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EDITORS

CANCER PRECURSORS

Epidemiology, Detection, and Prevention

Springer

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Cancer Precursors

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Foreword by Joseph F. Fraumeni, Jr., MD, MSc

With 50 Figures

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Cancer Precursors

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Foreword

Dramatic advances in our understanding of cancer causation have come from epidemiologic and laboratory research, particularly over the past two decades. These developments have included a broadening interest in the critical events that take place during the early stages of the dynamic multistep process leading to invasive cancer. Increasingly, cancer epidemiologists are pursuing research into the origins and natural history of premalignant lesions, including intermediate or surrogate endpoints, a trend accelerated by the development of molecular technologies that are revolutionizing our understanding of the transformation of normal to malignant cells. There seems little doubt that this emerging knowledge will provide further insights not only into carcinogenic processes, but also into more sensitive methods of early detection and more effective means of prevention.

In this book, Drs. Franco and Rohan have succeeded in preparing a comprehensive, timely, and critical review of the substantial progress that has been made in our understanding of cancer precursors. They have enlisted experts in the field who have contributed authoritative chapters on the precursors to a wide variety of cancers, with emphasis on etiology and natural history, including the role of environmental and heritable factors that provoke normal cells to undergo malignant transformation. Epidemiologic data are linked whenever possible to molecular as well as classical cellular pathology, providing a fuller understanding of the causal events and mechanisms that initiate the carcinogenic process.

It is generally understood that preventing cancer is far preferable to treating it. While opportunities now exist for primary and secondary prevention of certain cancers, we are still limited by an incomplete understanding of causal factors and precursor lesions that hold the key to advances in cancer prevention. However, as a result of conceptual breakthroughs in our understanding of the fundamental mechanisms of cancer, there is growing optimism that the incorporation of molecular and genetic probes into epidemiologic and clinical approaches will more fully illuminate events on the causal pathway to cancer. By identifying and deploying sensi-

tive biomarkers of carcinogenic exposure, susceptibility genes, and intermediate outcomes, it should be possible to more precisely define individuals at elevated risk of cancer, and to design and test novel approaches to diagnostic and preventive interventions.

This optimism is tempered, however, by the formidable challenges for epidemiologic and multidisciplinary research to identify, select, measure, validate, and integrate biomarkers that are predictive of cancer risk and amenable to preventive measures. While this book presents a wealth of information about cancer precursors, it also indicates the complexity of the task ahead for epidemiologists, as well as clinicians, molecular biologists, and other scientists, whose work on precursors may usher in new strategies to eliminate cancer before it develops and escapes control.

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Preface

The purpose of this book is to bring together in one place reviews of the descriptive, analytical, and molecular epidemiological research on cancer precursors at specific anatomical locations, as well as a discussion of the methodological issues associated with the study of cancer precursors. We feel that such a book is particularly timely since the last few years have brought considerable progress in our understanding of the early natural history of cancer and of the etiology of precursor lesions. There have also been improvements in the means of detecting precursor lesions, either directly or via testing of surrogate biomarkers. While progress has perhaps been more rapid for cancer precursors at those anatomical sites which are more accessible and therefore more amenable to study, there is now a considerable body of knowledge bearing on the topic of precursor lesions at many sites.

The book is divided into five sections. Part I seeks to place subsequent chapters in context by providing brief overviews of the molecular basis of carcinogenesis and of the histological aspects of cancer precursors.

Part II addresses some of the issues related to the measurement, interpretation, and study of precursor lesions. Specifically, this section includes a chapter on the conceptual basis for studying precursor lesions, and on the practical aspects of obtaining, processing, and analyzing tissues containing either precancerous lesions or specimens enabling biomarkers of their presence to be detected. Intermediate markers (surrogate endpoints) have an increasingly important role to play in cancer research, and Part II also includes a chapter on the theoretical and practical problems involved in the use of surrogate endpoints in experimental and observational studies of cancer. The final chapter in this section discusses the assessment of epidemiologic relationships involving cancer precursors and the impact of measurement error on the study of such relationships.

The main section of the book, Part III, contains reviews of cancer precursors at the most important anatomical sites at which solid tumors occur. These reviews include discussion of the epidemiol-

ogy of these lesions, and where appropriate, aspects of their detection and prevention. Somewhat inevitably, the authors have taken different approaches in responding to their task, given that there are considerable between-site differences in the current state of knowledge and that much of the information regarding risk factors for cancer precursors overlaps with that available for invasive cancers of the same organ site.

Part IV includes chapters on various aspects of the control of cancer precursors. A chapter on screening addresses issues concerning the role of secondary prevention of cancer precursors, with particular emphasis on screening for precursors of cervix and colorectal cancer, for which the relevant concepts are most developed. A chapter on chemoprevention discusses the use of precancerous lesions and early associated biomarkers as surrogate endpoints to characterize cancer chemopreventive efficacy. The third chapter of this section summarizes evidence-based policy recommendations from different national and international agencies on screening and prevention, with particular emphasis on cancer precursors.

Part V, the final section of the book, contains a brief chapter in which we attempt to peer into the future to anticipate how research on the etiology, detection, and prevention of cancer precursors might develop.

The book includes contributions by well-established scientists who work on topics related to the biology, epidemiology, and control of cancer precursors, and these scientists have written their chapters in the knowledge that the target audience encompasses a broad professional base, including basic cancer researchers, epidemiologists, oncologists, molecular biologists, pathologists, health policy professionals, and graduate students in cancer-related fields. We thank the contributors for their superb efforts to make their chapters accessible to such a wide audience. We also appreciate their patience and diligence in revising their chapter manuscripts in response to our editorial requests to meet the common style and content structure that we attempted to impose upon the contributions within each section.

the contributions of his collaborators in the UCSF anal neoplasia cohort study: Elizabeth Holly, Mary Ralston, Naomi Jay, Michael Berry, Maria Da Costa, and Teresa Darragh, and in the cost-effectiveness analysis study: Suzanne Goldie, Milton Weinstein, and Karen Kuntz. E. Franco's contributions were supported by a Distinguished Scientist Award from the Medical Research Council of Canada.

Finally, a short note on the history of this book. Over the last 11 years, the editors have collaborated closely on various projects on cancer epidemiology and prevention and on methodological issues related to error in the measurement of intermediate endpoints for cancer. The decision to jointly edit this book was taken about two years ago and was a natural consequence of this long-standing collaboration. Bringing this writing and editing project to bear fruit required more hours and exchanges of electronic mail messages and phone conversations than we care to count. The order of our names on the masthead reflects nothing other than a simple alphabetical listing. We both enjoyed producing this tome immensely, and we sincerely hope that the reader will find it a valuable resource.

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Contents

Part III   Site-Specific Precancerous Conditions

Part IV   Control of Cancer Precursors