Susan G. Komen for the Cure
Research Grants – Fiscal Year 2011

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Development of an individualized risk prediction model for women with atypical hyperplasia

Investigator(s): Derek Radisky, PhD, Lynn Hartmann, MD
Mayo Clinic and Foundation, Jacksonville, FL

Awarded: $597,939.00
Grant Mechanism: Investigator Initiated Research
Research Focus: Early Detection

Public Abstract:
Women with atypical hyperplasia of the breast (atypia) are known to have a four-fold increased risk for subsequent development of breast cancer; recent long-term follow-up of a cohort of women with atypia by our study group has documented that women with atypia have an ~ 30% risk of developing breast cancer within 25 years. Atypia is diagnosed in approximately 40-50,000 women each year in the US, and these women are frequently counseled to pursue strategies of heightened screening, along with tamoxifen or raloxifene. Occasionally prophylactic surgery is considered. Unfortunately, the field is limited by the lack of accurate information about the risk for individual women with atypia. There are two breast cancer risk prediction models that practitioners use, which incorporate the presence of atypia—the Gail and the IBIS (Tyrer-Cuzick) models—but our group has shown and published that both of these perform no better than chance alone for individual women with atypia. Thus, there is currently no effective method for predicting the specific risk of breast cancer for an individual woman with atypia. Generally speaking, the cancers for which we can best predict disease susceptibility are those where we can directly examine the tissue at risk (for example, cervix or colon) for evidence of premalignant change. To facilitate the development of tissue-based breast cancer risk prediction for women with atypia, we have identified a cohort of 630 women who were diagnosed with atypia between 1969 and 2001; 130 of these women have developed breast cancer to date. Importantly, there is benign tissue available for all these women for in-depth pathologic study and biomarker development. Currently there are no methods for assessing subsequent cancer risk that make effective use of the pathological information contained within the breast biopsy showing atypia. Our proposal is designed to fill this critical gap. We aim to develop an individualized breast cancer risk prediction model for women with atypia that utilizes clinical as well as biopsy characteristics. Our model will integrate risk factors obtained from a study-specific questionnaire and the patient's medical history with risk factors related to tissue structure and gene expression patterns that can be assessed from the breast biopsy used to diagnose atypia. We predict that our new breast cancer risk model will be of great utility to women with atypia, providing better risk stratification before selecting surveillance and risk-reduction strategies. The result of implementing this model will be earlier disease detection, and hence reduced mortality, through heightened surveillance when appropriate. Additionally, by accurate, early identification of those women at greatest risk for breast cancer, we can recommend appropriate risk reduction maneuvers, expected to reduce incidence of the disease. Conversely, if our model can accurately predict low risk for a subset of women with atypia, this knowledge may reduce their psychological stress and avoid unnecessary interventions. Beyond risk prediction, this research has the potential to contribute to a better understanding of the pathways and mediators that drive the progression of breast cancer from atypia, leading in the future to the identification of new targets for physiologic risk reduction strategies.