Chemoprevention of Premalignant Lesions of the Upper Aerodigestive Tract

Guest Editors

Stimson P. Schantz
Memorial Sloan-Kettering Cancer Center
Head and Neck Service
New York, NY

Waun Ki Hong
University of Texas
M.D. Anderson Cancer Center
Head, Neck and Thoracic Medical Oncology
Houston, TX

Charles W. Boone
Division of Cancer Prevention and Control
Chemoprevention Investigational Drug Unit
National Cancer Institute
National Institutes of Health
Bethesda, MD

Gary J. Kelloff
Division of Cancer Prevention and Control
Chemoprevention Investigational Drug Unit
National Cancer Institute
National Institutes of Health
Bethesda, MD
Foreword ................................. 1

INTRODUCTORY REMARKS

Development of Chemopreventive Agents for Lung and Upper Aerodigestive Tract Cancers
Gary J. Kelloff, Charles W. Boone, Vernon K. Steele, Marjorie Perloff, James Crowell, and Linda A. Doody ................................. 2

Chemoprevention Strategies: The Relevance of Premalignant and Malignant Lesions of the Upper Aerodigestive Tract
Stimson P. Schantz ........................................... 18

Carcinogen Biomarkers Related to Smoking and Upper Aerodigestive Tract Cancer
Stephen S. Hecht, Steven G. Carmella, Sharon E. Murphy, Peter G. Foiles, and Fung-Lung Chung .................................................. 27

PREMALIGNANT LESIONS IN THE UPPER AERODIGESTIVE TRACT

Overview
Charles W. Boone ............................................... 36

Intraepithelial Neoplasia, Surrogate Endpoint Biomarkers, and Cancer Chemoprevention
Charles W. Boone and Gary J. Kelloff ........................................... 37

Premalignant Lesions of the Upper Aerodigestive Tract:
Pathologic Classification
John D. Crissman, Daniel W. Visscher, and Wael Sakr .................................................. 49

Early Lung Cancer as a Potential Target for Chemoprevention
Myron R. Melamed and Betty J. Flehinger ............................................... 57

Cytologic Diagnosis of Oral, Esophageal, and Peripheral Lung Cancer
Leopold G. Koss .................................................. 66

(continued on next page)
ANIMAL MODELS

Overview
Richard C. Moon ................................................. 82

The Hamster Cheek Pouch Carcinogenesis Model
Irma B. Gimenez-Conti and Thomas J. Slaga ........... 83

Esophageal Carcinogenesis in the Rat: A Model for Aerodigestive Tract Cancer
Michael J. Wargovich and Osamu Imada .................. 91

Lung Tumors in Strain A Mice: Application for Studies in Cancer Chemoprevention
Gary D. Stoner, Gabriela Adam-Rodwell, and Mark A. Morse ............ 95

Hamster Bronchial Carcinogenesis Induced by Carcinogen-containing Sustained Release Implants Placed Endobronchially: A Clinically Relevant Model
William G. Hammond and John R. Benfield .................. 104

ASSAYS FOR MARKERS OF CHRONIC CARCINOGEN EXPOSURE AND THEIR MODULATION BY CHEMOPREVENTIVE AGENTS

Overview
Stimson P. Schantz ............................................... 118

Molecular Epidemiology of Lung Cancer and the Modulation of Markers of Chronic Carcinogen Exposure by Chemopreventive Agents
Frederica P. Perera, Deliang Tang, Ricardo A. Grinberg-Funes, M. Anne Blackwood, Christopher Dickey, William Blaner, and Regina M. Santella ............. 119

Metabolic Activation, DNA Adducts, and H-ras Mutations in Human Neoplastic and Non-neoplastic Laryngeal Tissue

DNA Adducts in Model Systems and Humans
Kenneth W. Turteltaub, Chris E. Frantz, Moire R. Creek, John S. Vogel, Nancy Shen, and Esther Fultz .................. 138

VIRUSES IN HEAD AND NECK CANCER

Overview
Leslie Brand ...................................................... 149

Epstein-Barr Virus and Nasopharyngeal Carcinoma
Gary R. Pearson .................................................. 150

Papillomaviruses in Head and Neck Disease: Pathophysiology and Possible Regulation
Bettie M. Steinberg and Karen J. Auborn ................. 155

INTERMEDIATE BIOMARKERS

Differentiation Markers

Overview
Reuben Lotan .................................................... 165

Squamous Cell Differentiation Markers in Normal, Premalignant, and Malignant Epithelium: Effects of Retinoids
Reuben Lotan .................................................... 167

(continued on next page)
Prospective Trial Evaluating Immunocytochemical-based Sputum Techniques for Early Lung Cancer Detection: Assays for Promotion Factors in the Bronchial Lavage
Frank Scott, Frank Cuthitta, Anthony M. Treston, Ingalill Avis, Prabodh Gupta, John Ruckdeschel, Karen Kelly, Steven Plantadosi, Melvyn Tockman, and James Mulshine ..... 175

Oncogene Mutations as Intermediate Markers
David Sidransky, Jay Boyle, Wayne Koch, and Peter van der Riet ..... 184

TGF-α and EGFR in Head and Neck Cancer
Jennifer R. Grandis and David J. Tweardy ..... 188

Premalignant Lesions of the Upper Aerodigestive Tract: Biomarkers of Genetic Alterations, Proliferation, and Differentiation
John D. Crissman, Daniel W. Visscher, and Fazlul H. Sarkar ..... 192

Tissue Autofluorescence as an Intermediate Endpoint in Cancer Chemoprevention Trials
Stimson P. Schantz and Robert R. Alfano ..... 199

Genetic Biomarkers

Overview
Ugo Pastorino ..... 205

Clinical Experience With the Micronucleus Assay
Harinder S. Garewal, Lois Ramsey, George Kaugars, and Jay Boyle ..... 206

Chromosomal Biomarkers in the Clonal Evolution of Head and Neck Squamous Neoplasia
Thomas E. Carey, Maria J. Worsham, and Daniel L. Van Dyke ..... 213

Blood Group Antigens and Integrins as Biomarkers in Head and Neck Cancer: Is Aberrant Tyrosine Phosphorylation the Cause of Altered α6β4 Integrin Expression?
Thomas E. Carey, Thankam S. Nair, Catherine Chern, Monica Liebert, H. Barton Grossman, Gregory T. Wolf, and Carter VanWaes ..... 223

Early Genetic Changes During Upper Aerodigestive Tract Tumorigenesis
Walter N. Hittelman, Narin Voravud, Dong M. Shin, Jin Soo Lee, Jae Y. Ro, and Waun Ki Hong ..... 233

Genetic Changes in Lung Cancer
Ugo Pastorino, Gabriella Sozzi, Monica Miozzo, Elda Tagliabue, Silvana Pilotti, and Marco A. Pierotti ..... 237

CANDIDATE CHEMOPREVENTIVE AGENTS IN CLINICAL TRIALS

Overview
Waun Ki Hong ..... 249

Micronuclei: A Potential Intermediate Marker for Chemoprevention of Aerodigestive Tract Cancer
Steven E. Benner, Michael J. Wargovich, Scott M. Lippman, and Waun Ki Hong ..... 250

Fenretinide (4-HPR) in Chemoprevention of Oral Leukoplakia
Fausto Chiesa, Nicoletta Tradati, Marino Marazza, Nicoletta Rossi, Patrizia Boracchi, Luigi Mariani, Franca Formelli, Roberto Giardini, Alberto Costa, Giuseppe De Palo, and Umberto Veronesi ..... 255

Beta-Carotene and Vitamin E in Oral Cancer Prevention
Harinder S. Garewal ..... 262
N-Acetyl-L-Cysteine
Nico De Vries and Silvio De Flora .......................................................... 270

Oltipraz: A Laboratory and Clinical Review
Al B. Benson III .......................................................... 278

A Review of the Use of Antioxidant Supplements in the Treatment of Human Oral Leukoplakia
George E. Kaugars, Sol Silverman, Jr., John G.L. Lovas, Richard B. Brandt, Joan S. Thompson, and Vishwa N. Singh .......................................................... 292

PANEL STATEMENT

Strategy for Design of Clinical Trials of Chemopreventive Agents
Stimson P. Schantz, Co-Chairman
Waun Ki Hong, Co-Chairman
Charles W. Boone
Gary J. Kelloff .......................................................... 299

Author Index .......................................................... 301

Subject Index .......................................................... 302

FRONT COVER: Histological section from a bronchial biopsy of a heavy smoker. From the work of Dr. Walter N. Hittelman, Chief, Section of Cellular Oncology, Department of Clinical Investigation, The University of Texas M.D. Anderson Cancer Center, Houston, TX. Contributed by Dr. Charles W. Boone, Chemoprevention Investigational Drug Unit, National Cancer Institute, in conjunction with the Medical Arts and Photography Branch, National Institutes of Health, Bethesda, MD.