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OVERVIEW

Assays for Markers of Chronic Carcinogen Exposure and Their Modulation by Chemopreventive Agents

This session provided a basis for understanding the latest advances in assays of chronic carcinogen exposure. Such markers would be relevant if their association with the subsequent cancer-bearing state could be clearly identified. Furthermore, the strength of these markers would be based on their relevance to the carcinogenic process.

Beginning the session with an overview of molecular epidemiology of lung cancer, Perera described measuring exposure to polycyclic aromatic hydrocarbons, cigarette smoke, ethylene oxide, styrene, and 4-aminophenyl identified with biomarkers including DNA and protein adduct formation, sister chromatid exchange, gene mutation, and/or oncogene activation.

A detailed study of one assay of carcinogen exposure involved DNA adduct analysis of human laryngeal tissue by ^{32}P-postlabelling. Stern and colleagues revealed the presence of adducts only in mucosa derived from smokers. Furthermore, smoking cessation for ten months resulted in no detectible adducts. Significantly, levels of DNA adduct formation correlated with levels of Phase I enzyme activity, specifically P4502C and P450IA1. Demonstrating the interaction of tobacco carcinogens, active carcinogen-activating enzymes, and DNA damage within upper aerodigestive mucosa represents a significant advance.

Despite the above identified advances, questions related to DNA adduct detection remain unanswered. Using ^{32}P-postlabelling in combination with accelerator mass spectrometry, Turtletaub and colleagues report that adduct levels do not necessarily correlate with target tissue response. This discrepancy may possibly reflect repair capacities within various tissues.

It is evident from this session that advances in the field are being made. Also evident is that assays of carcinogen exposure are facilitated by investigating diseases of the upper aerodigestive mucosa. The association of mucosal diseases to carcinogen exposure is evident. Furthermore, upper aerodigestive mucosa lends itself to repeat examination. Targeted biopsies are readily performed. Finally, as emphasized in this session, these markers can be used as intermediate endpoints for assessment of both the mechanisms and efficacy of chemopreventive agents.

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