proteins and cytoskeleton suggesting that it may play a role in transducing a signal from the cell membrane to the nucleus.

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MUTATIONS THAT ALTER THE FUNCTION OF GROWTH REGULATING GENES IN HUMAN BREAST CANCER

M.A.J. van Dijk, A.N. Floore, L.J. van 't Veer
The Netherlands Cancer Institute, Amsterdam, The Netherlands

Elevated levels of estrogen receptors (ER) are found in sixty percent of breast carcinoma and correlate with a better prognosis when patients are treated with antiestrogens. However, forty percent of the patients with an ER positive tumor do not respond to this treatment. Recent findings suggest that variant estrogen receptors may be present in these tumors that are non-functional or non-responsive, or on the contrary are responsive to antiestrogens. The expression of ER is routinely measured either by immunohistochemical staining or by a radioactive ligand binding assay, but neither method is suitable to detect variant receptors with altered function. We have developed a rapid functional screening method in yeast, that allows us to determine the prevalence and functional activity of variant estrogen receptors among normal receptors. The assay can discriminate between constitutively active, inactive and inducible ER variants.

The functional integrity of p53 tumor suppressor gene has been related to radiation or chemotherapy response. We are testing the functional activity of p53 of breast carcinoma also in a yeast growth assay. Frequently detected point mutations in p53 have all been associated with functional inactivation of the protein.

Testing functional activity of genes may prove to be of greater importance in predicting the outcome of therapy than merely analyzing their presence and may lead to improved treatment selection for breast cancer patients.

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CYTOGENETICS OF MESENCHYMAL TUMORS

F. Mitelman
University of Lund, Sweden

The cytogenetic information on solid tumors is in many respects only fragmentary and for many tumor types the knowledge is extremely limited. Furthermore, most solid tumors are characterized by very complex karyotypes which means that it is practically impossible to distinguish the pathogenetically relevant aberrations from the confusing variety of seemingly random changes that accumulate during tumor progression. In spite of all these shortcomings, an increasing number of characteristic and even specific karyotypic changes have been identified in both benign and malignant tumors of different histologic subtypes. Several of these aberrations, in particular those found in malignant mesenchymal tumors, have been characterized at the molecular level, e.g., t(12;16)(q13;p11) in myxoid liposarcoma, t(2;13)(q35;q14) in alveolar rhabdomyosarcoma, t(X;18)(p11;q11) in synovial sarcoma, t(11;22)(q24;q12) in Ewing's sarcoma, Askin's tumor and peripheral neuroepithelioma, t(12;22)(q13;q12) in clear cell sarcoma of tendons and aponeurosis, and t(11;22)(p13;q12) in the desmoplastic small round cell tumor. All these aberrations lead to the generation of fusion genes and result in the formation of presumably tumorigenic chimeric proteins.