Your Genes, Environment and Breast Cancer Risk: the Two Sister Study

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Why do some women develop breast cancer and not others? And why do some women develop breast cancer at a much younger age? We know that factors like weight, alcohol consumption and hormone replacement therapy, among others, may affect breast cancer risk. But some women with one or more risk factors will never get breast cancer, while some women with no apparent risk factors will still develop the disease.

These questions prompted Komen grantee Dr. Clarice Weinberg, and her colleagues Drs. Dale Sandler and Lisa DeRoo, to conduct a study on how a woman's genes and her environment might affect her risk of breast cancer. In 2008, the researchers launched the Two Sister Study, funded by Komen with a 5-year, $1.75 million grant, along with funding from the National Institute of Environmental Health Sciences (NIEHS).

The Two Sister Study builds upon the work of the Sister Study and focuses on women who developed breast cancer at a young age, with the idea that this group of women can help us learn a lot about the genetic and environmental causes of breast cancer. What makes the Two Sister Study unique is that it gathers data from sisters, who share similar genes and possibly environmental backgrounds.

The Two Sister Study enrolled over 1,400 women recently diagnosed with early-onset breast cancer (under the age of 50), 1,700 of their sisters from the Sister Study (who did not have breast cancer), and parents when possible. Participants provided detailed information about family and medical history, diet, occupation, as well as house dust and DNA samples. After collecting hundreds of samples and surveys from study participants, their sisters and families, Dr. Weinberg and her collaborators identified new potential risk factors for young women. Specifically, the research team found that women who were sensitive to certain hormonal changes differed in their risk for early-onset breast cancer.

They found that **reduced risk** was associated with:

- Fertility treatments to stimulate ovaries when it does not result in pregnancy.
- Night sweats and hot flashes in pre-menopausal women, which are symptoms typically associated with menopause.
- History of pregnancy-associated hypertension (high blood pressure).
- Hormone replacement therapy with estrogen alone.

Dr. Weinberg also found that women who suffered from menstrual migraines were less likely to develop hormone receptor negative breast cancer (estrogen receptor-negative and progestin-receptor negative). Together, these findings suggest that a young woman's overall response to hormones during the different phases in her life may be related to her risk of developing breast cancer early.

The initial results from the Two Sister Study about a woman's response to hormones add to our knowledge of breast cancer risk factors and early-onset breast cancer. Data from the study are still being analyzed in efforts to identify other risk factors for breast cancer. "The rich data (we have) developed through this family-based study offers a unique window on little-studied possible mechanisms," says Dr. Weinberg. Data on genetic mutations that impact early-onset breast cancer will continue to be mined for years to come as scientists continue to identify both genetic and modifiable (e.g. behavioral) factors related to survival and good health in survivors of young onset breast cancer.

The genetic data collected through this research project are now publically available through the NIH's CIDR dbGap website for researchers to use at: http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000678.v1.p1.

Jack Taylor: Senior Investigator, NIEHS

Dale Sandler: Chief, Epidemiology Branch and Principal Investigator, NIEHS

Lisa DeRoo: Staff Scientist, NIEHS and University of Bergen, Norway

Clarice Weinberg: Chief, Biostatistics & Computational Biology Branch and Principal Investigator, NIEHS Stephanie London: Deputy Chief, Epidemiology Branch and Principal Investigator, NIEHS

Paula Juras: Project Officer, NIEHS

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