GENES, CHROMOSOMES, AND NEOPLASIA

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The University of Texas System Cancer Center
M. D. Anderson Hospital and Tumor Institute
33rd Annual Symposium on Fundamental Cancer Research

Genes, Chromosomes, and Neoplasia

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This volume is a compilation of the proceedings of The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute 33rd Annual Symposium on Fundamental Cancer Research, held March 4–7, 1980, in Houston, Texas.

The material contained in this volume was submitted as previously unpublished material, except in the instances in which credit has been given to the source from which some of the illustrative material was derived.

Great care has been taken to maintain the accuracy of the information contained in the volume. However, the Editorial Staff and The University of Texas System Cancer Center cannot be held responsible for errors or for any consequences arising from the use of the information contained herein.

Preface

This volume, based on the 1980 symposium on Fundamental Cancer Research of M. D. Anderson Hospital and Tumor Institute, reviews our current understanding of the alterations in normal genetic material that occur prior to or as a consequence of cancer in the organism. Major sections discuss chromatin and chromosome structure, the *src* gene, gene expression, and the genetics of human cancer.

Frank Ruddle and T. C. Hsu, two pioneers who continue to advance the understanding of genetic mechanisms, set the stage by giving histories of somatic cell genetics and cytogenetics and projecting future advances. Insights available from the analysis of the structure of chromatin and chromosomes are provided by Potu Rao, Elton Stubblefield, and Albert Ting of Bert O'Malley's group.

Viral oncogene studies have contributed much to the understanding of neoplastic transformation. This monograph devotes several chapters to the *src* viral locus and its normal homologue, the *sarc* locus.

Gene expression is examined in subsequent chapters by, for example, Donald Robberson, who carefully models the expression of genetically altered mitochondrial DNA, supporting the model with electron micrographic evidence. Somatic cells, rat hepatoma cells, enzymes in human tumor cell lines, and DNA-transformed cells further the discussion of gene expression in normal and malignant cells.

Gene amplification is reviewed by Albert Levan and O. J. Miller. In his survey of 4 years' work on the SEWA mouse tumor, Levan concludes that C-bandless chromosomes and double minutes are in the same category of cytogenetic phenomena. Miller discusses methylation's role in controlling amplification.

Part of the evidence for a genetic cause for neoplastic transformation has been the finding of specific chromosome changes in cells from particular cancers. Among those discussed in this book are human leukemia, for which chromosome changes have led to the identification of new entities, lymphoma and the 14q+ anomaly, and ovarian cystadenocarcinomas and the 14q+ and 6q− anomalies. Experimental animal tumors are also reviewed in light of specific chromosome changes.

The monograph concludes with four discussions of particular human populations and with a summary by James Evans. Relatives of breast cancer patients, Utah Mormons, relatives of lung cancer patients, and patients with polyposis of the colon and their relatives are analyzed for the insight they provide into

the relation of genetics and cancer. For example, the problem of altering a familial predisposition to cancer is covered by John Mulvihill.

This volume will be of interest to basic researchers in disciplines concerned with the cellular basis of cancer, including cell and molecular biologists, and to medical epidemiologists and human geneticists.

Editors' Foreword

"Genes, Chromosomes and Neoplasia" was the topic for the 33rd Annual Symposium on Fundamental Cancer Research, which was held in Houston March 4–7, 1980. This was a timely topic because of the increase in evidence that nonrandom chromosome changes are associated with certain tumors. The symposium was well attended, with 734 scientists participating representing 38 states and 18 foreign countries. At this symposium, Dr. T. C. Hsu became the first staff member of The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute to receive the Bertner Award.

As cochairpersons, we acknowledge our appreciation to members of the organizing and advisory committees for their advice and guidance.

Our appreciation and special thanks are due to Frances Goff and her staff for the many functions that they have expertly performed. We also wish to thank Forma Scientific, Scimetrics, Beckman Instruments, Inc., Dolan Scientific, and GIBCO Laboratories for providing funds for the hospitality room wherein speakers and other participants could meet and discuss topics of mutual interest. Our appreciation is also extended to the National Cancer Institute and American Cancer Society, Texas Division, without whose support this meeting could not have been held. We wish to thank the staff of the Graduate School of Biomedical Sciences of The University of Texas Health Science Center at Houston for their assistance. The efforts of the Departments of Scientific Publications and Public Information and Education are also appreciated, especially the efforts of Walter J. Pagel and Leslie Wildrick, who played important roles in the compilation and manuscript editing of this volume.

Finally we acknowledge the interest, concern, and efforts of Dr. R. Lee Clark, President Emeritus, and Dr. Charles A. LeMaistre, President, The University of Texas System Cancer Center.

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Introductory Remarks

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Welcome to the 33rd Annual Symposium on Fundamental Cancer Research sponsored each year by The University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute. M. D. Anderson hosts the Symposium on Fundamental Cancer Research so that scientists may exchange ideas about a particular topic of current interest.

This year's symposium, entitled "Genes, Chromosomes, and Neoplasia" was an exciting one. It comes at a time when scientists are poised on the brink of gleaning new insights into the control mechanisms of the cell. This knowledge is now accessible because of new techniques that recently have come into use in the sciences of cell biology and cytogenetics.

One of those new techniques, in particular, has not only excited scientists, but captured the imagination of the public through the news media. After only 3 to 4 years of serious study, recombinant DNA techniques already have shown themselves capable of producing hormones and other natural substances in large amounts. This ability to propagate specific DNA fragments is a genetic technique that is without previous counterpart. But recombinant DNA also shows promise of revealing the molecular events taking place in normal and abnormal cells. Recombinant DNA is making it possible to analyze the structure and organization of genes on a scale not imaginable only a few years ago.

I am sure you can imagine how such new basic research discoveries excite those involved in the treatment of cancer. At M. D. Anderson a comprehensive program of basic research undertaken since the early 1940s already has provided a solid foundation for progress in the successful treatment of many types of cancer.

But all of these modes of treatment have been developed to fight a disease that was already present, a disease whose origins and causes were a mystery. The search for new ways of halting a cancer's progression will certainly continue I hope that recent developments in cellular biology will one day enable scientists to find methods to correct cellular abnormalities, thereby eliminating diseases such as cancer before they occur.

I am sure you are all aware of just how far these recent developments have brought the science of cytogenetics. But perhaps by looking at the last symposium held by M. D. Anderson on this topic, we can see just how far this decade's developments have taken us in the understanding of cellular processes.

In 1969, M. D. Anderson's 23rd Annual Symposium was devoted to "Genetic Concepts and Neoplasia." Some of you who are here today presented papers at the symposium that pointed to possibilities that are now fact—made possible because specific technologies available today were not then known to be possible.

That symposium took place the year before Doctors T. C. Hsu and Frances Arrighi reported on their studies of chromosome banding patterns in 1970. That discovery enabled chromosomes to be banded into patterns—what they described as looking like bands on "argyle socks." That discovery also led the way to finding specific chromosome abnormalities common to specific types of cancer, particularly leukemias.

When those common rearrangements have been identified, in some cases they have been found to be diagnostic and predictive of how certain types of cancer will respond to therapy. Now, studies are being conducted to determine chromosome abnormalities in samples of solid tumors.

Other new techniques discovered in the last decade and now being perfected include gene sequencing, location of integrated viral segments, gene transfer, and gene amplification. These techniques have enabled scientists to conduct more precise experiments with heretofore unexpected results, all of which lead to a better understanding of the role of genetics in the cancer cell.

In this year's monograph, authors will be discussing some new and exciting findings. Perhaps we will look back on these reports 10 years hence with equal interest. The authors will be discussing how they have used the new techniques to come up with some interesting observations about the behavior of normal and abnormal cells. They will be looking at the cell from the microscopic structure of the chromosome itself, the chromosome at the molecular level, and the structure of specific genes. Some of the interesting discussions we can look forward to include those about gene transfer and how it has been used to probe cancer cells, the avian sarcoma virus and how it is involved in cancer in birds, double minutes and the role they play, chromosomal rearrangements in cancer cells, and the exciting area of gene amplification. The last session will be devoted to the practical application of what we've found out about cancer genetics.

I cannot close these remarks without adding my congratulations to this year's Bertner Award winner, Dr. T. C. Hsu. Dr. Hsu has been a member of our faculty since 1955 and recently was honored with an appointment to the Olga Keith Wiess Chair for Cancer Research here at M. D. Anderson.

In the short time that I have known Dr. Hsu, I have been immensely impressed by the startling contributions he has made to the entire field of cell biology. His laboratory here at M. D. Anderson continues to be a focal point of research and education in cytology and cytogenetics.