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Somatic mutations leading to incomplete extinction of HLA class I were associated with replication error phenotype-positive colorectal carcinoma

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Abstract: Hereditary non-polyposis colorectal carcinoma (HNPCC) is one of the prevalent inherited cancers in the general population. Underlying biological process impaired in HNPCC is DNA mismatch repair, which results in microsatellite instability and accumulation of frame-shift mutations within the tumor cells. Protein products of the mutant alleles are expected to be the alteredself to the host immune system and become targets for the tumor-specific cytotoxicity. To explore the mechanism for HNPCC tumor cells to escape from the immune surveillance, we investigated the mutations in the beta 2 microglobulin (B2M) and HLA class I genes as well as the microsatellite instabilities in the colorectal cancers. It was found that either a frame-shift mutation of B2M gene or allele loss of HLA class I genes, which would lead to the extinction of HLA class I expression, were more prevalent in the HNPCC tumors than in the non-HNPCC tumors. Interestingly, none of the tumors exhibited complete loss of B2M or HLA class I genes. These observations strongly suggested that the extinction of HLA class I should be kept incomplete, because the complete loss might activate natural killer cells.

Key words: HLA class I, beta 2 microglobulin, colorectal cancer, HNPCC, immune surveillance

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