TCF4 may act as a tumor suppressor gene in colorectal carcinogenesis

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Colorectal cancer (CRC) is one of the leading malignancies as being the third most cause of cancer causing death in the world. Carcinogenesis is a complex process caused by various genetic and epigenetic changes in various genes like tumor suppressor genes, DNA repair genes, translation regulatory genes and others. The Wnt/β-catenin pathway plays multiple and diverse roles in development by regulating gene expression via T-cell factor/Lymphoid enhancer-binding factor (Tcf/Lef) DNA binding factors. Misregulation of this pathway is thought to initiate colon adenoma formation. The Wnt pathways with its molecular gladiator Tcf4 plays an important role in transforming a normal tissue into a malignant one. In this study, we aimed to investigate the role of aberrations in Tcf4 gene in the pathogenesis of CRC in the Kashmiri population.

Materials and Methods: We examined the paired tumor and normal-tissue specimens of 100 CRC patients from Apr 2010-June 2013, from Department of Surgery, Government Medical College, Srinagar and its associated hospital Shri Maharaja Hari Singh Hospital (SMHS) and analysis of promoter hypermethylation for exon 1 and intron 8 of Tcf4 gene was also carried out using Methylation-specific PCR (MS-PCR).

Results and Conclusion: Promoter hypermethylation of Tcf4 of the exon 1 of Tcf4 gene among 100 CRC cases was found to be 66 per cent (66 of 100) and for intron 8, it was 70%. Besides in both cases of males and females, the hypermethylation status of intron 8 is more than exon 1 of Tcf4, the study confirms the role of epigenetic gene silencing of the pivotal molecular gladiator, Tcf4, of the Wnt pathway in the development of CRC in the Kashmiri population. So, it was concluded that Tcf4 promoter may be used as a diagnostic tool for colorectal carcinogenesis and therefore can be used a marker for its diagnosis.

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