ABSTRACT

Breast cancer is an increasingly common cause of morbidity and mortality in black South African women. Of all diagnosed cases of breast cancer in European populations, approximately 5-10% of these arise due to an inherited mutation in a cancer susceptibility gene. *BRCA1* and *BRCA2* gene mutations are the primary contributors to inherited breast cancer (IBC). However, mutations in other high, moderate and low susceptibility genes have also been identified. Previous studies indicate that approximately 10% of young black South Africans with breast cancer have a deleterious mutation in either *BRCA1* or *BRCA2* gene**.** It would, therefore, be pertinent to determine what is contributing to disease in the remainder of the young high-risk black South African breast cancer patients by investigating other genes which are known to confer cancer susceptibility.

In addition to a breast cancer syndrome, biallelic *BRCA2* mutations can also result in a Fanconi anaemia (FA) phenotype. Previous studies have identified overlapping *BRCA2* mutations, c.582G>A and c.5771_5774delTTCA, in patients with either breast cancer or FA. Approximately 80% of black South African patients with FA are found to be homozygous for the c.637_643delTACCGCC mutation in the *FANCG* gene. The relationship between this *FANCG* mutation and breast cancer in the black South African population has not been previously determined.

The main aim of the study was to increase current knowledge of the molecular basis of breast cancer in the black South African population. The study initially focussed on genotyping the two *BRCA2* mutations (c.582G>A and c.5771_5774delTTCA) in a sample of black South African women with breast cancer to determine the frequencies of these proposed common mutations in this population. This was followed by the construction of haplotypes using the *BRCA2* mutations to evaluate the presence of a founder effect for each mutation. The study also aimed to screen for the *FANCG* c.637_643delTACCGCC mutation in breast cancer patients to determine its role in breast cancer development.