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Abstract: Chemotactic cytokines play a role in angiogenesis and attraction of immune cells. However, their contribution to tumor formation remains incompletely understood. In a previous transcriptome study, we identified a family of structurally related chemokines of the CXC-family to be specifically up-regulated in colorectal cancer. The aim of the present study was to investigate the regulation of their expression in colon cancer cells and to test the hypothesis that altered CXC-chemokine expression is related to critical clinical parameters, such as survival or metastasis formation. Expression levels of interleukin-8 (CXCL-8) and growth-related oncogenes 2 and 3 (GRO-2/CXCL-2 and GRO-3/CXCL-3) were quantified using qRT-PCR in 97 patients with completely resected colon carcinoma and correlated with clinical parameters. Moreover, 16 samples of normal mucosa, nine samples of benign adenoma, and 11 samples of liver metastasis were analyzed. Next, the regulation of chemokine expression in response to various stimuli was tested in colon cancer cell lines (HT29, HCT116, CaCO2). Expression of GRO-2, GRO-3, and IL-8 was significantly increased in colon cancer as compared to normal colon tissue. Expression of GRO-2 and GRO-3 was already enhanced in premalignant adenomas, and GRO-3 was
significantly down-regulated in liver metastasis as compared to the primary tumor. Importantly, expression of GRO-3 was significantly higher in patients with local versus systemic disease. Moreover, IL-8 expression was significantly associated to overall post-operative survival. Finally, all chemokines were strongly induced by IL-1alpha in the colon cancer cell lines tested, indicating a potential link to inflammatory processes. In accordance with earlier findings, we report here a significantly increased expression of GRO-2, GRO-3, and IL-8 in colon carcinoma as compared to normal tissue. Furthermore, GRO-3 was related to metastasis formation, and IL-8 was associated with survival, suggesting a potential predictive power of these markers.

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