

mammary cancer incidence in controls from 95% to 15%; carcinoma multiplicity in rats receiving 800 mg DHEA per kg diet was reduced by more than 85% from control levels. In a separate study, the 400 mg/kg diet dose of DHEA reduced the incidence of mammary cancer to 5% from 80% found in controls fed the basal diet. Reductions in mammary cancer incidence and multiplicity associated with DHEA administration were accompanied by large increases in cancer latency. Evaluation of mammary gland wholemounts from animals fed DHEA demonstrated a massive induction of lobuloalveolar differentiation. These results indicate the dietary supplementation with non-toxic dose levels of DHEA has chemopreventive efficacy approaching that of endocrine ablation. This protection may be mediated by the induction of differentiation in the mammary gland, during which sensitive mammary parenchymal structures (terminal end buds) are stimulated to develop into structures (alveolar buds) less sensitive to carcinogenic insult. © 1993 Wiley-Liss, Inc.

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Trapping of Genes Induced Upon Growth Arrest After Treatment With Antiestrogen or Retinoids Using Retroviral Promoter Trap

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Abstract Although chemopreventive anti-steroids such as the antiestrogens are thought to act through competitive inhibition of agonist binding to estrogen receptors, it has been postulated that the estrogen receptor changes its conformation when bound to a strong antiestrogen such as ICI-164,384. We hypothesized that such conformationally changed receptors could bind specific recognition sequences in the genome and activate specific genes that might be involved in growth arrest. In order to identify such genes with a functional assay, we used a retroviral gene trap U3lacZ. We have now isolated MCF-7 breast cancer cell line clones in which the lacZ reporter gene is inserted into the genes activated by either ICI-164,384 or retinoic acid. One such clone, B4, was further characterized. In B4, lacZ activity is induced by ICI-164,384 or *trans*-retinoic acid, and repressed after treatment with estradiol. Cloning of the 5'-flanking genomic sequence in this clone will be possible using polymerase chain reaction.

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High Resolution Image Cytometry for Quantitative Assessment of Ductal Carcinoma *In Situ* of the Breast

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