New Identified Genetic Variants are Proven to be Associated with Breast Cancer Susceptibility and Aggressiveness in the Tunisian Population

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**Background:** Single nucleotide polymorphisms (SNPs) may be causally related to breast cancer risk or be indirectly associated with breast cancer risk through linkage disequilibrium with a causal sequence variant. Risk-associated SNPs will have different frequencies among women with or without breast cancer and can be detected using genetic association studies. Recently, several genome-wide association studies (GWAS) have identified novel risk alleles for breast cancer including those related to FGFR2, TNRC9, MAP3K1, LSP1 genes and other locus. Replication in independent population samples is essential for validation of the results of any genome-wide association. Since the genetic variants (SNPs) are common, they are likely to be shared across different populations with diverse ancestry backgrounds. It would be of interest to determine and investigate the potential implications of these novel markers revealed by genome-wide association studies to predict the "sporadic" breast cancer risk and progression in MENA populations.

**Methods:** Using TaqMan® SNP genotyping assays, we characterize the variation of 9 SNPs (include rs1219648, rs2981582, rs8051542, rs12443621, rs3803662, rs889312, rs3817198, rs13387042 and rs13281615) for 520 patients with sporadic breast cancer and 360 healthy controls in the Tunisian population. The association between the genotypes and breast cancer susceptibility and tumors characteristics was estimated by computing odds ratio (OR) and 95% confidence levels from logistic regression analyses. Association of the genetic marker with the rates of breast cancer overall survival was assessed using univariate analysis.

**Results:** Two genetic variants in FGFR2 are significantly associated with the risk of breast cancer: rs1219648 AG/GG (OR=1.23, P=0.002) and rs2981582 AG/AA (OR=1.33, P=0.003). Two significantly increased risks of breast cancer were respectively associated with T allele of rs8051542 in TNRC9 (OR=1.43, P=0.0003) and C allele of rs889312 in MAP3K1 (OR=1.33, P=0.006). The AG and GG genotypes of rs2981582 in FGFR2 have a significant association with a high risk of lymph node metastasis and a decreased overall survival in breast cancer patients.

**Conclusion:** Our results for the first time replicated the results of breast cancer GWAS in the Arabic population and indicated that some polymorphisms are associated with increased breast cancer risk and disease progress in the Tunisian population.

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The Association of Adiponectin Gene Variants rs2241766 [+45T/G] and rs1501299 (276G > T) in Arab Patients Presenting with Acute Coronary Syndrome

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**Background:** Adiponectin is a fat derived hormone, known to decrease in type-2 diabetes (DM) and coronary artery disease (CAD). Moreover, our previous study showed that total adiponectin and its HMW isoform decreased in acute coronary syndrome (ACS) patients compared to healthy controls. The adiponectin gene ADIPOQ is located on chromosome 3q27. Two single nucleotide polymorphisms (SNPs) (rs1501299 and rs2241766) in ADIPOQ gene and their possible associations with ACS were investigated among Arab patients resident in Qatar.

**Methods:** A case-control association study was performed on 142 (ACS) Arab patients and 115 Arab healthy controls from Qatar. Genotypes were determined using TaqMan real time PCR assay. Serum adiponectin level was determined using ELISA.

**Results:** The GG, GT and TT genotype frequencies of the rs2241766 [+45 T/G] variant showed significant difference between the control and (ACS) cases [45.2%, 40.0%, 14.8% vs. 46.2%, 25.0%, and 28.8%, p=0.0001], respectively. In contrast, there was no significant association between the control and (ACS) cases in the GG, GT and TT genotype frequencies of the rs1501299 (276G > T) [39.8%, 49.1%, 11.1% vs. 41.7%, 48.3%, and 10.0%, p=0.94], respectively. The T allele was the minor allele for both rs2241766 and rs1501299 with a frequency of (0.31) and (0.25) respectively. All allele frequencies were in equilibrium for HWE among study subjects [P=0.51] for SNP rs2241766 and (p=0.12) for rs1501299. Using logistic regression analysis with adjustments of age and body mass index, only the T allele of rs2241766 variant was significantly associated with risk of (ACS) with odds ratio of 2.430, (95% CI 1.010-5.563) with the (p=0.047) among subjects using the genetic dominant model. Furthermore, using dominant genetic model, linear regression analysis showed an inverse significant association between the SNP rs2241766 (+45G>T) in the adiponectin gene and serum adiponectin levels (r= -0.621 p=0.001) among all subjects. By contrast, no significant association was found between rs1501299 (276G>T) and adiponectin level.

**Conclusion:** This study suggests that rs2241766SNP (+45T>G) in the adiponectin gene is associated with high risk for ACS, and has an effect on the serum adiponectin levels in Arab populations.

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