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OVERVIEW

Animal Models

Chemoprevention of experimental carcinogenesis requires that chemopreventive agents prevent initiation of transformation or arrest or reverse the progression of transformed malignant cells in order to delay or prevent the development of invasive disease. To achieve its preventive role, a chemopreventive agent must enhance the physiological process that protects the organism against the growth of abnormal cells which have the potential to develop into invasive cancer. Experimentally, the efficacy of a potential chemopreventive agent can be evaluated in animal models of carcinogenesis. Several tumor models for various target organs are available to study modulation of the carcinogenic process by such agents. However, for a tumor system to qualify as an effective experimental chemoprevention model, several criteria should be satisfied: (a) development of the cancer should be relatively rapid (approximately six to nine months); (b) cancer should develop only in the tissue of interest, *i.e.*, be target-organ specific; (c) tumors should be histopathologically comparable to those found in humans; (d) the model should mimic the growth characteristics of the human counterpart (hormone dependence, metastasis, *etc.*); and (e) the inducing agent (chemical carcinogen, radiation) should cause little or no systemic toxicity. Using these criteria, several tumor models have proved valuable for determining the chemopreventive efficacy of several classes of chemopreventive agents.

In this session, four models for cancer of the aerodigestive tract are presented. A model which compares favorably with the events involved in the development of premalignant and malignant lesions in human oral cancer is discussed by Dr. I. Gimenez-Conti. In her presentation, Dr. Gimenez-Conti describes several morphological, biochemical and molecular changes in the hamster cheek pouch model which have been identified during development of human oral cancer.

Dr. M. Wargovich discusses a model for esophageal carcinogenesis and describes the morphological changes induced by the chemical carcinogen, nitrosomethylbenzylamine. He also shows that such changes may be inhibited by several classes of phytochemicals with emphasis directed towards the thioether constituents of garlic.

Two models for lung tumorigenesis are described by Drs. G. Stoner and W. Hammond. Dr. Stoner describes the parameters for inducting lung tumors in the strain A mouse and shows that several phytochemicals inhibit the induction of these tumors, which in several cases correlates with a reduction in the level of carcinogen-specific DNA adducts. Dr. Hammond describes a unique model in which a carcinogen pellet is placed in the bronchus of the Syrian hamster. He also describes the kinetics of carcinogen release from the pellet which result in a sustained carcinogen release and tumor development in a localized area of the bronchus. He further discusses the potential of this model system for chemoprevention studies.

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