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The role of *RAD51* and *BRCA2* genes in colorectal cancer progression among Saudi population

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Background & Aim: DNA repair system plays an essential role in the protection against carcinogens. Given the important roles of *RAD51* and *BRCA2* in the repair mechanism, it is not surprising that mutations in these genes can affect the chromosomal integrity consequently leading to tumorigenesis. The aim of this study was to evaluate the link between *RAD51* and *BRCA2* expressions, single nucleotide polymorphisms (SNPs) and susceptibility to colorectal cancer (CRC) in Saudi population.

Methodology & Results: Gene expression was investigated in 25 CRC and adjacent normal tissues using RT-PCR. All tissues, expressed *RAD51* and *BRCA2* but to different extents. High expression levels were observed associated with early stages of tumor and this finding confirmed at the protein levels by immunohistochemistry assay. Furthermore, promoter methylation status was determined by methylation specific-PCR. Un-methylated CpG islands were observed at the *RAD51* promoter in all normal and cancerous tissues. However, only 30% of the cancerous tissues had un-methylated *BRCA2* CpG islands compared to the normal tissues. Also, blood samples from 102 CRC patients and matched controls used to investigate SNPs in *RAD51* and *BRCA2* genes using TaqMan genotyping assay. No association was observed between *RAD51* polymorphisms (rs1801320, rs1801321) and CRC risk. Significant relationship was detected between *BRCA2* gene polymorphisms (rs1799944, rs1801406 and rs7334543) and CRC where the mutant alleles posed to provide protective effect against CRC risk in Saudi. Haplotyping *BRCA2* SNPs suggested AAA haplotype as a predisposition factor to CRC development.

Conclusion: Alteration in *RAD51* and *BRCA2* expression levels might be an early event in colorectal carcinogenesis. These findings might provide a value for using *RAD51* and *BRCA2* as prognostic.

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