CHARACTERIZATION OF GERMLINE MUTATIONS IN THE BREAST CANCER GENE 1 - EXON 15

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ABSTRACT

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Breast cancer is the most common malignancy in women and is the leading cause of death in women between the ages of 40 and 55. The genetic analysis of families with multiple cases of breast cancer has lead to the identification of two breast cancer susceptibility genes, the breast cancer gene 1 (BRCA1) and the breast cancer gene 2 (BRCA2). It is estimated that about 5% of all cases of breast cancer are transmitted as an autosomal dominant genetic trait, and a fairly high proportion of these are associated with a BRCA1.

The aim of this study is to detect germline mutations in the Exon 15 of the BRCA1 in selected Sri Lankan breast cancer patients and there by, to provide a stepping stone in the isolation of common germline mutations in BRCA1. Subjects screened for mutations were women clinically diagnosed and prior to treatment for breast cancer at the National Cancer Institute, Maharagama and the National Hospital of Sri Lanka, Colombo. Following the extraction of genomic DNA the target sequence of interest was amplified by the polymerase chain reaction. 60 subjects were analyzed as such. Out of the 60 samples screened, 51 were successfully amplified. Only these 51 samples were analyzed by Single strand conformation polymorphism and Hetero duplex analysis. Sequence variants usually show differences in mobility, and the presence of mutations is revealed as the appearance of new bands. Sequencing can further illuminate such samples.

The 51 patient samples screened by Single strand conformation polymorphism and Hetero duplex analysis did not show any mobility difference when compared with the normal control sample indicating that the samples did not give an indication of a mobility shift of either SSCP or HDA for the exon 15 of BRCA1. One reason for this could be the overall low prevalence of mutations in this exon. Such negative test result in women who has breast cancer is not informative. It is likely that a mutation might be present in any other exon other than exon 15 or that a mutation might be present in any other gene other than BRCA1. Screening a larger number of patient's with a positive family history for breast cancer could overcome this. Further studies are needed to identify mutations present and currently work is in progress to identify mutations common to Sri Lankan breast cancer patients.