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Gene Expression Changes in Colorectal Cancer during Metronomic Chemotherapy and High-Concentration Drug Administration

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Abstract

5-fluorouracil (5-FU) and oxaliplatin, either alone or in combination, are widely used in chemotherapy for advanced colorectal cancer. Among chemotherapeutic strategies, metronomic chemotherapy has recently demonstrated promising efficacy against otherwise chemoresistant neoplasms. However, data on the efficacy of metronomic applications in cancer stem cells are lacking. This cell population is characterized by resistance to most chemotherapeutic models. In this study, we investigated the efficacy of metronomic chemotherapy and compared it with high-concentration administration of 5-FU and oxaliplatin and their combination in colon adenocarcinoma cells and colon cancer stem cells. We assessed changes in expression levels of specific genes involved in 5-FU and oxaliplatin resistance (thymidylate synthase, DNA (cytosine-5)-methyltransferase 1, dihydrofolate reductase, serine hydroxymethyltransferase, DNA excision repair protein, dihydropyrimidine dehydrogenase) in relation to drug administration schedule using quantitative real-time polymerase chain reaction. We also examined changes in cell viability. Metronomic chemotherapy showed greater efficacy in gene expression levels in colorectal cancer cells, while high, single-concentration administration was more effective in colon cancer stem cells. Regarding cell viability, no significant change was observed between metronomic and single-dose treatments. These results suggest that metronomic chemotherapy may be more effective than high-dose chemotherapy in some patients with colorectal cancer, though high, single-concentration administration may be more effective against cancer stem cells.

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