Pharmacogenetics Approach to Combinatorial 5-Fluorouracil Treatments of Colorectal Cancer

Mehmet Kadir Erdoğan¹, Hakan Aşkın²
¹Department of Biology, Faculty of Arts and Sciences, Bingöl University, 12000, Bingöl, Turkey
²Department of Molecular Biology and Genetics, Faculty of Sciences, Atatürk University, 25000, Erzurum, Turkey

Background: Worldwide, colorectal cancer (CRC) is a major reason of cancer-related death, approximately 1.2 million new cases are reported each year and more than half die from the disease. 5-Fluorouracil (5-FU) is the backbone in the clinical treatment of advanced CRC, it has raised the whole survival of affected patients from 10 to 18-24 months. However, beside the antitumor effect most toxicities attributed to the drug and observed severe side effects. Therefore, novel and better treatments are still needed.

Methods: 5-Fluorouracil-based chemotherapeutic regimens are established as a fundamental standart treatment for metastatic colorectal cancer. 5-FU exerts its anticancer influences by inhibition of thymidylate synthase (TS), the rate-limiting enzyme in the pyrimidine nucleotide synthesis. TS converts deoxyuridine monophosphate to deoxythymidine monophosphate (dTMP). Inhibition of TS results in less dTMP and inhibition of DNA synthesis and repair.

Combinational drug therapies are used together with chemotherapy or when chemo is no more working, they have less severe side effects. Many 5-FU plus drug or natural products treatments are administered to patients. Therapeutic agents such as oxaliplatin and irinotecan in combination with 5-FU, 5-FU plus levamisole (LEV), 5-FU plus leucovorin (LV) or FOLFOX4 (5-FU/LV/oxaliplatin) have increased response in advanced disease and improved survival rates.

Results and Conclusion: Personalized cancer research and pharmacogenetics is aimed to improve the efficacy of anticancer drugs, increase clinical benefits of therapy and diminish adverse reactions in patients. The optimal drug combinations will improve our ability to overcome the limitations of treating the colorectal cancer in the future. New combinational approaches can offer us safer and more effective therapy for the treatment of CRC.