

Handbook of Experimental Pharmacology

Volume 156

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Mechanisms in Carcinogenesis and Cancer Prevention

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With 30 Figures and 24 Tables

ISBN 978-3-642-07859-0 ISBN 978-3-662-08602-5 (eBook)
DOI 10.1007/978-3-662-08602-5

Cataloging-in-Publication Data applied for
Bibliographic information published by Die Deutsche Bibliothek
Die Deutsche Bibliothek lists this publication in the Nationalbibliografie;
detailed bibliographic data is available in the Internet at
<<http://dnb.ddb.de>>.

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© Springer-Verlag Berlin Heidelberg 2003
Originally published by Springer-Verlag Berlin Heidelberg New York in 2003
Softcover reprint of the hardcover 1st edition 2003

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Cover design: design & production GmbH, Heidelberg
Typesetting: SNP Best-set Typesetter Ltd., Hong Kong

27/3020/kk – 5 4 3 2 1 0 – printed on acid-free paper



Eino Hietanen (13.10.1947–16.09.2002)

This book is dedicated to my long-time friend, Eino Hietanen, MD, PhD, who passed away unexpectedly on September 16th, 2002. Eino was a compassionate physician and a steadfast and innovative toxicologist with deep understanding of research and commitment to better protect people from environmental insults and to advance public health. Eino's abilities are dearly missed.

Harri Vainio

Preface

Overall, cancer is a preventable disease. Modifiable external factors, discovered by epidemiological studies during the last 50 years, account for a majority of all cancer deaths. Tobacco smoking remains the largest etiological contributor to cancer, while the contribution of inadequate diet and obesity may be equally important, but much more difficult to quantify. Most of the biological agents with established carcinogenic potential are rare in high-resource countries, but important in low-income countries. The association of human papillomaviruses (HPVs) with cervical neoplasia is very strong. Persistent infections with HPV types that carry a high oncogenic risk lead to invasive cervical neoplasia. After 20 years of intensive research, a point has been reached at which prevention of cervical cancer by vaccination against HPV infection will be possible in the foreseeable future.

Implementation of cancer prevention takes place slowly and incrementally, rather than through major breakthroughs. Avoidance of tobacco smoke, including environmental tobacco smoke, is a first priority in prevention. With respect to diet, increased consumption of fruits and vegetables and reduced consumption of refined carbohydrates, salt, red meat and animal fat are likely to contribute substantially to the primary prevention of cancer. Increased physical activity, avoidance of excessive alcohol intake, avoidance of obesity and overweight throughout life are also desirable. Vaccination against hepatitis B and control of transmission of hepatitis C virus and some of the HPVs will have a modest impact in developed countries, but a major impact in developing countries. Avoidance of exposure to sunlight, strict control of occupational exposures and a sound environmental policy can also contribute to the avoidance of a small fraction of the cancer burden.

Carcinogenesis is a multiyear, multistep, multipath disease of progressive genetic and associated tissue damage. The past two decades have been golden years for the genetics of cancer. It has become clear through the work of several research groups that both inherited and sporadic cancers arise through defects of misregulations of their genomes. The cartography of the order, accumulation and interactions of genetic lesions during tumor initiation and progression is reasonably detailed for many human tumor types. Such information is proving to be tremendously valuable in grouping patients into prognostic categories, and also in opening new avenues for mechanism-based cancer prevention.

The good news is that basic research into molecular genetics and biology of cancer is delivering better diagnoses and smarter drugs. However, despite increasing research and development efforts in cancer prevention, new drug approvals for preventive indications have been slow to emerge. New preventive strategies with earlier endpoints, such as intraepithelial neoplasia, may provide practical and feasible approaches to the rapid development of new tools to treat and prevent precancer rather than full-blown invasive cancer. Most of these approaches still need to be fully tested before they can be more widely adopted. The ultimate prize, which could be available within the next 10–15 years, would be a preventive tool that works on the particular genes in a particular sequence of events. Genetic tests may one day accurately identify those precancers that are likely to become invasive and spread. The tests may also tell physicians to which drugs a given precancer is most vulnerable.

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Lyon, June 2002

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