

Silencing of tumor suppressor genes RASSF1A, SLIT2, and WIF1 by promoter hypermethylation in hereditary breast cancer

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Promoter hypermethylation is gaining strength as one of the main mechanisms through which tumor suppressor genes are silenced during tumor progression. Three tumor suppressor genes are frequently found methylated in their promoter, in concordance with absence of expression, RASSF1A, SLIT2, and WIF1. In addition, a previous array-CGH analysis from our group showed that these genes are found in deleted genomic regions observed in hereditary breast cancer tumors. In the present work we analyzed the methylation status of these three tumor suppressor gene promoters in 47 hereditary breast cancer tumors. Promoter methylation status analysis of hereditary breast tumors revealed high methylation frequencies for the three genes (67% RASSF1A, 80% SLIT2, and 72% WIF1). Additionally, the presence of methylated PCR products was associated with absence of protein expression for the three genes and statistically significant for RASSF1A and WIF1. Interestingly, methylation of all the three genes was f