLARK, JR., M.D., M.Sc., D.Sc. (HON.)

Director and Surgeon-in-Chief,

*The University of Texas M. D. Anderson Hospital
and Tumor Institute,
Houston, Texas*

WITH RECENT ACCOMPLISHMENTS in various fronts of cancer research, it is reasonable to predict that we are at the threshold of being able to unify many theories of carcinogenesis. Much of this progress has resulted from a cooperative approach among the various disciplines involved. Through such an approach, specialized information from other disciplines is available for a particular problem. This is precisely the incentive for the annual symposia on fundamental cancer research; namely, to review one timely facet of our knowledge that bears close relationship to cancer, to bring this facet up-to-date through review by various workers, and to exchange ideas through discussions of the points at issue. By such speculation and discussion, a means is provided for workers in the various disciplines of research to coordinate their efforts toward a solution of the problem of cancer.

The topic of this Fourteenth Annual Symposium on Fundamental Cancer Research is Cell Physiology of Neoplasia. Each of the distinguished investigators will report on the part of cell physiology that he knows best because he personally has explored it and has furthered our insight into how these problems relate to cancer.

In 14 years this annual symposium has grown from a small local meeting to become a conference whose speakers and audience attend from all areas of the United States and from a number of

foreign countries. The first symposium was held in 1946, but not until 1952, at the sixth symposium, did the program begin to point up one central theme. That year the theme was "Nutritional Factors." In succeeding years, symposia were held on "New Methods of Microscopy and Cell Research," "Tissue Culture," "Histochemistry," "Nucleic Acid Metabolism," "Viruses and Tumor Growth," "Radiation Biology and Cancer," and, last year, "Genetics and Cancer."

The papers presented at these meetings have grown in scope and volume to such an extent that they merit publication in a separate monograph series. Collected papers from the 1959 symposium, *Genetics and Cancer*, were published nine months after the meeting was held, and we hope to continue rapid publication of the symposium proceedings. The present volume, *Cell Physiology of Neoplasia*, is the fourth monograph in the series.

Cell physiology is but one of the many phases of cancer research that are in progress throughout the world. Working on the hypothesis that the laws of chemistry and physics govern the activities of individual cells, cytologists have unraveled many of the mysteries of the cell's activities. Today cytologists study not just morphology and fine structure of cell components, but also their function in relation to cell metabolism. They study not only the chemistry of constituents of cellular material, but also the roles of these substances in cell growth and development. In short, the trend in present cytological studies is to correlate morphological and physiological properties of cells to reveal the nature of the cell's machinery and the principles governing the cell's functions. Our aim at this symposium is to gain knowledge of these mechanisms in order to gain more understanding of the cancer problem. Eventually, we hope that these findings will contribute to the treatment of cancer patients or to the prevention of neoplasms in human beings.

In modern cell research, a multitude of experimental tools and methods is employed. Judicious choice of material also plays an important part in determining the success of any research project. Although our ultimate aim may be the transfer of experimental information to human welfare, certain results can be obtained best from experimental organisms, whether they be mice, rats, rabbits, chickens, frogs, plants. In these discussions, a variety of experimental materials and techniques is represented. Tissue culture, micromanipulation, electron microscopy, tracer techniques, cytochemical and cytophysical methods and many others all render

indispensable assistance to the investigators. One of the investigators, Dr. Caspersson, contributed to the growth of biochemical and biophysical cytology when he developed ultraviolet microspectrophotometry.

Recent events have intensified several aspects of cytological investigations of cancer, among which are the nucleic acids, chromosomes and viruses.

The nucleic acids, which hold the secret of life, have received widespread attention during recent years. In October 1959, Ochoa and Kornberg received the Nobel Prize in medicine for their work in synthesizing DNA and RNA. Since the nucleic acids are essential to all living matter, further understanding of these substances probably could supply the answer to the uncontrolled growth characteristic of all cancers. Consequently, several papers in this monograph have been devoted to the nature, synthesis and use of nucleic acids by cells.

Chromosomes have been the subject of much research since the last century, primarily because they are the material basis of heredity. One of the early workers to implicate the chromosomes in cancer was the German scientist Theodor Boveri. The greater rate of mitosis, along with aberrant division figures in many of the cancer tissues, led Boveri to formulate his heralded theory of the origin of cancer in 1914.

However, the chromosomes of man could not be analyzed satisfactorily because of technical difficulties. Dr. Hsu pioneered development of the hypotonic solution pretreatment methods which opened the door to accurate analysis of mammalian chromosomes. This in turn led to renewed interest in the chromosomes of cancer tissues and to discoveries by Ford, Lejeune and others of chromosomal abnormalities in cells of patients afflicted by a number of congenital diseases.

Many contemporary investigators support Boveri's notion that chromosomal imbalance resulting from abnormal mitosis causes a cell to become malignant. In this volume, his thesis will be re-evaluated by Dr. P. C. Koller of the Chester Beatty Research Institute in London.

Viruses were first implicated in connection with cancer some 50 years ago by Rous. Through the efforts of Bittner, and of Stewart, of Gross, and of Dmochowski, viral etiology of some mammalian tumors has been firmly established. We now face an array of problems concerning virus-cell relationships, such as how viruses attack

cells, how an infected cell behaves, and how a virus causes a normal cell to become malignant. A number of papers, therefore, have been devoted either completely or partially to these intriguing subjects.

Acknowledgment is gratefully made of the efforts of Dr. T. C. Hsu, chairman of the 1960 symposium committee and the members of the committee. Committee members working with Dr. Hsu were Mr. Joe E. Boyd, Jr., Drs. Jeffrey P. Chang, Leon L. Dmochowski, Felix L. Haas, Saul Kit, and H. Grant Taylor. Honorary chairman of this symposium was Dr. T. S. Painter of The University of Texas, who has devoted his scientific life to the study of the cell. Serving as chairmen of the various sessions were Dr. Hsu; Dr. M. J. Kopac, New York University, New York City; Dr. C. M. Pomerat, The University of Texas Medical Branch, Galveston; Dr. Jerome T. Syverton, University of Minnesota School of Medicine, Minneapolis; and Dr. J. Herbert Taylor, Columbia University, New York City.

THE NUCLEUS

Chromosome Behavior in Tumors: Readjustments to Boveri's Theory

P. C. KOLLER, PH.D., D.SC.

*Professor of Cytogenetics,
Chester Beatty Research Institute,
Institute of Cancer Research,
London, England*

At the turn of the century von Hansemann described in detail various abnormalities of cell division in human tumors. About the same time Boveri, the pioneer of experimental cytology, was studying the effect of double fertilization on the cleavage division of sea urchin eggs. He found mitotic irregularities in the developing larvae similar to those seen in tumors and described by von Hansemann; Boveri noted the formation of cell groups lacking organization, which closely resembled cancerous tissue. Boveri inferred that the two phenomena were causally related and in 1902, when he published these observations, suggested that tumorous growth might be brought about by abnormal mitotic processes, particularly those processes involved in multipolar division. He found that such divisions result in an irregular distribution of chromosomes and argued that the unbalanced cells produced have the potentiality for unrestricted proliferation.

Boveri was not satisfied with a theory only; he was well aware that experimental verification was required, and for this he searched. When, however, 12 years later, he was forced by circumstances to present his studies, Boveri failed to provide substantial evidence in favor of his theory. The book: "Zur Frage der Entstehung maligner Tumoren" (1914) is no more than a speculative