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RESEARCH HIGHLIGHTS

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Basic Research

Ovarian Cancer Cell Proteins May Be Useful for Early Detection

Ovarian cancer, the most lethal of the gynecologic cancers, often remains undetected until it is in later stages. Proteomic technologies offer the possibility of developing an early-detection diagnostic assay. Researchers from the School of Medicine at Tufts University in Boston, MA, the National Cancer Institute in Bethesda, MD, and Northwestern University Medical School in Chicago, IL, presented the results of a study examining the serum from patients with ovarian cancer (n = 115) and unaffected women (n = 127). Mass spectrometry and Western blotting were used to identify low–molecular-mass proteins that bound to the carrier protein, albumin. An iterative searching algorithm was used to identify a proteomic pattern that discriminated between cancer and noncancer serum samples. The cluster pattern that emerged was 100% sensitive and 100% specific. Novel biomarkers were identified from the clusters. The researchers concluded that albumin is a significant source of diagnostic information. Their work suggests that science may be able to identify diagnostic markers useful for detecting early-stage ovarian cancer in women at high risk and in the general population.

Progesterone Receptor Antagonists Prevent Carcinogen-Induced Breast Cancer in Rats

Researchers from Schering AG Corporate Research in Berlin, Germany, presented the pharmacologic characterization of a novel progesterone receptor antagonist. Progesterone is known to contribute to the proliferation of mammary tumors. The progesterone receptor antagonist demonstrated antiprogestagenic and antiproliferative activity in animal models. In human breast cancer models, the antagonist suppressed the growth of established tumors. In rats, the progesterone receptor antagonist prevented tumor growth that normally occurs in response to treatment with nitroso-methylurea and dimethyl-benzathracene. The researchers concluded that the biologic response to the antagonist does not result solely from its antiprogesterone effects. The compounds appear to be able to induce tumor cell differentiation that leads to apoptosis, suggesting a unique mechanism of action.

High Levels of Cancer-Causing Agent Are Present in the Amniotic Fluid of Female Smokers

Researchers from the University of Louisville in Kentucky measured levels of polycyclic aromatic hydrocarbons (PAHs) in amniotic fluid from female smokers who smoked half a pack per day to more than two packs per day and nonsmokers between the 16th and 20th weeks of pregnancy. Previous work by these scientists examining serum had shown a clear correlation between maternal smoking and fetal exposure to smoke PAH carcinogens, including 4-aminobiphenyl and benzo(a)pyrene. PAHs were found in nearly all of the amniotic fluids examined. Maternal smoking levels correlated with the amount of PAHs in the amniotic fluid. For example, 1-hydroxypyrene levels ranged from 1.54 +/– 0.12 micrograms/l in nonsmokers to 11.72 +/– 0.67 micrograms/l in women who smoked more than two packs per day. This tenfold increase in PAHs also was found for hydroxylated benzo(a)pyrene derivatives, which ranged from 1.41 +/– 0.13 micrograms/l for nonsmokers to 11.56 +/– 0.59 micrograms/l for women who smoked more than two packs per day. The researchers suggest that these harmful environmental carcinogens during early gestation may place the fetus at risk for genotoxic and teratogenic events.

Pentobarbital Inhibits Colon Cancer Cell Metastasis in Mouse Model

Nembutal® (pentobarbital, Abbott Laboratories, Abbott Park, IL) acts on gamma-aminobutyric acid (GABA) receptors to suppress the central nervous system. GABA receptors also are present in colon and ovarian cancer cells. Researchers at the University of Texas M.D. Anderson Cancer Center in Houston investigated the ability of Nembutal to suppress cancer cell growth and metastasis using a mouse model. They examined several colon cancer (KM12SM, HT29, RKO) and ovarian cancer (SKOV3ipl, HeyA8, OVCAR3, 222) cell lines for the expression of GABA receptors using Western blots. The receptors were present on all colon cancer cells lines and most ovarian cancer cell lines. Cytotoxicity assays measuring cellular respiration demonstrated that continuous exposure to 50 micrograms/ml of Nembutal for 96 hours reduced cell proliferation by 50%. KM12SM cells were injected into the cecum or spleen of nude mice, and tumor growth and metastasis were measured. In these experiments, mice were anesthetized with either methoxyflurane by inhalation or Nembutal by intraperitoneal injection (50 micrograms/ml). Primary tumors developed in the cecums of 9 of 10 mice anesthetized with methoxyflurane compared to 7 of 10 mice anesthetized with Nembutal. The mean weights of the tumors were 1.08 g +/– 0.19 and 0.38 g +/– 0.13 (p = 0.04) for the methoxyflurane and Nembutal groups, respectively. Primary tumors developed in the spleens of 8 of 10 mice in the methoxyflurane group compared to 4 of 10 mice in the Nembutal group. The mean weights of the tumors were 2.08 g +/– 0.73 and 0.53 g +/– 0.39 (p = 0.048) for the methoxyflurane and Nembutal groups, respectively. In the mice that had splenic injections, liver metastasis occurred in 80% of the methoxyflurane group and 20% of the Nembutal group (p = 0.007). The researchers concluded that this is the first evidence that Nembutal is an inhibitor of colon cancer and that this result may have important therapeutic applications.

Erythropoietin Improves Learning and Memory Outcomes After Whole Brain Irradiation in Mouse Model

Erythropoietin is a renal hormone known to be important in red blood cell production. Erythropoietin also is known to enter the central nervous system when administered systemically. Researchers from Sunnybrook and Women's College Health Sciences Centre in Toronto, Canada, presented the results of a study of the neuroprotective effects of erythropoietin in a mouse model. Experimental dose groups of 10 mice were established. Animals received 0, 2, 8, 17, or 22 Gy of whole brain irradiation. Erythropoietin doses of 1,000, 5,000, or 10,000 units/kg were given intraperitoneally one hour following radiation. Open field, hole-board,

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