ANALYSIS OF THE THYMIDYLATE SYNTHASE GENE STRUCTURE IN COLORECTAL CANCER PATIENTS, AND ITS POSSIBLE RELATION WITH THE 5-FLUOROURACIL DRUG RESPONSE

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Thymidylate synthase (TS) catalyzes methylation of deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP) and is the target of anticancer chemotherapeutic agents as 5-fluorouracil (5-Fu). Barbour et al., Kawate et al., and others researchers showed that variant structural forms of TS or in tumour cell lines or in bacterial complementation system confer resistance to fluoropyrimidines (1-2). In an our previous paper (3) we did not find a substitution of the Tyrosine to Histidine at the residue 33 of the TS protein chain in human colorectal cancer samples, that has been previously detected by Barbour et al 1992 in mammalian and bacterial cells.
Here, we intend to proceed on the use of sequencing techniques to see if any TS variant form could be present in human samples from patients who underwent surgery for primary colorectal cancer (CRC) and previously untreated and try to find a relationship between any hypothetical TS variant form and the 5-Fu treatment. We performed the TS-DNA gene sequence in 68 cancer samples from patients of different Dukes' stages (A, B and C) and histological grade. We did not find any mutation in the TS-DNA structure. We intend even to evaluate the TS gene structure of the D Dukes' metastatic CRCs: in these tumours, could be possible to find mutations related with their higher genomic instability, explaining, so their 5-Fu drug resistance, and a worse prognosis.

Bibliografia

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