

3rd World Conference on

BREAST AND CERVICAL CANCER

September 24-25, 2018 Abu Dhabi, UAE

Association and additive effects of single-nucleotide polymorphisms in pre-miR-182 and TOX3 with breast cancer susceptibility

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Breast Cancer (BC) is one of the most frequent tumors affecting women worldwide. Single-Nucleotide Polymorphisms (SNPs) in microRNAs (miRNAs) likely contribute to BC susceptibility. Using Sanger sequencing, we detected rs4541843:C>T (pre-miR-182 boundaries) in 99 BRCA1/2-negative BC patients from high-risk families. While mir-182 is known to be involved in breast carcinogenesis, there are no association studies in the literature regarding the contribution of rs4541843 to BC susceptibility. Therefore, we evaluated the association of the SNP rs4541843:C>T with BC risk in non-carriers of BRCA1/2 mutations from a South American population. The SNP was genotyped in 440 BRCA1/2-negative Chilean BC cases and 1048 controls. The frequency of rs4541843-T was higher in cases than controls (0.46 vs. 0.31, p=0.01). Furthermore, homozygous T/T- and T-allele carriers (C/T + T/T) had a significantly increased BC risk (OR=1.5 [95% CI 1.0-2.2] p=0.03 and OR=1.2 [95% CI 1.0-1.5] p=0.01, respectively), indicating that the T allele is positively associated with BC susceptibility. This is the first association study on rs454183 and BC risk. In our previous work, we showed that TOX3-rs3803662:C>T was significantly associated with familial BC risk. Given that TOX3 is a target of miR-182 and that both the TOX3 rs3803662-T and pri-miR-182 rs454183-T alleles are associated with elevated BC risk, we evaluated their combined effect. Risk of familial BC increased in a dose-dependent manner with the number of risk alleles (p-trend=0.0005), indicating an additive effect.

Biography

Sebastian Morales Pison is a Biotechnology Engineer, completed his Masters in Biotechnology and currently pursuing his PhD in Biomedical Sciences at the University of Chile. He has expertise in cancer genetics, with a research focus on genetic variants in microRNA genes associated with familial breast cancer. He has published original scientific articles with novel findings on Chilean familial breast cancer patients.

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