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Progress Report, May 2001 – May 2002  
“Breast Cancer Susceptibility and DNA Damage/Repair”

U.S. Department of the Army  
Grant # DAMD17-01-1-0578

The study is based on breast cancer cases and matched controls from a cohort of women (New York University Women’s Health Study—NYUWHS) who have been followed up for 7-13 years since they donated a blood sample and completed a health, lifestyle and dietary questionnaire to determine the incidence of breast cancer. The original proposal was to genotype 6 polymorphisms in the genetic pathways for DNA repair or protection against DNA damage in 200 cases and 200 matched controls.


We expanded the study to 300 cases and 300 controls. For about 40% of subjects we had blood clots or cell aggregates (left after separating out the serum) from which to extract DNA, but for the remainder we had to extract it from the serum. There was abundant DNA in the clots and cell aggregates but much less in the serum.

Before genotyping a locus we conducted a quality control/validity check. This included performing analyses on two samples from each of about 70 women. We concentrated on the adequacy of the DNA samples from serum because of concerns about the amount and integrity of the DNA in serum and therefore ran 50 pairs comparing a serum and clot sample. For one locus we found that we had to adjust the conditions of the PCR and hybridization for the serum-based DNA in order to get good agreement with the corresponding clot-based DNA. Had we not run this comparison, we would not have known that the serum-based DNA was giving us inaccurate readings based on our initial optimization.

We have completed the genotyping of three of the proposed loci (XPD, XRCC1 and MnSod) and are in the midst of analyzing those data.

We have requested an unfunded extension of the study for another year (until June 30, 2003). The other three loci will be completed and the results written up during that time period.

Signed: \_\_\_\_\_

  
Roy E. Shore, PhD, DrPH