Aim: Colorectal cancer (CRC) is one of the main inflammation-cancer association models. Polymorphisms in genes involved in the inflammatory process, as TLR2, may be interesting targets for potential CRC molecular markers. We aimed to evaluate the association of the functional polymorphism TLR2 -196 to -174 del with CRC development, and its influence on relative mRNA and protein expression.

Methods: Altogether 434 DNA samples (194 patients / 240 controls) were genotyped from peripheral blood leukocytes or tumor tissue cells by PCR allele specific. Multiple logistic regression was performed to evaluate the association between the polymorphism and CRC risk (log-additive, dominant and recessive models), adjusted to risk factors. Relative quantification (RQ) of mRNA expression was performed in 40 samples by qPCR (TaqMan® gene expression assay). Protein expression was evaluated in 20 tumor and respective adjacent normal tissue by immunohistochemistry. Immunostaining was evaluated in the epithelial cytoplasm by densitometric analysis.

Results: The variant TLR2 -196 to -174 del was associated with increased risk of CRC according to dominant (OR = 1.72, 95%CI = 1.03 to 2.89, p = 0.038) and log-additive (OR = 1.59, 95%CI = 1.02 to 2.48, p = 0.039) models. The mRNA RQ showed a significant increase in TLR2 expression (RQ= 2.36) in tumor tissue when compared to adjacent normal tissue (p < 0.0001). In agreement, the immunohistochemistry showed positive immunostaining in 84.2% of tumors samples and the mean optical densitometry values for TLR2 in tumor tissue (157 a.u.) were statistically higher compared to the adjacent normal tissue (109 a.u., p < 0.0001). When tumor samples were stratified according to the polymorphisms in promoter region, carriers of TLR2 -196 to -174 del variant had an RQ median for mRNA about 2-fold higher (RQ= 2.21) when compared to wild genotype (p= 0.035).

Conclusions: The polymorphic variant TLR2 -196 to -174 del is associated with increased CRC risk and enhances the TLR2 mRNA expression. In addition, both TLR2 mRNA and protein expression are increased in tumor tissue, emphasizing its important role in colorectal carcinogenesis.

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