Protein-based tumor biomarker predicts breast-cancer survival

December 5 2006

The first and largest clinical trial of its kind confirms that a protein called p27 may be a valuable tool for predicting survival after a diagnosis of breast cancer.

The findings, by lead author Peggy Porter, M.D., of Fred Hutchinson Cancer Research Center, in collaboration with colleagues from nine other institutions, appear in the Dec. 6 issue of the Journal of the National Cancer Institute.

More than a decade ago, Porter and colleagues at the Hutchinson Center identified p27, a protein that prevents cells from dividing. Since then, several population-based and clinical studies at the Hutchinson Center and elsewhere have indicated that abnormally low levels of this protein in tumor cells are associated with poor prognosis for breast and other cancers. This link suggests that p27 may be a useful clinical biomarker, or predictor, of breast-cancer survival. However, such attempts to determine the prognostic value of p27 have been limited by the fact that the women studied have not received uniform treatment, so it has been unclear whether certain treatments may impact the strength of p27 as a predictor of outcome.

Now, for the first time, researchers have confirmed the link between low p27 expression and decreased breast-cancer survival in a large randomized, controlled clinical trial of two standard chemotherapy drugs.

"Being able to look at the impact of p27 on breast-cancer outcome in a clinical setting in which all the women were treated similarly allows us to tease out the relationship between the expression of this protein and breast-cancer mortality. Until now, we haven't been able to look at this," said Porter, a member of the Hutchinson Center's Human Biology and Public Health Sciences divisions.

The researchers found that low p27 expression is associated with poor breast-cancer prognosis, particularly among women with hormone-receptor-positive tumors, which depend on the hormones estrogen and progesterone to grow. Specifically, they found the five-year survival was 91 percent in women whose tumors had high p27 expression, as compared to a survival rate of 85 percent in women whose tumors exhibited low p27 expression. The researchers found no association between p27 expression and decreased survival among women with hormone-receptor-negative tumors.

The multicenter study involved more than 3,000 women nationwide (median age 47) with newly diagnosed moderate-risk, primary breast cancer who underwent treatment with doxorubicin and cyclophosphamide. The trial was designed to assess the effectiveness of giving the drugs together (concurrently) or one after the other (sequentially). The study was conducted through the Southwest Oncology Group, one of the largest cancer clinical trials cooperative research efforts in the United States.

Tissue samples for the study were provided by several SWOG clinical-trial groups (the Eastern Cooperative Group, North Central Cancer Treatment Group, and Cancer and Leukemia Group B). "The collaboration among these groups enabled us to gather enough data to produce statistically significant results," said Porter, whose Hutchinson Center team analyzed more than 2,000 breast-tumor samples for p27 expression. The specimens were analyzed via tissue microarray, a

relatively new technique that mimics high-throughput methods originally developed for large-scale genetic analysis.

Using this method, many tumor samples can be analyzed for protein expression at once.

While the findings suggest that p27 may be a useful clinical tool for predicting breast-cancer mortality, more work needs to be done before it sees widespread use, Porter said.

"I think p27 has clinical potential, but we still need to define which patient populations are going to benefit most. Right now it looks like it may be most useful for predicting outcome and tailoring treatment in women whose tumors are hormone-receptor positive," Porter said.

Source: Fred Hutchinson Cancer Research Center