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Correlative analysis of *hMLH1* and *hMSH2* with *APC* gene in sporadic colorectal cancer in young north Indian patients**Kim Vaiphei and Vikas Gupta**

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Sporadic Colorectal Cancer (CRC) in patients is increasing rapidly in Indian population and half of the patients are less than 50 years of age. No comprehensive molecular study has been carried out to analysis the basis for the disease occurring in younger individuals. The study investigated frequency of *hMLH1* and *hMSH2* genes and *hMLH1* and *hMSH2* proteins expressions, their prognostic significance and correlated with the Adenomatosis Polyposis Coli (*APC*) gene mutational status by DNA sequencing in young CRC patients. Protein expression and promoter methylation of *APC*, *hMLH1* and *hMSH2* and Mismatch Repair genes (MMR) were analyzed by immunohistochemistry and Methylation-Specific PCR (MSP), respectively and correlated with patient's data. Of 100 CRC, *hMLH1* and *hMSH2* loss were observed in 18 and 12, reduced expressions in 50 and 38, respectively, 5 failed to express. Promoter hyper-methylation for *hMLH1* was detected in 50 and *hMSH2* in 10. Combination of methylation of *hMLH1* and *hMSH2* gene was observed in 8 tumors. Significant correlation was observed between histological tumor grade, methylation status and *hMLH1* gene expression ($p < 0.05$). Normal expression for *hMLH1* and *hMSH2* was observed in all un-methylated tumors. Promoter methylation of *hMLH1* and *hMSH2* failed to influence survival and correlated with loss of protein. *APC* gene mutation was observed in 45% patients with no differential in distribution. Our observations suggest inactivation of MMR gene via hyper-methylation lead to functional loss resulting in tumor aggressiveness and role of *APC* gene appeared not to play a major role in tumor progression in these young patients.

Biography

Kim Vaiphei is currently serving as a Professor at Department of Histopathology, Post Graduate Institute of Medical Education and Research, Chandigarh, India. She has received MBBS in 1983 and MD Pathology in 1987. She is a Fellow of International Union against Cancer (UICC-WHO), National Academy of Medical Sciences India and Indian College of Pathology. She holds various levels of faculty positions in the Department of Histopathology, PGIMER and remained as Professor since 2006. Her area of research includes molecular pathways of cancer development. She has more than 300 publications and attended more than 50 national and more than 20 international conferences.

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