Predicting individual breast cancer risk may be possible

August 12 2013

Harvard Stem Cell Institute Principal Faculty member Kornelia Polyak, of Dana-Farber Cancer Institute and Harvard Medical School, lead the study that identified p27 as a possible marker for breast cancer risk. Credit: B. D. Colen/Harvard University

An international scientific collaborative led by the Harvard Stem Cell Institute's Kornelia Polyak, MD, PhD, has discovered why women who give birth in their early twenties are less likely to eventually develop breast cancer than women who don't, triggering a search for a way to

confer this protective state on all women.

The researchers now are in the process of testing p27, a mammary gland progenitor marker, in the tissue of thousands of women collected over a 20-year period—women whose histories have been followed extremely closely—to see if it is an accurate breast cancer predictor in a large population of women. If the hypothesis is confirmed, likely within a few months, Polyak says the commercial development of a clinical test for breast cancer risk would follow.

In a paper just published in the journal *Cell Stem Cell*, the researchers describe how a full-term pregnancy in a woman's early twenties reduces the relative number and proliferative capacity of mammary gland progenitors—cells that have the ability to divide into milk-producing cells—making them less likely to acquire mutations that lead to cancer.

By comparing numerous breast tissue samples, the scientists found that women at high risk for breast cancer, such as those who inherit a mutated BRCA1 or BRCA2 gene, have higher-than-average numbers of mammary gland progenitors. In general, women who carried a child to full term had the lowest populations of mammary gland progenitors, even when compared to cancer-free women who had never been pregnant. In addition, in woman who gave birth relatively early, but later still developed breast cancer, the number of mammary gland progenitors were again observed to be higher than average.

"The reason we are excited about this research is that we can use a progenitor cell census to determine who's at particularly high risk for breast cancer," said Polyak, a Harvard Stem Cell Institute Principal Faculty member and Harvard Medical School professor at the Dana-Farber Cancer Institute. "We could use this strategy to decrease cancer risk because we know what regulates the proliferation of these cells and we could deplete them from the breast."

Research shows that two trends are contributing to an increase in the number of breast cancer diagnoses—a rise in obesity and the ever-increasing number of women postponing child bearing. The scientists' long-range goal is to develop a protective treatment that would mimic the protective effects of early child bearing.

The research, which took five years to complete, began with conversations between Polyak and John Hopkins University School of Medicine Professor Saraswati Sukumar, PhD. The two scientists formed collaborations with clinicians at cancer centers that see large numbers of high-risk women in order to obtain breast tissue samples. They also worked with genomics experts and bioinformaticians to analyze gene expression in different breast cell types. At times, Polyak and Sukumar had trouble convincing others to help with the study, which is unique in the breast cancer field for its focus on risk prediction and prevention.

"In general people who study cancer always want to focus on treating the cancer but in reality, preventing cancer can have the biggest impact on cancer-associated morbidity and mortality," Polyak said. "I think the mentality has to change because breast cancer affects so many women, and even though many of them are not dying of breast cancer, there's a significant personal and societal burden."

More information: www.cell.com/cell-stem-cell/abstract/S1934-5909%2813%2900197-5

Provided by Harvard University