Colorectal cancer (CRC) is one of the most common cancer worldwide. The current mainstay of CRC treatment is surgery and chemotherapy. However, the statistics still show alarming numbers - there were nearly 1.4 million new cases and 0.7 million deaths in 2012. Therefore, it is essential to find new combination of drugs that would improve the efficacy of current CRC treatment. In our studies we have shown that DNA methylation inhibitors enhance the cytotoxic effect of irinotecan, a topoisomerase I inhibitor that constitute the backbone of chemotherapy for CRC. Moreover, we have noted that DNA methylation inhibitors increase the sensitivity of CRC cells to topoisomerase II inhibitors, including etoposide, doxorubicin and mitoxantrone. The mechanism of this synergistic effect is not known. The aim of our project is to define the role of DNA methylation in this combinatorial treatment. DNA methylation refers to the addition of a methyl group to the cytosine nucleotides. DNA methylation has an influence on the structure of DNA, gene expression, and genomic stability through, for example, repression of transposable elements. In our project we will be using methods such as liquid chromatography-mass spectrometry (LC-MS) and pyrosequencing for analysis of DNA methylation levels. We will be also using qRT-PCR and western blotting to measure changes in the expression of selected genes upon treatment with DNA methylation inhibitors. The results of our studies may represent a highly effective combination therapy against CRC and possibly other cancers.