SNPs in ultraconserved elements and familial breast cancer risk.

Ultraconserved elements (UCEs) are segments of >200 bp length showing absolute sequence identity between orthologous regions of human, rat and mouse genomes. The selection factors acting on these UCEs are still unknown. Recent studies have shown that UCEs function as long-range enhancers of flanking genes or are involved in splicing when overlapping with exons. The depletion of UCEs among copy number variation as well as the significant under-representation of single-nucleotide polymorphisms (SNPs) within UCEs have also revealed their evolutional and functional importance indicating their potential impact on disease, such as cancer. In the present study, we investigated the influence of six SNPs within UCEs on familial breast cancer risk. Two out of six SNPs showed an association with familial breast cancer risk. Whereas rs9572903 showed only a borderline significant association, the frequency of the rare [G] allele of rs2056116 was higher in cases than in controls indicating an increased familial breast cancer risk ([G] versus [A]: odds ratio (OR) = 1.18, 95% confidence interval (CI) 1.06-1.30, P = 0.0020; [GG] versus [AA]: OR = 1.41, 95% CI 1.15-1.74, P = 0.0011). Interestingly, comparing with the older age group, the ORs were increased in woman younger than 50 years of age ([G] versus [A]: OR = 1.27, 95% CI 1.11-1.45, P = 0.0005; [GG] versus
[AA]: OR = 1.60, 95% CI 1.22-2.10, P = 0.0007) pointing to an age- or hormone-related effect. This is the first study indicating that SNPs in UCEs might be associated with cancer risk.