Update of Genetics in Colorectal Carcinomas: Genomic Instability and Somatic Evolution

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Abstract

***Introduction**: Currently, there are two contrasting viewpoints on what drives the process of carcinogenesis. The genomic (DNA or chromosomal) instability model contends that an increased mutation rate early in carcinogenesis is necessary for the multistage process, while the somatic evolution model postulates that normal mutation rate with selective advantage and clonal expansion is sufficient to cause cancer. **Methods**: Evidence from colorectal carcinoma (CRC) for and against the two models are compared and contrasted. **Results**: With the exception of hereditary non-polyposis colorectal carcinoma (HNPCC) where DNA instability attributable to mismatch repair deficiency is clearly demonstrated, the majority of CRC appear to progress through the selection of a series of mutations without the need of first acquiring a mutator phenotype. Aneuploidy or chromosomal instability is more likely to be a consequence of non-random selection of mutations in genes residing on the chromosome rather than the direct cause of cancer. Nevertheless, aneuploidy and / or DNA alterations can lead to secondary instability, hence, contributing to the phenotypes associated with carcinoma. **Conclusions**: Present knowledge, thus, points to multiple, mutually non-exclusive pathways for different cancer populations, further emphasising tumour heterogeneity.*

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