# Abstract

Breast cancer is the leading cause of cancer among women worldwide. Many studies shows that breast cancer is associated with higher dietary fat contents and saturated fatty acid levels. However, polymorphisms in 'candidate' genes, especially involving in lipid metabolism, are less examined. Two genes in particular, peroxisome proliferator-activated receptor alpha (PPAR a) and apolipoprotein E (ApoE), are attractive candidates. To determine whether genetic variants in PPAR a and ApoE genes are associated with the development of breast cancer, the genotypic frequency of the PPAR a and ApoE polymorphisms and the association of these polymorphisms with breast cancer risk were studied. The polymorphisms of PPAR a and ApoE genes were determined by denaturing gradient gel electrophoresis (DGGE) and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. We found two missense mutants of PPAR a: S24F and V227A. However, there was no significant correlation between PPAR a polymorphisms (S24F, L162V and V227A) and breast cancer risk ($p > 0.05$). The ApoE e4 polymorphism was associated with breast cancer risk ($p = 0.006$) and with HER-2/neu negative status ($p = 0.004$). Variation in the coding region of

PPAR a is unlikely to be a major cause of breast cancer, and then we investigated a possible synergistic effect of PPAR a and ApoE polymorphisms on the risk for breast cancer. Carries of a PPAR a-F24 allele and an ApoE e4 allele showed higher risk for breast cancer than carriers of a PPAR a-F24 allele and an ApoE e3 allele. The same results were found in carriers of a PPAR a-F24 allele and an ApoE e2 allele. In addition, carriers of a PPAR a-V227 allele and an ApoE e4 allele presented with an increased risk for breast cancer. HER-2/neu negative status correlated with carries of an ApoE e4 allele and a PPAR a- F24 or V227 allele. Carriers of a PPAR a-F24 allele and an ApoE e4 allele presented with a decreased risk for ductal carcinoma in situ. Patients with a PPAR a-F24 allele and an ApoE e2 allele showed higher lymphatic invasion, than with a PPAR a-F24 allele and an ApoE e3 allele. These results suggest that ApoE4 may be a risk factor for breast cancer. A synergistic effect of ApoE4 and PPAR a polymorphisms (F24 or V227 allele) may increase the risk for breast cancer.