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FAT10通过激活RhoA介导肝细胞性肝癌侵袭转移*

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FAT 10promotes invasion and metastasis of hepatocellular carcinoma through activating RhoA

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摘要 图/表 参考文献(0) 相关文章 (15)

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摘要

目的：探讨FAT 10与肝细胞性肝癌（hepatocellularcarcinoma ，HCC ）恶性病理特征间的相关性，及FAT 10对细胞骨架蛋白F-actin的影响及可能的机制。方法：通过免疫组织化学技术检测108 例肝癌组织标本中FAT 10及active-RhoA蛋白表达，分析它们与患者临床病理特征之间的相关性及二者间的相关性；用7721、HepG2 肝癌细胞株瞬时转染质粒过表达FAT 10，用Huh 7 及LM3 细胞株转染siRNA 干扰FAT 10表达，利用Westernblot方法检测过表达和干扰FAT 10后肝癌细胞中active- 、total-RhoA 和ROCK 蛋白表达的变化；利用免疫荧光检测7721细胞过表达FAT 10后细胞骨架蛋白F-action 的变化。结果：免疫组织化学结果及临床数据的关联性分析表明：高表达FAT 10或active-RhoA均与肝癌转移和复发密切相关（FAT 10：复发P = 0.004，转移P = 0.031；active-RhoA：复发P = 0.026，转移P = 0.036），且二者的表达水平之间呈明显正相关（P < 0.001）；生存分析的结果表明：高表达FAT 10或RhoA组患者预后明显差于各自低表达组（FAT 10：P = 0.026；active-RhoA：P = 0.019）。 Westernblot检测显示过表达FAT 10增加active-RhoA和ROCK 蛋白表达；反之，干扰FAT 10则抑制active-RhoA和ROCK 蛋白表达（均P < 0.01）。 免疫荧光显示肝癌细胞株7721过表达FAT 10可促进细胞骨架蛋白F-actin的表达和胞膜聚积及连续性变化。结论：FAT 10与肝癌恶性病理特征密切相关；并可能通过激活RhoA促进肝癌细胞骨架改变。

关键词 ： FAT 10， active-RhoA， 肝细胞性肝癌， 细胞骨架蛋白， 侵袭， 转移

Abstract :

Objective:To investigate the correlation of FAT 10expression with the malignant characteristics of hepatocellular car -cinoma (HCC), and to explore the effect of FAT 10on RhoA and cytoskeleton of HCC. Methods:Immunohistochemistry (IHC) was used to detect the FAT10expression level of 108 HCC patients, and the correlation between the expression of FAT10and the malignant characteristics of HCC patients was analyzed. We transiently transfected plasmids with overexpressed FAT 10using 7721and HepG2 cells or interfered with FAT10expression using siRNA in Huh 7 and LM3 cells. Active-RhoA, total-RhoA, and ROCK protein expres-sion levels were detected by Western blot analysis after overexpression or interference. We also used immunofluorescence to detect changes in the cytoskeleton protein F-actin after FAT10overexpression in7721cells.Results:Correlation analysis showed that both ac-tive-RhoA and FAT10expression levels were significantly correlated with clinical malignant characteristics by using IHC (RhoA: me-tastasis, P=0.036 and recurrence, P=0.026; FAT 10: metastasis, P=0.031 and recurrenc P=0.004). In addition, active-RhoA expression level was correlated with FAT10(P=0.000). Survival analysis showed that the prognoses of low-expression active RhoA (P=0.019) or FAT 10(P=0.026) groups were significantly better than those of the high-expression groups. Western blot analysis showed that FAT10 increased the expression of active-RhoA and ROCK. However, the expression of active-RhoA and ROCK decreased after FAT 10inter -ference. F-actin expression increased in the 7721cells with overexpressed FAT 10(all P<0.01). Moreover, FAT10facilitated F-actin ag -gregation on cell membrane and changes in F- actin. Conclusion:FAT 10is correlated with the malignant characteristics of HCC and may promote changes in HCC cytoskeleton induced by active-RhoA.

Key words : FAT 10 active-RhoA hepatocellular carcinoma cytoskeleton protein invasion metastasis

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