

Capture-RT-PCR Assay of mRNA in Breast Tumors: *int-2* and HERV-K *env* mRNA

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Abstract Gene expression at the mRNA level is likely to be a rapidly responding intermediate biomarker for use as a surrogate endpoint in Phase II clinical trials of breast cancer. Using a technology called "capture-RT-PCR," we have been able to show ectopic *int-2* mRNA expression in 7/9 breast tumors, including two fibroadenomas. The level of expression varied, high expression being observed in three tumors. Frequent expression of *int-2* in breast tumors is contrary to published reports, possibly reflecting differences in technology. *int-2* expression in fibroadenomas suggests that the marker may precede malignancy. Conversely, if fibroadenomas are not premalignant, *int-2* expression may be gratuitous. These alternatives need to be tested in a clinical trial. Human endogenous retrovirus K (HERV-K) *env* gene expression was detected in only 1/7 breast tumors. Expression of this retroviral gene is more restricted than *int-2* expression. *c-myc* was expressed in all 10 tumors studied, albeit at widely varying levels. Expression of *prad1* and *erbB-2* are under study. Gene expression will be compared with gene amplification. It is anticipated that a capture-RT-PCR assay simultaneously signifying levels of expression of several oncogenes/anti-oncogenes will be a most informative surrogate endpoint biomarker.

In particular, chaotropic salt methods that simplify sample preparation and mRNA isolation and reduce these combined steps to a 10 minute procedure will be presented. © 1993 Wiley-Liss, Inc.

Dehydroepiandrosterone: A Chemoprotective Steroid

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Abstract Dehydroepiandrosterone (DHEA) and its sulfate conjugate, DHEAS, are steroids found in high concentration in human plasma. Levels peak in young adulthood and decrease steadily with age as the incidence of cancer increases. Several studies have found that low serum levels of DHEA or DHEAS or their urinary metabolites were associated with the presence or development of breast cancer. Dietary administration of DHEA significantly reduces the incidence of spontaneously and chemically induced mammary tumors in animals. DHEA also has potent chemoprotective actions in several other target organs against a variety of carcinogens. DHEA's mechanism of action is not known but may be due to its uncompetitive inhibition of glucose-6-phosphate dehydrogenase. Animal studies and tissue culture