RESEARCH HIGHLIGHTS FROM THE 93RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH
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BASIC RESEARCH

New Marker Identified for Metastatic Breast Tumors

Researchers at the University of Michigan reported results from a study suggesting that RhoC may be a marker for metastatic breast tumors, regardless of tumor size. RhoC-GTPase is member of the ras superfamily of proteins, which are known to affect cell polarity and motility. In this research, 182 breast tissues from 164 patients were examined by immunohistochemistry using a polyclonal antibody raised against RhoC. Data were analyzed quantitatively according to the intensity of antibody staining. RhoC was expressed in 36 of 114 (32%) invasive carcinomas and strongly correlated with tumor stage. It showed a high specificity for detecting metastatic tumors (88%), especially those smaller than 1 cm (92%). RhoC was not expressed in normal breast tissue, fibrocystic disease, atypical hyperplasia, or ductal carcinoma in situ. Researchers are continuing to work with tissues that overexpress HER2/neu and are negative for progesterone receptors, both of which are suggestive of poor prognosis. Identification of a biomarker for small invasive tumors would improve the selection of appropriate initial aggressive treatment for these tumors.

Receptor Tyrosine Kinase Mutation May Be Associated With Shorter Survival

Receptor tyrosine kinases in the epidermal growth factor receptor or fibroblast growth factor receptor (FGFR) families are thought to play a role in numerous cancers. Collaborative research from Germany (Martinsried and Munich) suggested that a mutation in FGFR may be associated with shorter survival for patients with head and neck squamous cell carcinoma. A single nucleotide polymorphism that inserts either a glycine or arginine was identified in FGFR4. The arginine substitution was shown to be a marker for poor prognosis. Quantitative evaluation of 104 head and neck squamous cell carcinoma tissues for this mutation demonstrated the mutation in 59 tumors. Examination of clinical data revealed that the mutation correlated with reduced overall survival (p = 0.02; log-rank test). The researchers suggested that these findings may serve to identify a new diagnostic biomarker and therapeutic target for this type of cancer.

New Ovarian Cancer Biomarker, Haptoglobin Alpha Chain, Identified

Researchers at the University of Michigan tested a new biomarker for ovarian cancer. They found that RhoC may be a marker for metastatic breast tumors, regardless of tumor size. RhoC-GTPase is a member of the ras superfamily of proteins, which are known to affect cell polarity and motility. In this research, 182 breast tissues from 164 patients were examined by immunohistochemistry using a polyclonal antibody raised against RhoC. Data were analyzed quantitatively according to the intensity of antibody staining. RhoC was expressed in 36 of 114 (32%) invasive carcinomas and strongly correlated with tumor stage. It showed a high specificity for detecting metastatic tumors (88%), especially those smaller than 1 cm (92%). RhoC was not expressed in normal breast tissue, fibrocystic disease, atypical hyperplasia, or ductal carcinoma in situ. Researchers are continuing to work with tissues that overexpress HER2/neu and are negative for progesterone receptors, both of which are suggestive of poor prognosis. Identification of a biomarker for small invasive tumors would improve the selection of appropriate initial aggressive treatment for these tumors.

Potential New Treatment Reduces Pancreatic Tumors and Metastasis

Researchers in Osaka, Japan, identified the hepatocyte growth factor (HGF) antagonist NK4, a peptide that may prove to be useful in treating pancreatic cancer. This malignancy is highly aggressive and resistant to treatment. NK4 is actually a fragment HGF that interferes with HGF binding to its cell surface receptor (c-Met). The interaction of HGF and c-Met stimulates intracellular signaling, causing cancer cells to invade normal tissues and metastasize. NK4 not only blocks HGF signaling but also inhibits blood vessel formation (angiogenesis) that is necessary for tumor growth. In this study, mice were injected with pancreatic cancer cells. After four days, they were treated daily with either NK4 or saline as a control. After 28 days, the tumors in the NK4-treated mice were one-third the size of the tumors in the control mice. Furthermore, blood vessel growth and metastasis were reduced significantly in the treated mice. In a second experiment, the NK4 treatment was withheld until late-stage cancer had developed (24 days). All of the mice in the control group had died by 69 days; however, 60% of the NK4 mice remained alive on day 70. The researchers plan to expand this work toward the development of human trials with NK4.

CLINICAL RESEARCH

Chemically Induced Hypothyroidism May Improve Survival for Patients With Recurrent Gliomas

High doses of tamoxifen previously have been shown to down-regulate protein kinase C-a, producing a cytostatic and apoptotic effect on glioma cells. The insulin-like growth factor-1 inhibits the apoptotic effects of tamoxifen on cell cultures and it modulated by the thyroid hormone. Researchers at Cleveland Clinic Cancer Center in Ohio reasoned that inhibition of thyroid gland function may enhance the effectiveness of tamoxifen in patients with recurrent gliomas, aggressive brain tumors that generally are unresponsive to chemotherapy. In the trial, 38 patients were treated with propylthiouracil 600–1,000 mg per day and Lugol’s solution 30 mg three times a day for 14 days. For 22 patients, tamoxifen 240 mg per day was begun within one month of entry into the study. For the remaining patients, tamoxifen was begun only when they were chemically hypothyroid. Of the 18 patients who became chemically hypothyroid, 5 (28%) had a significant reduction in tumor size. However, tumor size was not reduced for any of the patients who remained euthyroid. Toxicities included one occurrence of each of the following: deep vein thrombosis, nausea and vomiting, fatigue, and ataxia. One patient became symptomatic from hypothyroidism. Furthermore, the median survival for the hypothyroid group was 10.6 months compared with 3.1 months for the euthyroid group. Three of the patients who became hypothyroid survived more than two years, whereas the longest surviving patient of the euthyroid group lived eight months. This treatment now is being tested in patients with newly diagnosed glioma.