ELSEVIER

Archives of Medical Research 41 (2010) 182–189

Archives of Medical Research

ORIGINAL ARTICLE

Elevated Serum Level of IL-23 Correlates with Expression of VEGF in Human Colorectal Carcinoma

Biljana Ljujic,[a] Gordana Radosavljevic,[a] Ivan Jovanovic,[a] Sladjana Pavlovic,[a] Nemanja Zdravkovic,[a] Marija Milovanovic,[a] Ljubisa Acimovic,[a] Milan Knezevic,[a] Dragic Bankovic,[b] Dusica Zdravkovic,[a] and Nebojsa Arsenijevic[a]

[a]*Center for Molecular Medicine, Faculty of Medicine, University of Kragujevac, Serbia*
[b]*Faculty of Science, University of Kragujevac, Serbia*

Received for publication October 22, 2009; accepted January 29, 2010 (ARCMED-D-09-00518).

Background and Aims. Interleukin-23 (IL-23) has a role in inflammatory bowel diseases (IBD) as a condition of higher risk of colorectal carcinogenesis. Vascular endothelial growth factor (VEGF) is overexpressed in IBD and colorectal carcinoma. Therefore, we aimed at uncovering the relationship between serum level of IL-23 and expression of VEGF in colorectal cancer (CRC) patients and to establish the relationship between VEGF and p53 and serum levels of IL-23, as well as its possible role in carcinogenesis of colorectal carcinomas.

Methods. Levels of IL-23 from serum samples of patients with colorectal carcinoma ($n = 40$) and healthy control samples ($n = 37$) were examined for IL-23-Ab using an ELISA assay. We also determined the expression of VEGF and p53 by immunohistochemistry in 59 cases of CRC.

Results. We found significantly higher serum levels of IL-23 in patients with CRC compared to control subjects (IL-23; mean 189.46 pg/mL vs. mean 34.77 pg/mL, $p = 0.033$). We also detected higher serum levels of IL-23 in patients with overexpressed VEGF ($p = 0.028$). Our results also showed that concomitant expression of VEGF and increased serum levels of IL-23 are in positive correlation with histological grade 2 ($p < 0.05$).

Conclusions. Our data indicate that serum IL-23 levels are significantly elevated in CRC vs. control patients and are strongly associated with overexpression of VEGF, thus they may play an important role in carcinogenesis of CRC.

Key Words: IL-23, VEGF, p53, Colorectal carcinoma.

Introduction

Hypoxia is a microenvironmental feature of tumors and chronically inflamed tissues. Intratumoral hypoxia has been shown to be a predictor of early distant relapse in node-negative breast (1), cervical (2) and colorectal cancer (CRC) (3). Under pathological conditions like inflammation or cancer, hypoxia induces synthesis of subunit α of HIF-1 (hypoxia-inducible factor). HIF-1α binds with constantly expressed HIF-1β and the complete molecule of HIF-1 can perform its functions (4). Moreover, hypoxia is a potent stimulator of vascular endothelial growth factor (VEGF) expression (5). VEGF has been well established to have an important role in carcinogenesis (6). A factor that regulates hypoxic angiogenesis is HIF-1α, and it has been shown to be upregulated in CRC (7) and also correlates with VEGF expression in CRC (3).

Chronic inflammation has been associated with the initiation and progression of many types of cancer (8,9). A classic example of the connection between inflammation and cancer is the increased risk of CRC in patients with IBD (10,11). A possible explanation is that high levels of inflammatory mediators that are produced in this setting

Address reprint requests to: Biljana T. Ljujic, MD, Center for Molecular Medicine, Faculty of Medicine, University of Kragujevac, Svetozara Markovica 69, 34 000 Kragujevac, Serbia; Phone: +38134306800; FAX: +38134306800 ext 112; E-mail: bljujic74@gmail.com

0188-4409/$–see front matter.
doi: 10.1016/j.arcmed.2010.02.009