

Metabolomics and pharmacogenetics based 5-fluorouracil monitoring in colorectal cancer patients

ABSTRACT

Objective: To provide quick and accurate clinical diagnostic tools those are currently not available leading to improper management of colorectal cancer (CRC) patients. **Methods:** The metabolomic profiles of 10 CRC patients treated with 5-fluorouracil and 24 healthy volunteers were analysed. The subjects were genotyped for UGT1A1*28, DPYD 1896 T>C and DPYD*5. **Results:** Our results show alterations in the metabolism of bile acid, glycolysis and fatty acid in patients. The distinctive metabolite profiles established using PLSDA identify several biomarkers for diagnostic use in clinical settings. The predictive PLSDA model revealed 100% accuracy of metabolites differentiating CRC patients and healthy volunteers. In addition, the metabolic profiles associated with different genotypes of DPYD and UGT1A1 explains the impact of genetic variation on differential drug responses. **Conclusion:** Pharmacogenetics and metabolomics profiles are potential platforms for more comprehensive monitoring of patient's disease progress and drug response. Further study is however needed to validate the use of biomarkers identified.

Keyword: 5-fluorouracil (5-FU); Colorectal cancer (CRC); Metabolomics; Pharmacogenetics; Polymorphism