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Novel somatic frameshift mutations of genes related to cell cycle and DNA damage response in gastric and colorectal cancers with microsatellite instability

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ABSTRACT

Aims and background. Microsatellite instability (MSI) in sporadic gastric cancer (GC) and colorectal cancer (CRC) causes frameshift mutations in gene sequences that contribute to cancer pathogenesis. Many mutations have already been identified in these two cancer types, but some are still undiscovered.

Methods. We analyzed seven genes (cell cycle control and DNA damage signaling/repair-related genes) with seven or more mononucleotide repeats in 30 GC samples with high MSI (MSI-H), 15 GC samples with low MSI (MSI-L), 45 GC samples that were microsatellite stable (MSS), 33 CRC samples with MSI-H, 15 CRC samples with MSI-L, and 45 CRC samples that were MSS. Single-strand conformation polymorphism (SSCP) and DNA sequencing were used for the analysis.

Results. We found somatic frameshit mutations of the *KNTC1* (6.7% GC, 12.1% CRC), *ZC3H13* (3.3% GC, 15.2% CRC), *CENPH* (6.7% GC), *TOPBP1* (3.0% CRC), *NDC80* (3.0% CRC), *RIF1* (6.7% GC), and *NBS1* (3.3% GC, 3.0% CRC) genes in the cancers with MSI-H. Mutations were detected in MSI-H, but not in MSI-L or MSS samples.

Conclusions. Novel frameshift mutations occurred in seven genes in GC and CRC with MSI-H. The results of our study suggest that the mutations might contribute to the development of GC and CRC with MSI by deregulation of the cell cycle and DNA damage signaling/repair. Free full text available at www.tumorionline.it

Key words: MSI, mutation, mononucleotide repeats, gastric cancer, colorectal cancer.

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