

HGF和VEGFR-3在大肠癌中的表达及其在淋巴管生成和转移中的作用

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Expression of HGF and VEGFR-3 in Colorectal Carcinoma and Their Role in Lymphangiogenesis and Lymphatic Metastasis

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全文: PDF (1906 KB) HTML (0 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 目的

观察肝细胞生长因子(HGF)和血管内皮生长因子受体3(VEGFR-3)在大肠癌组织中的表达,检测大肠癌组织中的微淋巴管密度(LMVD),探讨HGF和VEGFR-3在大肠癌淋巴管生成及转移中的作用。

方法

应用免疫组织化学(SABC)法检测52例大肠癌、20例大肠息肉组织和20例健康对照组织中HGF和VEGFR-3的表达,并应用podoplanin标记淋巴管,检测各组组织中的淋巴管密度,结合大肠癌患者的临床病理资料,分析其相关性。

结果

(1)大肠癌组织中HGF和VEGFR-3均被染成棕褐色或棕黄色,阳性表达率分别为75%、67.3%,相对表达量分别为(0.36 ± 0.07)、(0.41 ± 0.10),均明显高于大肠息肉组[25%、30%;(0.24 ± 0.06)、(0.28 ± 0.03)]和正常大肠组织[15%、10%;(0.23 ± 0.06)、(0.21 ± 0.03)]的表达($P < 0.01$)。且微淋巴管密度(LMVD)也明显增多[(4.13 ± 1.99) vs. (2.59 ± 1.46) vs. (2.40 ± 1.44)], $P < 0.01$ 。 (2)大肠癌组织中HGF、VEGFR-3的相对表达量, LMVD三者间呈两两正相关。39例HGF表达阳性的大肠癌,其LMVD明显大于HGF表达阴性者[(4.25 ± 2.13) vs. (2.73 ± 1.54)], $t = 3.051$, $P = 0.003$; 35例VEGFR-3表达阳性的大肠癌,其LMVD也明显大于VEGFR-3表达阴性者[(3.79 ± 1.26) vs. (2.64 ± 1.32)], $t = 3.235$, $P = 0.002$ 。 (3)HGF、VEGFR-3和LMVD的表达与大肠癌患者年龄、性别以及肿瘤分化程度无关($P > 0.05$),但与Dukes分期($P = 0.034$, $P = 0.021$, $P = 0.006$)、淋巴管有无转移明显相关($P = 0.015$, $P = 0.012$, $P = 0.001$)。

结论

HGF与大肠癌的淋巴管生成及转移有一定的相关性,并可能通过VEGF-C、D/VEGFR-3信号途径间接促进淋巴管增生,从而促进肿瘤细胞的淋巴转移。

关键词: 大肠癌 肝细胞生长因子 血管内皮生长因子受体3 微淋巴管密度

Abstract: Objective

To investigate the role of hepatocyte growth factor(HGF) and vascular endothelial growth factor receptor 3(VEGFR-3) in lymphangiogenesis and lymphatic metastasis of colorectal carcinoma by analyzing the expression of HGF and VEGFR-3, and calculating lymphatic vessel density (LMVD) in colorectal carcinoma.

Methods

The expression of HGF and VEGFR-3 in specimens of 52 colorectal carcinoma, 20 colorectal polyps tissues and 20 colorectal normal tissues was evaluated by immunohistochemistry utilizing streptavidin-biotin complex. LMVD in colorectal carcinoma was calculated by using podoplanin as the specific marker of lymphatic endothelium. And the clinicopathological features of colorectal carcinoma were analyzed.

Results

(1) The stainings of brown and filemot in cytoplasm were observed as the positive expression of HGF and

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EGFR-3 proteins. The positive rate(75% , 67.5%) and mean value [(0.36 ± 0.07) , (0.41 ± 0.10)] of HGF and VEGFR 3 expressions in specimens of colorectal carcinoma were significantly higher than those of the colorectal polyps tissues[25%,30%; (0.24 ± 0.06) , (0.28 ± 0.03)] and the normal bowel tissues(15% 10%; 0.23 ± 0.06 0.21 ± 0.03) (P < 0.05). The LMVD of colorectal carcinoma was also significantly higher than those of the colorectal polyps tissues and the normal bowel tissues [(4.13 ± 1.99) vs. (2.59 ± 1.46) vs. (2.40 ± 1.44) , P < 0.01]. (2) A significant correlation was found between either two of LMVD, the mean value of HGF and VEGFR 3 in specimens of colorectal carcinoma. The positive expression of HGF was found in 39 cases of colorectal carcinoma, and their mean LMVD was higher than that in the negative ones [(4.25 ± 2.13) vs. (2.73 ± 1.54) , t= 3.051 , P = 0.003]. The positive expression of VEGFR 3 was observed in 35 cases of colorectal carcinoma, and their mean LMVD was higher than that in the negative ones [(3.79 ± 1.26) vs. (2.64 ± 1.32) , t= 3.235 , P = 0.002]. (3) The expression of HGF, VEGFR 3 and LMVD in colorectal carcinoma was no correlation with age, gender and degree of differentiation, but significant correlation with Dukes' staging(P= 0.034 , P= 0.021 , P = 0.006) and lymph node metastasis(P= 0.015 , P= 0.012 , P = 0.001).

Conclusion

The positive expression of HGF is related with colorectal cancer lymphangiogenesis and lymphatic metastasis. It seems that HGF induces lymphangiogenesis indirectly through VEGF-C,D/VEGFR-3 signaling pathway and contributes to lymphatic metastasis in colorectal carcinoma.

Key words: Colorectal carcinoma Hepatocyte growth factor Vascular endothelial growth factor receptor3 Lymphatic vessel density

收稿日期: 2008-07-28;

引用本文:

熊枝繁,于欢,曹仕琼等. HGF和VEGFR-3在大肠癌中的表达及其在淋巴管生成和转移中的作用[J]. 肿瘤防治研究, 2009, 36(10): 838-843.

XIONG Zhi-fan, YU Huan, CAO Shi-qiong et al. Expression of HGF and VEGFR-3 in Colorectal Carcinoma and Their Role in Lymphangiogenesis and Lymphatic Metastasis[J]. CHINA RESEARCH ON PREVENTION AND TREATMENT, 2009, 36(10): 838-843.

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