

## RESEARCH HIGHLIGHTS

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#### Basic Research

#### Low-Dose Cyclooxygenase-2 Inhibitor and Fish Oil Component May Reduce Risk of Colon Cancer

Studies have suggested that nonsteroidal anti-inflammatory drugs and diets rich in polyunsaturated fatty acids (PUFAs) can reduce the risk of colorectal cancer. Researchers from the Institute for Cancer Prevention, American Health Foundation–Cancer Center in Valhalla, NY, presented the results of a study of the combined effect of a cyclooxygenase-2 inhibitor, celecoxib, and an n-3 PUFA, docosahexanoic acid (DHA), which is a component of fish oil, on colon cancer cells in a cell culture. The results showed that a high dose of celecoxib (150 mcM) or DHA (300 mcM) induces apoptosis and inhibits cell proliferation. Synergy occurs at lower doses when the two agents are combined, 50–100 mcM celecoxib and 100 mcM DHA. Key molecular targets of celecoxib and DHA were suppressed at these low doses. This work suggests that the combination of celecoxib and DHA warrants further investigation in preclinical studies.

#### New Gene Is Associated With Breast Cancer

Researchers from the University of Rochester and Vaccinex Inc., both in Rochester, NY, have identified a novel gene, C35, that could become a target for breast cancer therapies. In a study of 35 grade II and III infiltrating ductal carcinomas, 34% expressed the protein encoded by the C35 gene as well as the HER2-neu protein known to be a marker of poor prognosis in breast tumors. Another 31% that did not express HER2-neu did have the C35 protein. All tissues that had the HER2-neu protein also had the C35 protein. When the researchers examined normal tissues, they found that the C35 protein was present at very low levels in normal breast epithelium and in the Leydig cells of the testes. They also found that they could generate specific cytotoxic lymphocytes using C35 peptides. This work suggests that C35 may be a novel target for breast cancer therapy. The cellular immune response may make C35 a suitable target for immuno-

therapy. Researchers also are working to develop a diagnostic test for C35 protein or antibodies in blood samples.

#### Clinical Research

#### Low-Dose Tamoxifen May Enhance Compliance in Treating Breast Cancer

A randomized trial directed by researchers at the Division of Cancer Prevention European Institute of Oncology in Milan, Italy, involved 120 women with estrogen receptor- (ER-) positive breast cancer. The study examined treatment with 1, 5, or 20 mg of tamoxifen daily for four weeks prior to surgery. The results were compared with two nonrandomized control groups: 34 women with ER-negative breast cancer and 29 women with ER-positive breast cancer. Ki-67 levels, a marker for tumor proliferation, were measured before and after tamoxifen treatment. Tamoxifen was shown to significantly reduce Ki-67 levels in the tissues, but no associated drug dose effect existed. Even though more of the drug accumulated in tumors of patients taking 20 mg tamoxifen daily, no correlated reduction in Ki-67 occurred. Because lower doses of tamoxifen are associated with a lower risk for complications such as endometrial cancer, the researchers suggest that patients may achieve maximum benefit from lower doses. On the other hand, researchers found that other disease markers were tamoxifen-dose dependent: insulin-like growth factor-1, cholesterol, triglycerides, and antithrombin III. Lower doses of tamoxifen would reduce the beneficial effects associated with these markers.

#### Serum Caveolin-1 May Be a Predictor of Prostate Cancer Progression

Caveolin-1 (cav-1) is important in signaling pathways, molecular transport, and cellular proliferation and differentiation. Cav-1 was shown previously to be increased in metastatic prostate cancer and to be a predictor of recurrent disease after radical prostatectomy. Researchers from Baylor College of Medicine in Houston, TX, developed a highly specific and sensitive enzyme-linked immunosorbent assay to measure cav-1 levels in serum. Serum from four groups was analyzed: group one (control) from patients with prostate-specific antigen levels below 1.5 ng/ml for two years (n = 115), group two from patients with clinical benign prostatic hyperplasia (BPH) (n = 149), group three from patients with clinically localized prostate cancer prior to radical prostatectomy

(n = 119), and group four from patients with recurrent prostate cancer prior to radical prostatectomy (n = 23). The median serum cav-1 levels for group three (0.429 ng/ml) were statistically higher than those of either group one (0.214 ng/ml, p = 0.267) or group two (0.127 ng/ml, p = 0.175). No statistical difference existed in serum cav-1 levels between groups one and two. The serum cav-1 level also was shown to be a significant predictor of time to recurrence (p = 0.0074, Cox proportional hazard model). The researchers concluded that cav-1 may be an important biomarker to differentiate prostate cancer and BPH. It also may be a significant predictor of disease recurrence.

#### Serum IGF-1 May Predict Favorable Outcomes for Patients With Renal Cell Carcinoma

Researchers from Umea, Sweden, presented the results of a study of serum leptin, IGF-1, and prealbumin at the time of diagnosis for 256 patients with renal cell carcinoma. IGF-1 and prealbumin levels were inversely proportional to tumor stage and grade. Eighty-six patients were alive at the time of follow-up (median 61.5 months). Tumor stage and IGF-1 levels were shown by multivariate analysis to predict survival. Other variables, such as age, gender, serum leptin, and prealbumin, did not predict survival. IGF-1 levels greater than the median value of 55 ng/ml were correlated with a more favorable outcome compared to lower levels. These data suggest that IGF-1 level may be a useful prognostic indicator.

#### Estrogen Receptor Alpha Levels in Prostate Tissue Differ Among Men According to Ethnicity

Hispanic and Asian American men have a lower incidence and mortality rate for prostate cancer compared to African American men. The molecular mechanisms underlying this difference may involve estrogen receptor alpha. Researchers from Baylor College of Medicine in Houston, TX, and the University of California, San Francisco, used cDNA microarrays, quantitative polymerase chain reaction, and immunohistochemistry

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