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Interleukin-17 may be a valuable serum tumor marker in patients with colorectal carcinoma

G. RADOSAVLJEVIC[1], B. LJUJIC[1], I. JOVANOVIC[1], Z. SRZENTIC[3], S. PAVLOVIC[1], N. ZDRAVKOVIC[1], M. MILOVANOVIC[1], D. BANKOVIC[2], M. KNEZEVIC[1], LJ. ACIMOVIC[1], N. ARSENIJEVIC[1]

[1]Center for Molecular Medicine, Faculty of Medicine, University of Kragujevac, Serbia;e-mail: perun.gr @gmail.com, [2]Faculty of Science, University of Kragujevac, Serbia; [3]Hospital "Blazo Orlandic", Bar, Montenegro.

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The promotion of tumor growth is due to a combination of several mechanisms, including angiogenesis and the abundance of cell-derived inflammatory cytokines. The aim of this study was to investigate the serum levels of interleukin 17 (IL-17) and the expression of p53 and Vascular Endothelial Growth Factor (VEGF), in order to determine the relationship between these markers and serum IL-17 levels in patients with colorectal carcinoma.

Serum levels of the proinflammatory cytokine IL-17 in patients with colorectal carcinoma (CRC) (n=40) and in a healthy group (n=37) were analysed by ELISA. Surgically resected specimens of 59 colorectal carcinomas were studied by immunohistochemical staining for VEGF and p53.

Analyses by ELISA showed significantly higher IL-17 serum levels in patients with colorectal carcinoma than in control subjects (IL-17; mean 128.52±47.62 pg/ml vs. mean 101.91±22.46 pg/ml; p=0.022). We also found an inverse correlation between p53 expression and the level of IL-17 in the serum of patients with CRC. In fact, the serum concentration of IL-17 was significantly higher in patients who did not express p53 (p=0.023). There was no significant correlation between the expression of p53 and VEGF. However, concomitant expression of VEGF and p53 showed a significant correlation with the histological and nuclear grade of the carcinoma.

The data presented in our study indicate that IL-17 might act as a valuable tumor marker in patients with CRC and that combined analysis of p53 and VEGF expression might provide additional information about tumor features.

Key words: colorectal carcinoma (CRC),interleukin-17 (IL-17), p53, vascular endothelial growth factor (VEGF)

Tumor growth, expansion and metastasis are promoted by the development of vascular networks (i.e., angiogenesis), which deliver essential nutrients to the growing tumor [1, 2]. Tumor angiogenesis is a critical step in the growth and metastatic spread of colorectal cancers. The survival and growth of colorectal tumors (CRCs), and thus their metastases, depend upon the balance of endogenous angiogenic and anti-angiogenic factors such that the outcome favours increased angiogenesis [3].

Vascular Endothelial Growth Factor (VEGF) is one of the most potent angiogenic factors known, and is a key molecule in orchestrating the formation and function of vascular networks. VEGF, also known as vascular permeability factor, in conjunction with the leaky state of microvessels, may cause extravasation of tissue metalloproteinase and promote cancer cell invasion into the circulation [4, 5]. VEGF is overexpressed by the vast majority of solid human cancers and has been found to correlate with a poor prognosis [2, 6–11]. In addition to its angiogenic activity, VEGF may also act as an immunosuppressant by inhibiting dendritic cell maturation [12].

Experimental results have shown that some tumor suppressor genes are involved in the regulation of angiogenesis [13]. The protein p53 has a variety of important functions in cellular integration, including cell growth control, response to DNA damage, checkpoint mechanisms during the cell cycle, regulation of transcription and control of genomic stability. The frequency of p53 gene mutations is elevated in colon, stomach, breast, and lung cancers, as well as in leukaemia, osteosarcoma, ovarian cancer, and brain tumors [14]. Interesting data have been reported on the genetic inactivation of p53 in cancer cells, showing that the loss of wild-type p53 function contributes to the activation of the angiogenic switch in tumors [15]. In human colon cancer cell lines expressing mutant p53, transient restoration of wt p53 function by adenovirus-mediated gene transfer has been found to down-regulate VEGF expression [16].