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Peo C. Koller

The Role of Chromosomes in Cancer Biology

With a Foreword by Sir Alexander Haddow

With 42 Figures

Springer-Verlag Berlin · Heidelberg · New York 1972

Peo C. Koller, Ph. D., D. Sc., Professor Emeritus, University of London. Formerly Professor of Cytogenetics, Chester Beatty Research Institute, Institute of Cancer Research, London

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To Karin

Foreword

For many years Professor KOLLER has possessed an international reputation in the fields of cytogenetics and karyology, both in their fundamental aspects and in their relation to the problems of tumour causation, especially to the role of heterochromatin, and few men have made a greater contribution.

The role of the chromosome complex in carcinogenesis has exerted a natural fascination for many decades, but there can be little doubt of the great advances in knowledge and understanding which have accrued of recent years. Although it is probable that the key event in the inception of particular tumours resides in a delicate molecular rearrangement, and is hence undetectable by conventional microscopical methods, nevertheless a large proportion is accompanied by karyotypic variation and relatively gross changes in chromosomal number, order and arrangement, witness the discovery of the Philadelphia chromosome and its consequences. Further, any such changes in the chromosomal apparatus must inevitably be attended by profound repercussions in the cytoplasm with all that this must mean in protein synthesis and cellular behaviour. It would be idle to pretend that any such problems have finally been solved, and they still contain an element of mystery, as can be seen through a quotation from the address given at the Symposium on "Genetics and Cancer", (Houston, 1959) by DARLINGTON, one of the founders of the discipline of Cytogenetics:

"*Thus there seems no reason to doubt that variations in chromosome numbers occur in tumours not because they matter more, but because they matter less, than elsewhere ... the cell has become less dependent on nuclear balance than in regular development.*"

But it is one function of the present work still further to stimulate our comprehension of these remarkable changes. Although mountains of effort have been expended in attempts to decipher the mode of action of the carcinogenic hydrocarbons, amines and other classes of chemical carcinogen—so far with little success or precision—much progress has come of recent years through study of the reactive alkylating carcinogens. At one stage it almost appeared that the tumour nucleus in such cases might bear, as it were, an imprint of the alkylating carcinogen which induced its appearance. Be that as it may, we are now approaching ever more accurate knowledge of highly specific interactions between these substances and chromosomal DNA-molecules, especially the purines, so bringing about alterations in base sequence and other effects upon the chemical integrity of chromosomal DNA, with all the attendant consequences.

The book describes the molecular organization and function of chromosomes, as well as the consequences of chromosomal aberrations in human development. Not the least impact of cytology on medicine has been of a highly practical kind, and thus the

book also contains accounts of the cellular features of primary tumours and ascitic fluid, and of the cytological actions of radiation and drugs and discusses their relevance to therapy.

On every ground of timeliness and authority, I recommend it warmly, in the certain hope that it must prove of utmost value, at once to those who are already acquainted with its subject matter and to those who are entering a fascinating field.

May 1972 A. HADDOW

Preface

Transformation of a normal cell to a cancer cell is a biological event; it may be referred to as mutation which occurs either at the level of the gene or chromosome. The latter includes the integration of oncogenic viruses into the host cell's DNA. Whatever the mechanism responsible for neoplastic transformation is, it has eventually to affect the genome of the cell. The physical basis of the cancerous cell behaviour is fixed in the molecular organization of the chromosomes and during mitosis it is transmitted through the chromosomes to descendent generations of cells. Abnormal mitosis is a common phenomenon in tumour tissue and has been recognised to be the main cause of chromosomal irregularities which are characteristic features of cancer cells. Already at the turn of the century the possible role of chromosome changes in the aetiology of cancer was being discussed. The discovery of a chromosomal basis of certain pathological syndromes in man e. g. Down's, Klinefelter's, Turner's syndromes, has shown the consequences of anomalous chromosome constitution, and gave new stimulus for similar investigations in tumours.

During the past decade the study of chromosomal aberrations and their significance in the development and progression of tumours became a rapidly expanding branch of cancer research. It has been demonstrated that most malignant growths are of mosaic composition, containing a variety of cell types distinguishable from normal cells and frequently from each other, by their chromosome patterns. The concept of *selective cellular proliferation* has been derived from information gained by studies on karyotypic variation in the cell population of tumours. Chromosome analyses have already brought a clearer understanding of such dynamic processes as cell competition, selection and adaptation, all of which operate within a cancerous growth and have a role in tumour progression and their response to treatment.

I do not intend to present a comprehensive review of the vast literature which has grown up around this subject, full of many paradoxes, discrepancies and descriptions of unexplained phenomena. My aim is to show the value of the information which has been obtained from such studies by considering the chromosomes of cancer cells as a phenotypic characteristic and not solely as the cell components representing the genotype. I hope that colleagues engaged in diverse aspects of cancer research will find the information in the book of interest and help in their own field of study, and those who wish to enter into tumour cytogenetics may find it a useful introduction.

PEO C. KOLLER

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