Breast Cancer is one of the most prominent cancers among women worldwide, and this is particularly true in Malaysia, where it constitutes a significant proportion of cancer cases. According to the article, “Mutation Analysis of the BRCA1 Gene in Malaysian Breast Cancer Patients,” in 1995, breast cancer accounted for 9.6% of cancer admissions in government hospitals and 20% of 317 women who died of breast cancer were below the age of 40[1], Researchers have linked the early onset cancer susceptibility gene, also known as BRCA1, to hereditary breast and ovarian cancer. Germline mutations in the BRCA1 gene have also been found to significantly increase the risk of developing both breast cancer and ovarian cancer[1]. According to the article, most recognized BRCA1 mutations are from those of Caucasian origin whereas information on the BRCA1 mutations in the Malaysian ethnic group is lacking[1]. To better explore this knowledge gap, scientists carried out a detailed analysis of the BRCA1 gene in patients in Malaysia, focusing on the main ethnic groups: Chinese, Indians, and Malays. The study aimed to perform a comprehensive analysis of the BRCA1 gene in hopes of identifying mutations that could contribute to breast cancer susceptibility. Experiments were focused on patients with early-onset breast cancer and a family history of breast cancer to better understand the BRCA1 gene mutation spectrum in the population. The entirety of the BRCA1 gene coding region was investigated using direct sequencing in Malaysian patients with early onset breast cancer and in patients with two or more relatives that have had breast cancer and/or ovarian cancer[1]. The BRCA1 gene was screened in two clinically selected groups. The first group was composed of patients with histologically confirmed breast cancer before the age of 35 and the second group was composed of patients with histologically confirmed breast cancer having two or more relatives with breast and/or ovarian cancer with no regard to age[1]. A total of 30 patients were included in the study, 16 patients from the Malays ethnic group, 9 patients from the Chinese ethnic group, and 5 patients from the Indian ethnic group[1]. Blood was collected from patients followed by the use of Polymerase Chain Reaction and direct sequencing to analyze the entire coding region of the BRCA1 gene[1]. Results identified a frameshift mutation found in exon 21 in nucleotide 5447 codon 1776 in one 32-year-old patient from Malaysian origin which was predicted to result in a premature stop codon at position 1829[1]. This mutation is said to disrupt the involvement of the BRCA1 gene in DNA binding and protein-protein interaction[1]. In addition to this frameshift mutation, eight polymorphisms were identified, all of which were found in patients from the Chinese, Malay, and Indian ethnic groups with the exception of one polymorphism which was only found in the Malay and Chinese groups[1]. The eight polymorphisms included 2201C>T, 2430T>C, 2731C>T, 3232A>G, 3667A>G, 4427T>C, 4956A>G, and IVS8-57delT[1]. The number of patients with the polymorphism were as follows, 4/30, 18/30, 19/30, 14/30, 19/30, 18/30, 20/30, and 16/30 respectively[1]. BRCA1 mutations were identified in 4.3% of patients aged 35 years or lower, similarly, studies done in the Caucasian populations showed a 5.7% to 6.2% of BRCA1 mutations[1]. In addition, a study of 169 cases of women with a history of one to 11 breast cancer cases in the family only reported 27 BRCA1 mutations[1]. These results, indicating the lack of BRCA1 mutations among breast cancer patients with a family history of breast cancer could be due to other breast cancer susceptibility genes such as BRCA2 and PTEN[1]. It could also be due to mutations in the noncoding regions of BRCA1 which could affect RNA transcription, splicing, and stability[1]. Further research should be performed to investigate the possible existence of other breast cancer susceptibility genes, as well as mutations in the non-coding regions of the BRCA1 gene. It would also be useful to utilize advanced genetic testing methods rather than mutational analysis by direct sequencing which could have missed large deletions or rearrangements.

Works Cited

1. Balraj, P. et al. Mutation analysis of the BRCA1 gene in Malaysian breast cancer patients. *Singapore Med J*; https://pubmed.ncbi.nlm.nih.gov/12188064/ (2002).