Abstract

The choice of treatment strategy in patients with malignant disease depends on various clinical and molecular biological factors. Although several molecular predictive biomarkers have already been proposed, only a few of them are used in clinical practice and the number is still not enough for reliable personalized medicine. Given the lack of treatment success results in many colorectal cancer (CRC) patients, there is an urgent need for personalized medicine to identify new predictive biomarkers.

One of the main clinical challenges in the treatment of advanced CRC is the development of chemoresistance to systematic chemotherapy. Early detection of resistant cancer cells clones could lead to changes in treatment regimens but it requires a long-term follow up of patients and monitoring of specific markers of chemoresistance.

The aim of this master's thesis has been to determine the biomarkers associated with chemoresistance to 5–FU drug, one of the most used chemotherapeutics in the treatment of CRC patients. In the first step, the whole transcriptome of maternal (sensitive) and resistant DLD–1 (line resistant to 40 μM 5–FU and line resistant to 160 μM 5–FU) cell lines using the next generation sequencing (NGS) has been analyzed. Through bioinformatic analyses, potential candidate genes (*HIST1H2BE*, *CD44*, *DKK1*, *ALDH1L1* and *ABCC2*) were selected for subsequent validation in samples from CRC patients treated with 5–FU. These samples included tumor tissue and adjacent unaffected mucosa from CRC patients identified with chemoresistance or complete response to therapy.

Based on the data validation we confirmed the gene expression trend for the *CD44*, *DKK1*, *ABCC2* and *ALDH1L1* genes. The potential use of new discovered markers in clinical practice in CRC patients could lead to improvements in CRC treatment.

Keywords:

colorectal cancer, chemoresistance, 5–fluorouracil, biomarkers