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Foreword

Progress in Cancer Chemoprevention: Biomarkers and Cohorts

Collaborative chemoprevention projects between the United States (US), China, Korea, and Japan are desirable because each country contributes significant specialized resources and expertise, making the projects proceed more rapidly than they could in any one country alone. The US offers experience in managing short-term Phase II chemoprevention trials, and experience in quantitative measurement of surrogate endpoint biomarkers, including molecular markers, in tissue and cytologic samples, using computer-assisted image analysis to increase precision and objectivity.

Japan has multiple research activities related to the discovery of new chemopreventive agents, particularly those from food, and a pharmaceutical industry capable of supplying new and innovative drugs in the kilogram amounts required for clinical toxicology testing and clinical trials.

Chinese and Korean research institutes have identified many cohorts with premalignant leasions suitable for chemopreventive intervention. Examples of such cohorts of interest are ductal carcinoma *in situ* of the breast, oral leukoplakia, respiratory metaplasia and dysplasia, colon polyps, low-stage bladder and prostate neoplasms, prostatic intraepithelial neoplasia, and cervical intraepithelial neoplasia.

Evaluation of chemopreventive strategies requires good agents, reliable biomarkers, and suitable cohorts. This volume deals with biomarkers and cohorts, and Volume 1 is concerned primarily with chemopreventive agents.

Intermediate endpoint biomarkers for cancer chemoprevention trials may be detected and quantitated at the clinical, tissue, cellular, and molecular levels. Examples of the different levels are colon polyps (clinical level), plaques of carcinoma *in situ* seen grossly by colposcopy or bronchoscopy (clinical level), intraepithelial neoplasia seen in histological sections (tissue level), nuclear atypia seen in cytological smears from sputum, cervix, or bladder (cellular level), and sites of p53 positive staining within nuclei (molecular level).

Surrogate endpoint biomarkers at the histological level, as measured by computer-assisted quantitative image analysis, are discussed by C.W. Boone (Chemoprevention Branch, National Cancer Institute, Bethesda, MD) and J. Bacus (Bacus Laboratories, Elmhurst, IL). The applicability of computer-assisted imaging to measure molecular markers is also discussed.

The subject of molecular markers of oncogenes and oncogene expression, as used diagnostically or modulated by chemopreventive agents, is presented by a number of speakers, including J.K. Lin (National Taiwan University, Taipei, Taiwan) on protein kinase C and nuclear oncogene expression, M. You (Medical College of Ohio, Toledo, OH) on genetic and epigenetic alterations in mouse lung tumors, M.W. Anderson (University of Cincinnati College of Medicine, Cincinnati, OH) on genetic markers in early detection of lung cancer, S.J. Cheng (Cancer Institute, Chinese Academy of Medical Sciences, Beijing, China) on molecular and cytologic alterations in early stages of lung carcinogenesis, A.J.P. Klein-Szanto (Fox Chase Cancer Center, Philadelphia, PA) on chemopreventive efficacy of 2-difluoromethylornithine (DFMO) and development of biomarkers in mouse skin tumor model, and G. Dong (National Institute of Deafness and Communication Disorders, National Institutes of Health, Bethesda, MD) on genes differentially expressed in progression of malignant transformation in murine squamous cell carcinoma. With regard to cohorts for chemoprevention trials, for breast, C.J. Fabian (University of Kansas Medical Center, Kansas City, KS) describes breast cytology and biomarkers obtained by random fine needle aspiration, and G.Y.C. Wong (Strang Cancer Prevention Center, New York, NY) discusses a dose-range finding study of indole-3-carbinol for breast cancer prevention.

For uterine cervix, M.F. Mitchell (University of Texas M.D. Anderson Cancer Center, Houston, TX) discusses polyamine measurements in uterine cervix connected with use of DFMO, W.S. Ahn (Catholic University Medical College, Seoul, Korea) describes effects of retinoic acid on colposcopic changes in Korean patients with cervical dysplasia, and R.D. Chen (Cancer Institute, Chinese Academy of Medical Sciences, Beijing, China) presents a study of retinamide II for cervical precancerous lesions.

For colon, M.Lipkin (Strang Cancer Prevention Center, New York, NY) tells of new rodent transgenic models for studies of chemoprevention of colon cancer, and D. Brenner (University of Michigan Medical School and Veterans Affairs Medical Center, Ann Arbor, MI) describes the clinical development of aspirin as a chemopreventive agent in colon.

For esophagus, L.D. Wang (Henan Medical University, Zhengzhou, Henan, China) describes cell proliferation in esophageal and gastric cardiac epithelia of subjects in a high-incidence area for esophageal cancer in northern China. T.W. Kensler (Johns Hopkins University School of Public Health, Baltimore, MD) describes an oltipraz chemoprevention trial in Qidong, Jiangsu Province, China.

For prostate, L.W.K. Chung (University of Virginia Health Sciences Center, Charlottesville, VA) discusses human prostate cancer models for chemoprevention, and H.Y.E. Zhau (University of Virginia Health Sciences Center, Charlottesville, VA) talks about an interracial comparative study of prostate cancer among patients from the United States and Japan.

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