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OVERVIEW

Premalignant Lesions of the Breast: Animal Models

Tumor models for various target organs are available to study modulation of the carcinogenic process by exogenous factors. Most of the models are designed to satisfy several criteria: (1) development of tumors should be relatively rapid (approximately 6 months); (2) tumors should only develop in the tissue of interest (target organ-specific); (3) histopathologically, the tumors should resemble human breast cancers; (4) growth characteristics of the tumors should mimic the human counterpart (hormone dependence, metastasis, *etc.*); and (5) the inducing agent (chemical carcinogen, radiation) should cause little or no systemic toxicity. Among the existing models for experimental carcinogenesis studies, some offer specific advantages. Most frequently employed in chemoprevention studies are two tumor models using either 7,12-dimethylbenz(*a*)anthracene (DMBA) or *N*-methyl-*N*-nitrosourea (MNU) as carcinogens to induce mammary cancer in rats. Both the DMBA- and MNU-induced mammary tumor models have been used successfully for chemoprevention studies, resulting in a 90–100% incidence of mammary tumors within a period of 6 months. The majority of cancers induced by these carcinogens are ovarian hormone-dependent; a small percentage remain hormone-dependent. Earlier chemoprevention studies were conducted with the DMBA-induced cancer model; however, the MNU-induced mammary cancer model has remained a model of choice for several reasons: (1) DMBA-induced tumors are encapsulated and do not metastasize; (2) DMBA must be metabolized to an active form; and (3) DMBA induces a high incidence of adenomas and fibroadenomas. These complications do not arise in the MNU-induced cancer model.

In this session, Dr. Michael Gould discussed a new model for breast cancer in which the mammary epithelial cells are transfected *in situ* with retroviruses containing activated *ras* or *neu* oncogenes. Although further characterizations of these models are required, they promise to be useful for identifying potential chemopreventive agents for breast cancer. Dr. Gould also discussed the role of monoterpenes in preventing *ras*-induced mammary tumors.

Dr. Arthur Schwartz described the effect of dehydroepiandrosterone (DHEA), and a fluorinated analog of DHEA which lacks androgenic or estrogenic activity, on the inhibition of cancer development in the MNU-induced mammary tumor model. Dr. Schwartz also indicated that the inhibitory effect of these agents may be mediated through inhibition of glucose-6-phosphate dehydrogenase and the pentose-phosphate pathway.

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