

## **Molecular Pathology of Colorectal Cancer**

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Morphologic and genetic progression to colorectal cancer (CRC) in an adenoma-adenocarcinoma sequence and in hereditary CRC syndromes is well described. Chromosomal instability and mutation of the APC gene, the K-ras proto-oncogene, and the p53 suppressor gene are common. Microsatellite instability due to abnormal nucleotide mismatch repair that results in numerous mutations, especially in repeated nucleotide sequences (microsatellites), is a second important molecular pathway to CRC. Recent studies have shown that methylation of CpG islands is also common in CRC. CpG islands are 0.5–2 kilobase regions rich in cytosine-guanosine dinucleotides that are present in the 5' region of about one half of all human genes. The recently discovered CpG island methylator phenotype (CIMP) has widespread concordant transcriptional silencing of numerous genes. These three major molecular pathways of chromosomal instability, microsatellite instability, and CIMP predominate during development of colorectal neoplasia.