# GENETICS, CELL DIFFERENTIATION, AND CANCER

Editor
PAUL A. MARKS

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# GENETICS, CELL DIFFERENTIATION, AND CANCER

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# Editor's Foreword

This volume reports the proceedings of the seventh Bristol-Myers Symposium on Cancer Research. The third and sixth symposia (from Stanford and Milan, respectively) were primarily oriented toward clinical treatment. The first, second, fourth, and fifth volumes described basic subjects like effects of drugs on the cell nucleus (Baylor), molecular targets for drug action (Yale), tumor cell heterogeneity (Hopkins), and chromosomes as they relate to cancer (Chicago).

The title of this symposium at the Memorial Sloan-Kettering Cancer Center is "Genetics, Cell Differentiation, and Cancer." Thus, it covers many topics introduced at the University of Chicago symposium held in 1982. It is extraordinary to reflect how much basic research has accumulated in the intervening two years, an indication of the accelerating pace of basic research in cancer.

Among many other themes, the current volume highlights the importance of protein factors in the growth, differentiation, and control of cells. It is singularly apt that tumor necrosis factor, first characterized at the Memorial Sloan-Kettering Cancer Center a dozen years ago, has now been cloned by a number of laboratories around the world and is entering clinical trial. The finding at Sloan-Kettering and elsewhere, that $\gamma$ interferon is highly synergistic with TNF, suggests avenues for clinical exploration. Finally, it is not far-fetched to speculate that as many as a half dozen lymphokines might be used together in patient treatment, involving such diverse elements as interleukin II, tumor inhibitor factor, transforming growth factor, lymphotoxin, etc.

Maxwell Gordon
Series Editor

# Foreword

A century ago, the public's perception of cancer was still medieval; it was considered a disease of shame. When we think of impressive advances in prevention and treatment during the past few decades, we must also be thankful for the changes in public perception and acceptance that now permit us to discuss cancer with relative freedom and candor.

The intense public interest in news about all aspects of cancer research extends to basic science as well as to clinical applications. In recent years, the public has learned of stunning advances in the understanding of how normal cells grow and develop and of what happens when the controls to that growth and development break down. Never before in the history of molecular biology have there been so many ideas to be tested. Never before have there been so many techniques to evaluate them.

But there is another perspective as well. In the weeks just before this symposium was held, the British scientific journal *Nature* reversed its earlier editorial position, saying it had been "overly optimistic" in predicting the speed with which oncogene research would lead to an understanding of the cause of some forms of cancer. And it is indeed the case that although remarkable progress has been made in some areas, the problem of solving the cancer riddle remains a vast one.

It was to these unsolved problems that the distinguished scientists participating in the seventh annual Bristol-Myers Symposium on Cancer Research addressed themselves. The symposium series is an integral part of the $8.34 million, no-strings-attached program of unrestricted grants for cancer research our company has sponsored since 1977 at 17 institutions in the United States and abroad.

The symposium organized by Memorial Sloan-Kettering Cancer Center had special meaning to us because it took place during Memorial Sloan-Kettering's centennial year and was held in New York, the city that has been our

company's corporate headquarters for more than 80 years. With the publication of these proceedings, we are pleased that the important insights shared with the investigators attending the 1984 symposium can now be shared with a broader audience.

Richard L. Gelb
Chairman of the Board
Bristol-Myers Company

# Preface

The Memorial Sloan-Kettering Cancer Center celebrated its Centennial Year in 1984. As the major scientific meeting in this hundredth year, the symposium "Genetics, Cell Differentiation, and Cancer," the seventh annual symposium on cancer research, was organized by the Center and sponsored by the Bristol-Myers Company. This volume is composed of papers delivered by scientists who participated in this conference.

Remarkable progress has been made in our understanding of the nature of carcinogenesis and, in particular, of the role of protooncogenes and oncogenes in the transformation of normal to abnormal cells. As these proceedings demonstrate, work in several areas, including studies on DNA replication, protein synthesis, embryologic development, DNA and RNA viruses, growth factors, and receptors, are coming together to provide us with an understanding of the process of transformation on a molecular and cellular level. This volume provides elegant testimony to the importance of studies on prokaryotes, simple eukaryotic organisms such as yeast, and *Drosophila* in providing insight into the nature of cancer. The first series of papers in these proceedings reports on studies of DNA replication, DNA structure, RNA synthesis, and control of gene expression. Subsequent papers review recent research on oncogenes and their role in inducing malignant growth.

The organizing committee for this symposium comprised Drs. Dorothea Bennett, Bayard D. Clarkson, William Hayward, Samuel Hellman, Paul A. Marks, Malcolm Moore, Lloyd J. Old, and Richard A. Rifkind. We are grateful to all of the participants who made this symposium and this volume which records its proceedings such a memorable scientific event.

We are particularly appreciative of the support of Mr. Richard Gelb, Chairman of the Board of the Bristol-Myers Company and his colleagues, in particular Mr. Harry Levine, Ms. Ann Wyant, and Ms. Kathryn Bloom.

Ms. Suzanne Rauffenbart and Ms. Suzanne Emery of the Memorial Sloan-Kettering Cancer Center provided excellent staff work in all details related to the organization of the symposium. We also thank Ms. Helene Friedman for her expert assistance in the preparation of these proceedings.

Paul A. Marks

# Abbreviations

*abl*, Abelson murine leukemia virus (mouse)
ad, adenovirus
AIDS, acquired immunodeficiency disease syndrome
ALL, acute lymphoblastic leukemia
AML, acute myelogenous leukemia
ALV, avian leukosis virus
ARC, AIDS-related complex
ATTB, bacterial attachment site
ATL, adult T-cell leukemia
att, attachment site
ATP, adenosine triphosphate
attP, phage attachment site

BCGF, B-cell growth factor
*bgl*I, restriction enzyme
BLV, bovine leukemia virus

c, cellular
CAT, chloramphenicol acetyl transferase
CFUe, colony-forming unit for erythropoiesis
CMGF, cellular myeloid growth factor
CML, chronic myelogenous leukemia
CMP, cytidine monophosphate
*c-onc*, cellular or protooncogenes
CSA, colony-stimulating factor
CTP, cytidine triphosphate

d, deoxy
DBP, DNA binding protein