Investigation of Functional Roles of Novel Fluorouracil Drug Resistance Genes of Colorectal Cancer through Combination with Data Mining and In Vitro Experiment Approach

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Abstract

Colorectal cancer (CRC) is the third most common cancer in the world, with nearly 1.8 million new cases diagnosed in 2018. Surgery is the treatment for early-stage tumors. 5 Fluorouracil (5-FU) can reduce the primary tumor size in advanced stage CRC, but patients often relapse during treatment because of 5-FU resistance, therefore, it is important to identify drug resistance genes of CRC and find out the treatment method. In this study, we identified differentially expressed of 5-FU drug resistance genes from Gene Expression Omnibus (GEO) dataset (GSE77180) and next-generation sequencing (NGS) of 5-FU drug resistance cell line. Here, we established a long-term 5-FU drug resistant CRC cell model and explored the cellular events underlying 5-FU treatment. Knockdown of 5-FU drug-resistant genes (APOBEC3B, APOBEC3H, CCNE2, and COL12A) could increase 5-FU drug sensitivity. In contrast, transient transfection of 5-FU drug-resistant genes (APOBEC3B, APOBEC3H, CCNE2, and COL12A) could enhance 5-FU drug resistance of HCT116 cells. Taken together, our results revealed that APOBEC3B, APOBEC3H, CCNE2, and COL12A play a crucial role in the 5-FU resistance of CRC cells and indicated that would be a promising therapeutic strategy to overcome 5-FU drug resistance in CRC.

Keywords

Colorectal cancer, 5-FU, drug resistance.