DNA methylation marker shows promise for detecting breast cancer risk

By Pamela Kidron

DNA methylation could prove to be an effective indicator of breast cancer risk, according to a new study published online April 11 in the Journal of the National Cancer Institute.

DNA methylation is a form of epigenetic modification that may control gene regulation, but is not directly part of the DNA sequence. In this study, NIEHS epidemiologists Jack Taylor, M.D., Ph.D., and Zongli Xu, Ph.D., discovered that, by measuring such epigenetic modifications, it's possible to capture changes in susceptibility to breast cancer that result from factors such as aging or the environment — changes that genetic studies of DNA sequence do not capture.

Taylor's group found that evidence of this modification was a better predictor of breast cancer risk than other approaches, such as the Gail model, which relies on known risk factors including age; reproductive, medical, and family history; and common polymorphisms. However, Taylor cautions that the work is the first study of its kind and that these measurements are not yet accurate enough for clinical use.

Taylor has duel appointments in the NIEHS Epidemiology Branch and the Laboratory of Molecular Carcinogenesis. (Photo courtesy of Steve McCaw)

NIEHS Sister Study yields valuable data

Working with DNA extracted from white blood cells in blood samples, Taylor and his colleagues assessed the methylation profile of 27,000 sites across the genome. They used samples from a cohort of women in the NIEHS Sister Study, a nationwide study of women who have had a biological sister with breast cancer. The Sister Study is designed to explore genetic and environmental determinants of breast cancer.

The NIEHS team used the data to examine whether these sites were different in those who later developed breast cancer than those who did not. They also examined the predictive power of blood methylation, compared with the Gail model, and 10 common polymorphisms that are associated with breast cancer risk.

The data provided evidence that there are differences in blood DNA methylation in those who ultimately develop breast cancer. These differences are detectable months to years before the clinical diagnosis of breast cancer.

Of the 250 differentially methylated sites the team identified, 188, or 75.2 percent, were undermethylated. The prediction accuracy via methylation was 66 percent, compared to 56 percent for the Gail model and 59 percent for genome-wide association study polymorphisms.

"While methylation profiling of blood holds promise for detecting and predicting breast cancer, we have to be careful," cautioned Taylor. "The next step is to replicate these methylation findings in other studies."

Xu is a staff scientist in the NIEHS Epidemiology Branch and first author on the paper. (Photo courtesy of Zongli Xu)

Because of the possibility that effects could differ by race or ethnicity, Taylor and the team restricted their analysis to non-Hispanic whites. Now, the findings must be replicated in studies of other ethnic groups. Also, the study was done with women who each had a sister with breast cancer, and it cannot be assumed that these results would apply to women with a different family history.
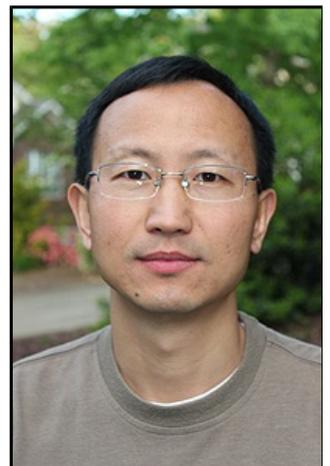
Producing a diagnostic tool

The study may help researchers move closer to developing a blood test that can predict a woman's chances of developing breast cancer. Women with elevated risk could then be monitored closely. Early diagnosis of breast cancer, before it spreads, is essential for successful treatment.

Breast cancer is the most common cancer in women and the leading cause of cancer mortality worldwide. Some 40,000 people die annually from breast cancer in the United States.

Taylor heads the NIEHS Molecular and Genetic Epidemiology Group, which works toward understanding the interaction between genes and environmental exposures in human carcinogenesis. The Sister Study is led by NIEHS Epidemiology Branch Chief Dale Sandler, Ph.D.

(Pamela Kidron is a contract writer with the NIEHS office in Bethesda, Md.)