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# The KRAS Mutations in Colorectal Cancer: A Genetic Analysis

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## INTRODUCTION

Colorectal Cancer (CRC) occurrence is increasing, even though there have been tremendous improvements in the diagnosis and treatment. The process of developing cancer is typically thought as a series of stages beginning with a mutagenic incident known as tumour development. The adenoma-carcinoma sequence is regarded as a classic example of spontaneous colon cancer in colorectal cancer. Numerous signal transduction pathways, including the Wnt/-catenin signalling cascade, the apoptotic signalling cascade, and Mitogen-Activated Protein Kinase (MAPK), are implicated in this process. It turned out that the conventional adenoma-carcinoma sequence's beginning cause was an APC gene mutation. Due to the absence of Wnt signaling's inhibitory effect in cells with mutant APC genes, -catenin accumulates and, after being translocated into the nucleus, functions as a co-activator of T-Cell Factor (TCF)-Lymphocyte Enhancer Factor (LEF).

## DESCRIPTION

The important cell cycle regulating genes cyclin D1 and c-Myc are transcriptionally activated by the -catenin/TCF-LEF complex, which in turn promotes tumour development. In this case, APC suppression controls the development of adenomas in the colon (*i.e.*, gut), which are subsequently stimulated to develop into colon malignancies in the presence of other mutations, such as those in the TP53 and KRAS genes. By using a combination of DNA hybridization tests and tissue sectioning techniques shows that over one-third of human colorectal tumours contained RAS gene mutations, and that the mutations typically occurred before the beginning of malignancy. Further studies showed that the frequency of KRAS mutations varied from 25% to 52% and that they were generally found at codons 12 and 13, in exon 2, of the KRAS gene's coding area. The glycine residues in the GTP-binding pocket, which are essential for GTPase function, are affected by single base changes in codons 12 and 13. As a result, these KRAS mutations stabilise the protein in its prolonged active state, increasing the signalling pathways downstream. The MAPK and AKT pathways, which enable tumour cells to multiply in the absence of growth stimuli and lengthen their survival, are the two key downstream signalling pathways. In addition, KRAS can control the production of the gene for Vascular Endothelial Growth Factor (VEGF), increase Wnt signalling by inhibiting GSK-3beta, and advance tumour growth by collaborating with Wnt signalling.

KRAS not only plays a significant role in the development and progression of colorectal cancer, but it also has an impact on how it is treated. In patients with colorectal cancer, KRAS gene mutations are significant predictors of response to cetuximab or panitumumab therapy. Cetuximab and panitumumab are not effective in patients with mutant KRAS, but are effective in those with wild-type KRAS. While this was going on, some studies claimed that the KRAS mutation was a poor predictor of Overall Survival (OS) and Recurrence-Free Survival (RFS).

## CONCLUSION

Although it is clear that KRAS is crucial for both the treatment of patients with colorectal cancer and the carcinogenesis of colorectal epithelial cells, KRAS mutations are, only identified in 50% of patients. In other words, the wild type is present in about 50% of cases. It is possible that people who have mutant or wild-type KRAS will exhibit various biological traits due to their different gene mutation spectra. In order to better understand the occurrence, progression, and therapy of colorectal cancer, studies may find it useful to compare thegene mutation profiles of patients with and without a KRAS mutation.

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