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Meeting abstract

Oncogenic viruses in nipple aspirate fluid: biomarkers for breast cancer risk assessment?

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It would be a considerable advantage to be able to identify women at high risk for developing breast cancer to justify closer follow-up and use of multiple methods to ensure early detection. At present, the only high risk individuals identifiable with a biomarker are those ≈5% with a strong familial history of breast cancer. For the remaining 95% there is a lack of such biomarkers. Three independent epidemiologic studies found that women with mammary epithelial cells (MEC) in their nipple aspirate fluids (NAF) were more likely to subsequently develop breast cancer than women without cells. A possible explanation for this is that early stages of breast carcinogenesis and tumor progression most likely involve MEC hyperplasia triggered by a carcinogenic agent. Viruses cause several major human cancers (e.g. primary liver cancer and cervical cancer). Recent studies found bovine leukemia virus (BLV), Epstein-Barr virus (EBV), and human papilloma virus (HPV) more frequently in breast tissues of women with breast cancer vs. those with no breast cancer history.

The objective in this study is to determine if oncogenic viruses in NAF MEC can serve as biomarkers to identify women at high risk for breast cancer. Specific aims are 1) to test the feasibility of detecting genomes of BLV, EBV, and HPV in MEC from NAF using in situ PCR, which allows localization of the signal to individual cells; 2) to determine if viral presence in NAF correlates with viral presence in matching breast tissue from the same donor; 3) to determine if viruses are present more frequently in women with breast cancer history than those without. The pilot grant from the Dr. Susan Love Research Foundation has enabled us to tackle some of the technical challenges (specific aim #1). The first challenge was to minimize loss of NAF MEC from the slide during the PCR reaction. We found that neither modifications of fixation nor addition of viscous additives could improve adherence when NAF cells were sparse. Therefore, we will use only samples with at least 100 cells per slide to assure adherence of enough cells to analyze. The second challenge is to screen for 3 viruses using one NAF preparation per donor, since that is all that is available to us. We have worked out a scheme whereby all three viruses could be amplified simultaneously and then detected individually with specific DNA probes in one in situ hybridization reaction. Each probe would have a different label incorporated into its DNA, with the final detection signal fluorescing at different wavelengths. We have begun to test this triple label system using three control cell lines each harboring one of the three viruses.

Specific aims #2 and #3 involve analysis of patient samples for the presence of the three oncogenic viruses. With co-funding from the Avon Foundation, we have begun the acquisition of matching tissue sections and NAF (cytospun onto slides) from the same donor, provided by Drs. Krishnamurthy and Kuerer at M.D. Anderson Cancer Center in Houston, TX. Women with NAF cell abnormalities are 4–5 times more likely to develop breast cancer than women with no NAF. This pilot study aims to determine if that risk is related to oncogenic viruses and to eval-

uate the feasibility of detecting these viruses in NAF. The results could be translational, enabling identification of women at higher risk of developing breast cancer, just as HPV screening of cervical samples is now being used.